

**Gene networks and transcription factor motifs defining the  
differentiation of human embryonic stem cells into  
hepatocyte like cells**

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## **Zusammenfassung**

Das Potenzial von humanen embryonalen Stammzellen (hESCs), in Hepatozyten-ähnliche Zellen (hepatocyte like cells, HLCs) zu differenzieren, ermöglicht Hepatozyten in unbegrenzter Anzahl für pharmakologische und toxikologische Untersuchungen sowie für Zelltherapien zur Behandlung von Leberversagen herzustellen. Obwohl zahlreiche wissenschaftliche Untersuchungen über die erfolgreiche Herstellung von HLCs aus hESCs berichten, existieren immer noch kontroverse Angaben über die Ausprägung des Differenzierungsgrades zu homogenen Populationen von reifen Hepatozyten.

Das primäre Ziel dieser Promotionsarbeit war es, ein umfassenderes Verständnis der Eigenschaften von stammzellabgeleiteten HLCs zu erreichen. Hierfür wurden durch die Verwendung eines bewährten Protokolls hESCs zu HLCs differenziert. Die Charakterisierung und Identität der stammzellabgeleiteten HLCs erfolgte durch die Ermittlung der Genexpressionsnatur mittels GeneChip® Human Genome U133 Plus 2.0 Arrays. Die HLCs Genexpressionsnatur wurde anschließend mit der Genexpressionsnatur von hESCs und von frisch isolierten adulten Hepatozyten sowie von bis zu 14 Tage lang kultivierten adulten Hepatozyten verglichen. Durch die Anwendung eines breiten Spektrums von bioinformatischen Analyseprogrammen konnten die Gennetzwerke für erfolgreiche und erfolglose Hepatozytendifferenzierung sowie die involvierten regulativen Transkriptionsfaktoren identifiziert werden.

Die Analyse der regulatorischen Gennetzwerke zeigte, dass HLCs einen hybriden Zelltyp darstellen, welcher Gensignaturen von Leber-, Darm-, Bindegewebs- und Stammzellen zeigt. Der unerwünschte "Colon"-Phänotyp stand hierbei im Zusammenhang mit

Transkriptionsfaktoren wie KLF5 und NKX2-3 sowie dem CDX2-Transkriptionsnetzwerk. Durch Clusteranalysen konnten stark korrelierende Gengruppen identifiziert werden, welche sowohl mit Funktionen der reifen Leber und einer Herunterregulierung der Zellproliferation zusammenhängen, als auch dem Expressionslevel der adulten Hepatozyten nahe kamen.

Allerdings erreichten drei weiteren Gencluster nicht das Expressionslevel adulter Hepatozyten. Zwei dieser Cluster beinhalteten die Schlüsseltranskriptionsfaktoren SOX11, FOXQ1 und YBX3. Die dritte nicht erfolgreich exprimierte Clustergruppe, welche u.a. durch die Transkriptionsfaktoren HNF1A, CAR, FXR und PXR kontrolliert wird, zeigte signifikante Überschneidungen mit Genen, die in kultivierten Hepatozyten eher unterdrückt waren als in frisch isolierten Hepatozyten. Dies deutet darauf hin, dass in den gegenwärtig verwendeten *in-vitro* Kulturbedingungen essentielle Stimuli für den Erhalt der Genexpression von Hepatozyten fehlen. Demzufolge könnten hierdurch auch die vergleichbaren Defizite von HLCs erklärt werden.

Zusammenfassend kann festgestellt werden, dass durch den in dieser Arbeit verwendeten Ansatz zur Untersuchung von Genregulationsnetzwerken wichtige Transkriptionsfaktoren identifiziert werden konnten, welche sich als Interventionsziele zur Verbesserung der Differenzierung von hESCs zur reiferen HLCs anbieten.

## Summary

In the past decade, it has been recognized that human embryonic stem cells (hESCs) differentiation into hepatocyte like cells (HLCs) could offer an unlimited supply of hepatocytes for pharmacology, toxicology, and cell therapy for liver failure. Many research efforts claimed to have successfully engineered HLCs from hESCs. However, the degree of differentiation and identity of HLCs remains controversial.

The primary goal of this thesis work was to obtain a comprehensive understanding of HLCs identity. Thus, HLCs were differentiated from hESCs using a well-established protocol. Genome-wide gene expression programs of hESCs and HLCs were analyzed using GeneChip® Human Genome U133 Plus 2.0 arrays. The resulting gene expression profiles of HLCs and hESCs were compared to freshly isolated adult hepatocytes and adult hepatocytes cultivated for up to 14 days. Application of a broad range of bioinformatic tools and data mining approaches led to elucidation of gene networks and transcription factors (TFs) involved in the regulation of gene expression suggesting successful and failed hepatocyte differentiation.

Gene regulatory network analysis revealed that HLCs represent a hybrid cell type with features of the liver, intestine, fibroblast, and stem cells. The undesirable “colon” phenotype was associated with TFs such as KLF5, NKX2-3, as well as CDX2 transcriptional networks. Cluster analysis identified highly correlated groups of genes associated with mature liver functions and downregulated proliferation-associated genes, which approach levels of adult hepatocytes. However, three further clusters failed to reach the gene expression levels of adult hepatocytes. Key TFs of two of these clusters include SOX11, FOXQ1, and YBX3. The third

cluster group, controlled by TFs such as HNF1A, CAR, FXR, and PXR, significantly overlaps with genes that are repressed in cultured adult hepatocytes relative to freshly isolated adult hepatocytes, suggesting that the current *in vitro* conditions lack stimuli essential for maintaining gene expression in hepatocytes, which consequently explains the corresponding functional deficiency of HLCs.

In conclusion, the present gene regulatory network approach identified critical transcription factors for interventions to improve differentiation of hESCs to functional matured hepatocytes.

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## **Dedication**

This work is dedicated to Sir Francis Bacon (22 January 1561 – 9 April 1626), author of “*Novum Organum Scientiarum*”.

## Glossary

<b>Term</b>	<b>Description</b>
%	Percent
° C	Degree Celsius
µg	Microgram
µl	Microliter
µm	Micromolar
Alexa Fluor® 488	Fluorescent synthetic green dye
aRNA	Amplified RNA
BMPs	Bone morphogenetic proteins
BSA	Bovine serum albumin
cDNA	Complementary deoxyribonucleic acid
CO <sub>2</sub>	Carbon dioxide
Cy®3 dye	Bright, orange fluorescent dye
DAPI	4',6-diamidino-2-phenylindole-a fluorescent stain
DMEM	Dulbecco's Modified Eagle Medium
DMSO	Dimethyl sulfoxide
DNA	Deoxyribonucleic acid
FBS	Fetal bovine serum
FDR	False discovery rate
FGFs	Fibroblast growth factors
GlutaMAX™	Alternative to L-glutamine
GO	Gene Ontology
H <sub>2</sub> O	Water
hESCs or ESC	Human embryonic stem cells
HGF	Hepatocyte growth factor
hHEPs or FH	Freshly isolated adult human hepatocytes
HLCs or HLC	Hepatocyte like cells
iPSCs or ihPSCs or iPS	Human induced pluripotent stem cells
L-15 basal medium	Leibovitz L-15 cell culture Medium
ml	Milliliter
MTeSR™	Maintenance medium for hESCs and iPSCs from stem cell technologies
ng	Nanogram
nM	Nanomolar
PBS	Phosphate buffered saline
RNA	Ribonucleic acid
RPM	Revolutions per minute
RPMI 1640	Roswell Park Memorial Institute medium 1640-cell culture
RT-qPCR	Real-time quantitative polymerase chain reaction
SEM	Standard error of the mean
TFs or TF	Transcription factors
Wnt3a	Wingless-type MMTV integration site family, member 3A

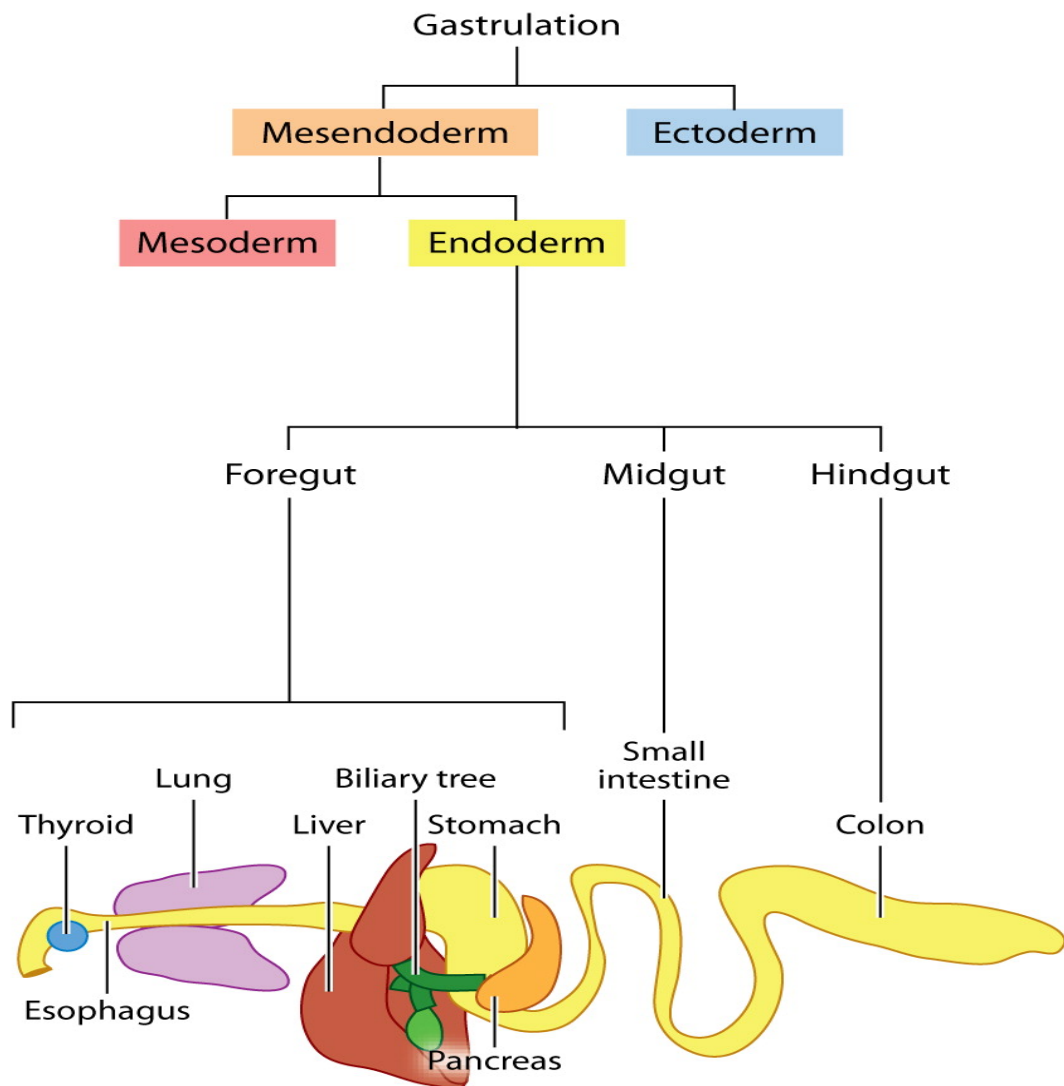


## **1 Introduction**

The liver is the largest gland, accounting for about 2 to 5% of total body weight, and a key metabolic organ [1]. It is responsible for over 500 functions in metabolism, detoxification, and synthetic processes [2]. Liver-related research was hampered by limited availability of the donor livers [2]. Over the last decade, *in vitro* generation of cell types from stem cells have been idealised as an alternative source to cell types in the liver [3, 4]. For this reason, it is paramount to understand the liver's basic developmental stages, as well as differentiation mechanisms, maturation mechanisms, and their cell types [1]. Additionally, it is essential to determine how cells in the adult liver organise to create the three-dimensional structure that is so critical for liver function [1].

### **1.1 Embryonic liver development**

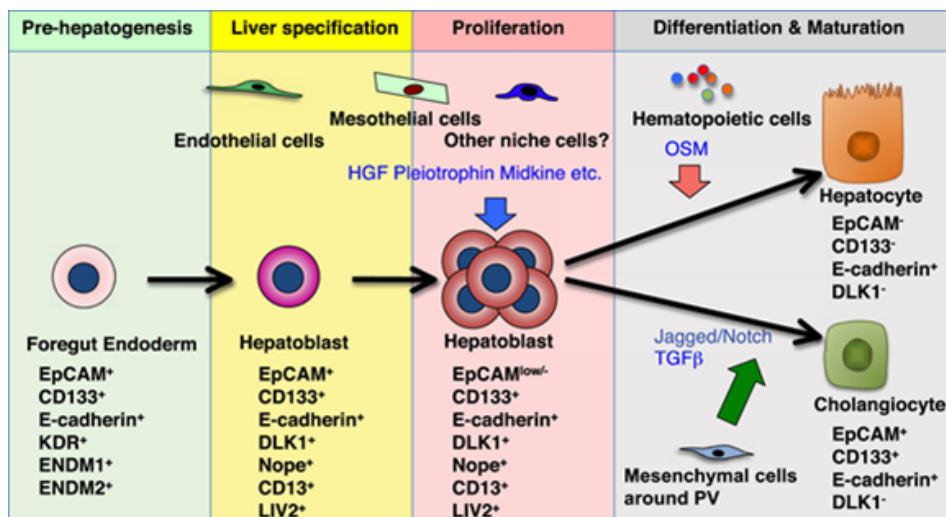
The liver development is a sequential process comprised of the various signalling processes that take place in spatial and temporal patterns [5]. Different vertebrate models are studied inclusively to understand various morphological transitions of liver development and differentiation [6, 7]. During embryonic gastrulation, the epiblast of the fertilised egg passes through the primitive streak and is incorporated into the endoderm and mesoderm (Fig. 1) [6]. After gastrulation, the endoderm transforms into a rudimentary gut tube along the dorsal-ventral and anterior-posterior axes, which is then subdivided into three developmental domains foregut, midgut, and hindgut (Fig. 1) [6]. Liver development is initiated from the foregut endoderm (Fig. 1) and is controlled by a series of mutual interaction with the neighboring mesoderm [6]. During liver development, the tissue morphogenesis and cell identity is tightly controlled [6].



**Figure 1: Schematic representation of liver specification**

*During gastrulation, germ layer ectoderm and a transient precursor cell population, namely mesendoderm are formed. From mesendoderm, two germ layers, mesoderm and endoderm, are formed. After gastrulation, the endoderm transforms into the primitive gut tube, which is subdivided into foregut, midgut and hindgut regions. Embryonic liver originates from the foregut endoderm. (Adapted from [6])*

The mouse embryonic liver development originates from the ventral foregut endoderm on an embryonic day 8 (E8) [8]. The mouse liver development and maturation is accompanied by different cellular stages, cell to cell interactions (Fig. 2) and are characterized by various molecular markers (Fig. 2) [7]. The foregut endoderm cell population destined for hepatic fate begins to express transcription factors HHEX and HNF4A, hepatic genes alpha-fetoprotein (AFP) and albumin (ALB) [7]. The formation of the hepatic diverticulum, an outpocket of ventral foregut epithelium adjacent to the developing heart (Fig. 3) on E9 is the first morphological sign of liver development [5].



**Figure 2: Schematic Model of Regulatory Mechanisms and Cell Surface Markers for Hepatic Epithelial Cells during Mouse Liver Development**

*The representative cell surface markers are shown. While EpCAM is transiently downregulated in hepatoblasts at the midgestational stage, its expression is restored in cholangiocytes, but not in hepatocytes, later on. DLK1 is also expressed in hepatoblasts but is not expressed in mature hepatocytes or cholangiocytes. (Adapted from [7])*

While the anterior portion of the hepatic diverticulum develops into the liver and the intrahepatic biliary tree, the posterior part of the hepatic diverticulum develops into the gallbladder and extrahepatic bile ducts (EHBD) [5, 9]. At E9.5, the hepatoblast emerges as a

split from the epithelium and migrates into the adjacent septum transversum mesenchyme (STM) to materialise the liver bud [5]. The hepatoblast expresses gene markers including EPCAM, CD133, CDH1, DLK1, IGDCC4, CD13 and LIV2 (Fig. 2) and is capable of differentiating into both hepatocytes and cholangiocytes (Fig. 2) [7]. Delta-Like homolog 1 (DLK1) is expressed early at E9.0 and decreases in the neonatal stage, disappearing entirely in adult hepatocytes [7, 10]. The loss of CDH1 (E-cadherin) from hepatoblast is vital for the migration and formation of liver bud [1, 11]. Fetal liver kinase FLK1 and growth factors HGF, midkine, and pleiotrophin are required for differentiation of hepatoblast into liver bud [12, 13]. Liver fibroblast and stellate cells are contributed by the STM [5].

Between E10–15 continuous growth of the liver bud leads to the formation of the fetal liver and become a principal site of hematopoiesis [5]. The fetal liver is a core player in hematopoietic cell differentiation from its precursor cells. Oncostatin M, a cytokine produced by the blood cells, is responsible for the hepatocyte maturation (Fig. 2) [14]. It has been reported that notch signalling pathway is essential for the biliary system development (Fig. 2) [15].

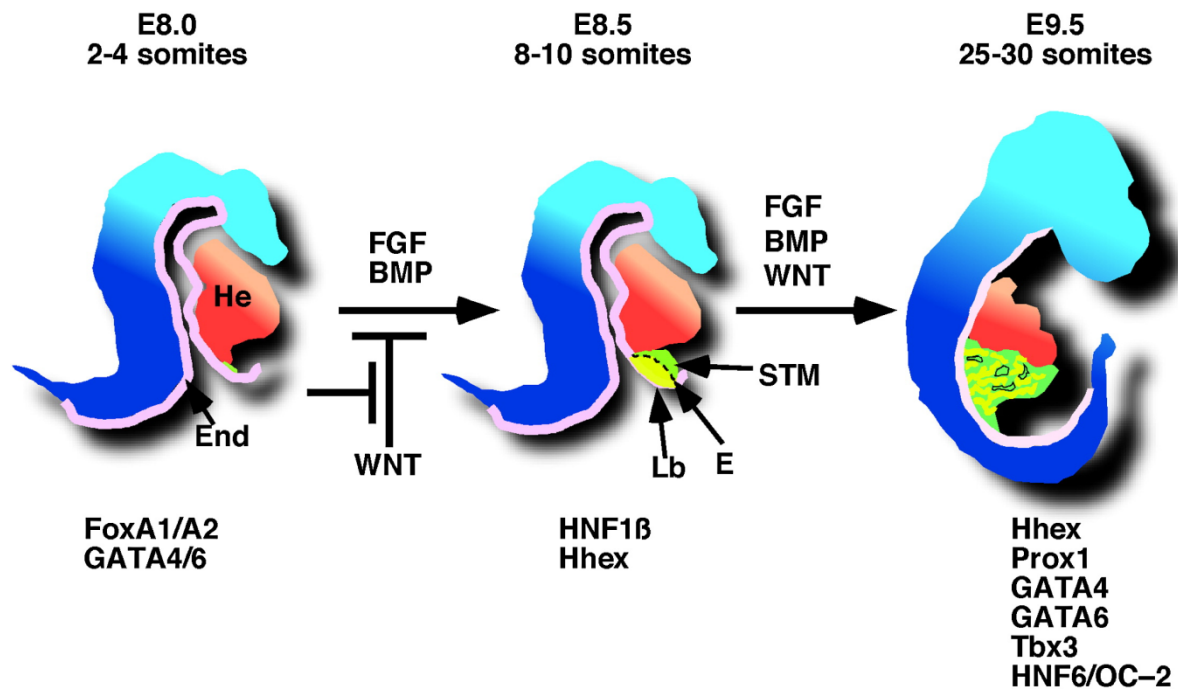
The liver fate specification and development is guided by three major pathways such as fibroblast growth factors (FGFs), bone morphogenetic proteins (BMPs) and wnt signalling (Fig. 3) [1]. Both FGFs and BMPs have an inductive role in liver development [16, 17]. FGFs molecules are secreted from the developing heart while BMPs are secreted from the septum transversum mesenchyme (STM) [1]. The FGFs mediated hepatic induction is concentration dependent and controlled by the position of the endoderm relative to the heart [18]. FGFs control the induction of hepatic genes through activation of the mitogen-activated protein kinase (MAPK) pathway and are independent of phosphoinositide 3-kinase (PI3K) signalling

[19]. Numerous FGFs such as FGF1, FGF2, FGF8 and FGF10 are expressed in the cardiac mesoderm during the onset of hepatogenesis [20]. A zinc finger transcription factor GATA4 regulates the expression of BMP4 [17]; both GATA4 and BMP4 are essential for early liver development (Fig. 3) [1]. Purportedly there is flexibility on the relative timing of BMPs and FGFs to induce the differentiation of the distinct population of hepatic progenitors [21]. In the suggested model, transforming growth factor-beta (TGF- $\beta$ ) acts as a developmental timer by preventing hepatic endoderm from differentiating inappropriately [21]. Moreover, it ensures that the endoderm retains competence for hepatic lineage [1, 21].

In contrast to FGFs and BMPs, the contribution of Wnt signalling in liver development is relatively complex [1]. At early stages, Wnt signalling represses liver development by inhibiting a crucial hepatic regulator HHEX, while in later stages wnt signalling promotes hepatogenesis (Fig. 3) [22]. The studies conducted on the zebrafish model suggested that Wnt protein Wnt2B is essential for the onset of hepatic differentiation of the progenitor cells. However, there is a mechanism to compensate for the loss of Wnt2B [23].

Apart from different signalling pathways, the liver specification and development is guided by a set of regulatory factors (Fig. 3) [24, 25]. Transcription factors FOXA1, FOXA2 and GATA4 [26], are expressed in the anterior endoderm [1] and termed as “pioneer factors” because they are essential in creating competence for liver development (Fig. 3) [27]. However, later stages of liver development happen independently of FOXA1 and FOXA2 (Fig. 3) [28]. These three factors are capable of binding enhancers of albumin before the onset of its expression [29, 30]. Moreover, GATA6 and GATA4 contributes to hepatoblast development by enabling HHEX expression [31-33]. Hepatocyte nuclear factor HNF1B is also essential for hepatic specification, and studies conducted in mouse models suggest that

lack of HNF1B will severely compromise ALB, FOXA1, and FOXA2 expression in the liver bud (Fig. 3) [34].



**Figure 3: Mechanism controlling early development of the hepatocytes**

*Illustration showing the onset of differentiation of liver parenchymal cells indicating signalling molecules and transcription factors with proven regulatory roles. Initial functions of Wnt signalling promote posterior endodermal identity at the expense of anterior (e.g., prospective hepatic) identity, and must be inhibited anteriorly by local Wnt antagonist expression before liver development can proceed further. Later functions of Wnt signalling act in parallel with BMP and FGF signalling to drive hepatic specification, expansion, and differentiation. Foregut endoderm (End; pink), heart (He; red), liver bud (Lb; yellow), septum transversum mesenchyme/lateral plate mesoderm (STM; green), and vascular endothelial cells. (E; black). (Adapted from [1])*

The hepatoblast migration is highly regulated by homeodomain factors ONECUT1 and ONECUT2 [35]. The prospero-related homeobox transcription factor PROX1 regulates the hepatoblast proliferation and migration from the primary liver bud [36]. T-Box factor TBX3 (upstream of PROX1) promotes a hepatocyte specification of hepatoblast while repressing a

cholangiocyte fate [37]. There is an incredible synergy between different signalling pathways and transcription factors (Fig. 3) to coordinate the liver development.

After a detailed study, it has been found that HNF1A, HNF1B, FOXA2, HNF4A, ONECUT1 and NR5A2 are responsible for forming core regulatory circuitry of liver development [38]. Each of these TFs regulates each other, among them HNF1A, FOXA2, HNF4A, and ONECUT1 are auto-regulators [39]. Moreover, these TFs also regulates peripheral TFs by occupying their promoters [1]. Wilms Tumor factor 1 (WT1), expressed in mesothelial cells, is also essential for hepatic stellate cell and liver development [40].

## **1.2 Postnatal liver development**

The liver will continue to develop even after birth (postnatal period), which may extend up to 5 years in humans [41]. During this phase of growth the liver acquires its adult gene expression program, which is essential for various physiological processes, including the drug metabolising enzymes [42, 43]. The postnatal developmental period is unique because hepatocytes proliferation and differentiation happen simultaneously [44]. During this time, the liver tends to achieve 2-5% weight [1] of the whole body [44]. The nuclear receptors NR1I2, NR1I3 and HNF4A, are key factors responsible for regulating the gene expression of the postnatal liver [44-46]. The significance of HNF4A in maintaining mature hepatocyte characteristics in the adult liver is supported by the fact that HNF4A alone bind 12% of human hepatocyte genes at the whole genome level [47].

Experimental studies indicate that levels of Beta-catenin is increased in the cytoplasm from postnatal day 5 to 20. Moreover, knockdown of Beta-catenin results in a smaller liver size

highlighting its importance in the liver growth. Therefore, canonical wnt signalling is important for liver growth [48]. Besides wnt signalling, the postnatal liver size and maturation is regulated by yes-associated protein (YAP) [49], a downstream effector of the hippo signalling pathway [50]. YAP critically regulates gene expression by coordinating with HNF4A, HNF1B, PXR, and CAR [44]. The hippo and YAP may act as a switch between cell maturation and proliferation [44]. However, a central regulatory mechanism which guides postnatal liver development is still largely unknown [44].

### 1.3 Adult liver and stem cells

The liver parenchyma and non-parenchyma represent highly heterogeneous cell types consisting primarily of hepatocytes, cholangiocytes/bile duct, endothelial cells, sinusoidal endothelial cells, pit cells, kupffer cells, and the stellate cells [1] (Table 1). Each cell type carries out specific functions (Table 1). Moreover, heterotypic cell-cell interactions are essential for proper liver function [51].

Cell Type	Position in Liver	Function
<b>Hepatocyte</b>	Parenchyma	~70% of liver cell population Protein secretion Bile secretion Cholesterol metabolism Detoxification Urea metabolism Glucose/glycogen metabolism Acute phase response Blood clotting

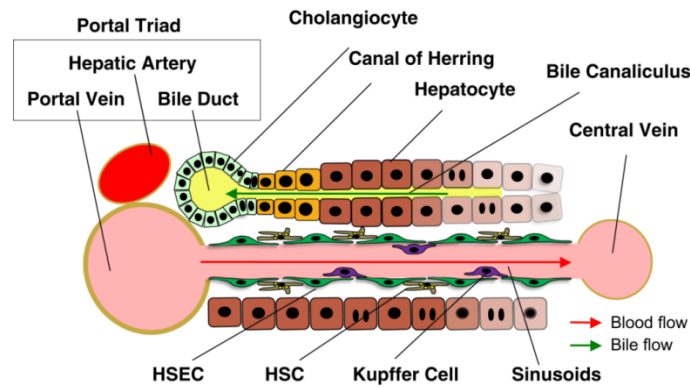


<b>Cholangiocyte/bile duct cell</b>	Duct epithelium	<p>~3% of liver cell population</p> <p>Form bile ducts to transport bile</p> <p>Control rate of bile flow</p> <p>Secrete water and bicarbonate</p> <p>Control pH of bile</p>
<b>Endothelial cell</b>	Vasculature	<p>Form veins, arteries, venuoles, and arterioles</p> <p>Control blood flow</p> <p>Contribute toward parenchymal zonation</p>
<b>Liver sinusoidal endothelial cell</b>	Sinusoids	<p>~2.5% of lobular parenchyma</p> <p>Form sinusoidal plexus to facilitate blood circulation</p> <p>Highly specialized</p> <p>Allow transfer of molecules and proteins between serum and hepatocytes</p> <p>Scavenger of macromolecular waste</p> <p>Cytokine secretion</p> <p>Antigen presentation</p> <p>Blood clotting</p>
<b>Pit cell</b>	Liver natural killer cells	<p>Rare</p> <p>Cytotoxic activity</p>
<b>Kupffer cell</b>	Sinusoids	<p>~2% of liver</p> <p>Scavengers of foreign material</p> <p>Secrete cytokines and proteases, etc.</p>
<b>Hepatic stellate cell</b>	Perisinusoidal	<p>~1.4% of liver cells</p> <p>Maintenance of extracellular matrix, Vitamin A, and retinoid storage</p> <p>Controls microvascular tone</p> <p>Activated to become myofibroblast</p> <p>Contributes toward regenerative response</p>

		to injury Secretion of cytokines
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**Table 1: Predominant cell types and their functions within the adult liver**  
(Adapted from [1])

Despite the cellular heterogeneity (Table 1), the liver is a relatively homogenous organ [52]. The fundamental architectural unit of the liver is the liver lobule (Fig. 4) [1]. The hepatocytes are parenchyma of the liver and carry out most of the metabolic and synthetic functions (Table 1). Hepatocytes are polarised epithelial cells, and their basolateral surfaces face sinusoidal endothelial cells (Fig. 4), which facilitates the exchange of molecules between the hepatocytes and blood vessels [1]. Tight junctions between neighboring hepatocytes form a canaliculus, which surrounds each hepatocyte [1]. Bile secreted from the hepatocytes is collected by the canaliculi and exported in a sequential manner to the gallbladder for storage [7].

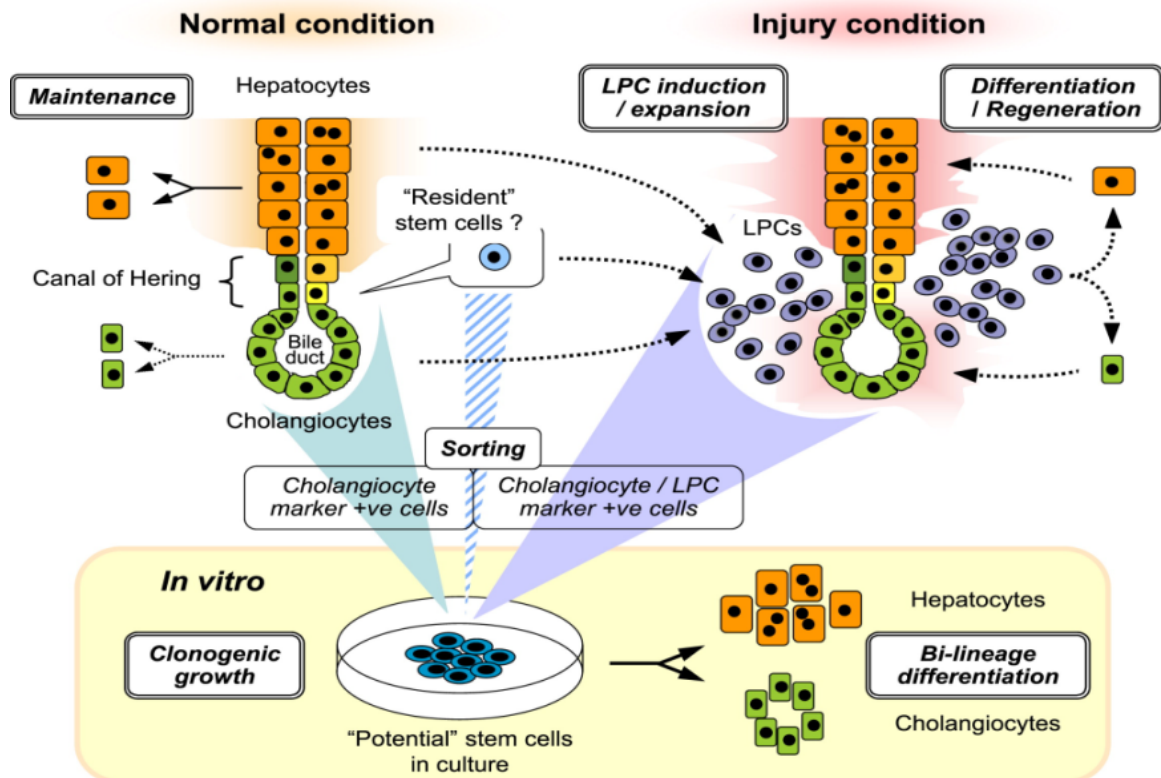


**Figure 4: Schematic Overview of Liver Lobule**

*The portal triad consists of the portal vein, hepatic artery, and bile ducts. Blood from the portal vein and the hepatic artery flows toward the central vein between hepatocytes through the sinusoids surrounded by fenestrated hepatic sinusoidal endothelial cells (HSECs). Bile produced by hepatocytes is collected into bile ducts via the bile canaliculi. Kupffer cells, resident macrophages of the liver, are located at the luminal side of sinusoids, while hepatic stellate cells (HSCs) are positioned in close proximity to HSECs at the “space of Disse,” a location between hepatocytes and a sinusoid. The canal of Hering is the junctional region between hepatocytes and bile ducts. (Adapted from [7])*

Apart from different cell types (Table 1), the occurrence of stem cells in the adult human liver is well documented (Fig. 5) [7, 53]. However, the presence of stem cells in the normal liver remains controversial [54]. Adult liver stem cells are critical for tissue turnover and tissue repair when the liver is subjected to injury [7]. Unlike other organs (intestine and epidermis), hepatocytes turnover is slow [55] and in normal conditions hepatic tissue maintenance is achieved by the proliferation of mature hepatocytes, which happens throughout the liver parenchyma (Fig. 5) [7].

Potential liver stem cells are identified based on cholangiocyte molecular markers such as EPCAM [56], CD133 [57] and MIC1-1C3 [58], which implicates the biliary system as a compartment that harbours “resident” liver stem cells (Fig. 5) [7]. Supporting this hypothesis is that fact that, EPCAM positive cells can be isolated from postnatal livers and fetal livers also contain human hepatic stem cells (hHpSCs) [59]. Moreover, experimental findings suggest that multipotent progenitor stem cells may be harbored in the peribiliary glands of the adult human liver, which can give rise to hepatocytes, cholangiocytes and pancreatic islets [60].



**Figure 5: Stem/Progenitor Cells in Adult Liver under normal and injured Conditions**

Under normal physiological conditions, the homeostatic maintenance of hepatocytes is achieved predominantly by the proliferation of mature hepatocytes. Upon certain types of injury condition, unique epithelial cell populations with an immature phenotype, called adult liver progenitor cells (LPCs), emerge and expand, and are thought to contribute to the regeneration process due to their bilineage differentiation potential to both hepatocytes and cholangiocytes. Although the origin of LPCs is still not clear, the dominant theory is that they are derived from the canal of Hering, which may harbor putative “resident” stem cells as the exact cell of origin. Purification by cell sorting and subsequent culture experiments have demonstrated that the cholangiocyte marker-positive population from normal liver, as well as the cholangiocyte/LPC marker-positive subset from injured liver, contains a “potential” liver stem cell population defined *in vitro* by clonogenicity and bilineage differentiation potential. (Adapted from [7])

Liver progenitor cells (LPCs) are another class of stem cells known to appear only when the liver is injured (Fig. 5) [7]. It has been demonstrated *in vitro* that LPCs are bipotential in nature (Fig. 5). Multiple studies suggest that the site of origin of LPCs may be the canal of Hering (Fig. 5); LPCs are identified using molecular markers such as CK19, EPCAM, and CD133. However, there is no direct proof for the origin of LPCs because there is a lack of genuine

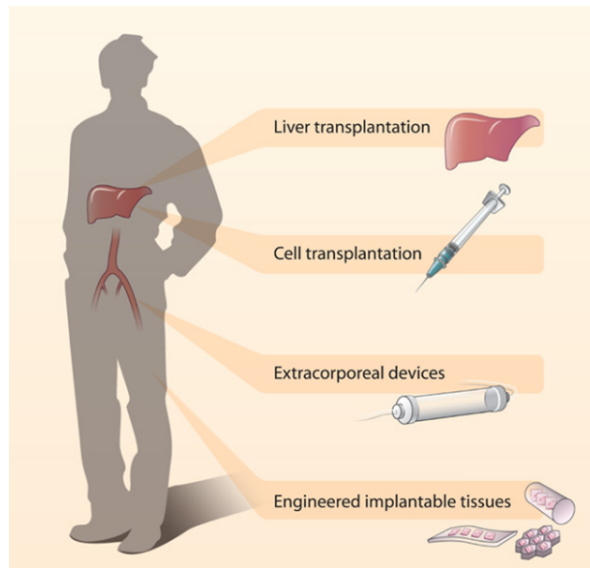
molecular markers; these three previous markers are also used to isolate cholangiocytes from the normal liver, which is also capable of differentiating into both hepatocyte and cholangiocyte *in vitro* (Fig. 5).

When the normal liver is treated with N, N'-Dicyclohexylcarbodiimide (DDC) a transmembrane molecule TACSTD2 (paralog of EPCAM) is expressed only in LPCs, but not in cholangiocytes [56]. Therefore, TACSTD2 would be a potential LPCs specific marker and may be used for further research. Forkhead Box L1 (FOXL1) and G Protein-Coupled Receptor 5 (LGR5) are being actively pursued to establish their use in LPCs related research [7]. Activation of LPCs is usually accompanied by inflammatory responses, inflammatory molecules such as tumor necrosis factor-alpha (TNF-alpha), interleukin-6 (IL6) and interferon-gamma (INFG), which is coherent with the notion that LPCs are activated under chronic liver injury conditions [61-63]. Proliferation and differentiation of LPCs are regulated by hepatocyte growth factor (HGF) and epidermal growth factor (EGF) [64, 65].

Although there have been advances in LPCs research, but the origin and possible role in the liver biology of LPCs remains elusive [54].

#### **1.4 Liver diseases and therapeutic Possibilities**

Despite the unique capacity of the liver for regeneration, continuous insults lead to liver diseases associated with high morbidity and mortality rates, affecting over 600 million people around the globe [3]. Most liver processes are interconnected with functions of various organs; clinical and pathological studies have confirmed that liver diseases can manifest as systemic illness [2]. Liver diseases are predominantly divided into three categories [2].



**Figure 6: Organ transplantation and cell-based therapies**

*Currently, liver transplantation is the primary treatment for patients with liver failure and is the only therapy shown to improve survival. Because of the limited number of livers suitable for transplantation, advanced surgical procedures including split liver and partial donor transplants have been pursued clinically. Additionally, a diverse range of cell-based therapies are currently being explored to treat liver disease and liver failure. These include the transplantation of various adult and stem cell-derived cell populations, the development of extracorporeal BAL devices, and the implantation of engineered tissues. (Adapted from [2])*

#### **1.4.1 Chronic disease caused by metabolic dysfunction**

These diseases are caused by defective secretion of key proteins, which are important for liver-based metabolism and functions. Urea cycle disorders, Crigler-Najjar syndrome, phenylketonuria and oxalosis are examples of metabolic liver diseases. Moreover, this type of liver diseases shows no signs of any structural or cellular damage in patients. Until now, these categories of patients are treated with organ transplantation. However, the clinical manifestation of these diseases may offer an ideal situation for cell-mediated therapy (Fig. 6).

#### **1.4.2 Acute liver failure caused by direct injury and loss of hepatocytes**

Direct liver injury leads to necrosis of hepatocytes that signal the production of liver enzymes such as alanine transaminase and aspartate transaminase. These two enzymes are an

indicator of hepatocyte injury, but not a sign of liver failure. Organ transplantation is the successful treatment option available for acute hepatic failure. It is unclear yet, how hepatocyte transplantation is useful in treating these patients. However, extracorporeal devices like artificial liver may provide a clinical bridge to manage symptoms until the endogenous liver recovers (Fig. 6).

#### **1.4.3 Chronic liver failure caused by tissue damage and remodelling (or) cirrhosis**

This class of liver diseases are a severe and chronic form of liver failure. Cirrhosis causes dysfunction of the liver, which eventually lead to secondary dysfunction of the kidney and lung. Hepatitis B or C infection, alcohol abuse, fat accumulation and autoimmune reactions are considered to be the major causes of cirrhosis. Also, antitrypsin deficiency, Wilson's disease, cystic diseases, and hemochromatosis include some of the inborn metabolic errors, which cause structural liver damage with cirrhosis, liver failure. Orthotopic liver transplantation is the definitive therapy for this category of patients (Fig. 6).

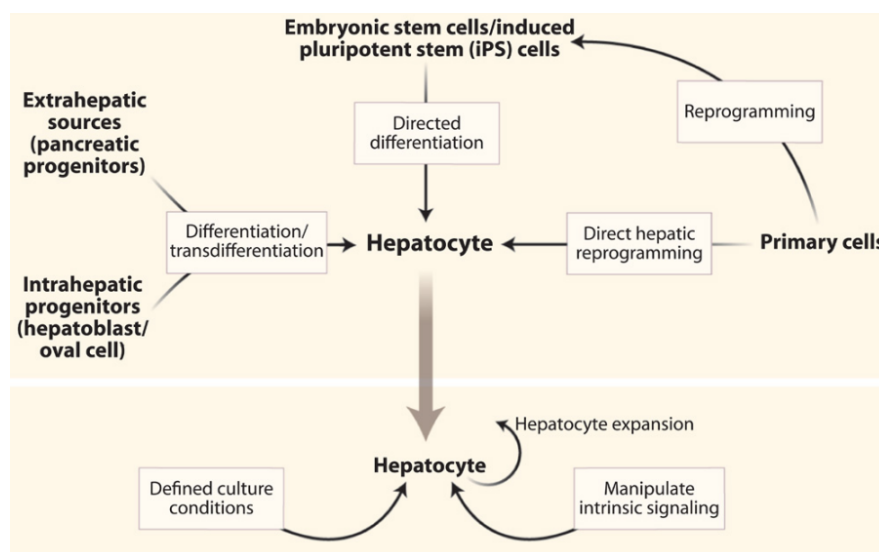
The liver (partial or full organ) and the hepatocyte transplantation are the universal treatment options available for various liver diseases [2, 3]. In some metabolic disorders, normal hepatocyte transplantation in 2-5% of the liver parenchyma might be good enough to improve/regain liver function significantly [66]. For successful transplantation, different surgical options are considered based on the availability of donor organs such as split liver transplants and living-related partial donor [67]. However, liver and mature hepatocytes transplantation is limited by the insufficient availability of source material [3].

For the generation of hepatocytes in large volumes, researchers are trying to induce and support the proliferation of adult hepatocytes in *in vitro* conditions but these efforts are

unsuccessful [68]. Moreover, attempts to prevent dedifferentiation of hepatocytes *in vitro* set-up are also highly unsuccessful [69]. Therefore, continuous research efforts are placed to find an alternative source for generating sufficient hepatocytes for cell-mediated therapy as well as drug discovery and biomedical applications [3].

### 1.5 Generation of Hepatocyte Like Cells (HLCs)

For the last few decades, an endeavour has been made to generate hepatocyte like cells from different cell sources (Fig. 7). These cell sources are weighed using parameters such as ethics, safety, supply, and scalability [3, 70, 71]. Among various cellular sources, Human Embryonic Stem Cells (hESCs) are one of the winners, although there are significant ethical issues associated with them [72]. Since discovery in 1998, hESCs have been considered as the “holy grail” of cell-mediated therapy and biomedical applications because of their self-renewal, proliferative nature and their ability to differentiate into any cell types in the presence of appropriate niches/cues [73, 74].





## **Figure 7: Sources of hepatocytes**

*Obtaining appropriate sources of hepatocytes is a major limitation for developing cell-based therapies for treating liver disease. Many different approaches are under investigation including methods for improving the expansion of primary human hepatocytes in vitro, the directed differentiation of pluripotent stem cells (both ESCs and iPSCs), and the differentiation of either intrahepatic or extrahepatic adult progenitor cells, as well as new methods for the direct reprogramming of adult somatic cells to hepatic cells. (Adapted from [2])*

Typical HLCs differentiation protocols are designed using existing knowledge of liver development and maturation that have been accumulated over the years from studies conducted in different vertebrate models [3]. These methods are a miniature of the hepatocyte developmental window, which contains appropriate molecular and cellular signals to induce hepatic lineage.

Differentiation of hESCs into HLCs is performed using two different approaches, (i) “Directed differentiation” in which cytokines are applied systematically and (ii) “Direct conversion” in which hepatic transcription factors are overexpressed to achieve hepatic phenotype [75-77]. Sometimes both of these previous approaches are mixed to achieve a successful HLCs derivation. Freshly isolated adult hepatocytes are considered as “gold standard” to which gene expression profiles, as well as the functionality of derived HLCs, are compared [3].

In 2003, the first method to differentiate HLCs from hESCs was reported by Rambhatala and colleagues [78]. Since then, various groups across the world are in search of possible modifications to improve HLCs differentiation to obtain more homogeneous population. HLCs differentiation protocols vary significantly in terms of hESCs culturing that are either in a monolayer or aggregated in three-dimensional structures called “embryoid bodies” (EBs) [75]. The creation of embryoid bodies from hESCs is achieved either by suspension culture or using an extracellular matrix (ECM) coated culture plates [75].

## **1.6 HLCs differentiation using embryoid bodies**

hESCs differentiation into three germ layers such as the ectoderm, mesoderm and endoderm is highly spontaneous [73]. These endodermal cells express nascent hepatic markers such as alpha-fetoprotein (AFP) and albumin (ALB) [79]. These methods do not use 'Activin A' to induce endoderm [75]. In 2004, Lavon and colleagues reported that hESCs can be differentiated into HLCs using an embryoid body approach, which can express ALB and is capable of growing *in vitro* for a few weeks [80]. Two years later, Bharvand and colleagues published an efficient EBs based protocol, which uses three-dimensional collagen type I scaffold with the sequential supplementation of different growth factors [81]. However, the EBs based HLCs differentiation is no longer preferred due to the lower differentiation efficiency and unpredictable outcomes [75].

## **1.7 Methodical differentiation of hESCs into HLCs**

In monolayer culturing conditions, these protocols first differentiate the hESCs into definitive endodermal cells that are then further differentiated into hepatoblast and HLCs. Since hepatocytes are derivative of endoderm, the formation of endoderm is the first step in a multistep hESCs differentiation towards HLCs [82, 83]. Endoderm lineage is induced using a high concentration of Activin A, which mimics the nodal signalling pathway of embryonic gastrulation [83]. Activation of nodal signalling pathway leads to phosphorylation of TFs such as SMAD2 and SMAD3 [84]. Then these SMAD proteins are translocated to the nucleus and form a complex with transcription factor SMAD4 to initiate the activation of lineage-specific genes [75].

Definitive endoderm was obtained by overexpression of transcription factor SOX17 in hESCs [85]. In a detailed study on the effect of the extracellular matrix and different growth factors,

it had been concluded that matrigel and 100 ng/ml of ‘Activin A’ enhance the efficiency of HLCs differentiation [86]. The combination of ‘Activin A’ and FGF2 enhanced the expression of endodermal genes such as SOX17, FOXA2 and CXCR4 [87]. Use of Wnt3a in combination with ‘Activin A’ for endoderm induction was proven to be effective by Hay and colleagues [88]. The repression of ectoderm and mesoderm lineages in endoderm differentiation was achieved by applying a combination of FGF, TGF- $\beta$ , and wnt together with low BMP molecules [89].

Hepatic induction of endodermal cell population is achieved by the use of BMPs, FGFs, chemical antagonist and synthetic epigenetic modifiers in low serum conditions [75]. The combination of FGF2 and BMP4 increased expression of albumin in endodermal population. Moreover, the combination of bFGF and BMP4 or FGF4 and BMP4 were also given to similar outcomes [90]. The inductance of endoderm cell population to hepatoblast was attained by using DMSO, which modifies histone acetylation [91]. The hepatic induction was enhanced by the addition of a low amount of FGF2, whereas the higher amount favours pancreatic lineage [92]. Combinatorial use of FGF1/2/4 and BMP2/4 increased the expression of Epithelial Cell Adhesion Molecule (EPCAM) in multiple cell clusters with adjacent cell clusters positive of cytokeratin such as CK7, and CK19 was well documented [87].

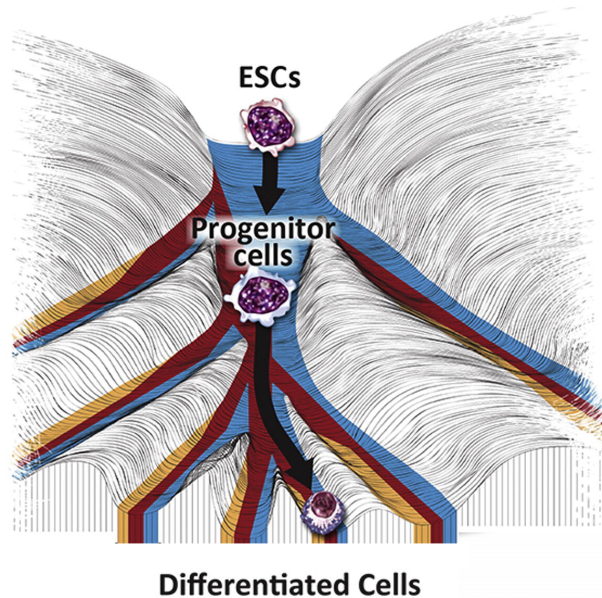
Finally, hepatocyte polygonal multinuclear morphology and maturation is obtained by the application of hepatocyte growth factor/epidermal growth factor, oncostatin M, insulin and cortisone (hydrocortisone and dexamethasone) at different levels and concentration [75]. Besides using a different combination of cytokines, overexpression of transcription factors in combination with cytokines is used to push hESCs towards hepatic lineage. For example, the sequential transduction of TFs such as SOX17, HHEX and HNF4A was performed to differentiate hESCs into HLCs [93].

Overall, most of the hepatocyte differentiation methods follow a similar regime of cytokines. However, the difference lies in the composition of cytokines used in each successive cellular stage and number of days accompanying specific cellular stages (definitive endoderm, hepatoblast and HLCs) [3].

## **1.8 Gene regulatory layers**

In 1961, Jacob and Monod suggested a general model of gene regulation in a seminal paper. Since then, numerous efforts have been made to understand gene regulation mechanisms and involvement of other molecular components [94]. Stereotype embryonic development and maintenance of the adult gene expression program is governed by multilayered, complex, interconnected regulatory and functional elements [95, 96], [97-101]. Many factors are responsible for this molecular and cellular complexity that have gathered over the course of mammalian evolution, which includes pervasive transcription [102, 103], epigenetics [104, 105], gene pleiotropy [106], post-transcriptional protein modifications [107], protein kinases [108], alternative splicing [109], trans-acting factors [110], cis-regulatory elements [111], and cell type-specific gene expression [112]. Understanding these different regulatory elements/factors will lead to comprehensive knowledge about the embryonic development and maintenance of differentiated cellular identity (adult cell/tissue types). Various research efforts such as “The Human Genome Project” (HGP) [113], “FANTOM Consortium” [114], “ENCODE Consortium” [115], “NIH Roadmap Epigenomics” [105], “GTEx”[116], “Human Kinome” [108] and “The Human Protein Atlas” [117] are conceptualized to understand the various gene regulatory and functional elements.

Since DNA is organised in chromatin fibres, genomic data access is controlled by an array of proteins including transcription factors (TFs), cofactors, chromatin remodelling proteins and histones [118]. In 1957, Waddington described the embryonic development using a term called “epigenetic landscape” where cellular differentiation and developmental (Fig. 8) competence is not part of the DNA sequence [96, 105]. A variety of histone and DNA modifications, mainly are responsible for chromatin structure realignment [119], which attract TFs toward DNA either initiate or repress gene expression.



**Figure 8: Waddington developmental canal**

*Waddington, following Morgan, characterized the process of development as essentially “epigenetic” and also introduced the metaphor of an “epigenetic landscape”, which he depicted with a ball rolling down a hill of bifurcating valleys symbolizing the specification of defined cell lineages and fates during the progress of differentiation. It is notable that Waddington’s usage of epigenetic to denote the origination and propagation of information about cellular states during differentiation differs considerably from its recent reformulation to mean “on the genome” and its association with chemical modifications. ESCs: embryonic stem cells. (Adapted from [96] and modified)*

TFs are one of the trans-acting factors and a prime factor in transcriptional gene regulation [94]. In humans, estimates show that there are 2000 to 3000 DNA sequence binding TFs [118], which accounts approximately 10% of genes [120]. In the human body, each tissue/organ expresses the combination of cell type-specific and ubiquitous TFs for its development, maintenance and function [118, 121]. Cell type-specific TFs expressions are unique to their respective cell types and responsible for the reorganisation of global TFs binding profiles [121]. Cell type-specific combinatorial TFs binding and interactions are [122] necessary to establish TF-mediated gene regulatory networks (GRNs) [123, 124], which defines cellular identity. GRNs are hierarchical in nature [125]. Typical GRNs dictate cellular physiological capabilities and determine the cellular response to environmental fluctuations [125].

### **1.9 Wherefore further research in HLCs**

Numerous publications suggest the satisfactory derivation of HLCs but their applications hit the roadblocks due to the immature nature of derived HLCs [3]. Since HLCs are obtained by mimicking molecular events of the liver development, their transcriptional program is overlooked and interpreted only in the context of hepatocytes with a handful of gene markers [126]. Such an overwhelming approach made our understanding more constrained [126]. Furthermore, little is known about the transcriptional regulatory networks controlling the HLCs differentiation program.

Previously, there are serious concerns about the transcriptome similarity between in *vitro* engineered cell types and its in *vivo* counterpart [127-129]. Moreover, it is widely accepted that in *vitro* culturing environmental conditions foist specific changes in cellular gene expression [105, 130]. A potential application of this acquired knowledge will help to improve

HLCs derivation methods to yield mature and homogenous hepatocyte populations in the future.

### **1.10 Objective of this work**

This Ph.D. thesis work was primarily done at the Institute of Neurophysiology at the University of Cologne (UKK). In this work, a gene expression program of HLCs was dissected in comparison with “gold standard” freshly isolated adult hepatocytes and cultivated hepatocytes (in both monolayer and sandwich conditions) using gene arrays.

For this purpose, embryonic stem cells were differentiated into HLCs using a well-known method. The authenticity of derived HLCs was checked by RT-qPCR and immunostaining assays. Then global gene expression of HLCs and hESCs was analyzed by gene arrays. The resulted gene expression profiles of HLCs and hESCs were compared with freshly isolated adult hepatocytes and cultivated adult hepatocytes by using a series of computational tools.

The following were key intentions of this study:

- A.** Differentiation of embryonic stem cells (hESCs) into hepatocyte like cells (HLCs)
- B.** Profiling global gene expression of HLCs as well as hESCs and comparing with freshly isolated adult hepatocytes and cultivated adult hepatocytes
- C.** Determining the state and identity of differentiation in HLCs and to estimate gene regulatory mechanism by transcription factors via “Network Influence Scores” (NIS) using CellNet platform
- D.** Generation of gene clusters based on similar gene expression patterns and identification of transcription factors associated with each cluster

**E.** Analysing correlation between genes downregulated during cultivation of adult hepatocytes and minimally upregulated genes in HLCs



## 2 Materials and methods

### 2.1 Materials

Following materials and equipment were used in cell culture, molecular biology and microarray analysis.

**Table 2 List of materials utilised in this study**

<b>List of molecular biology reagents, and instruments</b>		
<b>Item</b>	<b>Company</b>	<b>Catalogue no.</b>
4',6-Diamidino-2-phenylindole dihydrochloride (DAPI)	Invitrogen, USA	D21490
Automated cooling centrifuge - 5430R	Eppendorf, Germany	-
Bovine Serum Albumin	SERVA Electrophoresis, Germany	11946.01
Chloroform, Molecular biology grade	SIGMA-ALDRICH, USA	C2432
Donkey anti-goat IgG (H+L) Alexa Fluor- 488 conjugated	Dianova, Germany	705-486-147
Donkey anti-rabbit IgG (H+L) Cy3 conjugated	Dianova, Germany	711-166-152
Ethanol, Molecular biology grade - 1 liter	Merck, Germany	1009831000
Experion RNA StdSen starter kit	Bio-Rad, USA	700-7111
Experion™ Automated Electrophoresis System	Bio-Rad, USA	-
FluorPreserve™ Reagent	Merck, Germany	345787
Goat anti-Human DPPIV/CD26	R&D Systems, USA	AF1180
Mini plate spinner-MPS1000	Labnet, USA	-
Nanodrop ND-1000 UV-Vis spectrophotometer	Nanodrop, USA	-
Nuclease-Free Water (not DEPC-Treated)	Invitrogen, Ambion, USA	AM9937
Rabbit anti-Human serum albumin	Abcam, UK	ab2406
Real time PCR - 7500FAST	Applied Biosystems, USA	-

RNase-Free DNase Set	Qiagen, Germany	79254
RNeasy Mini Kit	Qiagen, Germany	74106
SuperScript® VILO™ cDNA Synthesis Kit	Invitrogen, USA	11754250
Taqman gene expression master mix	Invitrogen, USA	4369016
Thermomixer-1.5 ml microcentrifuge tube	Eppendorf, Germany	-
Triton™ X-100	SIGMA-ALDRICH, USA	X100
TRIzol® reagent	Invitrogen, USA	15596-018
TWEEN® 20	SIGMA-ALDRICH, USA	P9416
VORTEX GENIE-2	Scientific Industries, USA	-
<b>List of Cell culture, reagents and instruments</b>		
<b>Item</b>	<b>Company</b>	<b>Catalogue no.</b>
1X Dulbecco's Phosphate buffered saline	Invitrogen, USA	14040174
1X Dulbecco's Phosphate buffered saline- No calcium, magnesium	Invitrogen, USA	14190169
4-(2-Hydroxyethyl)piperazine-1-ethanesulfonic acid, N-(2-Hydroxyethyl)piperazine-N'-(2-ethanesulfonic acid, HEPES)	SIGMA-ALDRICH, USA	H4034
B-27® Supplement (50X), minus vitamin A	Invitrogen, USA	12587-010
Beta-Mercaptoethanol (50 mM)	Invitrogen, USA	31350010
Centrifuge- IEC CENTRA CL2	Thermo Scientific, USA	-
CO2 incubator -HERACELL 150i	Thermo Scientific, USA	-
Confocal microscopy-FV1000	Olympus, Japan	-
D-MEM/F-12 (1:1) (1X), liquid - with GlutaMAX™ medium	Invitrogen, USA	31331-093
DMSO, Cell culture grade	SIGMA-ALDRICH, USA	D2650
Fetal bovine serum	Invitrogen, USA	944855K
GlutaMAX™	Invitrogen, USA	35050-038
hESC-qualified Matrix, 5 ml *LDEV Free	BD Biosciences, USA	354277
Hydrocortisone hemisuccinate	SIGMA-ALDRICH, USA	H2270
Insulin solution Human	SIGMA-ALDRICH, USA	I9278

KnockOut™ D-MEM	Invitrogen, USA	10829-018
Knockout™ Serum Replacement	Invitrogen, USA	10828028
L-15 Medium	SIGMA-ALDRICH, USA	L1518
Laminar air flow bench- HB2448	Heraeus, Germany	-
Laminar air flow-EN12469	Thermo Scientific, USA	-
mFreSR™	Stem cell technologies, USA	05854
mTeSR™	Stem cell technologies, USA	05850
Non-essential amino acids	Invitrogen, USA	11140035
Penicillin-Streptomycin (10,000 U/ml)	Invitrogen, USA	15140122
Phase contrast microscope-Axiovert 25	Zeiss, Germany	-
Recombinant Human /Murine/Rat Activin A (E.coli derived)	Peprotech, USA	120-14E
Recombinant Human FGF-Basic (FGF2)	Peprotech, USA	AF-100-18C
Recombinant Human HGF	Peprotech, USA	100-39
Recombinant Human Oncostatin M/OSM	R&D Systems, USA	295-OM-010
Recombinant Human Wnt-3a	R&D Systems, USA	5036-WNP-010
RPMI-1640 medium	Invitrogen, USA	61870-044
Sodium pyruvate solution	SIGMA-ALDRICH, USA	S8636
StemPro® hESC SFM	Invitrogen, USA	A1000701
Stereo microscope-LEICA MZ 125	Leica Microsystems, Germany	-
Tryptose Phosphate Broth solution	SIGMA-ALDRICH, USA	T8159
Weighing balance-BP121S	Sartorius, Germany	-
William's E medium	Panbiotech, Germany	P04-29050
<b>List of microarray, instruments, kits, and reagents</b>		
<b>Item</b>	<b>Company</b>	<b>Catalogue no.</b>
3 IVT Express Kit	Affymetrix, USA	901229
Experion automated electrophoresis system	Bio-Rad, USA	701-7000
Experion RNA StdSen starter kit	Bio-Rad, USA	700-7111
GeneChip Fluidics Station 450	Affymetrix, USA	00-0079
GeneChip Hybridization Oven 645	Affymetrix, USA	00-0331

GeneChip hybridization, wash and stain kit	Affymetrix, USA	900720
GeneChip Scanner 3000 7G WholeGenome Association System	Affymetrix, USA	00-0362
Human Genome U133 Plus 2.0 arrays	Affymetrix, USA	900467
<b>List of plastic and glass consumables</b>		
<b>Item</b>	<b>Company</b>	<b>Catalogue no.</b>
1 ml pipettes	SARSTEDT AG & CO, Germany	86.1251.001
1.5 ml Microcentrifuge Tubes	Axygen, USA	MCT150-C
10 cm petri dishes	Corning Inc, USA	353003
10 microliter filtered tips	Nerbe plus GmbH, Germany	07-602-7300
10 ml pipettes	Labomedic, Germany	1110508
100 microliter filtered tips	Nerbe plus GmbH, Germany	07-642-7300
1000 microliter filtered tips	Nerbe plus GmbH, Germany	07-692-7300
15 ml tubes	Labomedic, Germany	1110502
1ml sterile syringe	BD plastipak, USA	300013
2 ml pipettes	SARSTEDT AG & CO, Germany	86.1252.001
20 microliter filtered tips	Nerbe plus GmbH, Germany	07-622-7300
200 microliter filtered tips	Nerbe plus GmbH, Germany	07-662-7300
25 ml pipettes	Labomedic, Germany	1110611
5 ml pipettes	Labomedic, Germany	1110507
50 ml tubes	Labomedic, Germany	1110503
6 cm petri dishes	Corning Inc, USA	353004
6-well cell culture plates	Corning Inc, USA	353046
Glass cover slips	VWR, Germany	16004-316
Glass Pasteur pipette	VWR, Germany	612-1701
MicroAMP fast optical 96-well plate	Applied Biosystems, USA	4346906
MircroAmp optical adhesive film	Applied Biosystems, USA	4311971
Stainless steel sterile needle 20 gauge	BD microlance, USA	301300
StemPro® EZPassage™ Disposable Stem Cell Passaging Tool	Invitrogen, USA	23181-010

Sterile cell scraper	Techno Plastic Products AG (TPP), Switzerland	99002
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**Table 3 List of TaqMan® gene expression Assays**

Following gene expression probes were obtained from Invitrogen, USA.

<b>Gene symbol</b>	<b>Assay ID</b>
ALB	Hs00910225_m1
ALDH1A1	Hs00946916_m1
CAR	Hs00901571_m1
CEBPA	Hs00269972_s1
CEBPB	Hs00270923_s1
CEBPD	Hs00270931_s1
E2F5	Hs00231092_m1
FGB	Hs00905942_m1
FOXA1	Hs04187555_m1
FOXA2	Hs00232764_m1
FOXA3	Hs00270130_m1
FOXQ1	Hs00536425_s1
GAPDH (Endogenous control)	4333764F
HNF1A	Hs00167041_m1
HNF4A	Hs00230853_m1
MYB	Hs00920558_m1
SOX11	Hs00846583_s1
TTR	Hs00174914_m1
YBX3	Hs04195573_u1

## 2.2 Methods

### 2.2.1 hESCs culturing and maintenance at the Institute of Neurophysiology, University of Cologne (UKK)

Human embryonic stem cell lines (WA09) was obtained from the Wicell Research Institute, USA. Permission to work with hESCs was given by the Robert Koch Institute, Berlin (AZ: 1710-79-1-4-48). H9 cells were maintained in irradiated embryonic fibroblast feeder cell lines (CF1 mouse strain) using Dulbecco's Modified Eagle Medium/Nutrient Mixture F-12 supplemented with 1% penicillin-streptomycin, 1% nonessential amino acids, 4 ng/ml of fibroblast growth factor-2 and 0.1 mM beta-mercaptoethanol. All cell cultures were performed at 37°C and 5% CO<sub>2</sub>. For every 5-7 days, cells were passaged using a STEMPRO® EZPassage™ tool under a stereomicroscope.

For feeder-free conditions [131], H9 cells were grown in matrigel coated culture dishes using mTeSR™ or StemPro® hESC serum-free medium supplemented with 0.1 mM beta-mercaptoethanol and 8 ng/ml of fibroblast growth factor-2. All experiments were carried out using hESCs of passage number between 35 and 70.

### 2.2.2 Differentiation of hESCs into hepatocyte like cells (HLCs)

H9 cells were differentiated into HLCs using a published procedure [88, 132]. Briefly, H9 cells were grown in a feeder-free environment using matrigel coated dishes. It is a prerequisite that seeded cells reach 60-70% confluency. Once the cells reached required confluency, hESCs (DAY0) was harvested using TRIzol® for RNA isolation, before the start of HLCs differentiation.

HLCs differentiation was initiated by washing cells twice with 1X PBS and refreshing with “**Definitive endoderm medium**” consisting of RPMI 1640-Glutamax basal media supplemented with 100 ng/ml of Activin A, 50 ng/ml of Wnt3a and 1XB27.

After 72 hrs, the differentiation medium was changed to “**Hepatoblast differentiation medium**” consisting of Knockout-DMEM media supplemented with 20% KSOR, 1% DMSO, 1% non-essential amino acid, 0.5% glutamax, and 0.1 mM beta-mercaptoethanol for 7 days.

Finally, “**Hepatic maturation medium**” consisting of L-15 media supplemented with 10 ng/ml HGF, 10% FBS, 20 ng/ml Oncostatin M, 8.3% tryptose phosphate broth, 10 µM hydrocortisone-21-Hemisuccinate and 1 µM insulin was used for hepatic maturation, which lasted for 7 days. The medium was refreshed daily in each stage of differentiation. On completion of differentiation at day18, HLCs were harvested using TRIzol® for RNA isolation.

HLCs-islands were collected from a heterogeneous population for RNA isolation as reported earlier [133]. Briefly, hepatocyte like islands were identified by phase contrast microscopical observation and mechanically dissected under a stereomicroscope. After dissection, hepatic islands were pooled and lysed using TRIzol® reagent. All TRIzol® cell lysates were stored at -80°C until further processing. RNA samples, including hESCs (DAY0), HLCs-total (DAY18), and HLCs-islands (DAY18) were analysed in triplicates using gene arrays.

### **2.2.3 Freshly isolated adult human hepatocytes and culturing**

Freshly isolated adult human hepatocytes (hHEPs, DAY0) were obtained under patient informed consent from liver sections of patients undergoing surgical liver resection (following the 1975 declaration of Helsinki) as previously described [134]. Hepatocytes were obtained by two-step collagenase-I perfusion of liver sections. A detailed protocol for isolation was described in Godoy et al. 2013 [134]. Freshly isolated hepatocytes from three independent donors were lysed using TRIzol®, stored at -80°C until RNA was isolated and analysed for global gene expression.

hHEPs (DAY0) were cultured using Williams' medium E supplemented with 10% fetal bovine serum, 1 mM insulin, 15 mM HEPES, 0.8 µg/ml hydrocortisone, 1% penicillin-streptomycin, 1% glutamax, 1% non-essential amino acids and 1 mM sodium pyruvate in matrigel coated culture plates with a density of 150, 000 cells/cm<sup>2</sup>. These cultivated adult hepatocytes were used as positive control for immunostaining.

#### **2.2.4 RNA isolation and cDNA synthesis**

Stored TRIzol® cell lysates were thawed and proceeded for RNA isolation. Total RNA was purified using the RNeasy mini kit as per manufacturer's protocol. Concisely, cell lysates were homogenized using 20 gauge syringe needle. After successful homogenization, the samples were encouraged for phase separation by the addition of 0.2 milliliters of chloroform for each 1 milliliter of TRIzol®. Phase separation of the lysates was allowed to take place at room temperature for 2-5 minutes. After 5 minutes, lysates were centrifuged at a 14,000 RPM for 15 minutes at 4 °C. After completion of centrifugation, only an upper layer was removed and collected in a new 1.5-milliliter microcentrifuge tube. Precipitation of RNA was achieved by the addition of an equal volume of ice-cold ethanol and mixed gently. From now on, all centrifugation steps take place at room temperature. The resultant mixture was added to the RNeasy spin column and centrifuged at 11,500 RPM for 30 seconds. After discarding the flow-through, 350 microliters of RW1 buffer was added to the spin column and centrifuged at 11,500 RPM for 30 seconds. Spin column was digested using RNase-free DNase to remove the genomic DNA. For each column, a mixture of DNase (10µl) + RDD buffer (70 µl) was added to the column and incubated for 15 minutes at room temperature. After 15 minutes, DNase digestion reaction was arrested by the addition of 350 microliters of RW1 buffer and spin column flow-through was discarded. Spin column was washed twice, in a back to back manner using RPE buffer by centrifuging at 11,500 RPM for 30 seconds. The empty spin



column was dried by centrifuging at 14,000 RPM for 2 minutes. Finally, RNA was eluted by the addition of 20-25 microliter water (RNase, DNase-free). Purified RNA was quantified using ND-1000 UV-Vis spectrophotometer. For microarray analysis, RNA Integrity Number (RIN) was evaluated using Experion RNA StdSen starter kit and Experion automated electrophoresis system. RNA samples with RIN more than 8.0 were used for microarray analysis.

1 µg or 500 ng of total RNA was employed for cDNA synthesis using Vilo Superscript cDNA synthesis kit as per manufacturer’s protocol. The reaction mixture composition was indicated in Table 4. Initially, the reaction mixture was incubated for 10 minutes at 25°C. On completion of the initial incubation, cDNA synthesis was continued for 60 minutes at 42 °C. Then cDNA synthesis was terminated by incubating at 85 °C for 5 minutes. Resultant cDNA was stored in -20 °C until used for RT-qPCR assays.

<b>Componentes</b>	<b>volume per 20 µl-single reaction( µl)</b>
5X VIL <sup>o</sup> ™ Reaction Mix	4
10X SuperScript® Enzyme Mix	2
water	12
RNA	2 (1 µg or 500 ng)
<b><i>Total volume</i></b>	<b><i>20µl</i></b>

**Table 4 cDNA synthesis reaction mixture**

### **2.2.5 RT-qPCR assays**

The RT-qPCR reaction was carried out using TaqMan gene expression assays in a 7500 fast real-time cycler as per manufacture’s protocol (Table 5). cDNA of 2 microliters was used in 20 microliter PCR reaction (Table 6), which ran in three replicates for each gene (Table 3).

H<sub>2</sub>O was used as negative control. Relative gene expression (delta-delta Ct method [135]) was calculated using DataAssit software version 3.01 from Applied Biosystems, USA. For gene expression computation, either hESCs or hHEPs was used as calibrator and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) was used as the housekeeping gene.

RAMP rate	Reaction volume	Cycling conditions				
		Parameters	UNG incubation	Polymerase activation	40 cycles	
					Denature	Anneal/extend
		Temperature (degree celcius)	50	95	95	60
<b>Standard</b>	20 $\mu$ l	Time(mm:ss)	2:00	10:00	0:15	1:00

**Table 5 RT-qPCR cycling conditions**

PCR componenets	volume per 20 $\mu$ l-single reaction( $\mu$ l)
20 $\times$ TaqMan <sup>®</sup> Gene Expression Assay	1
2X TaqMan gene expression master mix	10
water	7
cDNA	2
<b><i>Total volume</i></b>	<b><i>20 <math>\mu</math>l</i></b>

**Table 6 RT-qPCR reaction mixture composition**

### 2.2.6 Immunostaining assay

Immunostaining was preceded with fixation of hESCs and HLCs cells with ice-cold methanol at -20°C for 10 minutes. Adult hepatocytes cultured in matrigel were fixed with ice-cold methanol at -20°C for 10 minutes and used as positive control. After washing three times with 1X PBS, fixed cells were permeabilized using Triton-X 100 (1:50) for 30 minutes at room

temperature. After permeabilization, cells were again washed three times with 1X PBS. Then, cells were blocked with a blocking buffer made by dissolving 3% of BSA and 1% Tween-20. Overnight incubation of ALB (1:50) and DPPIV (1:100) was performed at 4°C diluted in 1X PBS (contains 0.3% BSA and 1% Tween-20). Secondary antibodies donkey anti-goat IgG (H+L) Alexa Fluor-488 conjugated (1:100) and donkey anti-rabbit IgG (H+L) Cy3 conjugated (1:100) dissolved in 1X PBS (contains 0.3% BSA and 1% Tween-20) were used and incubated for 2 hours at room temperature. DAPI counterstaining (1:10000) in distilled water was performed for 90 minutes at room temperature. Finally, stained cells were washed with 1X PBS and mounted with FluorPreserve™ reagent. The scanning of mounted glass slides was performed using a confocal microscope.

### **2.2.7 Microarray analysis**

Transcriptome analysis of all samples was performed using Affymetrix Human Genome U133 Plus 2.0 arrays as per manufacture's protocol. Briefly, 100 ng of total RNA was amplified using Gene chip 3' IVT Express Kit as per manufacture's guidelines. The resulted aRNA was purified using magnetic beads and 15 micrograms of aRNA hybridized onto the human genome U133 plus 2.0 chips in a gene chip hybridization oven-645. Then chips were stained and washed using an Affymetrix HWS kit. The chips were scanned with Affymetrix gene chip Scanner-3000-7G. The quality control analysis was performed using the GCOS software of Affymetrix.

### **2.2.8 Gene array data of HLCs and stem cells from our collaborators**

Gene array data (Human Genome U133 Plus 2.0 arrays) of HLCs and stem cells (hESCs and ihPSC) were obtained from two collaborating partners for comparative study. Between two collaborators, one is a Medical Research Council (MRC), United Kingdom and another is Collectis stem cell company (CEL), Sweden. MRC's HLCs differentiated from human

embryonic stem cells (ESC), and detailed differentiation protocol can be found elsewhere [136]. On the other hand, CEL's HLCs differentiated from both human embryonic stem cells (ESC) and induced pluripotent stem cells (ihPSC), independently [136].

### **2.2.9 Gene array data of cultured primary adult hepatocytes**

For comparative analysis with HLCs, gene array data of *in vitro* cultivated adult hepatocytes were obtained. Gene array data (Human Genome U133 Plus 2.0 arrays) of cultured primary adult hepatocytes under two different conditions, the collagen monolayer and collagen sandwich conditions were generated at "Leibniz Research Centre for Working Environment and Human Factors", Dortmund. In both conditions, primary adult hepatocytes were cultured for various time points like 01, 02, 03, 05, 07, 10, and 14 days using the previously published method (Godoy et al. 2013) [134]. Briefly, isolated human hepatocytes were removed from the debris by percol centrifugation method and plated (6-well plate) in both collagen-I coated (monolayer, at a density of 104,166) and between two layers of collagen-I gel (collagen sandwich, at a density of 88,542). The cells were cultured in serum-free William's E medium for the indicated time. The medium was refreshed daily.

### **2.2.10 Microarray data analysis by our bioinformatic collaborator**

Our collaborator at the Leibniz Institute for Natural Product Research and Infection Biology, Hans-Knöll-Institute (HKI) in Jena (Germany) performed all microarray data analysis. This analysis includes gene array data of UKK, MRC, CEL, freshly isolated adult hepatocytes and cultivated adult hepatocytes. Affymetrix gene expression data were preprocessed using 'affyPLM' packages [137] of the Bioconductor project [138]. Processing and visualisation (principal component analysis) of data were performed using MATLAB tools (Mathworks, USA).

### **2.2.11 Computation of differentially expressed genes**

To obtain the genes with the strongest evidence of differential expression, a linear model fit was applied for each genes using ‘limma’ (Linear Models for Microarray data) packages [139]. Gene array data from freshly isolated adult hepatocytes (hHEPs) was used as reference. The custom chip definition file from Brainarray [140] based on UniGene ID’s was used to annotate gene probesets. A false positive rate of  $\alpha=0.05$  with FDR correction [141] and a fold change greater 2 was taken as the levels of significance.

### **2.2.12 Fuzzy clustering**

The time profiles of the differentially expressed genes in stem cells and HLCs were scaled between their corresponding absolute temporal extreme values to focus subsequent cluster analysis on the qualitative behavior of the expression profiles. The time series clustered using fuzzy c-means [142] (fuzzy exponent=1.5; Maximum number of iterations=200; minimum cost function improvement=10<sup>-10</sup>). The optimum number (N) of the cluster was calculated by repeated calculations (number of iterations=100) of the fuzzy cluster index ‘separation index’. Fuzzy clustering identified twenty clusters and those with the strongest change in gene expression were selected, and similar gene expression patterns compiled into five cluster groups. The manually curated Gene Ontology database of BioBase Knowledge Library (BKL) of the ExPlain<sup>TM</sup> web service (BioBase GmbH, Germany) was used for gene ontology enrichment.

### **2.2.13 Gene ontology (GO) analysis**

Genes that show a change of the ratios higher or lower than 2-fold change in the arrays at any of the time points have been considered as upregulated or downregulated and subjected to gene ontology enrichment. Each cluster group was functionally categorized using BioBase knowledge library (BKL) of the ExPlain<sup>TM</sup> web service (BioBase GmbH, Germany). The

analysis performed on the list of genes corresponding to the combination of clusters into cluster groups.

#### **2.2.14 Transcription factor binding site (TFBS) enrichment analysis**

For identification of transcription factors whose binding sites are enriched in a given set of promoters, the PRIMA tool [143] of the Expander software version 6.1 was used [144]. The analysis was performed on genes belonging to the each cluster group that are significantly (p-value  $<0.05$ ) changed more than 2-fold. All the human genes (From Ensembl release 42) were used as background gene set, the threshold of the p-value set to 0.01 and the region was scanned from -3000 to +200.

#### **2.2.15 Identification of deregulated transcription factors**

To identify deregulated transcription factors in HLCs cluster groups, the genes were mapped to specific transcription factor using the database TRANSFAC professional and categorised using the ExPLAIN<sup>TM</sup> web service.

#### **2.2.16 Euclidean distance (ED) measurement**

To evaluate the differentiation process, the Euclidean distance between the different cell types was calculated based on the expression of the level of differentially expressed genes. The pairwise Euclidean distances were computed using the statistic toolbox of Matlab (Mathworks, USA) for genes with a fold change  $> 2$  and a fold discovery rate (FDR) corrected p-value less than 0.05.

#### **2.2.17 CellNet analysis**

CellNet tool was used to analyse tissue/cell identity based on global gene expression data of hESCs, ihPSC and HLCs from three independent labs UKK, MRC, and CEL and freshly isolated adult hepatocytes (hHEPs) as described in Cahan P et al. 2014 [126]. This algorithm also generates a metric for gene regulatory network associated with the genes belonging to

each tissue identity. The Network influence score (NIS) was computed for cell and tissues with a high value of the gene regulatory network to estimate the importance of transcription factors to normal and dysregulated gene regulatory network. Locally available R version of CellNet was used for all calculations (<http://pcahan1.github.io/cellnetr/>).

### **2.2.18 Statistics**

Results were presented as mean  $\pm$  SEM derived from three biological replicates. The graphical representations of data were performed using Graph Pad Prism version 4.0 (Graph Pad Software, USA).

### **3 Results**

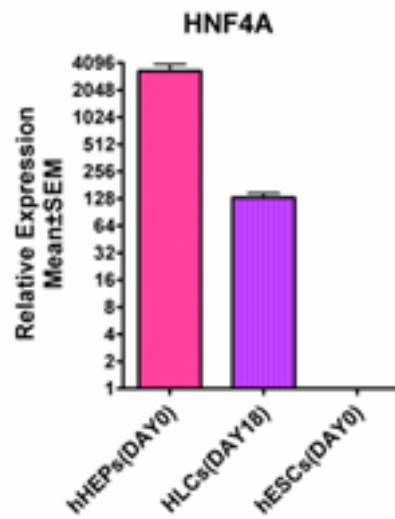
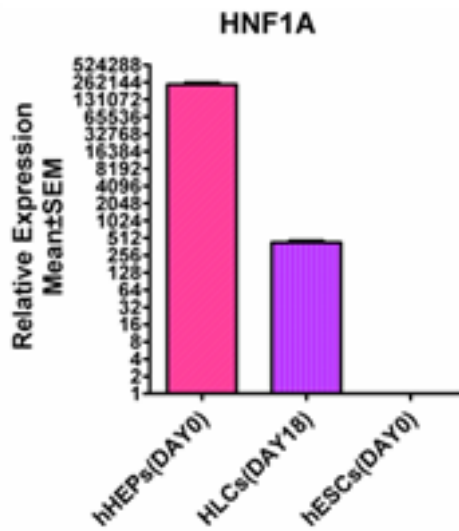
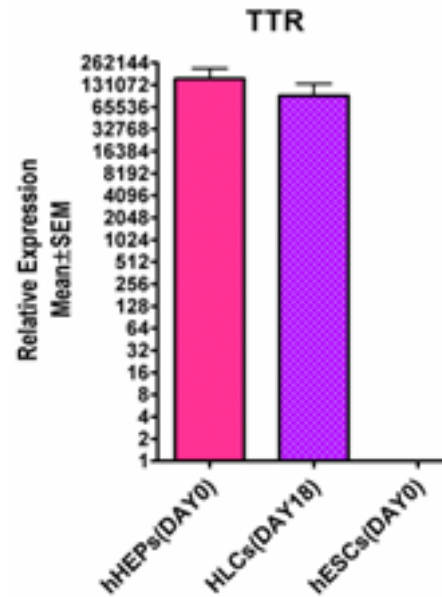
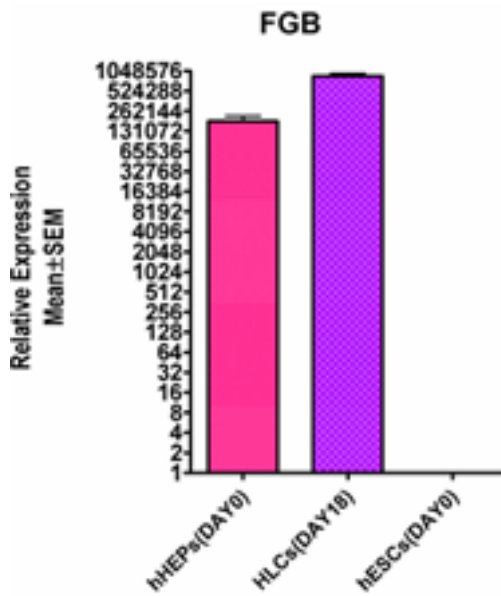
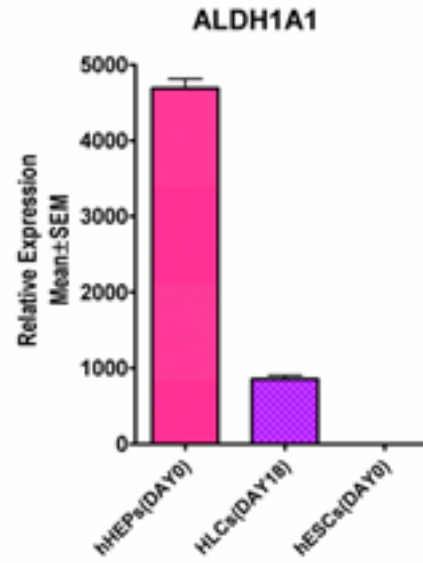
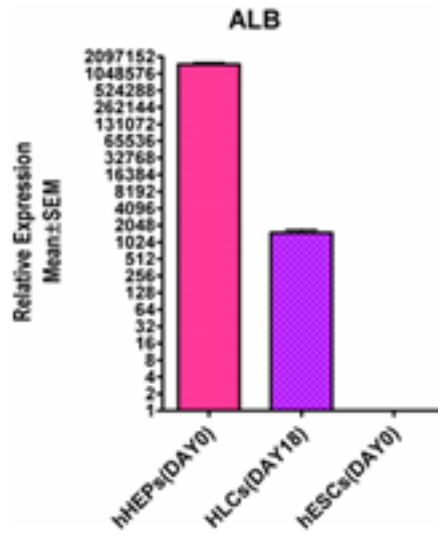
#### **3.1 Derivation of HLCs from human embryonic stem cells (hESCs)**

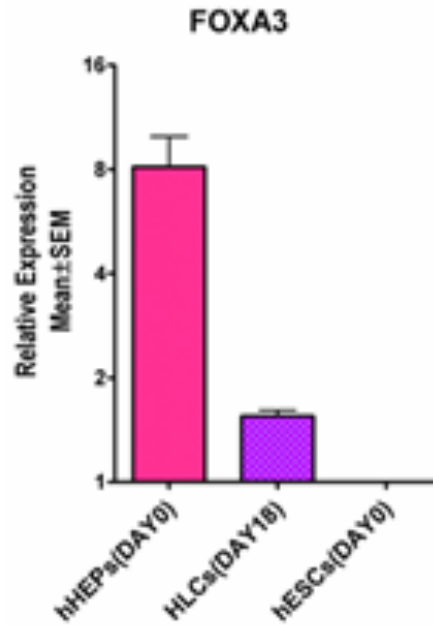
In Institute of Neurophysiology, University of Cologne (UKK) the primary objective was to differentiate hESCs (WA09) into hepatocyte like cells (HLCs). For this purpose, a previously published “Directed differentiation” method [88, 132] was employed. The authenticity of derived HLCs (DAY18) was checked by RT-qPCR and immunocytochemistry assays. Reproducibility of derivation was checked by performing three independent experiments. Freshly isolated primary adult human hepatocytes (hHEPs, DAY0) were used as a positive control. Primary hepatocytes were obtained from three independent donors.

Hepatocyte markers such as the transcription factors HNF4A, HNF1A, and FOXA3 [1], albumin (ALB), transthyretin (TTR), fibrinogen beta chain (FGB), and the metabolizing enzyme aldehyde dehydrogenase (ALDH1A1) were analyzed using RT-qPCR to compare the expression levels of the three cell types hESCs, HLCs and hHEPs. The result shows that expression levels of all genes are below detection limits for hESCs (Fig. 9). A strong increase in expression levels was observed in HLCs compared to hESCs (Fig. 9). However, expression levels in HLCs still were clearly lower compared to freshly isolated adult hepatocytes (hHEPs).

Next, immunostaining was applied to study whether HLCs adopt an epithelial morphology by analyzing expression of plasma protein albumin and the bile canaliculi marker DPP4, a well-established marker of hepatocyte polarity [145].





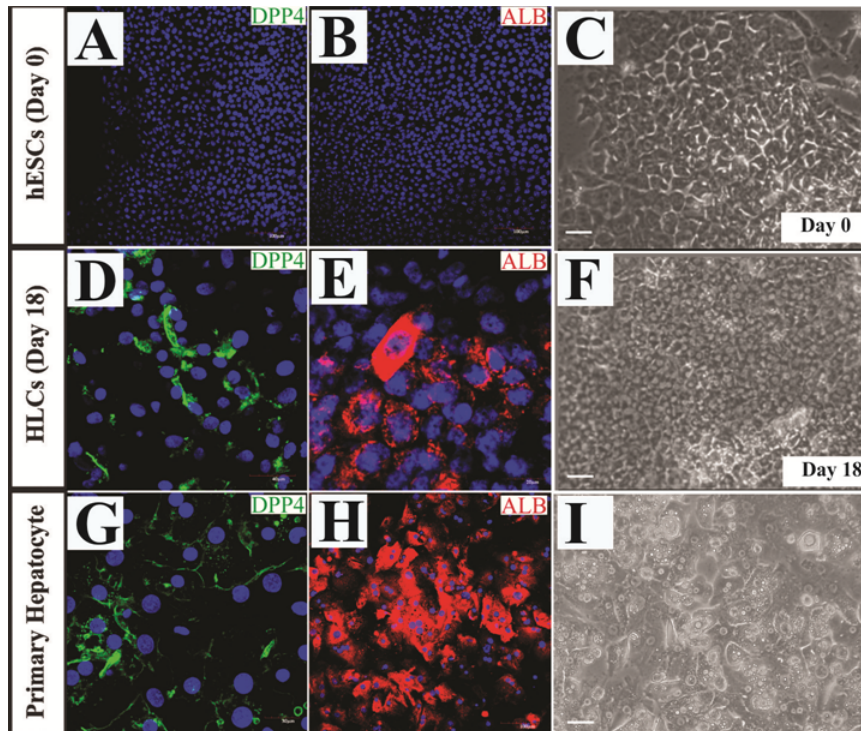


**Figure 9: Expression of hepatic gene markers in hESCs, HLCs, and hHEPs**

*The Strong increase in the expression of gene markers ALB, ALDH1A1, FOXA3, FGB, TTR, HNF4A, and HNF1A confirm hepatocyte like cells (HLCs) derivation from hESCs. However, the expression did not increase to the level of hHEPs. For the relative gene expression calculation, hESCs was used as calibrator and glyceraldehyde-3-phosphate dehydrogenase (GAPDH) as housekeeping gene. The mean and standard error of the mean (SEM) of gene expression levels were representative of three independent experiments. Freshly isolated adult hepatocytes (hHEPs) were obtained from three independent donors. ALB: Albumin; ALDH1A1: Aldehyde dehydrogenase family 1 Member A1; FOXA3: forkhead box A3; FGB: fibrinogen beta chain; TTR: transthyretin; HNF1A: Hepatocyte nuclear factor 1-Alpha; HNF4A: Hepatocyte nuclear factor 4-Alpha; hESCs (DAY0): human embryonic stem cells; HLCs (DAY18): hepatocyte like cells.*

The results of the immunostaining experiments show that hESCs express neither DPP4 nor albumin (Fig. 10A-C). After differentiation to HLCs staining for DPP4 became positive (Fig. 10D). DPP4 staining showed a pattern similar to primary human hepatocytes that used as positive control (Fig. 10G). In both HLCs and primary hepatocytes, the DPP4 signal was seen at the membrane surrounding small canaliculi. Albumin showed a clear cytoplasmic staining

in HLCs (Fig. 10E). A similarly positive result for albumin was obtained for the cultivated primary human hepatocytes (Fig. 10H).



**Figure 10: Immunostaining for ALB and DPPIV (Bile canaliculi) gene markers**

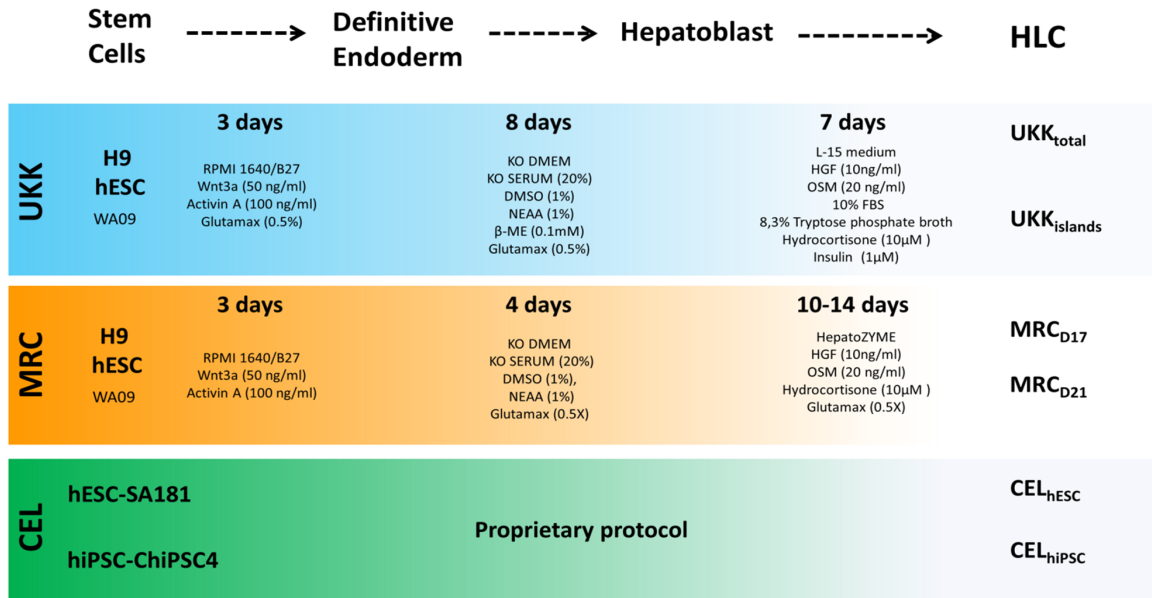
*Images A and B represents DPPIV, ALB for hESCs (DAY0) and image C represent a phase contrast microscopy image. Images D and E represents DPPIV, ALB for HLCs (DAY18) and image F represent a phase contrast microscopy image. Images G and H represents DPPIV, ALB for primary human hepatocytes and the image I represent phase contrast microscopy image of primary hepatocytes. Blue color represents DAPI cellular nuclei staining; Scale bar=100 micrometres; ALB: Albumin; DPPIV: Dipeptidyl peptidase-4; hESCs (DAY0): human embryonic stem cells; HLCs (DAY18): hepatocyte like cells.*

In conclusion, a robust method for derivation of HLCs from hESCs was established. Expression of genes typically expressed in human hepatocytes was verified using RT-qPCR. In addition, albumin and DPP4 immunostaining were positive. However, expression levels in HLCs were still lower compared to freshly isolated adult hepatocytes, suggesting that the differentiation process is still incomplete.

### **3.2 Global gene expression of HLCs, stem cells and primary hepatocytes**

An attempt to characterize the global gene expression of HLCs, hESCs, hiPSCs from three independent labs Institute of Neurophysiology of Uniklinik, köln (UKK), Medical Research Council, United Kingdom (MRC), and Cellartis (CEL), Sweden (Fig. 11) was realized using Affymetrix Human Genome U133 Plus 2.0 arrays. These labs generated HLCs using three published differentiation methods [146-148] (Fig. 11), i.e. “Directed differentiation”. Each of these methods consists of successive intermediate cellular stages such as definitive endoderm and hepatoblast when stem cells differentiate into HLCs (Fig. 11). However, these three methods differ in terms of growth factors use and the number of days accompanying each cellular stage (refer Fig. 11 for more details). Gene array data of HLCs and hESCs (Fig. 11 and Table 7) from UKK were generated in this Ph.D. thesis work. Conversely, the rest of gene array data (Fig. 11 and Table 7) were obtained from collaborating partners such as the MRC and CEL.

RNA of HLCs, hESCs and iPSCs at indicated time points (Fig. 11) were collected in biological triplicates and analyzed (Table 7). The population of HLCs from UKK were heterogeneous in nature, so total heterogeneous population, hepatocyte like islands were collected independently and analyzed (Fig. 11 and Table 7). For comparative global gene expression analysis, freshly isolated adult human hepatocytes (hHEPs, DAY0) from three independent donors were used. The samples above were fed into the bioinformatic pipeline.



**Figure 11: Schematic representation of the HLCs differentiation protocol used by three labs**

Three independent labs such as the Institute of Neurophysiology at University of Cologne, köln (UKK), Medical Research Council (MRC), United Kingdom, and Cellartis (CEL), Sweden generated HLCs from stem cells using three published differentiation methods, i.e. “Directed differentiation.” Each method consists of successive intermediate cellular stages such as definitive endoderm and hepatoblast when stem cells differentiate into HLCs. However, these three methods differ in terms of growth factors use and the number of days accompanying each cellular stage. RNA of HLCs, hESCs, and iPSCs at indicated time points were collected in biological triplicates and analyzed (refer Table 7). Differentiation of hESCs into HLCs from UKK was performed exclusively in this Ph.D. thesis work.

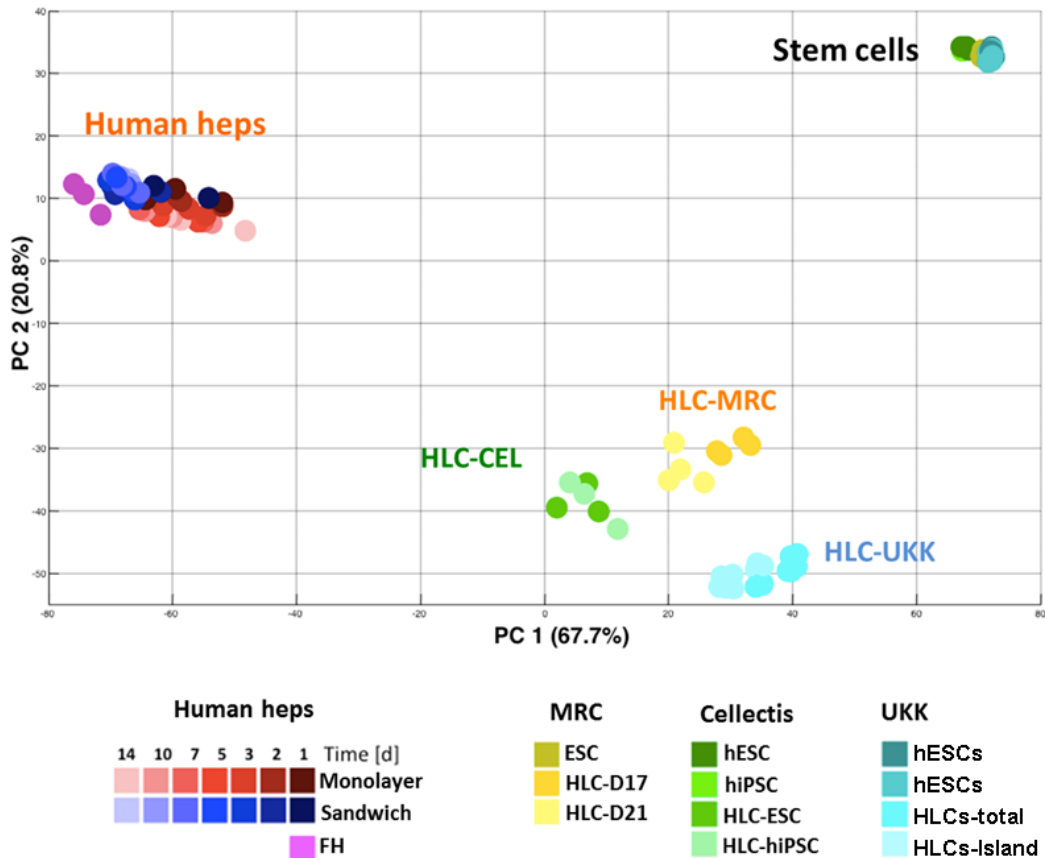
Abbreviation	Description
ESC-MRC	Embryonic stem cells from MRC
HLC-MRC-D17	Hepatocyte like cells form MRC, 17 days of differentiation
HLC-MRC-D21	Hepatocyte like cells form MRC, 21 days of differentiation
ESC-CEL	Embryonic stem cells from Cellartis
hiPSC-CEL	Human induced pluripotent stem cells from Cellartis
HLC-ESC-CEL	Hepatocyte like cells after differentiation of ESC from cellartis
HLC-hiPSC-CEL	Hepatocyte like cells after differentiation of hiPSC from cellartis
hESCs-UKK1	Embryonic stem cells from university of cologne, batch 01
hESCs-UKK2	Embryonic stem cells from university of cologne, batch 02
HLCs-total	Hepatocyte like cells after differentiation of ESC from UKK
HLCs-island	Hepatocyte like cells after differentiation of ESC from UKK

**Table 7 Overview of different samples from three labs analyzed by gene array**

*List of samples that were subjected to global gene expression analysis, which were obtained from three independent labs such as the Institute of Neurophysiology at University of Cologne (UKK), köln, Medical Research Council, United Kingdom (MRC), and Cellartis (CEL), Sweden. Gene array data of HLCs and hESCs from UKK were generated in this Ph.D. thesis work. The rest of gene array data were obtained from two collaborating partners such as the MRC and CEL.*

Computed differentially expressed genes among HLCs, hHEPs, hESCs [e.g. hHEPs vs. HLCs, hHEPs vs. hESCs and hHEPs vs. hiPSC] were filtered using a fold change 2 with a false discovery rate 5% that resulted in 10,420 genes and used for further analysis.

Principal component analysis (PCA) was used to identify cluster structure [149] in gene expression data. PCA of 1000 highest variant genes was used to understand the dynamics of gene expression (Fig. 12) and their manifestations as follows.



**Figure 12: Principal component analysis (PCA) biplot of different samples**

PCA plotted with 1000 highest variant genes in stem cells and HLCs. The cultivated adult hepatocytes in the collagen monolayer and sandwich conditions were also included in the biplot. HLCs differentiated from stem cells move towards freshly isolated adult hepatocytes but do not reach there yet. Presented data was representative of three biological array replicates of each sample. Gene array data of freshly isolated adult human hepatocytes (FH or hHEPs) were generated using hepatocytes from three independent donors. Gene array data of cultivated hepatocytes for monolayer and sandwich conditions were generated at “Leibniz research center for working environment and human factors,” Dortmund. PC1: Principal Component 1; PC2: Principal Component 2; Human heps: Includes cultivated adult human hepatocytes and freshly isolated adult human hepatocytes (FH); HLCs-total: the heterogeneous population of hepatocyte like cells(UKK); HLCs-island: hepatocyte like islands extracted from heterogeneous population (UKK); UKK: Institute of Neurophysiology at University of Cologne; MRC: Medical Research Council, United Kingdom; CEL: Cellartis, Sweden.

- A. HLCs differentiated from hESCs, iPSCs approach towards hHEPs but do not reach the position of hHEPs (labeled as ‘FH’ under Human heps in Fig. 12). It suggests a partial

gain of hepatic transcriptomic characteristics. Selective profiling of the HLCs-island had little effect on the global gene expression profile of HLCs (Fig. 12). These two observations were confirmed by Euclidean distance analysis (Table 8).

Samples	Euclidean distance to hHEPs (DAY0) (10,420 genes; 2-fold)	Euclidean distance to hHEPs (DAY0) (%)
hESCs (DAY0)	212.94	100
HLCs-total	185.01	86.9
HLCs-island	178.44	83.8

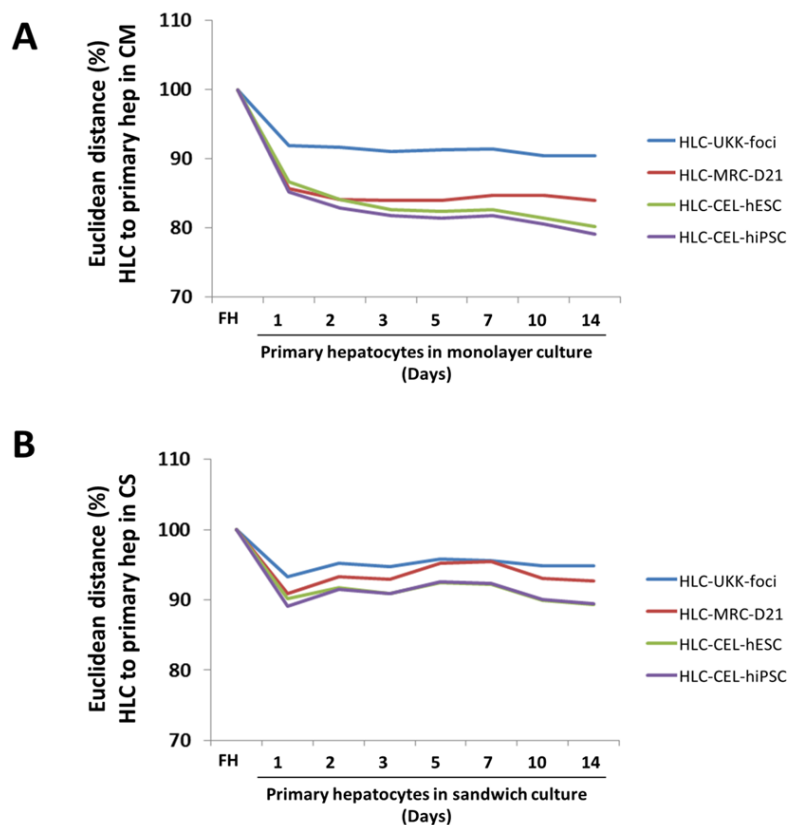
**Table 8 Euclidean distance measurement**

*Euclidean distance between freshly isolated adult human hepatocytes (hHEPs) and hESCs, HLCs from UKK was calculated using a statistic toolbox of Matlab (Mathworks Inc., USA). Differentially expressed 10,420 genes at a fold change 2 with the false discovery rate adjusted  $p$ -value  $\leq 0.05$  was used for Euclidean distance measurement. The Euclidean measurement of HLCs was scaled to the values of hESCs that were set to 100%. HLCs-total: the heterogeneous population of hepatocyte like cells (UKK); HLCs-island: hepatocyte like islands extracted from the heterogeneous population (UKK); hESCs: human embryonic stem cells.*

- B. Even though HLCs from three labs positioned as a distinct cluster, their distance to pluripotent cells and adult hepatocytes was relatively same, suggesting that HLCs from three different labs have a similar gene expression pattern (Fig. 12).
- C. Dedifferentiation of adult human hepatocytes *in vitro* and associated changes in gene expression pattern was well known [134]. Therefore, comparison of gene expression profiles of both monolayer and sandwich cultivated primary adult hepatocytes (up to 14 days) with HLCs suggests that prolonged cultivation brings primary adult hepatocytes



towards HLCs (labelled as under Human heps in Fig. 12). This observation was supported by the Euclidean distance (ED) measurement between primary hepatocytes (hHEPs or hepatocytes cultivated in monolayer or sandwich culture environments) and HLCs and hESCs (Fig. 13).

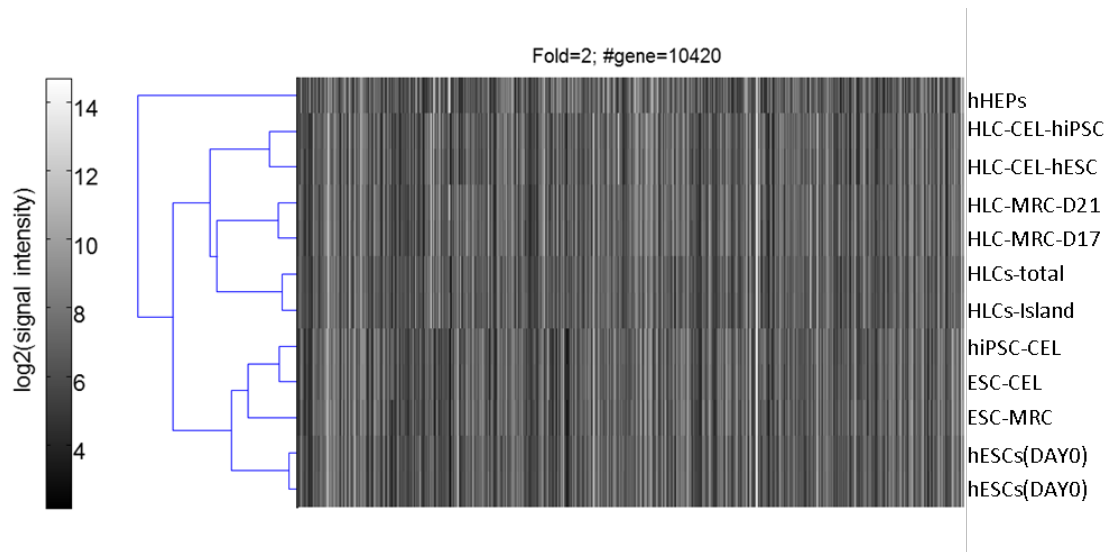


**Figure 13: Euclidean distance measurement among adult hepatocytes, hESCs, hiPSC and HLCs**

The Euclidean distance(ED) measurement between primary hepatocytes (hHEPs or cultivated in monolayer or sandwich culture environments) and HLC from UKK (HLCs-island), MRC (HLC-MRC-D21), and CEL (HLC-CEL-hESC and HLC-CEL-hiPSC). Euclidean distances were computed using all differentially expressed genes with a cut-off of 2-fold and a FDR adjusted  $p$ -value  $\leq 0.05$ . The ED of cultivated adult hepatocytes scaled to the values of hHEPs that were defined as 100%. HLCs-island: hepatocyte like islands extracted from the heterogeneous population (UKK); UKK: Institute of Neurophysiology at University of Cologne, Köln; MRC: Medical Research Council, United Kingdom; CEL: Cellartis, Sweden; hESCs: human embryonic stem cells; hiPSC: human induced pluripotent stem cells; CS: collagen sandwich; CM: collagen monolayer; FH or hHEPs: freshly isolated adult hepatocytes.

D. Pluripotent stem cells hESCs, iPSCs from different labs clustered closely. Likewise, freshly isolated primary hepatocytes from three independent donors were positioned in close proximity (Fig. 12).

Finally, the partial hepatic differentiation of HLCs was also confirmed by hierarchical clustering of 10,420 genes (Fig. 14).



**Figure 14: Hierarchical clustering of HLCs, hESCs, iPSCs and hHEPs**

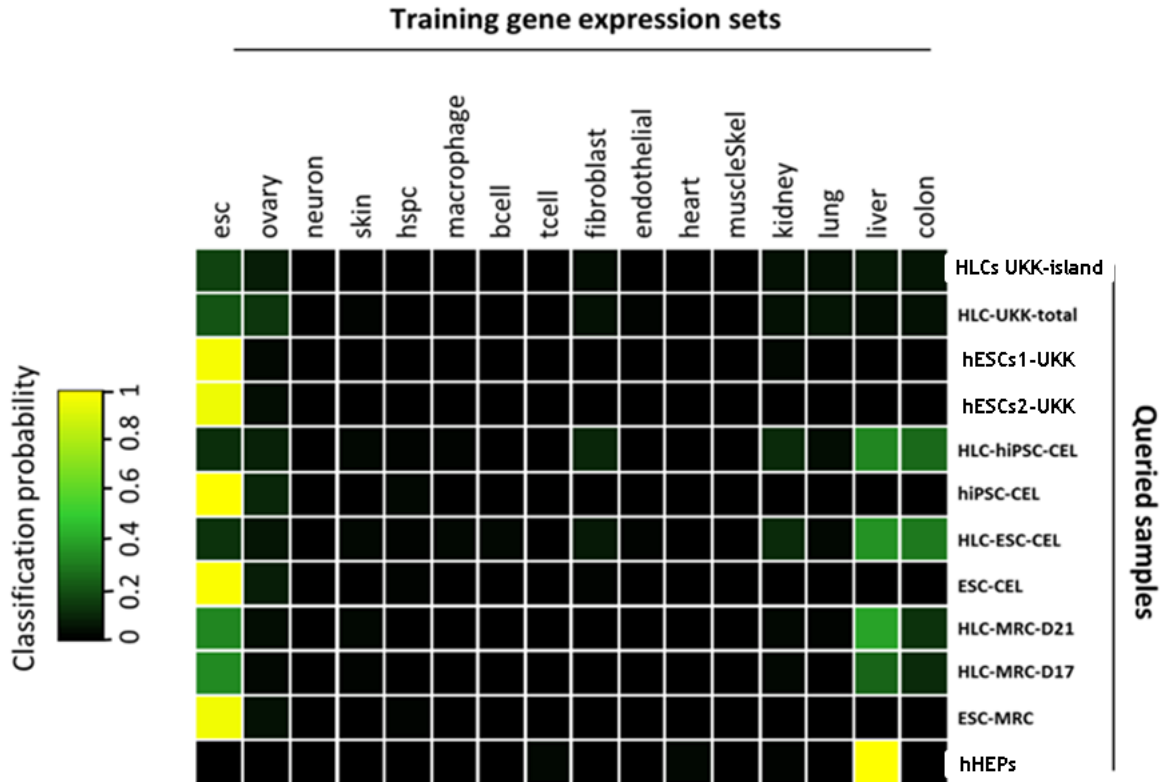
*Hierarchical clustering was used as an illustration of differentially expressed genes among different samples. Hierarchical clustering was performed for a set of 10, 420 genes with a fold change 2;  $p$ -value  $< 0.05$ . Dendrogram suggests all HLCs samples clustered towards freshly isolated adult hepatocytes (hHEPs). Gene probesets signal intensity (in log2 scale) was used as a scale for heatmap and suggest partial differentiation of HLCs. Presented data was representative of three biological array replicates of each sample. Gene array data of freshly isolated adult human hepatocytes (hHEPs) were generated using hepatocytes from three independent donors. HLCs-total: the heterogeneous population of hepatocyte like cells (UKK); HLCs-island: hepatocyte like islands extracted from the heterogeneous population (UKK); UKK: Institute of Neurophysiology at University of Cologne; MRC: Medical Research Council, United Kingdom; CEL: Cellartis, Sweden; hESCs: human embryonic stem cells.*

Collectively, the global gene expression analysis indicates that HLCs differentiated towards freshly isolated adult hepatocytes, but also inherited underdeveloped hepatic transcriptomic features.

### **3.3 Gene regulatory network analysis demonstrates multi-organ differentiation in HLCs**

Further characterization of HLCs from three independent labs such as the Institute of Neurophysiology, University of Cologne (UKK), Medical Research Council (MRC), United Kingdom, and Cellartis (CEL), Sweden was performed using the CellNet bioinformatic algorithm [126]. CellNet analyzes cellular identity using global gene expression profiles and gene regulatory networks of different human tissues and cell types. For this purpose, gene array data of HLCs, hESCs, and iPSCs from the aforementioned labs and freshly isolated adult hepatocytes (hHEPs) were analyzed in triplicates by CellNet.

The CellNet analysis indicated that hHEPs and embryonic stem cells (hESCs) scored a single tissue classification of “liver,” “esc” (Fig. 15), respectively. On the other hand, HLCs classified as mixed tissue types such as “liver,” “esc,” “colon” and “fibroblast” (Fig. 15).



**Figure 15: Cell and tissue type classification probability**

Freshly isolated adult hepatocytes (hHEPs), stem cells (hESCs, hiPSC) and hepatocyte like cells (HLCs) from three independent labs UKK, CEL, and MRC were analyzed by the CellNet algorithm. Global gene expression profiles of the aforementioned samples were analyzed and compared to the training expression profiles defining each of 16 human tissues or cells, as described in Cahan et al. 2014 [126]. The maximal classification scores were observed for hHEPs and hESCs from UKK corresponds to “liver” and “esc,” respectively. HLCs (total, island) from UKK were classified into different tissues such as “esc,” “liver,” “colon,” and “fibroblast.” Presented data was representative of three biological array replicates of each sample. Gene array data of freshly isolated adult hepatocytes (hHEPs) were generated using hepatocytes from three independent donors. HLCs-total: the heterogeneous population of hepatocyte like cells (UKK); HLCs-island: hepatocyte like islands extracted from the heterogeneous population(UKK); UKK: Institute of Neurophysiology at University of Cologne; MRC: Medical Research Council, United Kingdom; CEL: Cellartis, Sweden; hESCs: human embryonic stem cells; hiPSC: human induced pluripotent stem cells.

Moreover, the CellNet algorithm estimates a metric of the gene regulatory network (GRN) associated with the tissue classifications. The metric integrates TFs influence over gene

expression, based on studies such as Chromatin Immunoprecipitation Sequencing (ChIP-Seq) and gene expression profiles after TFs overexpression or knockdown [126].

In this regard, hESCs and hHEPs scored with a maximal GRN status, i.e. 1 for “stem cells” and “liver,” respectively (Fig. 16A). HLCs showed a strong but still incomplete decrease in the “hESCs” GRN status (Fig. 16A) suggesting stem cell characteristics linger in HLCs. Conversely, a strong increase in “liver” GRN status was detected in HLCs (Fig. 16A) than hESCs. Interestingly, the liver GRN status was reaching scores equal or higher than 0.5 in HLCs (Fig. 16A). Moreover, GRN status revealed an increase in “colon” and “fibroblast” status for HLCs (Fig. 16A), in agreement with the tissue classification (Fig. 15) analysis.

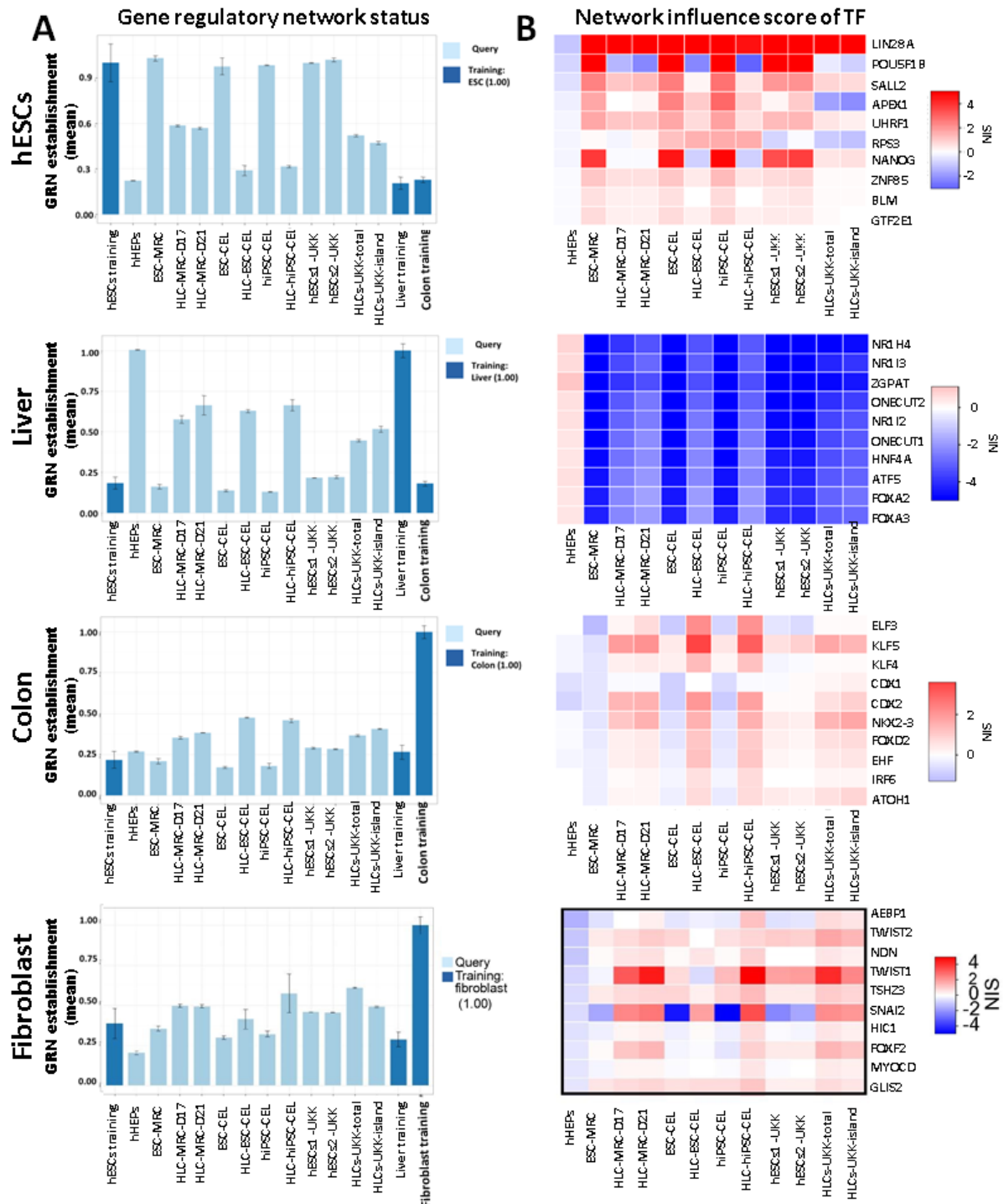
Finally, CellNet also generates a “Network Influence Score” (NIS), whereby the potential influence of each transcription factor on each gene regulatory network is estimated (Fig. 16B) [126]. The hESCs network contains TFs with well-known roles in stem cell biology such as NANOG and POU5F1B. The NIS of these TFs was high in hESCs and strongly reduced in HLCs (Fig. 16B). Nevertheless, TFs such as SALL2 and LIN28A remained with a high NIS in HLCs (Fig. 16B).

The NIS for the “liver” GRN identified several liver-enriched TFs such as NR1H4 (FXR), CAR (NR1H3), PXR (NR1H2) and HNF4A, whose low influence in hESCs was partially increased in HLCs (Fig. 16B).

In the same way, NIS analysis identified several colon-enriched TFs such as KLF5, CDX2, and NKX2-3, whose influence increased in HLCs than hESCs (Fig. 16B). The expression levels of KLF5 and CDX2 was increased in HLCs than in hHEPs (Fig. 17), supporting the estimation of their activity in HLCs. Furthermore, colon-enriched genes such as MEP1A and

CDH17 were also strongly induced in HLCs (Fig. 17). The tissue specificity of KLF5, CDX2, MEP1A, and CDH17 was validated using the human protein atlas portal [150] (Fig. 17). The protein atlas contains RNA and protein data of numerous tissues and cell types.

The NIS of fibroblast-enriched genes contains TFs such as TWIST1 and SNAI2, known to promote epithelial to mesenchymal transition (EMT), thereby representing an unwanted feature (Fig. 16B).

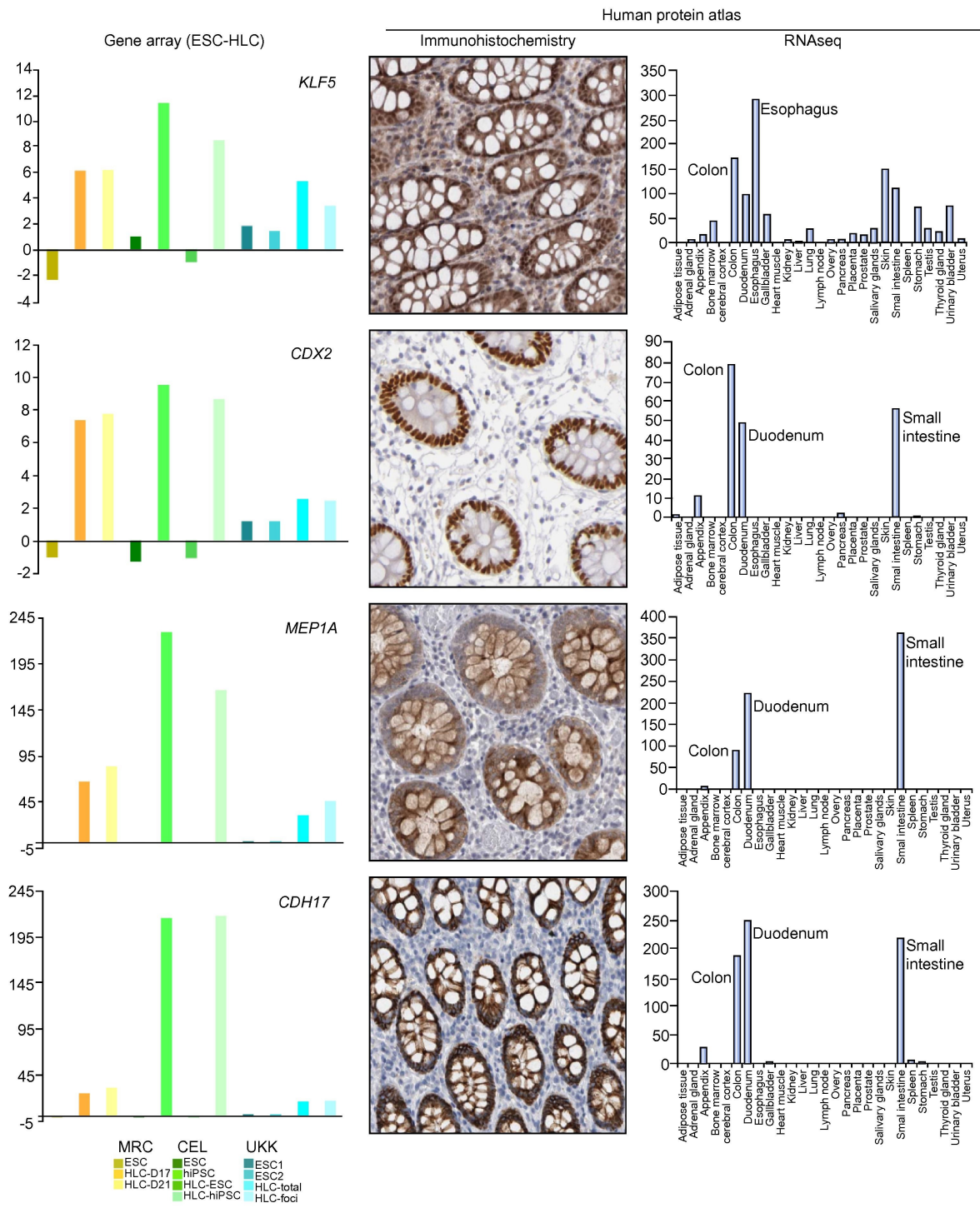


**Figure 16: CellNet enables identification of multi-tissue gene regulatory networks in HLCs from three labs (UKK, MRC, and CEL)**

*A) Gene regulatory network (GRN) status in hHEPs, hESCs, hiPSC, and HLCs Bars represent the strength of tissue-specific gene regulatory network. GRN for hESCs, liver, colon, and fibroblast was established by training in CellNet, representing the maximum*

value of 1.0. HLCs showed a strong, but still an incomplete decrease in the “hESCs” gene regulatory network status suggesting stem cell characteristics lingers in HLCs. A strong increase in “liver” gene regulatory network status was detected in HLCs than in hESCs. Interestingly, liver gene regulatory network status was reaching scores equal or higher than 0.5 in HLCs. Moreover, GRN status revealed an increase in “colon” and “fibroblast” status for HLCs. **B) Identification of transcription factors with the highest influence on the hESCs, liver, colon and fibroblast gene regulatory network** CellNet establishes a metric for the influence of TFs over the genes contained in each tissue GRN, i.e. Network Influence Score (NIS). The heat maps indicate the top ten TFs with the highest influence on each GRN. The hESCs network contains TFs with well-known roles in stem cell biology such as NANOG and POU5F1B. The NIS of these TFs was high in hESCs and strongly reduced in HLCs. Nevertheless, TFs such as SALL2 and LIN28A remained with a high NIS in HLCs. The NIS for the “liver” GRN identified several liver-enriched TFs such as NR1H4 (FXR), CAR (NR1H3), PXR (NR1H2) and HNF4A, whose low influence in hESCs was partially increased in HLCs. The NIS analysis identified various colon-enriched TFs such as KLF5, CDX2, and NKX2-3, whose influence increased in HLCs than hESCs. The NIS of fibroblast-enriched genes contains TFs such as TWIS1 and SNAI2, known to promote epithelial to mesenchymal transition (EMT), thereby representing an unwanted feature. Presented data was representative of three biological array replicates of each sample. Gene array data of freshly isolated adult hepatocytes (hHEPs) were generated using hepatocytes from three independent donors. HLCs-total: the heterogeneous population of hepatocyte like cells (UKK); HLCs-island: hepatocytes like island extracted from the heterogeneous population (UKK); UKK: Institute of Neurophysiology at University of Cologne; MRC: Medical Research Council, United Kingdom; CEL: Cellartis, Sweden; hESCs: human embryonic stem cells; hiPSC: human induced pluripotent stem cells; TFs or TF: transcription factors.





**Figure 17: Identification of colon-associated genes in HLCs from three labs (UKK, MRC, and CEL)**

The left side of the figure panel indicates the expression levels of the transcription factors *KLF5*, *CDX2*, and colon genes *MEP1A* and *CDH17* in hESCs and HLCs, which was extracted from gene array data. Expression levels of these colon-enriched genes increased in HLCs compared to hESCs. The tissue specificity for these genes was validated by querying the

*tissue-based map of the human proteome [150]. Here, representative pictures of immunostainings for the aforementioned genes are shown, indicating the nuclear expression of KLF5 and CDX2 in the colon crypts, and the membranous expression of MEPIA and CDH17. On the right side of the figure panel, the colon-enriched expression of these genes is also shown, which was extracted from RNA sequencing (RNA-seq) data. Presented data was representative of three biological array replicates of each sample. CDX2: CDX2 caudal type homeobox 2; KLF5: Kruppel-like factor 5; MEPIA: Meprin A, Alpha; CDH17: Cadherin 17, LI Cadherin; HLCs-total: the heterogeneous population of hepatocyte like cells(UKK); HLCs-island: hepatocytes like island extracted from the heterogeneous population (UKK); UKK: Institute of Neurophysiology at University of Cologne; MRC: Medical Research Council, United Kingdom; CEL: Cellartis, Sweden; ESCs: human embryonic stem cells; hiPSC: human induced pluripotent stem cells.*

In conclusion, CellNet unveiled details of the differentiation stage of HLCs, namely the acquisition of mixed phenotype with the partial loss of stem cell characteristics and gain of the hepatocyte, colon, and fibroblast lineages.

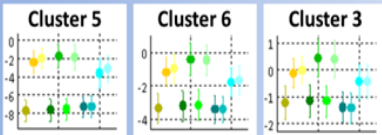
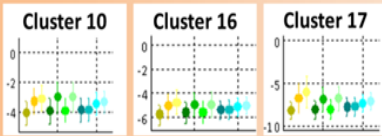
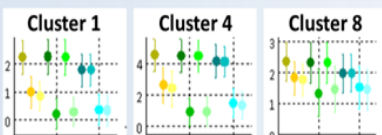


### **3.4 Cluster groups identify TFs between successful and insufficient differentiation processes**

Fuzzy c-means clustering is a pattern recognition algorithm [142] that could help to identify differentially expressed gene clusters in HLCs in comparison with freshly isolated adult hepatocytes (hHEPs). For this purpose, differentially expressed 10,420 genes (from earlier section 3.2) in hESCs and HLCs (total and island) from UKK were subjected to the Fuzzy c-means clustering.

Fuzzy clustering sorted differentially expressed genes into distinct clusters, and this precise clustering will allow to identify different biological process motifs in HLCs. Consequently, each cluster was analyzed for probable gene ontologies with the help of manually curated Gene Ontology database of BioBase Knowledge Library (BKL). Resulting gene ontologies with a p-value less than 0.05 were considered as statistically significant.

To further evaluate transcriptional regulation in HLCs, differentially expressed TFs and overrepresentation of transcription factor binding sites (TFBS) in the correlated gene groups were determined. For this purpose, gene clusters were subjected to transcription factors binding site analysis using Promoter Integration in Microarray Analysis Algorithm (PRIMA) of the EXPression ANalyzer and DisplayER (EXPANDER) version 6.1 [143, 144]. Twenty clusters were formed that were assigned to five cluster groups (Fig. 18) as below.

1. Cluster group II & I represents “Mature liver functions.”
2. Cluster group III & IV represents “Proliferation process”
3. Cluster group V represents “Extracellular matrix (ECM) and Migration”

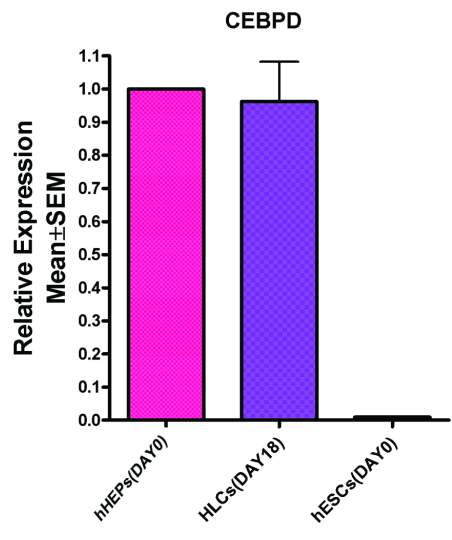
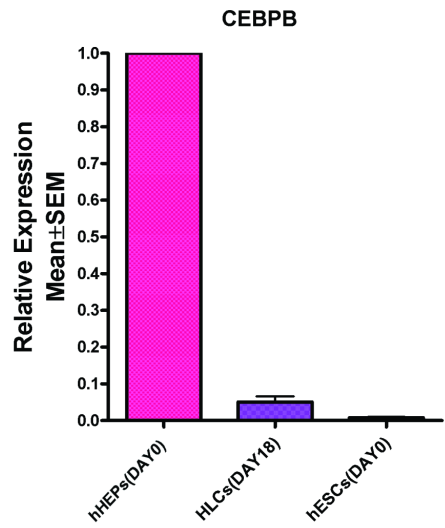
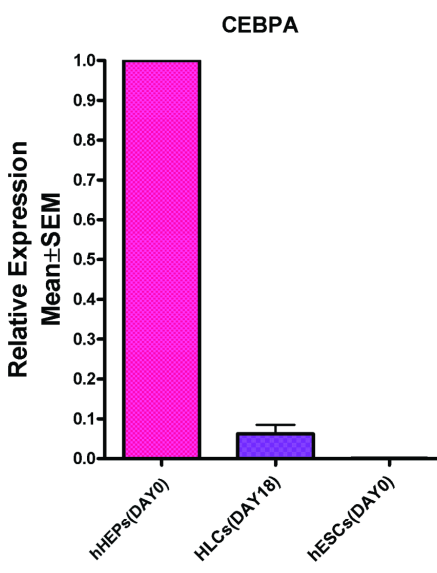
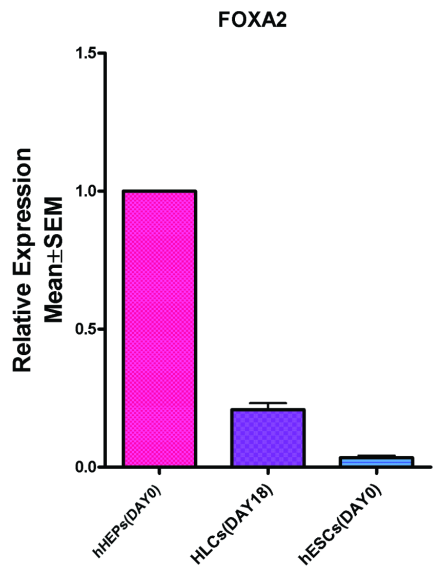
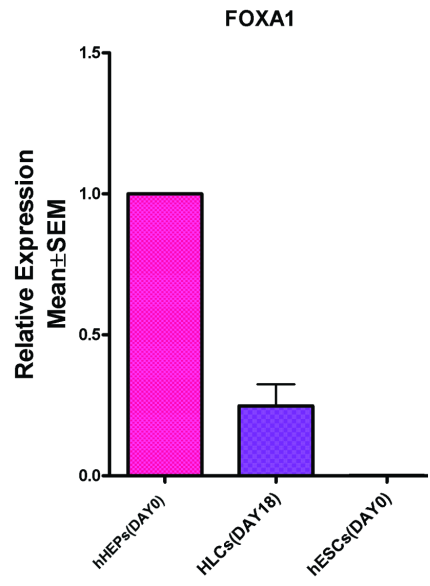
	Cluster groups	Number of genes	Representative genes	Representative TF	TFBS
Mature liver functions		1,057	ABCA1, APOA1, ALDH1A1, CYP1A1, GSTA, C3, C5, FGA, STAT4, IL1R1, A2M	FOXA1, FOXA2, CEBPA, CEBPD, HNF1B, PPARA, PPARG	HNF1
		447	CYP2E1, CYP3A4, SULT1E1, UGT2B15, C2, C6, C9, F5, F7, HPN, HRG	CAR, FXR, PXR, SHP	HNF1
Proliferation		1,562	CCNA1, CCNA2, CDC25A, CDK4, CDK7, PCNA	MYB, E2F5, E2F3, E2F7, TCF3, SOX2, SOX8	E2F, NF- $\kappa$ B, E2F, ZF5
		101	CCNB1, CCNB2, CDK1, ECT2, TOP2A, TTK	SOX11	n.s.
ECM Migration		505	COL1A1, COL4A1, FBN1, LAMB3, ITGA3, ITGA6, EGF, WNT5A	FOXQ1, YBX3, SOX4, TFAP2A, TWIST1	n.s.

## **Figure 18: Cluster groups represent complete and partial hepatic differentiation of HLCs**

*Fuzzy clustering of 10,420 differentially expressed genes in hESCs and HLCs generated 20 distinct clusters that represent well-defined gene expression patterns. These 20 clusters consist of 10,212 genes while 208 genes do not fit into any cluster regime and were classified as outliers. Five cluster groups such as Mature liver functions (Cluster group I and II), Proliferation process (Cluster group III and IV) and Extracellular matrix (ECM), migration (Cluster group V) were formed by selecting clusters containing genes with average fold changes over 5-fold. The cluster groups contain 3,217 genes, allowing for a more robust and precise bioinformatic analysis. The most relevant biological motifs and their representative genes were shown. Furthermore, the potential transcriptional mechanisms such as deregulated transcription factors and overrepresented transcription factor binding sites in each cluster group were also shown. TFBS: Transcription factor binding sites; TF or TFs: transcription factors; hESCs: human embryonic stem cells; HLCs: Hepatocytes like cells.*

### **3.4.1 Cluster group I: Mature liver functions**

Cluster group I consist of 1,057 genes (Appendix Table 9) with low expression in hESCs that increased after HLCs differentiation to levels comparable to those in hHEPs. Cluster group I are enriched in gene ontologies (GO) associated with mature liver functions, including “metabolic process” (GO:0008152), “catalytic activity” (GO:00038) and “immune system process” (GO:0002376). Hence, cluster group I represents successful HLCs differentiation. Cluster group I contains various TFs with known roles in hepatocyte differentiation, including transcriptionally upregulated HNF1A, HNF4A, FOXA1, FOXA2, CEBPA, CEBPB, and CEBPD (Fig. 18). The upregulation of aforementioned TFs was validated using RT-qPCR by comparing expression levels in hESCs, HLCs, and hHEPs (Fig. 19). Expression levels were normalized to those in hHEPs. Expression levels of FOXA1, FOXA2, CEBPA, CEBPB, and CEBPD was upregulated in HLCs than in hESCs (Fig. 19). Validation results of HNF1A and HNF4A were presented in earlier section 3.1 (Fig. 9).



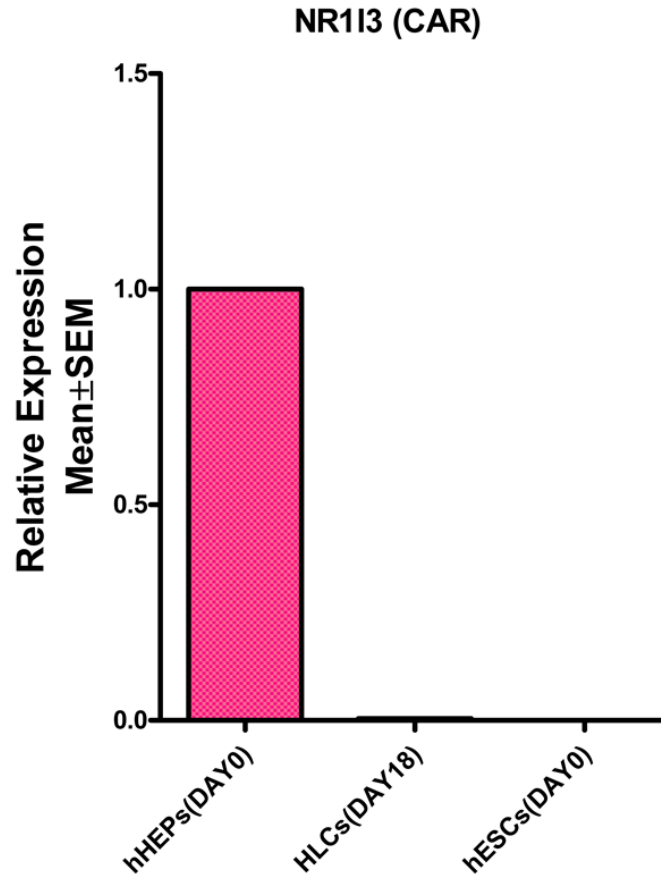
### **Figure 19: RT-qPCR validation of transcription factors belong to the cluster group I**

*Expression levels of transcription factors FOXA1, FOXA2, CEBPA, CEBPB, and CEBPD were analyzed in hESCs, HLCs, and hHEPs. All these genes were upregulated in HLCs than in hESCs. For the relative gene expression calculation, hHEPs was used as calibrator and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as housekeeping gene. The mean and SEM were computed from the expression levels of three biological replicates (hESCs and HLCs). Freshly isolated adult human hepatocytes (hHEPs) from three independent donors were used. FOXA1: Forkhead Box Protein A1; FOXA2: Forkhead Box Protein A2; CEBPA: CCAAT/enhancer-binding protein, alpha; CEBPB: CCAAT/enhancer-binding protein, beta; CEBPD: CCAAT/enhancer-binding protein, delta; hESCs (DAY0): human embryonic stem cells; HLCs (DAY18): hepatocyte like cells; SEM: standard error of the mean.*

Moreover, HNF1A binding sites were significantly enriched in cluster group I (Fig. 18). The increased expression of these TFs is consistent with successful hepatocyte differentiation of HLCs, since their role as inducers of liver-specific is well-established [151].

#### **3.4.2 Cluster group II: Mature liver functions**

Cluster group II consists of 447 genes (Appendix Table 10) with low expression in hESCs that were minimally induced after differentiation into HLCs. The enriched gene ontology terms were similar to the cluster group I such as “metabolic process” (GO:0008152), “catalytic activity” (GO:00038) and “immune system process” (GO:0002376). However, cluster group II genes did not reach the levels of hHEPs. This cluster group contains TFs controlling liver metabolic functions, such as CAR, FXR, SHP, and PXR (Fig. 18). These TFs were minimally induced in HLCs than in hHEPs. Expression of CAR was validated using RT-qPCR by comparing the expression levels in hESCs, HLCs, and hHEPs (Fig. 20). Expression levels were normalized to those in hHEPs. CAR is minimally induced in HLCs than in hHEPs (Fig. 20).



**Figure 20: RT-qPCR validation of transcription factor belongs to the cluster group II**

*Expression levels of transcription factor CAR was analyzed in hESCs, HLCs, and hHEPs. NR1I3 is minimally induced in HLCs than in hHEPs. For the relative gene expression calculation, hHEPs was used as calibrator and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as housekeeping gene. The mean and SEM were computed from the expression levels of three biological replicates (hESCs and HLCs). Freshly isolated adult human hepatocytes (hHEPs) from three independent donors were used. hESCs (DAY0): human embryonic stem cells; HLCs (DAY18): hepatocyte like cells; SEM: standard error of the mean; NR1I3: Nuclear Receptor Subfamily 1, Group I, Member 3.*

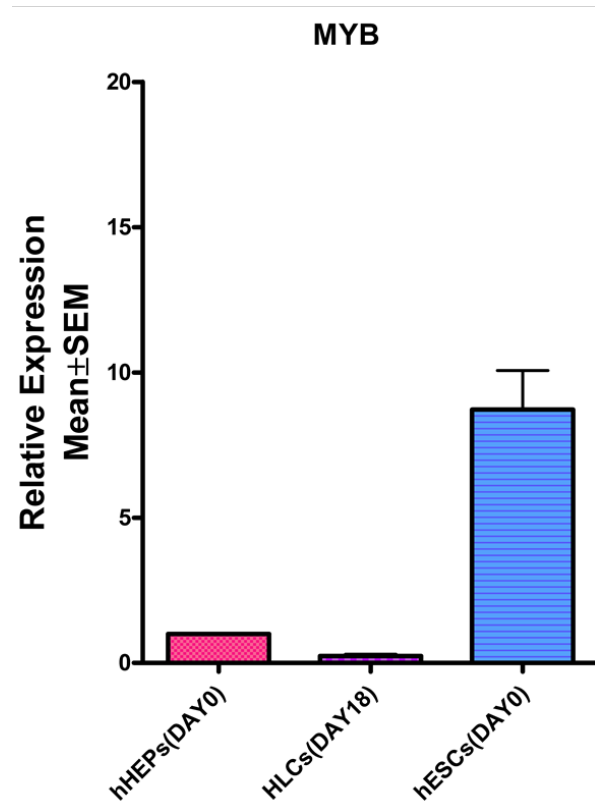
The low expression of these TFs in HLCs is consistent with the NIS results for the “liver” gene regulatory network (refer earlier section 3.3). The binding site for HNF1A was also overrepresented in cluster group II. The complexity of the gene regulatory networks is illustrated by the fact that overrepresented binding sites of HNF1A appear in both, cluster I and II. The difference between cluster group I and II may be due to HNF1A interaction

partners. Indeed, FXR and PXR functionally interact with HNF1A show low expression in HLCs.

### **3.4.3 Cluster group III: Proliferation process**

Cluster group III consists of 1,562 genes (Appendix Table 11) whose expression was high in hESCs and strongly decreased during differentiation into HLCs. Cluster group III enriched in GO terms such as “cell cycle” (GO:0007049), and “regulation of mitosis” (GO:0007088). Genes in these categories include cyclins as well as cyclin-dependent kinases, and the involved transcriptionally upregulated TFs as well as overrepresented TFBS are well established as control factors of proliferation such as E2F5 and MYB (Fig. 18). Downregulation of cell cycle associated genes suggests repression of the self-renewal potential, a hallmark of pluripotent stem cell differentiation. This microarray finding was validated using RT-qPCR by analyzing the expression of MYB in hHEPs, HLCs, and hESCs (Fig. 21). Expression levels were normalized to those in hHEPs. MYB is highly expressed in hESCs and strongly reduced during HLCs differentiation (Fig. 21).





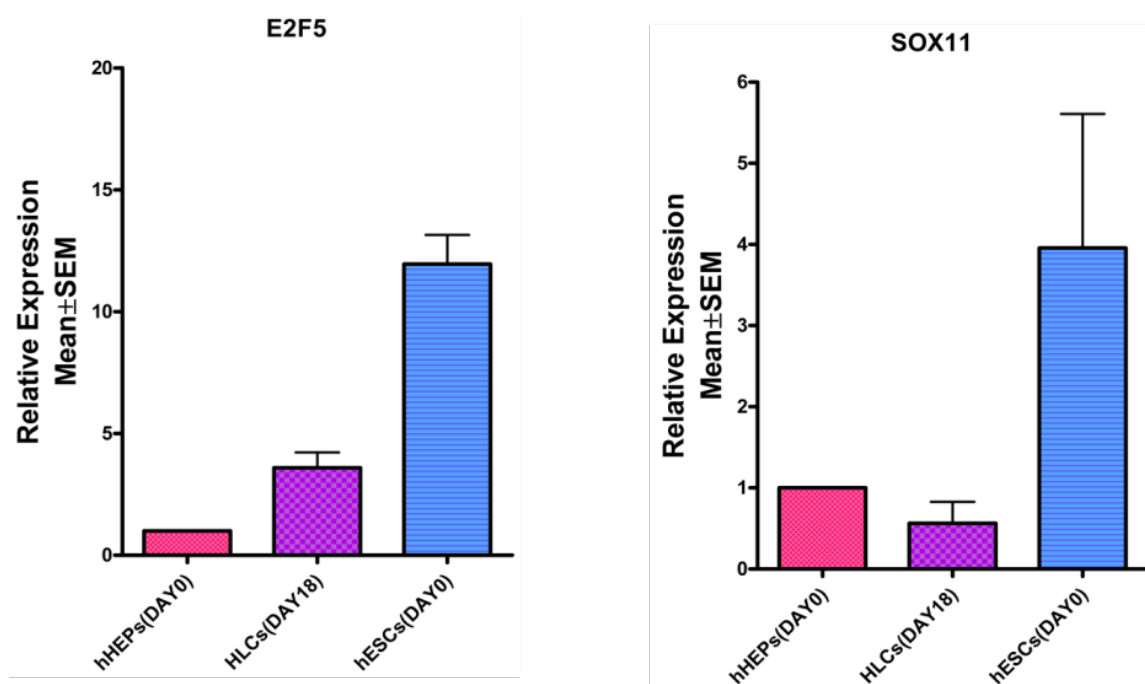
**Figure 21: RT-qPCR validation of transcription factor belongs to the cluster group III**

*The expression level of MYB was analyzed in hESCs, HLCs, and hHEPs. MYB is highly expressed in hESCs and decreased strongly during HLCs differentiation. The relative gene expression was calculated using hHEPs as calibrator and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as housekeeping gene. The mean and SEM were computed from the expression levels of three biological replicates (hESCs and HLCs). Freshly isolated adult human hepatocytes (hHEPs) from three independent donors were used. MYB: V-Myb Avian Myeloblastosis Viral Oncogene Homolog; human embryonic stem cells; HLCs (DAY18): hepatocyte like cells; hESCs: human embryonic stem cells; SEM: standard error of the mean.*

#### **3.4.4 Cluster group IV: Proliferation process**

Cluster group IV contains 101 genes (Appendix Table 12) with high expression in hESCs that did not decrease to the expression levels of hHEPs during HLCs differentiation. Cluster group IV associated to gene ontologies such as “regulation of nuclear division” and “regulation of mitosis”. Cluster group IV is part of the cell cycle process machinery. It includes genes such as CCBN1, CDK1, ECT2, TOP2A, and TTK. Although the expression of these genes was downregulated in HLCs compared to hESCs, their levels remained above those of hHEPs. It

contains only one TFs, i.e. SOX11 (Fig. 18). This finding was validated using RT-qPCR by comparing expression in hESCs, HLCs, and hHEPs (Fig. 22). Expression levels were normalized to those in hHEPs. While cell cycle associated transcription factor MYB expression strongly reduced in HLCs (Fig. 21), the expression levels of E2F5 remained elevated in HLCs (Fig. 22), suggesting that E2F5 may be responsible for the sustained expression of cell-cycle associated genes in cluster group IV.

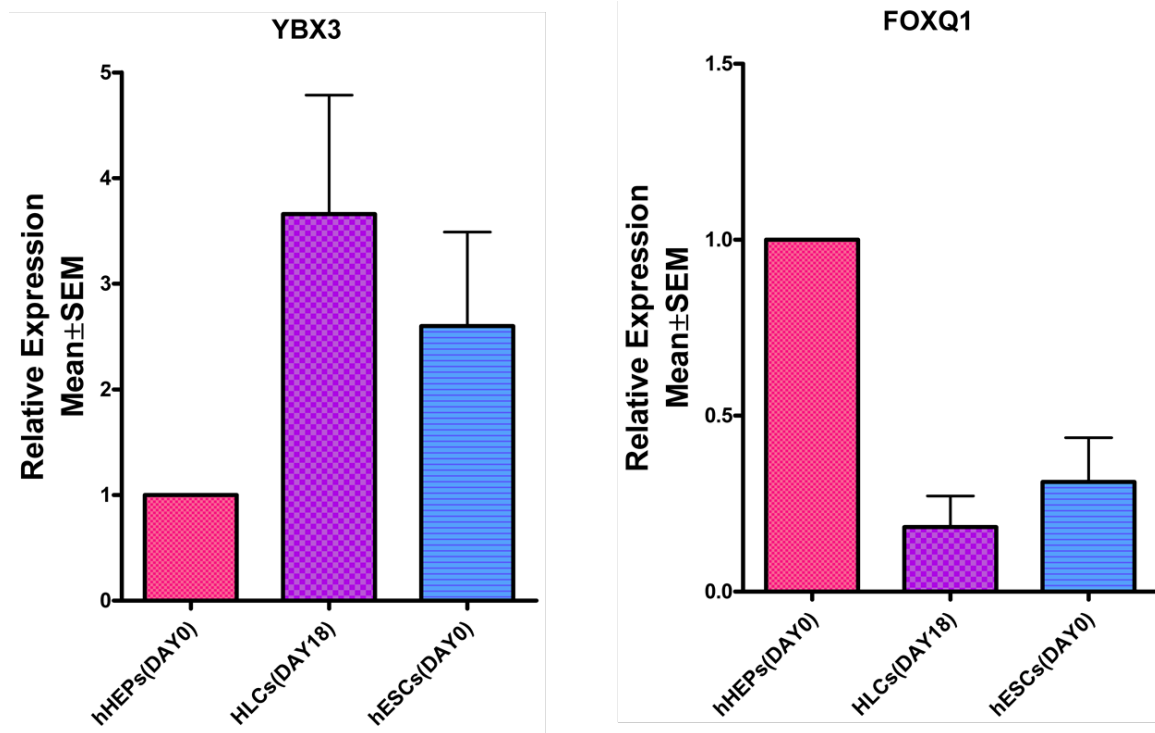


**Figure 22: RT-qPCR validation of transcription factors belong to the cluster group IV**

*Expression levels of SOX11 and E2F5 were analyzed in hESCs, HLCs, and hHEPs. E2F5 was highly expressed in hESCs and remained elevated in HLCs than in hHEPs. On the other hand, SOX11 is highly expressed in hESCs and downregulated during HLCs differentiation. The relative gene expression was calculated using hHEPs as calibrator and glyceraldehyde 3-phosphate dehydrogenase (GAPDH) as housekeeping gene. The mean and SEM were representative of three biological replicates for each cell type (hESCs and HLCs). Freshly isolated adult human hepatocytes (hHEPs) from three independent donors were used. hESCs (DAY0): human embryonic stem cells; HLCs (DAY18): hepatocyte like cells; SEM: standard error of the mean; E2F5: E2F Transcription Factor 5; SOX11: SRY (Sex Determining Region Y)-Box 11.*

### **3.4.5 Cluster group V: Extracellular matrix and Migration**

Cluster group V contains 505 genes (Appendix Table 13). These genes were expressed 4-fold higher in hESCs compared to hHEPs and which further increase during HLCs differentiation. GO terms such as “extracellular region” (GO:0005576) and “cell migration” (GO:0016477) were overrepresented in cluster group V. Genes in these categories include extracellular matrix genes such as collagens (e.g. COL1A1, COL12A1), other matrix genes (FBN1, LAMB3 and LAMA5), integrins (e.g. ITGA3, IGA6, and ITGAV) and cytokines (EGF, WNT5A). The deregulated TFs identified in this cluster group, including FOXQ1, YBX3, TWIST1, and SOX4, may be responsible for the immature nature of differentiated HLCs. For example, FOXQ1 is an oncogene found to be overexpressed in colorectal [152] and breast cancer [153], where it induces proliferation, dedifferentiation, and epithelial to mesenchymal transition. Moreover, FOXQ1 is also overexpressed in hepatocellular carcinoma and induces metastasis [154]. Likewise, YBX3 induces proliferation and dedifferentiation [155, 156]. The upregulation of TFs FOXQ1 and YBX3 was validated using RT-qPCR by analyzing the expression in hESCs, HLCs, and hHEPs (Fig. 23). Expression levels were normalized to those in hHEPs. Expression of YBX3 was increased in HLCs than in hESCs (Fig. 23). Therefore, cluster group V was considered to be the undesirable resultant of HLCs differentiation.



**Figure 23: RT-qPCR validation of transcription factors belong to the cluster group V**

Expression levels of *YBX3* and *FOXQ1* were analyzed in hESCs, HLCs, and hHEPs. The expression level of *YBX3* was increased in HLCs than in hESCs. For the relative gene expression calculation, hHEPs was used as calibrator and glyceraldehyde 3-phosphate dehydrogenase (*GAPDH*) as housekeeping gene. The mean and SEM were representative of three biological replicates (hESCs and HLCs). Freshly isolated adult human hepatocytes (hHEPs) from three independent donors were used. hESCs (DAY0): human embryonic stem cells; HLCs (DAY18): hepatocyte like cells; SEM: standard error of the mean; *YBX3*; Y Box Binding Protein 3; *FOXQ1*: Forkhead Box Q1.

In conclusion, cluster group analysis reveals gene groups representing successful and failed outcomes in HLCs differentiation. Moreover, identification of critical TFs responsible for aberrant gene clusters in HLCs, thereby giving a basis for overexpression or knockdown approaches to improve HLCs differentiation.

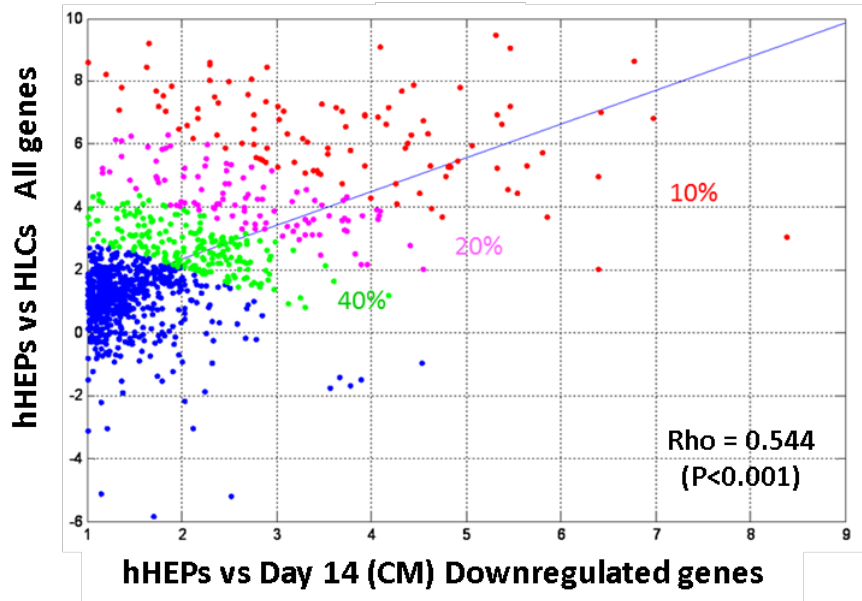
### 3.5 Cultivation-dependent repression of liver metabolism genes

It is well known that primary hepatocytes dedifferentiate in culture, whereby expression of many metabolic genes decreases. Intriguingly, *in vitro* dedifferentiated adult hepatocytes resemble stem cell derived HLCs, which can be seen from the PCA (refer earlier section 3.2, Fig. 12) and can also be objectified by the analysis of Euclidean distances (refer previous section 3.2, Fig. 13). Therefore, one might hypothesise that if the same genes which decrease during cultivation in adult hepatocytes also remain low after differentiation of stem cells into HLCs, this mutual deficiency may be due to failure of culture conditions to deliver critical factors of differentiation present in *vivo*, i.e. real liver tissue environment. To test this proposed theory, the correlation between downregulated genes after 14 days of monolayer culture of adult hepatocytes and the gene expression in HLCs minus expression in freshly isolated adult hepatocytes was studied.

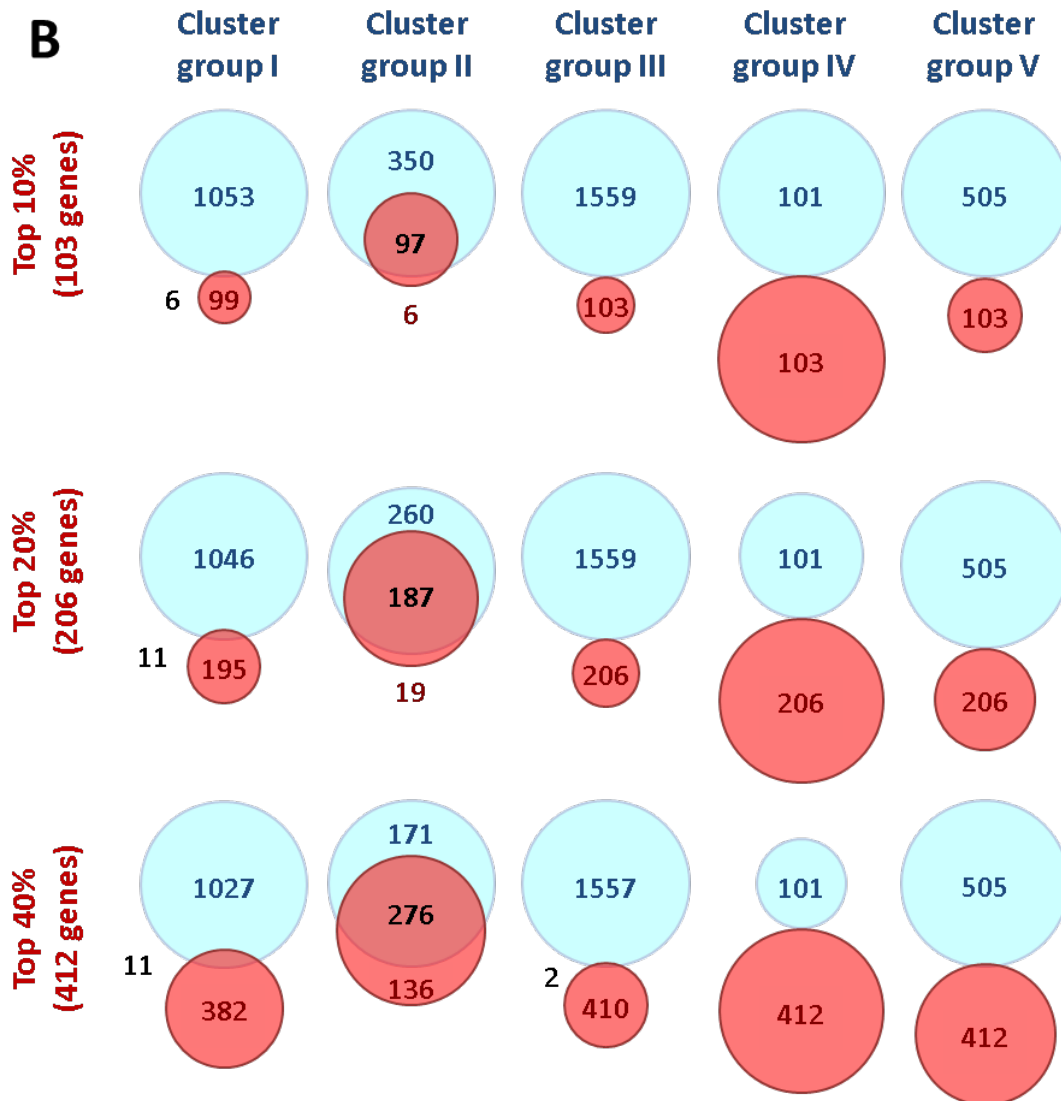
Interestingly, a highly significant correlation (Fig. 24A) was obtained ( $P < 0.001$ ;  $R = 0.54$ ). Further analysis of the 10, 20 and 40% genes with the highest correlation coefficients as indicated by red, purple and green colors (Fig. 24A), respectively was performed. Intriguingly, these genes (Fig. 24B) belong predominantly to the cluster group II (refer earlier section 3.4). This correlation remained high even when including the top 20 or 40 % genes (Fig. 24B). As described above, metabolism related GO terms are enriched in Cluster group II (refer earlier section 3.4). Likewise, metabolism GO terms were enriched in the top 10% to 40 % correlated genes. Notably, all of these genes are expressed at much lower levels in HLCs than in adult hepatocytes. The same genes were also downregulated during a 14 days cultivation period, when the hepatocytes were kept in two-dimensional monolayer cultures.

To see if decreased expression of metabolic genes is explained by a change in culture conditions. For this purpose, three-dimensional cultivation of hepatocytes was used. In three-dimensional (3D) culture system, hepatocytes were cultured between two layers of soft gel collagen. Three-dimensional system abolished the decrease in the expression of some genes including ADH1C, CYP4F2, CYP7A1, and HSD11B1, but the condition remained similar for the majority of genes.

**A**



**B**



**Figure 24: Comparable repression of metabolism associated genes during cultivation of adult hepatocytes and differentiated HLCs**

*A) Correlation between genes repressed in adult hepatocytes after 14 days of cultivation in two-dimensional (collagen monolayer) environments and genes deregulated in HLCs-islands compared to hHEPs. The red dots represent the top 10%, while the purple and green dots correspond to the additional 20 and 40% genes with the highest correlation. B) Venn diagram analysis indicates the high overlap between top 10, 20, and 40% correlated genes with genes in Cluster group II (from earlier section 3.4). The light blue circles represent genes in each Cluster group as described in Fig. 18 (from earlier section 3.4). Red circles represent genes in the top 10 to 40% with the highest correlation, as described in Fig. A. Gene array data of HLCs and cultivated adult hepatocytes (in monolayer and sandwich conditions) at different time points were generated in triplicates. Gene array data of freshly isolated adult hepatocytes (hHEPs) were generated using hepatocytes from three independent donors. HLCs-island: hepatocyte like islands extracted from the heterogeneous population (UKK); UKK: Institute of Neurophysiology at University of Cologne; CM: collagen monolayer.*

Taken together, mechanism inherent to *in vitro* culturing antagonizes the differentiation towards mature hepatocytes, affecting both the stability of adult hepatocytes and the potential for a gain of mature hepatocyte functions in HLCs.



## 4 Discussion

The differentiation of hESCs to hepatocyte like cells (HLCs) opens exciting new possibilities to generate an unlimited supply of human hepatocytes for numerous applications [157, 158]. Generation of HLCs similar to freshly isolated adult hepatocytes in terms of transcriptome and function is a desirable outcome of stem cell engineering [126, 159, 160]. Indeed, recent studies reported that hESCs derived HLCs exhibited liver functions [161, 162]. However, different critical viewpoints on the differentiation status of HLCs have been published [163].

Transcriptome analysis of embryos E20 to E32 had identified crucial TFs and putative molecular network responsible for early human organogenesis [164]. Therefore, transcriptome analysis of HLCs along with freshly isolated adult hepatocytes was performed to understand key TFs and gene networks that drive HLCs differentiation from hESCs. In this regard, HLCs generated from hESCs using a well-established protocol. Validation of differentiated HLCs was performed using RT-qPCR (Fig. 9) and immunostaining techniques (Fig. 10). Among the panel of markers used for HLCs validation, transcription factors such as HNF1A, HNF4A, and FOXA3 are critical for liver development [1, 5]. Moreover, these three transcription factors are also critical for proper functioning of the liver and maintaining the liver architecture. In adult hepatocytes, genome-wide chromatin immunoprecipitation assay suggests that HNF4A is capable of binding 12% of human hepatic genes [47]. However, comparative global gene expression analysis (Fig. 12 and 14) suggested that HLCs obtained partial hepatic transcriptomic features. The presence of DPPIV on the apical side of HLCs along with the cytoplasmic presence of albumin confirmed the epithelial polarity of derived

HLCs (Fig. 10). Hepatic epithelial morphology is important for proper functioning of the adult liver [7].

#### **4.1 Decoding cellular identity of HLCs**

The present genome-wide study demonstrates that the interpretation of HLCs almost fully differentiated hepatocytes might be further away from the truth than previously suggested. In reality, the hybrid phenotype of the liver, colon, stem cells and fibroblast is obtained (Fig. 15 and 16). This seems to be in agreement with established principles of human embryonic development. After gastrulation, the naive endoderm transforms into a primitive gut tube that becomes regionalized into foregut, midgut, and hindgut domains. As the development proceeds, the foregut develops into the liver while hindgut forms the large intestine. In line with this, a recent proteomics approach demonstrated that HLCs resemble embryonic than mature liver [165].

Results of the present GRN analysis show that HLCs represent a progenitor cell type, which has neither been classified as liver nor as colon, with high expression of the colon-associated TFs such as KLF5, CDX2, and NKX2-3 (Fig. 16 and 17). Nonetheless, the *in vivo* counterpart of HLCs is unclear. To further differentiate HLCs to pure populations of mature hepatocytes it will be useful to suppress TFs responsible for colon development in HLCs.

#### **4.2 Gene expression alternations during HLCs differentiation**

The fuzzy clustering analysis demonstrated that gene expression alternations during the HLCs differentiation process fall into five distinct groups (Fig. 18). Cluster group I supports the ‘favorable’ interpretation obtained in several previous studies. It contains hepatic metabolic genes that strongly upregulated during the differentiation process. However, it should be

considered that also cluster group II contains genes representative of normal liver functions, such as metabolism, and synthesis of coagulation and complement factors. In contrast to cluster group I they remain orders of magnitudes lower than those in adult hepatocytes. Interestingly, cluster group II genes overlap significantly with genes whose expression decreases during in *vitro* culturing of adult hepatocytes (Fig. 24A-B). This striking overlap could mean that the critical mechanisms responsible for maintenance of the liver's metabolic genes are generally absent in *vitro*. In this study, TFs responsible for maintenance of cluster group II in adult hepatocytes are identified, which may help to improve stem cell differentiation into matured HLCs (Fig. 18). The binding site of HNF1A, a TFs involved in the expression of genes characteristic of differentiated hepatocytes [151] is overrepresented in cluster group II genes. Moreover, 'liver transcription factors' such as CAR, FXR, and PXR are upregulated in HLCs but only to levels of much lower than those observed in adult hepatocytes.

The second 'favorable' Cluster group III contains proliferation-associated genes that are suppressed during the differentiation process, thereby reaching the low expression levels of adult hepatocytes. In contrast, cluster group IV is also associated contains proliferation-associated genes, but expression levels stay higher compared to adult hepatocytes. These genes are regulated by transcription factor SOX11 (Fig. 18). Cluster group V contains genes whose expression is upregulated in HLCs than in adult hepatocytes. These genes include extracellular matrix proteins and integrins as well as transcription factor TWIST1, which previously have been reported to be upregulated when adult hepatocytes dedifferentiate in culture [166-168].

These ‘unfavourable’ clusters (II, IV and V) contain totally 1,053 genes (28.7%) compared to the much higher number of 2,619 (71.3%) genes of the favourable clusters (I and III). Therefore, the majority of genes induced during differentiation approach similar to those of primary hepatocytes (Appendix Table 9 and 11). However, a major hurdle on the path to stem cell derived HLCs are control mechanisms of cluster groups II, IV, and V (Appendix Table 10, 12 and 13). Since the TFs controlling their expression have been identified in this study, research in future should aim at adjusting their activity to levels of adult hepatocytes.

### **4.3 Usage of HLCs in Biomedical Research**

Apart from a potential application of the HLCs for treatment of degenerative liver diseases, HLCs become very attractive in pharmacological and toxicological research [3]. Several studies have demonstrated the applicability of HLCs to study the development of liver disease and to elucidate liver toxicity mechanisms [169, 170]. Their applications are however, limited as they are classified as immature and hybrid cell types [2, 3, 126, 160, 171, 172]. A major drawback could be the fact that HLCs do not exhibit important phase I-II metabolizing enzyme activities [147, 158, 163]. Even after reaching an optimal matured state, a challenging issue remains to keep a functional and phenotypical stability of HLCs under long-term cell culture conditions [3, 172]. Moreover, transplantation studies conducted in mouse models suggest that HLCs exhibited minimal or even no functional improvement in the host environment [3].

The present dissertation contributes to the identification of key target transcription factors for improving maturation of HLCs (Fig. 18). Therefore, it opens new horizons for improving

maturation and functionality of HLCs for their application in regenerative medicine and drug discovery.

## **5 Conclusion**

The present comprehensive genome-wide study of hepatocyte like cells has potential applications in stem cell engineering of hepatocytes. This study is successful in revealing the strengths and limitations of current protocols aiming at the generation of hepatocyte like cells from human embryonic stem cells. The observation of colon fate specification and definition of five cluster groups, two are in agreement with hepatocyte like cells differentiation and three problematic clusters, and their assignment to key transcription factors give a basis for improvements of stem cell differentiation methods in future.

Overall, the presented findings will be helpful in designing novel differentiation protocols, which may yield mature hepatocyte populations.

## 6 Appendix

Fold > 5
Fold > 2
Fold < -5
Fold < -2

The values in the tables are fold changes.

**Table 9 Cluster group I: Mature liver functions**

Total number of genes: 1,057

*The list of 1057 genes represents a cluster group I that is responsible for mature liver functions as described in chapter 3.4.1, Fig. 18. Column 1(from left to right) represents the gene symbol and column 2 represents the corresponding gene description. Column 3 and 4 contain the fold change values of hHEPs vs. hESCs. Column 5 and 6 contain fold change values of hHEPs vs. HLCs. HLCs-total: the heterogeneous population of hepatocyte like cells; HLCs-island: hepatocyte like islands extracted from the heterogeneous population; hESCs: human embryonic stem cells; hHEPs: freshly isolated adult hepatocytes; vs.: versus.*

Symbol	Description	hESC1	hESC2	HLCs-total	HLCs-islands
EMC3	ER membrane protein complex subunit 3	-2.32	-2.38	-1.6	-1.52
MED8	mediator complex subunit 8	-2.52	-2.63	-1.22	-1.13
C6orf89	chromosome 6 open reading frame 89	-2.54	-2.61	-1.08	-1.17
TM9SF1	transmembrane 9 superfamily member 1	-2.33	-2.36	-1.66	-1.72
SLC12A7	solute carrier family 12 (potassium/chloride transporter), member 7	-2.86	-2.95	-1.29	-1.5
TMED4	transmembrane emp24 protein transport domain containing 4	-2.97	-3.13	-1.12	-1.1
SNX14	sorting nexin 14	-3.02	-2.98	-1.16	-1.14
QPRT	quinolinate phosphoribosyltransferase	-2.46	-2.81	-1.17	-1.15
ZNF654	zinc finger protein 654	-2.65	-2.83	-1.51	-1.61
TMEM9B	TMEM9 domain family, member B	-2.28	-2.38	-1.5	-1.5
GUK1	guanylate kinase 1	-2.38	-2.62	-1.14	-1.15
RIOK3	RIO kinase 3	-1.99	-2.04	-1.42	-1.44

MPPE1	metallophosphoesterase 1	-2.86	-2.88	-1.38	-1.21
RRBP1	ribosome binding protein 1	-2.12	-2.65	-1.36	-1.31
DNALI1	dynein, axonemal, light intermediate chain 1	-3.06	-2.82	-1.23	1.01
DNAJC1	DnaJ (Hsp40) homolog, subfamily C, member 1	-2.33	-2.84	-1.28	-1.24
KLHL8	kelch-like family member 8	-3.29	-3.17	-1.56	-1.66
SPRYD7	SPRY domain containing 7	-2.75	-2.71	-1.14	-1.3
FBXL17	F-box and leucine-rich repeat protein 17	-2.03	-2.26	-1.36	-1.6
TPST1	tyrosylprotein sulfotransferase 1	-2.9	-3.12	-1.31	-1.36
LYSMD3	LysM, putative peptidoglycan-binding, domain containing 3	-2.39	-2.52	-1.14	-1.02
FOXP1	forkhead box P1	-2.64	-2.38	-1.42	-1.38
HLA-C	major histocompatibility complex, class I, C	-2.71	-3	-1.27	-1.27
---		-2.59	-2.49	-1.41	-1.34
GOLGA5	golgin A5	-2.6	-2.67	-1.19	-1.01
FAM134A	family with sequence similarity 134, member A	-2.53	-2.66	-1.75	-1.98
PNPLA8	patatin-like phospholipase domain containing 8	-3.55	-3.81	-1.77	-1.42
ITFG1	integrin alpha FG-GAP repeat containing 1	-3.44	-3.74	-1.38	-1.4
TNFAIP1	tumor necrosis factor, alpha-induced protein 1 (endothelial)	-2.54	-2.62	-1.07	-1.26
TAB3	TGF-beta activated kinase 1/MAP3K7 binding protein 3	-2.48	-2.54	-1.82	-1.73
KIAA1715	KIAA1715	-3.61	-3.49	-1.19	-1.1
DNAJC3	DnaJ (Hsp40) homolog, subfamily C, member 3	-2.45	-2.5	-1.87	-1.7
PSAP	prosaposin	-2.71	-2.99	-1.3	-1.25
TMCC1	transmembrane and coiled-coil domain family 1	-2.7	-2.71	-1.42	-1.65
SDF4	stromal cell derived factor 4	-2.83	-3.09	-1.73	-1.93
REEP5	receptor accessory protein 5	-2.68	-2.65	-1.77	-1.62
CMPK1	cytidine monophosphate (UMP-CMP) kinase 1, cytosolic	-2.51	-2.77	1.01	1.06
RAB2A	RAB2A, member RAS oncogene family	-2.32	-2.55	-1.14	-1.19
TPRG1L	tumor protein p63 regulated 1-like	-2.46	-2.53	-1.68	-1.72
CHIC2	cysteine-rich hydrophobic domain 2	-2.13	-2.23	1	-1.28
CRELD1	cysteine-rich with EGF-like domains 1	-2.52	-2.46	-1.13	1.04
ASXL1	additional sex combs like 1 (Drosophila)	-2.11	-2.22	-1.4	-1.47
BLZF1	basic leucine zipper nuclear factor 1	-2.55	-2.54	-1.73	-1.36
PPCS	phosphopantothenoylcysteine synthetase	-3.41	-3.62	-1.86	-1.89
NDEL1	nudE neurodevelopment protein 1-like 1	-2.01	-2.17	-1.13	-1.22
GATC	glutamyl-tRNA(Gln) amidotransferase, subunit C	-3.47	-3.52	-1.84	-1.81
ZFH3	zinc finger homeobox 3	-1.92	-1.88	-1.17	-1.18
KLF3	Kruppel-like factor 3 (basic)	-2.87	-2.71	-1.78	-1.78
HSD17B14	hydroxysteroid (17-beta) dehydrogenase 14	-2.15	-2.27	-1.36	-1.12
KIF13B	kinesin family member 13B	-3.8	-3.79	-1.61	-1.69
NHLRC3	NHL repeat containing 3	-3.65	-3.64	-1.89	-1.71
SCYL1	SCY1-like 1 (S. cerevisiae)	-3	-3.21	-1.26	-1.22
EGLN1	egl-9 family hypoxia-inducible factor 1	-3.19	-3.55	-1.11	-1.34
PLEKHA1	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 1	-2.49	-2.59	-1.18	-1.23
EVI5	ecotropic viral integration site 5	-3.47	-3.82	-1.13	-1.16
EDEM3	ER degradation enhancer, mannosidase alpha-like 3	-2.82	-3.31	-1.52	-1.61
ZMYM6NB	ZMYM6 neighbor	-1.76	-1.8	-1.45	-1.49



ZNF148	zinc finger protein 148	-2.55	-2.63	-1.81	-1.57
USP38	ubiquitin specific peptidase 38	-2.58	-2.72	-1.81	-2.31
C11orf24	chromosome 11 open reading frame 24	-2.11	-2.08	-1.47	-1.47
DUSP3	dual specificity phosphatase 3	-2.1	-2.27	-1.54	-1.42
ALCAM	activated leukocyte cell adhesion molecule	-3.27	-3.36	-1.53	-1.47
DENND1B	DENN/MADD domain containing 1B	-2.84	-2.83	-1.65	-1.54
EXT1	exostosin glycosyltransferase 1	-1.9	-1.92	-1.07	-1.2
TMEM256	transmembrane protein 256	-2.57	-2.32	-1.39	-1.29
GPR39	G protein-coupled receptor 39	-1.75	-1.88	-1.45	-1.37
DNAJB2	DnaJ (Hsp40) homolog, subfamily B, member 2	-2.4	-2.56	-1.76	-1.81
RAB14	RAB14, member RAS oncogene family	-2.44	-2.64	-1.61	-1.91
DOPEY2	dopey family member 2	-3.45	-3.1	-1.61	-1.85
SCO2	SCO2 cytochrome c oxidase assembly protein	-2.52	-3.01	-1.28	-1.27
TMUB2	transmembrane and ubiquitin-like domain containing 2	-2.12	-2.05	-1.28	-1.16
DCAF10	DDB1 and CUL4 associated factor 10	-2.59	-2.76	1.02	-1.04
REEP3	receptor accessory protein 3	-2.31	-2.22	-1.28	-1.39
BAD	BCL2-associated agonist of cell death	-2.44	-2.5	-1.26	-1.12
RNF103	ring finger protein 103	-2.62	-2.66	-1.19	-1.12
ERMAP	erythroblast membrane-associated protein (Scianna blood group)	-2.38	-2.66	-1.89	-1.83
IFNAR2	interferon (alpha, beta and omega) receptor 2	-3.07	-2.96	-2.17	-1.96
ATP7A	ATPase, Cu <sup>++</sup> transporting, alpha polypeptide	-2.17	-2.02	1.02	-1.04
HGSNAT	heparan-alpha-glucosaminide N-acetyltransferase	-2.08	-2.13	-1.23	-1.3
FOXO3	forkhead box O3	-2.38	-2.05	-1.55	-1.74
APPBP2	amyloid beta precursor protein (cytoplasmic tail) binding protein 2	-3.22	-3.22	1.15	-1.07
CYB5R1	cytochrome b5 reductase 1	-3.11	-3.46	-1.83	-1.66
DST	dystonin	-2.29	-2.53	-1.52	-1.12
CAPN7	calpain 7	-2.34	-2.59	1.04	1.09
PLA2G15	phospholipase A2, group XV	-2.17	-2.3	-1.88	-1.88
LEPROT	leptin receptor overlapping transcript	-3.38	-3.57	-1.2	-1.21
GOLGB1	golgin B1	-3.1	-3.03	-2	-1.33
TBC1D2	TBC1 domain family, member 2	-2.48	-2.79	-2.18	-1.98
SCAPER	S-phase cyclin A-associated protein in the ER	-4.66	-3.86	-1.63	-1.25
SNX4	sorting nexin 4	-2.64	-3.06	-2.01	-1.65
TPRA1	transmembrane protein, adipocyte associated 1	-2.39	-2.39	-1.46	-1.37
DIP2C	DIP2 disco-interacting protein 2 homolog C (Drosophila)	-2.54	-2.54	-1.45	-1.58
TPK1	thiamin pyrophosphokinase 1	-3.14	-3.19	-1.41	-1.45
MOV10	Mov10, Moloney leukemia virus 10, homolog (mouse)	-2.02	-2.05	-1.38	-1.39
CEPT1	choline/ethanolamine phosphotransferase 1	-2.89	-3.14	-1.85	-2.16
SORCS2	sortilin-related VPS10 domain containing receptor 2	-2.31	-2.31	-1.75	-1.93
CASC4	cancer susceptibility candidate 4	-2.96	-3.12	-1.15	-1.18
SGPP1	sphingosine-1-phosphate phosphatase 1	-3.03	-2.95	1.27	1.28
WBP1L	WW domain binding protein 1-like	-2.1	-2.2	-1.11	-1.34
NCOA4	nuclear receptor coactivator 4	-2.02	-2.22	-1.55	-1.67
RAB21	RAB21, member RAS oncogene family	-2.49	-2.29	-1.66	-2.04
GINM1	glycoprotein integral membrane 1	-3.19	-3.17	-1.39	-1.35

LY6E	lymphocyte antigen 6 complex, locus E	-3.39	-3.36	-1.42	-1.41
TMEM219	transmembrane protein 219	-2.41	-2.65	-1.17	-1.04
CDK19	cyclin-dependent kinase 19	-1.8	-1.75	-1.1	-1.31
ABCG1	ATP-binding cassette, sub-family G (WHITE), member 1	-2.2	-2.1	-1.13	1.28
CLCN5	chloride channel, voltage-sensitive 5	-4.12	-4.07	-1.37	-1.52
ERAP1	endoplasmic reticulum aminopeptidase 1	-3.69	-3.6	-1.37	-1.53
DENND5B	DENN/MADD domain containing 5B	-2.85	-2.87	-1.51	-1.64
KLHDC10	kelch domain containing 10	-2.62	-2.53	-1.3	-1.4
ETHE1	ethylmalonic encephalopathy 1	-3.22	-3.09	-1.1	-1.07
RNPEPL1	arginyl aminopeptidase (aminopeptidase B)-like 1	-1.62	-1.7	-1.15	-1.16
TMEM187	transmembrane protein 187	-3.62	-3.66	-1.7	-1.77
SLC35B3	solute carrier family 35 (adenosine 3'-phospho 5'-phosphosulfate transporter), member B3	-2.81	-2.92	1.15	1.1
ITPRIPL2	inositol 1,4,5-trisphosphate receptor interacting protein-like 2	-1.99	-2.29	1.13	-1.27
IL22RA1	interleukin 22 receptor, alpha 1	-2.23	-2.39	-2.12	-1.91
FAM134C	family with sequence similarity 134, member C	-2.81	-2.86	-1.54	-1.81
MAFF	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog F	-2.42	-2.26	-1.05	-1.54
ATF6	activating transcription factor 6	-3.56	-3.35	-1.45	-1.43
FLJ20021	uncharacterized LOC90024	-2.02	-2.23	-1.41	-1.46
VAMP7	vesicle-associated membrane protein 7	-2.02	-2.1	-1.17	-1.18
LINC00674	long intergenic non-protein coding RNA 674	-2.7	-2.71	-1.39	-1.54
ATG4A	autophagy related 4A, cysteine peptidase	-2.6	-2.61	-1.66	-1.52
HEXA	hexosaminidase A (alpha polypeptide)	-2.32	-2.53	-1.12	-1
FAM73A	family with sequence similarity 73, member A	-3.81	-3.78	1.07	1.04
TMEM50B	transmembrane protein 50B	-3.53	-3.81	-1.4	-1.29
PLEKHA7	pleckstrin homology domain containing, family A member 7	-4.12	-3.59	-1.4	-1.85
FBXL3	F-box and leucine-rich repeat protein 3	-2.88	-3.01	-1.29	-1.37
PSME1	proteasome (prosome, macropain) activator subunit 1 (PA28 alpha)	-3.87	-3.69	-1.23	-1.21
ZBTB38	zinc finger and BTB domain containing 38	-1.59	-1.66	-1.6	-1.65
DNAH5	dynein, axonemal, heavy chain 5	-2.08	-2.04	-2.17	-2.22
IER5L	immediate early response 5-like	-2.2	-2.3	1.07	-1.03
PRKAB2	protein kinase, AMP-activated, beta 2 non-catalytic subunit	-2.18	-2.11	1.05	1.03
IFI35	interferon-induced protein 35	-2.98	-2.78	-2.1	-1.84
TAPBP	TAP binding protein (tapasin)	-1.75	-1.75	-1.16	-1.14
SLC1A4	solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	-2.48	-2.63	-1.7	-1.75
CBX4	chromobox homolog 4	-2.17	-2.05	1.12	-1.02
FAM174A	family with sequence similarity 174, member A	-4.28	-4.41	-1.04	-1.13
POLK	polymerase (DNA directed) kappa	-3.37	-3.81	-1.54	-1.24
TRIQQ	triple QxxK/R motif containing	-3.44	-3.55	1.18	1.25
JAK1	Janus kinase 1	-4.12	-4.5	-1.25	-1.36
PCMTD1	protein-L-isoaspartate (D-aspartate) O-methyltransferase domain containing 1	-4.16	-4.4	-1.36	-1.29

SOCS3	suppressor of cytokine signaling 3	-1.74	-1.94	1.22	-1.04
TET2	tet methylcytosine dioxygenase 2	-1.82	-1.84	-1.01	-1.15
GALE	UDP-galactose-4-epimerase	-2.84	-3.07	-1.86	-1.55
MAGI3	membrane associated guanylate kinase, WW and PDZ domain containing 3	-1.51	-1.72	-1.33	-1.41
EBF4	early B-cell factor 4	-2.11	-2.07	-1.5	-1.58
TESK1	testis-specific kinase 1	-1.96	-2	-1.33	-1.28
ACO2	aconitase 2, mitochondrial	-2.1	-2.41	-1.51	-1.38
ABHD5	abhydrolase domain containing 5	-1.89	-2.05	-1.74	-1.57
ZDHHC9	zinc finger, DHHC-type containing 9	-2.51	-2.54	-1.91	-1.95
LOC728431	uncharacterized LOC728431	-2.21	-2.15	-1.77	-1.47
MAN1A2	mannosidase, alpha, class 1A, member 2	-1.51	-1.67	-1.38	-1.35
HEBP1	heme binding protein 1	-5.83	-5.06	-1.27	-1.36
HNF1B	HNF1 homeobox B	-1.94	-2.09	-1.4	-1.25
RER1	retention in endoplasmic reticulum sorting receptor 1	-2.33	-2.37	-1.81	-1.78
LIG4	ligase IV, DNA, ATP-dependent	-3.39	-4.1	-2.3	-2.03
PPP3CC	protein phosphatase 3, catalytic subunit, gamma isozyme	-2.71	-3.05	1.4	1.51
CLDN3	claudin 3	-2.44	-2.33	-1.89	-1.69
FAM177A1	family with sequence similarity 177, member A1	-2.12	-2.01	-1.1	-1.06
TMEM59	transmembrane protein 59	-4.25	-4.18	-1.06	-1.03
KIAA0247	KIAA0247	-3.2	-3.5	-1.32	-1.6
ANKRA2	ankyrin repeat, family A (RFXANK-like), 2	-3.57	-3.83	1.14	1.05
RAB32	RAB32, member RAS oncogene family	-1.77	-2	-1.28	-1.3
LMO7	LIM domain 7	-2.19	-2.03	-1.76	-1.81
OSTF1	osteoclast stimulating factor 1	-2.41	-2.85	-1.43	-1.61
PDXDC1	pyridoxal-dependent decarboxylase domain containing 1	-2.1	-2.12	-1.11	-1.14
USP47	ubiquitin specific peptidase 47	-2.47	-2.69	-1.54	-1.36
SGMS1	sphingomyelin synthase 1	-2.53	-2.56	1.02	-1.19
LMNA	lamin A/C	-1.93	-2.12	-1.42	-1.38
CEP104	centrosomal protein 104kDa	-2.24	-2.22	-1.42	-2.02
ERBB2IP	erbb2 interacting protein	-3.02	-2.79	-1.87	-1.79
C19orf10	chromosome 19 open reading frame 10	-2.79	-3.19	-1.9	-2.04
SLC35A1	solute carrier family 35 (CMP-sialic acid transporter), member A1	-2.98	-3.44	-1.63	-1.74
ANAPC16	anaphase promoting complex subunit 16	-2.6	-2.55	-1.41	-1.54
CACNA1D	calcium channel, voltage-dependent, L type, alpha 1D subunit	-2.03	-1.98	-1.92	-1.72
TMEM106A	transmembrane protein 106A	-2.49	-2.49	-1.66	-1.63
KRBOX4	KRAB box domain containing 4	-3.51	-3.02	-1.62	-1.67
YPEL3	yippee-like 3 (Drosophila)	-2.7	-2.7	-1.41	-1.39
LAMB2	laminin, beta 2 (laminin S)	-4.6	-4.16	-1.7	-1.44
STAM2	signal transducing adaptor molecule (SH3 domain and ITAM motif) 2	-1.85	-2.07	-1.61	-1.56
NUCB2	nucleobindin 2	-4.04	-5.54	-1.35	1.23
NADSYN1	NAD synthetase 1	-2.44	-2.52	-2.05	-2
RND3	Rho family GTPase 3	-1.74	-1.78	1.2	-1
EPS8L2	EPS8-like 2	-2.99	-2.86	-1.29	-1.2

LCOR	ligand dependent nuclear receptor corepressor	-3.69	-3.69	-1.49	-1.45
OS9	osteosarcoma amplified 9, endoplasmic reticulum lectin	-2.22	-2.39	-1.37	-1.52
FNDC3A	fibronectin type III domain containing 3A	-1.98	-2.07	-1.5	-1.54
DCTN3	dynactin 3 (p22)	-1.96	-1.97	1.12	1.16
DUSP28	dual specificity phosphatase 28	-1.67	-1.61	1.01	-1.01
LOC100507557	uncharacterized LOC100507557	-3.25	-3.06	1.05	-1.1
FCHO2	FCH domain only 2	-2.66	-2.86	-2.02	-1.81
CTSL	cathepsin L	-4.22	-4.46	-1.24	-1.18
ELF1	E74-like factor 1 (ets domain transcription factor)	-3.12	-3.67	1.12	1.1
SIDT2	SID1 transmembrane family, member 2	-2.11	-2.04	1.25	1.19
FBXL4	F-box and leucine-rich repeat protein 4	-3.12	-3.39	-1.49	-1.64
STX17	syntaxin 17	-2.4	-2.38	-1.75	-1.74
LETMD1	LETM1 domain containing 1	-3.15	-2.99	-1.16	-1.04
FAM213A	family with sequence similarity 213, member A	-1.59	-1.72	-1.61	-1.61
RNH1	ribonuclease/angiogenin inhibitor 1	-2.49	-2.54	-1.33	-1.43
TMPRSS2	transmembrane protease, serine 2	-2.96	-2.87	-2.05	-1.91
AMICA1	adhesion molecule, interacts with CXADR antigen 1	-2.41	-2.49	-2.09	-2.04
ZNF800	zinc finger protein 800	-2.22	-2.44	-1.55	-1.62
MIEN1	migration and invasion enhancer 1	-2.4	-2.47	-1.45	-1.47
STS	steroid sulfatase (microsomal), isozyme S	-1.62	-1.67	-1.5	-1.59
AOAH	acyloxyacyl hydrolase (neutrophil)	-1.72	-1.67	-1.56	-1.61
IRF2BP2	interferon regulatory factor 2 binding protein 2	-2.94	-2.66	-1.53	-1.78
IL32	interleukin 32	-3.35	-3.84	-1.6	-1.29
MBTPS2	membrane-bound transcription factor peptidase, site 2	-2.69	-2.5	-1.43	-1.5
CD164	CD164 molecule, sialomucin	-2.23	-2.48	1.52	1.45
CADM1	cell adhesion molecule 1	-2.21	-2.49	1.11	-1.32
TRIM38	tripartite motif containing 38	-2.86	-2.78	1.05	1.07
HIPK3	homeodomain interacting protein kinase 3	-1.49	-1.44	-1.09	-1.06
ZNF823	zinc finger protein 823	-1.6	-2.18	1.11	-1.12
DHRS7	dehydrogenase/reductase (SDR family) member 7	-4.03	-3.49	-1.93	-1.75
GABARAP	GABA(A) receptor-associated protein	-2.04	-2.28	1.2	1.14
MLLT6	"myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 6"	-1.67	-1.83	-1.43	-1.36
GLRX	glutaredoxin (thioltransferase)	-2.94	-3.51	-1.07	1.04
BNIP3	BCL2/adenovirus E1B 19kDa interacting protein 3	-4.04	-5.01	-1.22	-1.6
FAM107B	family with sequence similarity 107, member B	-3.26	-3.37	-1.42	-1.36
CLN5	ceroid-lipofuscinosis, neuronal 5	-4.25	-4.7	-2.11	-2.03
SLC46A1	solute carrier family 46 (folate transporter), member 1	-1.99	-1.99	-1.52	-1.52
TAP1	transporter 1, ATP-binding cassette, sub-family B (MDR/TAP)	-2.16	-1.97	-1.48	-1.58
TRADD	TNFRSF1A-associated via death domain	-2.4	-2.43	-1.37	-1.48
MKNK1	MAP kinase interacting serine/threonine kinase 1	-2.37	-2.56	-1.39	-1.51
RHBG	Rh family, B glycoprotein (gene/pseudogene)	-1.93	-1.84	-1.32	-1.16
PERP	PERP, TP53 apoptosis effector	-1.34	-1.73	1.14	1.08
---		-4.71	-5.74	-1.55	-1.89

IAH1	isoamyl acetate-hydrolyzing esterase 1 homolog (S. cerevisiae)	-4.21	-4.05	-1.13	-1.03
CITED2	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 2	-3.07	-3.16	1.61	1.29
CAMTA2	calmodulin binding transcription activator 2	-1.76	-1.71	-1.03	-1.04
AFTPH	aftiphilin	-2.26	-2.34	-1.89	-2
C1orf85	chromosome 1 open reading frame 85	-2.18	-2.27	-2.17	-2.17
NDUFC2	NADH dehydrogenase (ubiquinone) 1, subcomplex unknown, 2, 14.5kDa	-1.65	-1.74	-1.49	-1.52
PEX11B	peroxisomal biogenesis factor 11 beta	-4.79	-4.93	-1.56	-1.7
KIFAP3	kinesin-associated protein 3	-3.74	-3.84	1.45	1.46
NEDD4	neural precursor cell expressed, developmentally down-regulated 4, E3 ubiquitin protein ligase	-4.8	-5.61	-1.14	-1.05
AKTIP	AKT interacting protein	-1.89	-2.01	-1.01	-1.07
SLC35D2	solute carrier family 35 (UDP-GlcNAc/UDP-glucose transporter), member D2	-4.37	-4.79	-1.09	1.03
DDIT3	DNA-damage-inducible transcript 3	-3.08	-3.43	-1.28	1.11
KDELR2	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 2	-2.39	-2.43	1.64	1.67
IFT20	intraflagellar transport 20 homolog (Chlamydomonas)	-3.3	-3.34	1.55	1.64
NEK7	NIMA-related kinase 7	-2.5	-3.08	1.76	1.55
ERBB3	v-erb-b2 avian erythroblastic leukemia viral oncogene homolog 3	-4.04	-3.39	-2.26	-2.09
CHURC1	churchill domain containing 1	-2.31	-2.25	-1.77	-1.67
RNF149	ring finger protein 149	-6.51	-6.84	-1.64	-1.84
NUCB1	nucleobindin 1	-2.43	-2.42	-1.64	-1.53
MERTK	c-mer proto-oncogene tyrosine kinase	-2.32	-3.14	1.3	1.62
RAPGEF5	Rap guanine nucleotide exchange factor (GEF) 5	-2.55	-2.75	-2.57	-1.93
TERF2IP	telomeric repeat binding factor 2, interacting protein	-2.99	-2.78	1.06	-1.09
NMT2	N-myristoyltransferase 2	-3.45	-3.16	-1.97	-2.06
PLOD1	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 1	-3.06	-3.04	1.88	1.79
HECA	headcase homolog (Drosophila)	-5.79	-5.24	-1.47	-1.62
RASSF4	Ras association (RalGDS/AF-6) domain family member 4	-2.26	-2.16	1.22	1.27
REV3L	REV3-like, polymerase (DNA directed), zeta, catalytic subunit	-3.95	-4.39	-2.25	-2.25
ZFYVE16	zinc finger, FYVE domain containing 16	-2.87	-3.18	-1.55	-1.26
ZBTB42	zinc finger and BTB domain containing 42	-1.96	-2.08	-1.5	-1.57
BRI3	brain protein I3	-3.07	-3.38	-1.85	-1.93
DERA	deoxyribose-phosphate aldolase (putative)	-4.1	-4.16	-1.62	-1.45
FAM91A1	family with sequence similarity 91, member A1	-2.1	-2.11	-1.49	-1.5
BTG1	B-cell translocation gene 1, anti-proliferative	-4.68	-4.24	-2.03	-1.98
UFL1	UFM1-specific ligase 1	-2.24	-2.35	1.14	1.34
TNRC18	trinucleotide repeat containing 18	-2.08	-2.53	1.02	-1.17
CD47	CD47 molecule	-3.16	-2.91	-1.11	-1.05
HINT3	histidine triad nucleotide binding protein 3	-3.36	-3.62	-2.4	-2.64
SPATA18	spermatogenesis associated 18	-2.08	-2	1.26	1.08
C6orf120	chromosome 6 open reading frame 120	-2.54	-2.58	-2.07	-2.16
MTM1	myotubularin 1	-2.28	-2.32	-2.2	-2.23

P4HB	prolyl 4-hydroxylase, beta polypeptide	-3.56	-4.13	-1.08	-1.13
SPAG1	sperm associated antigen 1	-2.42	-2.88	-2.14	-1.87
FBXL15	F-box and leucine-rich repeat protein 15	-2.31	-2.5	-1.52	-1.15
CLN3	ceroid-lipofuscinosis, neuronal 3	-1.67	-1.83	-1.26	-1.21
SERPINB1	serpin peptidase inhibitor, clade B (ovalbumin), member 1	-2.25	-2.74	-1.03	-1.09
SERTAD2	SERTA domain containing 2	-4.28	-4.84	-1.47	-1.71
TTC14	tetratricopeptide repeat domain 14	-2.49	-2.71	-2.26	-1.8
NINJ1	ninjurin 1	-2.2	-1.99	-1.62	-1.46
RPS27L	ribosomal protein S27-like	-1.99	-2.06	-1.89	-1.92
ZBTB41	zinc finger and BTB domain containing 41	-3.08	-3.03	-1.48	-1.01
CRTC3	CREB regulated transcription coactivator 3	-2.68	-2.54	1.16	1.11
DGAT1	diacylglycerol O-acyltransferase 1	-6.09	-6.03	-1.26	1.12
RAB7L1	RAB7, member RAS oncogene family-like 1	-5.26	-5.17	-2.01	-1.73
ADCY6	adenylate cyclase 6	-1.61	-1.58	1.31	1.27
NPHP3	nephronophthisis 3 (adolescent)	-2.79	-3.04	-1.58	-1.53
RFK	riboflavin kinase	-1.95	-2.16	-1.16	-1.23
NRIP1	nuclear receptor interacting protein 1	-2.43	-3.1	-2.2	-2.41
ACOT13	acyl-CoA thioesterase 13	-5.15	-4.73	-2.37	-1.77
TMEM139	transmembrane protein 139	-2.1	-2.04	-2.07	-2
NBR2	neighbor of BRCA1 gene 2 (non-protein coding)	-2.14	-2.14	-2.05	-1.94
DENND4C	DENN/MADD domain containing 4C	-2.92	-2.88	-1.26	-1.49
RAB4A	RAB4A, member RAS oncogene family	-2.03	-2.12	-1.94	-1.99
AP1M1	adaptor-related protein complex 1, mu 1 subunit	-2.16	-2.18	-1.46	-1.52
DAP	death-associated protein	-1.69	-1.69	1.34	1.39
CAMK2D	calcium/calmodulin-dependent protein kinase II delta	-2.67	-3.07	1.57	1.54
TMEM106B	transmembrane protein 106B	-2.36	-2.27	-1.15	1.03
STIM1	stromal interaction molecule 1	-2.31	-2.25	-1.84	-1.67
CAMSAP3	calmodulin regulated spectrin-associated protein family, member 3	-2.38	-2.29	-2.17	-2.09
CD151	CD151 molecule (Raph blood group)	-1.72	-1.87	1.03	-1
CAST	calpastatin	-4.38	-4.54	1.52	1.51
FAM162A	family with sequence similarity 162, member A	-2.83	-2.54	-1.21	1.09
SCARB2	scavenger receptor class B, member 2	-6.65	-6.6	-1.79	-1.86
IPP	intracisternal A particle-promoted polypeptide	-2.04	-1.98	-1.03	-1.2
LSMD1	LSM domain containing 1	-1.95	-2.27	-1.18	-1.12
NUMB	numb homolog (Drosophila)	-2.06	-2.18	-1.51	-1.66
TIPARP	TCDD-inducible poly(ADP-ribose) polymerase	-3.35	-4.3	-1.37	-1.46
TLCD2	TLC domain containing 2	-3.9	-4.14	-1.47	-1.43
CPPED1	calcineurin-like phosphoesterase domain containing 1	-3.33	-3.55	-2.84	-3.01
RAB22A	RAB22A, member RAS oncogene family	-2.03	-2.07	-1.32	-1.41
TCF25	transcription factor 25 (basic helix-loop-helix)	-2.3	-2.49	-1.45	-1.43
TMBIM1	transmembrane BAX inhibitor motif containing 1	-5.51	-5.08	-1.09	1.04
OSBPL2	oxysterol binding protein-like 2	-2.13	-2.24	-1.1	-1.16
IGF2R	insulin-like growth factor 2 receptor	-2.19	-2.37	-2.43	-2.68
LMAN2	lectin, mannose-binding 2	-2.45	-2.56	-2.16	-2.06
MGAT4B	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme B	-3.75	-3.76	-1.96	-2.24



LOC728730	uncharacterized LOC728730	-3.97	-3.7	1.29	1.77
PIGH	phosphatidylinositol glycan anchor biosynthesis, class H	-3.35	-3.78	1.74	1.68
SIAE	sialic acid acetyltransferase	-3.27	-3.54	-1.2	-1.14
CASP8	caspase 8, apoptosis-related cysteine peptidase	-1.67	-1.68	-1.52	-1.57
TNS3	tensin 3	-5.24	-4.38	-1.77	-2.8
DISP1	dispatched homolog 1 (Drosophila)	-2.42	-2.25	-1.41	-1.65
HMOX1	heme oxygenase (decycling) 1	-2.17	-1.9	-1.56	-1.87
DLC1	deleted in liver cancer 1	-1.87	-2.4	-1.13	-1.36
FEM1C	fem-1 homolog c (C. elegans)	-2.42	-2.13	-2.25	-2.55
SLC35F5	solute carrier family 35, member F5	-3.38	-3.9	1.37	1.2
ZNF846	zinc finger protein 846	-1.7	-1.69	1.32	1.34
HIGD1A	HIG1 hypoxia inducible domain family, member 1A	-1.48	-1.61	-2.06	-2.22
GOLGA2	golgin A2	-2.08	-2.31	1.09	-1.13
ERGIC1	endoplasmic reticulum-golgi intermediate compartment (ERGIC) 1	-2.73	-2.67	-1.74	-1.83
HIST1H2BI	histone cluster 1, H2bi	-1.65	-1.91	-2.09	-1.92
TSPAN31	tetraspanin 31	-3.14	-2.76	-1.35	-1.5
CTSA	cathepsin A	-3.64	-3.78	-2.48	-2.33
ZC3H12C	zinc finger CCCH-type containing 12C	-3.46	-3.25	1.04	-1.03
KBTBD3	kelch repeat and BTB (POZ) domain containing 3	-2.55	-2.48	-1.68	-1.41
MYO5B	myosin VB	-4.36	-4.24	-1.02	-1.03
MARCH2	membrane-associated ring finger (C3HC4) 2, E3 ubiquitin protein ligase	-2.45	-2.29	-1.68	-1.69
TNFRSF10D	tumor necrosis factor receptor superfamily, member 10d, decoy with truncated death domain	-1.53	-1.44	-1.36	-1.56
SPOP	speckle-type POZ protein	-2.26	-2.48	-1.66	-1.83
LTB	lymphotoxin beta (TNF superfamily, member 3)	-2.39	-2.51	-1.83	-1.5
FPGT	fucose-1-phosphate guanylyltransferase	-2.5	-2.55	-1.91	-1.92
ENPP4	ectonucleotide pyrophosphatase/phosphodiesterase 4 (putative)	-3.05	-3.13	-2.9	-2.24
EMP2	epithelial membrane protein 2	-3.32	-3.13	1.66	1.51
LMBRD2	LMBR1 domain containing 2	-2.66	-2.62	-2.24	-2.27
YPEL5	yippee-like 5 (Drosophila)	-1.81	-2.29	1.58	1.5
PECAM1	platelet/endothelial cell adhesion molecule 1	-1.67	-1.67	-1.16	1.07
ZNF395	zinc finger protein 395	-3.93	-4.04	2.07	1.97
PPP1R11	protein phosphatase 1, regulatory (inhibitor) subunit 11	-1.47	-1.6	-1.42	-1.6
NCOA1	nuclear receptor coactivator 1	-1.91	-2.11	1.16	1.22
PLEKHM3	pleckstrin homology domain containing, family M, member 3	-2.09	-2.19	-1.39	-2.01
OPTN	optineurin	-3.42	-4.18	1.7	1.64
SMYD2	SET and MYND domain containing 2	-1.37	-1.55	-1.23	-1.28
PITRM1	pitrilysin metalloproteinase 1	-1.88	-2.04	-1.51	-1.44
ALG9	ALG9, alpha-1,2-mannosyltransferase	-2.14	-2.14	-1.35	-1.48
HIPK2	homeodomain interacting protein kinase 2	-1.94	-1.92	-1.53	-1.81
MPZL2	myelin protein zero-like 2	-3.13	-3	-1.19	-1.14
BTBD6	BTB (POZ) domain containing 6	-1.52	-1.52	-1.5	-1.5
PMM1	phosphomannomutase 1	-4.15	-4.28	-1.29	-1.09

CD59	CD59 molecule, complement regulatory protein	-3.72	-3.76	1.19	1.18
ZNF224	zinc finger protein 224	-3.2	-3.14	-2.16	-1.83
ECE1	endothelin converting enzyme 1	-2.21	-2.23	-1.47	-1.54
RPS6KA3	ribosomal protein S6 kinase, 90kDa, polypeptide 3	-5.19	-5.54	-1.27	-1.02
MICALL2	MICAL-like 2	-1.88	-1.83	-1.39	-1.18
FGFR3	fibroblast growth factor receptor 3	-1.9	-2.24	-1.34	-1.38
SGMS2	sphingomyelin synthase 2	-3.09	-2.91	-1.12	-1.17
RNASE1	ribonuclease, RNase A family, 1 (pancreatic)	-1.58	-1.54	-1.1	1.07
SNX1	sorting nexin 1	-2.01	-2.19	-1.58	-1.57
CHID1	chitinase domain containing 1	-3.52	-3.85	-1.85	-1.82
BPNT1	3'(2'), 5'-bisphosphate nucleotidase 1	-2.93	-2.59	-1.87	-1.92
LOC286437	uncharacterized LOC286437	-2.96	-3.05	-2.73	-2.76
IRF6	interferon regulatory factor 6	-1.64	-1.64	-1.13	-1.16
PIEZO2	piezo-type mechanosensitive ion channel component 2	-1.43	-1.71	-1.59	-1.48
DOCK8	dedicator of cytokinesis 8	-2.22	-2.31	-1.25	-1.58
SHANK2	SH3 and multiple ankyrin repeat domains 2	-2.7	-2.29	-1.19	-1.41
FBXO17	F-box protein 17	-4.46	-4.46	-1.51	-1.28
NUDT19	nudix (nucleoside diphosphate linked moiety X)-type motif 19	-3.79	-3.93	-1.77	-2.3
ISG20	interferon stimulated exonuclease gene 20kDa	-2.62	-2.63	-1.03	1.29
KRT222	keratin 222	-2.06	-2.02	-1.87	-1.65
MBNL1	muscleblind-like splicing regulator 1	-5.42	-4.85	-2.36	-2.44
H1FO	H1 histone family, member 0	-4.64	-4.23	-2.07	-2.13
SPSB1	splA/ryanodine receptor domain and SOCS box containing 1	-1.95	-1.89	1.45	1.26
BCDIN3D	BCDIN3 domain containing	-1.54	-1.57	-1.47	-1.45
LAMTOR5	late endosomal/lysosomal adaptor, MAPK and MTOR activator 5	-2.18	-2.14	-1.43	-1.33
LRCH1	leucine-rich repeats and calponin homology (CH) domain containing 1	-2.45	-2.38	-1.51	-1.42
PIGB	phosphatidylinositol glycan anchor biosynthesis, class B	-3.11	-2.75	-1.56	-1.41
MAF	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog	-4.83	-4.75	-1.37	-1.39
APOBEC3F	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3F	-1.46	-1.55	-1.55	-1.49
MAB21L3	mab-21-like 3 (C. elegans)	-1.67	-1.7	-1.62	-1.57
C12orf23	chromosome 12 open reading frame 23	-4.27	-4.66	2.38	1.96
PTER	phosphotriesterase related	-3.87	-3.78	-3.28	-2.93
MAP3K2	mitogen-activated protein kinase kinase kinase 2	-3.31	-3.67	-2.3	-2.07
ATP9A	ATPase, class II, type 9A	-4.76	-3.74	-1.42	-1.31
TCAIM	T cell activation inhibitor, mitochondrial	-5.2	-5.32	-2.19	-1.83
SOAT1	sterol O-acyltransferase 1	-2.89	-3.09	-1.89	-2.14
PLEKHF2	pleckstrin homology domain containing, family F (with FYVE domain) member 2	-2.36	-2.2	-1.2	-1.67
ADCY9	adenylate cyclase 9	-3.18	-3.22	-1.55	-1.72
TRIM56	tripartite motif containing 56	-2.57	-2.6	-1.39	-1.77
PCYOX1	prenylcysteine oxidase 1	-5.93	-5.98	-1.89	-2.26



CGN	cingulin	-4.3	-4.13	-3.28	-3.06
HBP1	HMG-box transcription factor 1	-3.48	-3.43	-1.38	-1.42
CLIP1	CAP-GLY domain containing linker protein 1	-1.71	-2.17	1.03	1.09
SLC22A5	solute carrier family 22 (organic cation/carnitine transporter), member 5	-3.71	-3.64	1.73	1.51
CHMP2A	charged multivesicular body protein 2A	-4.32	-4.31	-1.62	-1.46
GOLGA4	golgin A4	-2.77	-3.22	-1.8	-1.1
MICAL2	microtubule associated monooxygenase, calponin and LIM domain containing 2	-1.78	-1.77	1.83	1.61
KBTBD11	kelch repeat and BTB (POZ) domain containing 11	-4	-3.65	-3.45	-3.02
IRF1	interferon regulatory factor 1	-2.57	-2.52	-1.74	-1.99
TRPV6	transient receptor potential cation channel, subfamily V, member 6	-2.2	-2.29	-1.9	-1.91
TMBIM6	transmembrane BAX inhibitor motif containing 6	-1.8	-1.92	-1.65	-1.58
RRAD	Ras-related associated with diabetes	-2.09	-2.04	-1.49	-1.51
CALCOCO2	calcium binding and coiled-coil domain 2	-5.47	-5.66	-1.28	-1.33
LIMCH1	LIM and calponin homology domains 1	-1.9	-2.04	1.18	1.28
CARD6	caspase recruitment domain family, member 6	-1.88	-1.68	-1.41	-1.32
NUDT16	nudix (nucleoside diphosphate linked moiety X)-type motif 16	-2.18	-2.11	-1.62	-1.58
KLF10	Kruppel-like factor 10	-2.48	-2.26	1.61	1.06
FZD4	frizzled family receptor 4	-1.34	-1.41	1.1	1.08
C8orf47	chromosome 8 open reading frame 47	-2.61	-2.48	-1.94	-2.61
PPA2	pyrophosphatase (inorganic) 2	-2	-2.09	-1.75	-1.76
SSR4	signal sequence receptor, delta	-1.77	-2.13	1.29	1.26
PHC2	polyhomeotic homolog 2 (Drosophila)	-2.03	-1.97	1.51	1.4
VPS54	vacuolar protein sorting 54 homolog (S. cerevisiae)	-2.24	-2.28	-1.01	-1.05
MVP	major vault protein	-4.23	-4	-1.07	-1.15
LINC00894	long intergenic non-protein coding RNA 894	-2.51	-2.36	-2.16	-1.6
FAM13C	family with sequence similarity 13, member C	-1.92	-1.8	-2.53	-2.39
HBEGF	heparin-binding EGF-like growth factor	-1.36	-1.4	-1.16	-1.36
MANSC1	MANSC domain containing 1	-4	-3.57	-2.7	-3.63
MRPS36	mitochondrial ribosomal protein S36	-1.88	-2.01	-1.92	-1.64
PLOD2	procollagen-lysine, 2-oxoglutarate 5-dioxygenase 2	-7.09	-8.15	-1.51	-1.93
RNF43	ring finger protein 43	-3.13	-2.98	-2.04	-2.12
PJA2	praja ring finger 2, E3 ubiquitin protein ligase	-2.53	-2.42	1.43	1.48
PDIA5	protein disulfide isomerase family A, member 5	-6.56	-6.93	-1.53	-1.25
C4orf3	chromosome 4 open reading frame 3	-3.89	-3.69	-1.96	-2.4
MXD1	MAX dimerization protein 1	-3.37	-3.25	-2.13	-1.97
NCF2	neutrophil cytosolic factor 2	-1.68	-1.66	-1.59	-1.58
RNF19A	ring finger protein 19A, RBR E3 ubiquitin protein ligase	-1.76	-2.22	-1.66	-1.66
IFNGR1	interferon gamma receptor 1	-2.44	-2.9	1.02	1.21
KIF16B	kinesin family member 16B	-2.41	-2.41	-1.91	-1.86
MBD6	methyl-CpG binding domain protein 6	-2.35	-2.39	-2.03	-2.2
KLHL28	kelch-like family member 28	-1.83	-2.07	-1.28	-1.18
CDKN1A	cyclin-dependent kinase inhibitor 1A (p21, Cip1)	-3.49	-2.88	1.78	1.53
IDS	iduronate 2-sulfatase	-1.76	-1.69	-1.06	-1.34
LRMP	lymphoid-restricted membrane protein	-1.22	-1.2	-1.15	-1.02

SERINC1	serine incorporator 1	-4.9	-5.51	-1.69	-2.01
PCED1A	PC-esterase domain containing 1A	-3.71	-3.89	-2.13	-1.82
C1orf63	chromosome 1 open reading frame 63	-3.61	-3.59	-1	1.78
NDFIP1	Nedd4 family interacting protein 1	-2.79	-2.8	-1.4	-1.5
ARHGDIB	Rho GDP dissociation inhibitor (GDI) beta	-1.98	-1.89	1.6	1.63
TMEM123	transmembrane protein 123	-1.38	-1.69	1.24	1.23
GALNT2	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2)	-1.67	-1.94	-2.18	-2.51
ASAH1	N-acylsphingosine amidohydrolase (acid ceramidase) 1	-2.43	-2.66	1.1	-1.04
TGM2	transglutaminase 2	-2.97	-2.81	1.02	-1.1
STAT4	signal transducer and activator of transcription 4	-1.37	-1.42	1.22	1.51
ADK	adenosine kinase	-2.97	-3.19	-1.83	-1.68
AES	amino-terminal enhancer of split	-2.14	-2.37	-1.93	-1.9
SMIM1	small integral membrane protein 1	-3.55	-3.87	1.72	2.03
TRIM63	tripartite motif containing 63, E3 ubiquitin protein ligase	-1.91	-1.94	-1.4	1.22
LACTB	lactamase, beta	-2.85	-3.2	-1.75	-1.69
SERINC2	serine incorporator 2	-2.88	-2.95	-2.45	-2.56
ATP1B1	ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, beta 1 polypeptide	-2.33	-2.76	2.35	1.91
ACVR1B	activin A receptor, type IB	-1.67	-1.65	-1.29	-1.38
LRRC31	leucine rich repeat containing 31	-1.94	-1.92	-1.62	-1.65
SUMF1	sulfatase modifying factor 1	-3.39	-3.01	-2.33	-2.93
RAP1A	RAP1A, member of RAS oncogene family	-3.22	-3.11	-1.38	-1.31
VPS13C	vacuolar protein sorting 13 homolog C (S. cerevisiae)	-3.1	-3.52	-2.11	-2.07
VRK3	vaccinia related kinase 3	-2.36	-2.34	-2.19	-2.25
NCKAP5	NCK-associated protein 5	-3.92	-3.79	-3.23	-3.38
COG1	component of oligomeric golgi complex 1	-2.16	-2.43	-1.67	-1.43
UBXN4	UBX domain protein 4	-1.87	-2.11	-1.26	-1.12
AAMDC	adipogenesis associated, Mth938 domain containing	-3.62	-3.7	-1.96	-1.85
PARP16	poly (ADP-ribose) polymerase family, member 16	-2.28	-2.27	-1.09	-1.11
GNS	glucosamine (N-acetyl)-6-sulfatase	-2.84	-3.02	1.07	1.14
SPAG5-AS1	SPAG5 antisense RNA 1	-1.32	-1.29	1.12	1.32
XPNPEP2	X-prolyl aminopeptidase (aminopeptidase P) 2, membrane-bound	-1.97	-1.95	-1.38	-1.18
TP53I13	tumor protein p53 inducible protein 13	-3.3	-3.37	-2.34	-2
WNT11	wingless-type MMTV integration site family, member 11	-2.44	-2.41	1.01	-1.08
RSL1D1	ribosomal L1 domain containing 1	-1.9	-1.97	-1.75	-1.78
OSMR	oncostatin M receptor	-2.78	-2.78	-1.17	-1.29
APLP2	amyloid beta (A4) precursor-like protein 2	-1.55	-1.81	1.2	1.21
ENPP7	ectonucleotide pyrophosphatase/phosphodiesterase 7	-1.43	-1.42	-1.28	-1.35
GSTM4	glutathione S-transferase mu 4	-2.01	-2.01	-1.73	-1.49
YIPF4	Yip1 domain family, member 4	-3.92	-3.67	1.18	-1.06
SLC25A44	solute carrier family 25, member 44	-1.86	-1.87	-2.6	-2.11
LPGAT1	lysophosphatidylglycerol acyltransferase 1	-5.32	-6.3	-1.9	-1.56
IRS1	insulin receptor substrate 1	-4.1	-3.6	-2.25	-3.31
LOC100506713	uncharacterized LOC100506713	-2.05	-2.08	-1.77	-1.8

PEX12	peroxisomal biogenesis factor 12	-2.1	-2.42	-1.15	-1.2
TMEM117	transmembrane protein 117	-2.9	-2.48	-1.15	-1.17
TOR1B	torsin family 1, member B (torsin B)	-2.05	-1.98	-1.42	-1.48
ABHD16A	abhydrolase domain containing 16A	-1.94	-2.15	-2.3	-2.31
SULF2	sulfatase 2	-1.31	-1.99	1.11	-1
RNASEL	ribonuclease L (2',5'-oligoadenylate synthetase-dependent)	-1.75	-1.84	1.18	-1.03
PRLR	prolactin receptor	-1.99	-2.01	-1.09	-1.19
CASP7	caspace 7, apoptosis-related cysteine peptidase	-7.45	-7.82	-2.51	-3
EPDR1	ependymin related 1	-1.59	-1.47	-1.94	-1.95
HIST2H2BE	histone cluster 2, H2be	-2.03	-2.25	-2.1	-2.12
PURA	purine-rich element binding protein A	-5.26	-6.1	-2.1	-2.35
TP53INP2	tumor protein p53 inducible nuclear protein 2	-2.68	-3.38	-1.63	-1.92
SMIM6	small integral membrane protein 6	-2.52	-2.18	-2.05	-1.96
SLC35A3	solute carrier family 35 (UDP-N-acetylglucosamine (UDP-GlcNAc) transporter), member A3	-2.93	-3.08	-3.41	-2.85
FLVCR2	feline leukemia virus subgroup C cellular receptor family, member 2	-2.43	-2.41	-2.17	-2.01
DCBLD1	discoidin, CUB and LCCL domain containing 1	-1.36	-1.61	-2.14	-2.23
ATP10D	ATPase, class V, type 10D	-4.09	-3.58	3.01	1.95
PSTPIP2	proline-serine-threonine phosphatase interacting protein 2	-3.48	-3.45	1.63	1.71
SCARB1	scavenger receptor class B, member 1	-3.8	-3.76	-2.25	-1.98
GLRX2	glutaredoxin 2	-1.4	-1.66	-2.61	-2.49
SSFA2	sperm specific antigen 2	-5.05	-5.45	1.4	1.12
KLF4	Kruppel-like factor 4 (gut)	-2.71	-3.09	-2.29	-2.66
PDE4DIP	phosphodiesterase 4D interacting protein	-2.46	-2.51	-1.77	-1.68
NOSTRIN	nitric oxide synthase trafficking	-1.75	-1.66	-1.05	1.26
HERPUD2	HERPUD family member 2	-2.32	-2.12	1.28	1.08
SOAT2	sterol O-acyltransferase 2	-1.98	-1.8	1.35	1.51
HECTD4	HECT domain containing E3 ubiquitin protein ligase 4	-2.5	-2.49	-1.75	-1.86
GRHL1	grainyhead-like 1 (Drosophila)	-4.27	-4.02	-1.26	-1.44
AMPD2	adenosine monophosphate deaminase 2	-2.18	-2.01	1.03	-1
IRAK4	interleukin-1 receptor-associated kinase 4	-1.93	-1.98	-1.65	-1.62
MICALCL	MICAL C-terminal like	-1.52	-1.38	-1.31	-1.23
ISG15	ISG15 ubiquitin-like modifier	-2.75	-2.81	-2.94	-2.51
DPP7	dipeptidyl-peptidase 7	-4.59	-4.55	-1.51	-1.32
PLA2G12A	phospholipase A2, group XIA	-3.77	-3.76	-2.13	-2.05
GOLIM4	golgi integral membrane protein 4	-1.91	-2.19	-2.27	-2.71
XPA	xeroderma pigmentosum, complementation group A	-2.3	-2.66	-2.51	-2.22
UBE2B	ubiquitin-conjugating enzyme E2B	-2.78	-2.8	-2.37	-2.63
NRTN	neurturin	-3.15	-2.68	-1.03	-1
BTG2	BTG family, member 2	-1.2	-1.35	1.37	1.44
HLA-J	major histocompatibility complex, class I, J (pseudogene)	-2.21	-2.41	-1.63	-1.42
PON2	paraoxonase 2	-5.61	-6.12	-1.21	-1.13
LCP1	lymphocyte cytosolic protein 1 (L-plastin)	-2.57	-2.49	-1.05	1.14
KIAA1598	KIAA1598	-4.57	-4.35	-1.87	-1.79
ETFA	electron-transfer-flavoprotein, alpha polypeptide	-2.97	-2.78	-1.59	-1.51

ANKS4B	ankyrin repeat and sterile alpha motif domain containing 4B	-2.36	-2.23	-2.08	-1.83
NDFIP2	Nedd4 family interacting protein 2	-2.5	-2.66	1.17	1.27
MIA2	melanoma inhibitory activity 2	-2.55	-2.5	-2	-1.57
GLT8D1	glycosyltransferase 8 domain containing 1	-3.27	-3.44	-1.03	-1.09
ZNF277	zinc finger protein 277	-2.85	-2.91	-1.83	-1.38
SOX6	SRY (sex determining region Y)-box 6	-2.18	-2.08	1.26	1.14
MIR22HG	MIR22 host gene (non-protein coding)	-2.97	-3.96	1.64	1.24
TRMT10A	tRNA methyltransferase 10 homolog A (S. cerevisiae)	-1.68	-1.66	-1.99	-2.11
TRAM2	translocation associated membrane protein 2	-1.01	-1.1	-1.13	-1.26
NAGPA	N-acetylglucosamine-1-phosphodiester alpha-N-acetylglucosaminidase	-1.63	-1.64	-1.75	-1.5
CCDC92	coiled-coil domain containing 92	-2.86	-3.51	-1.17	-1.25
ADCK2	aarF domain containing kinase 2	-1.98	-1.94	1.07	1.04
ARFGAP3	ADP-ribosylation factor GTPase activating protein 3	-4.2	-4.18	1.74	1.79
PCP4L1	Purkinje cell protein 4 like 1	-1.6	-1.69	-1.28	-1.04
LOC100507291	uncharacterized LOC100507291	-1.67	-1.7	1.02	1.14
RAMP1	receptor (G protein-coupled) activity modifying protein 1	-5.4	-4.6	-1.07	1.18
CYB561A3	cytochrome b561 family, member A3	-1.17	-1.16	-1.23	-1.23
DYNLT3	dynein, light chain, Tctex-type 3	-6.29	-6.26	-2.08	-1.49
EDEM2	ER degradation enhancer, mannosidase alpha-like 2	-2.25	-2.26	-1.74	-1.59
TIFA	TRAF-interacting protein with forkhead-associated domain	-5.22	-5.61	-1.6	-1.46
RASGRP3	RAS guanyl releasing protein 3 (calcium and DAG-regulated)	-1.3	-1.33	-1.27	-1.14
FNIP1	folliculin interacting protein 1	-2.37	-2.47	-1.67	-1.61
SRPR	signal recognition particle receptor (docking protein)	-2.46	-2.55	-1.7	-1.78
AGO4	argonaute RISC catalytic component 4	-2.21	-2.12	-1.53	-1.56
TIMP3	TIMP metalloproteinase inhibitor 3	-3.32	-3.32	2.11	1.59
TPP1	tripeptidyl peptidase I	-4.49	-4.62	-2.47	-2.38
TCEAL1	transcription elongation factor A (SII)-like 1	-4.99	-5.03	2.02	2.41
KIFC3	kinesin family member C3	-2.42	-2.63	-2.21	-2.29
AHNAK	AHNAK nucleoprotein	-3.98	-4.44	-1.21	-1.21
VAMP8	vesicle-associated membrane protein 8	-1.02	-1.65	-2.03	-2.03
MARVELD2	MARVEL domain containing 2	-2.02	-2.29	-3.07	-3.07
CXCL1	chemokine (C-X-C motif) ligand 1 (melanoma growth stimulating activity, alpha)	-2.97	-2.88	-3.11	-2.87
PHF11	PHD finger protein 11	-3.76	-4.01	-2.53	-2.55
DNAJB4	DnaJ (Hsp40) homolog, subfamily B, member 4	-3.1	-2.98	-1.95	-1.91
CHD9	chromodomain helicase DNA binding protein 9	-2.88	-2.58	-1.05	1.13
PLEKHA6	pleckstrin homology domain containing, family A member 6	-3.15	-3.32	-1.47	-1.58
WDR13	WD repeat domain 13	-4.32	-4.28	-1.52	-1.48
C5orf24	chromosome 5 open reading frame 24	-2.11	-2.35	1.28	-1.02
P4HTM	prolyl 4-hydroxylase, transmembrane (endoplasmic reticulum)	-1.44	-1.33	1.22	1.41

LINC01003	long intergenic non-protein coding RNA 1003	-4.19	-5.02	-1.9	-1.75
BBIP1	BBSome interacting protein 1	-2.84	-3.08	-1.92	-1.82
MEF2C	myocyte enhancer factor 2C	-1.45	-1.39	1.26	1.16
SPPL2A	signal peptide peptidase like 2A	-2.22	-2.77	-2.77	-2.46
TBRG1	transforming growth factor beta regulator 1	-1.82	-1.98	-1.75	-1.32
CAPN12	calpain 12	-3.93	-3.88	-1.8	1.05
TDRD7	tudor domain containing 7	-1.59	-2.37	1.05	1.15
MAGT1	magnesium transporter 1	-1.59	-1.59	-1.85	-2.1
RHBDD2	rhomboid domain containing 2	-1.28	-1.16	1.12	1.25
OTUD1	OTU domain containing 1	-2.28	-2.38	1.01	-1.19
---		-1.91	-2.09	-1.43	-1.55
ARRDC4	arrestin domain containing 4	-7.17	-6.25	2.76	1.99
CYSTM1	cysteine-rich transmembrane module containing 1	-2.19	-2.18	-1.06	1.26
RFTN1	raftlin, lipid raft linker 1	-2.92	-2.81	-1.12	-1.5
LNX1	ligand of numb-protein X 1, E3 ubiquitin protein ligase	-7.77	-5.22	-2.02	-2
C4orf33	chromosome 4 open reading frame 33	-2.17	-2.19	-1.6	-1.37
SLC19A3	solute carrier family 19 (thiamine transporter), member 3	-5.25	-4.69	-1.58	-1.82
TRIM14	tripartite motif containing 14	-2.04	-1.82	-2.23	-2.29
---		-2.14	-2.06	-2.92	-2.75
PAPSS2	3'-phosphoadenosine 5'-phosphosulfate synthase 2	-4.93	-4.64	-2.69	-2.25
SYNPO	synaptopodin	-2.33	-2.31	-1.42	-1.74
PLK2	polo-like kinase 2	-1.11	-1.32	1.15	-1.38
PDLIM5	PDZ and LIM domain 5	-1.9	-1.98	-2.07	-2.2
NEK6	NIMA-related kinase 6	-4.23	-4.62	-1.52	-1.6
INHBA	inhibin, beta A	-2.83	-2.98	1.08	1.11
KHNYN	KH and NYN domain containing	-1.48	-1.64	1.44	1.29
ACSS3	acyl-CoA synthetase short-chain family member 3	-1.03	-1.51	-2.32	-2.21
CXCL16	chemokine (C-X-C motif) ligand 16	-2.84	-2.71	1.07	1.44
AGA	aspartylglucosaminidase	-4.11	-4.48	-4.92	-4.68
LGALS3BP	lectin, galactoside-binding, soluble, 3 binding protein	-3.26	-2.99	1.24	1.22
NOL3	nucleolar protein 3 (apoptosis repressor with CARD domain)	-2.32	-2.4	-1.45	-1.47
SECISBP2L	SECIS binding protein 2-like	-1.76	-2.09	-1.07	-1.27
CAPN5	calpain 5	-1.99	-1.95	-1.9	-1.77
CLDN23	claudin 23	-2.5	-2.96	-3.38	-4.07
TOM1	target of myb1 (chicken)	-2.35	-2.52	-2.13	-1.85
FAM114A1	family with sequence similarity 114, member A1	-8.08	-7.36	1.68	1.52
CALML4	calmodulin-like 4	-3.73	-3.6	1.01	1.22
LOC100505812	uncharacterized LOC100505812	-1.37	-1.33	-1.38	-1.37
RNASET2	ribonuclease T2	-4.12	-3.9	1.51	1.53
NEDD9	neural precursor cell expressed, developmentally down-regulated 9	-1.53	-1.59	2	1.76
PDGFC	platelet derived growth factor C	-4.72	-5.16	-1.58	-2.21
PLLP	plasmolipin	-2.42	-2.33	1.2	1.42
FN1	fibronectin 1	-3.76	-4.08	1.8	1.6
TRAK2	trafficking protein, kinesin binding 2	-2.06	-2.14	-1.87	-1.67
DAZAP2	DAZ associated protein 2	-6.98	-6.77	-1.51	-1.52

ZFAND2A	zinc finger, AN1-type domain 2A	-6.58	-6.47	-2.34	-1.88
USP3	ubiquitin specific peptidase 3	-1.24	-1.39	-1.1	1.01
NPTXR	neuronal pentraxin receptor	-2.69	-2.19	-2.38	-2.56
FRK	fyn-related kinase	-4.39	-4.49	-3.38	-2.79
ERO1L	ERO1-like ( <i>S. cerevisiae</i> )	-2.49	-2.4	-1.19	-1.25
NUDT14	nudix (nucleoside diphosphate linked moiety X)-type motif 14	-1.53	-1.62	-1.88	-2.06
ZAK	sterile alpha motif and leucine zipper containing kinase AZK	-3.11	-3.26	-2.53	-3.09
AGPAT3	1-acylglycerol-3-phosphate O-acyltransferase 3	-4.07	-4.76	-1.84	-2.03
LOC100507311	uncharacterized LOC100507311	-1.53	-1.5	-1.14	-1.04
KDM6B	lysine (K)-specific demethylase 6B	-1.11	-1.24	1.33	1.13
PLA2G1B	phospholipase A2, group IB (pancreas)	-1.25	-1.25	-1.19	-1.12
TTC3	tetratricopeptide repeat domain 3	-2.8	-3.43	2.22	2.31
PHYHIPL	phytanoyl-CoA 2-hydroxylase interacting protein-like	-1.06	-1.04	-1.05	1
HIST1H2AE	histone cluster 1, H2ae	-1.28	-1.65	-2.52	-2.36
SPATA2L	spermatogenesis associated 2-like	-2.29	-2.46	-2.24	-2.69
NHSL1	NHS-like 1	-1.79	-1.92	-1.93	-2.2
NRP1	neuropilin 1	-4.12	-5.08	-1.08	-1.45
SLC33A1	solute carrier family 33 (acetyl-CoA transporter), member 1	-2.8	-3.05	-3.56	-3.12
LMBRD1	LMBR1 domain containing 1	-4.25	-4.86	-1.8	-1.88
ILVBL	ilvB (bacterial acetolactate synthase)-like	-2.8	-2.96	-2.3	-2.16
NCOA7	nuclear receptor coactivator 7	-10.56	-10.32	-2.06	-3.02
SLC5A9	solute carrier family 5 (sodium/sugar cotransporter), member 9	-3.16	-3.43	-2.85	-2.09
EMP1	epithelial membrane protein 1	-2.75	-2.52	-1.08	-1.32
SAT1	spermidine/spermine N1-acetyltransferase 1	-5.58	-5.46	1.57	1.78
LOC730101	uncharacterized LOC730101	-2.36	-2.57	-1.65	-1.76
CCL5	chemokine (C-C motif) ligand 5	-1.2	-1.23	-1.1	-1.05
AKAP13	A kinase (PRKA) anchor protein 13	-1.79	-2.06	-1.9	-2.19
ABHD3	abhydrolase domain containing 3	-8.12	-9.54	-2.94	-2.57
PPAPDC2	phosphatidic acid phosphatase type 2 domain containing 2	-2.32	-2.42	-2.49	-2.63
SLC9A3R1	solute carrier family 9, subfamily A (NHE3, cation proton antiporter 3), member 3 regulator 1	-1.41	-1.52	2.14	1.83
GSTO1	glutathione S-transferase omega 1	-1.47	-1.62	-2.33	-2.1
COLEC11	collectin sub-family member 11	-2.76	-2.77	1.59	1.16
PROSER2	proline and serine-rich protein 2	-6.05	-6.87	-1.84	-2.53
TM4SF20	transmembrane 4 L six family member 20	-1.45	-1.47	-1.41	-1.33
CFLAR	CASP8 and FADD-like apoptosis regulator	-3.57	-3.75	-2.25	-2.19
KLHL5	kelch-like family member 5	-4.07	-4.16	-4.93	-4.51
CMPK2	cytidine monophosphate (UMP-CMP) kinase 2, mitochondrial	-5.3	-5.42	-4.4	-4.28
MORC4	MORC family CW-type zinc finger 4	-8.45	-7.34	1.3	1.2
SH3BP5	SH3-domain binding protein 5 (BTK-associated)	-3.3	-3.47	2.17	1.83
SPTLC3	serine palmitoyltransferase, long chain base subunit 3	-5.06	-4.46	1.14	-1.04
IFI16	interferon, gamma-inducible protein 16	-3.5	-4.23	1.87	2.13



LSR	lipolysis stimulated lipoprotein receptor	-1.67	-1.75	-2.88	-2.73
CHMP4C	charged multivesicular body protein 4C	-1.2	-1.42	-1.62	-1.89
LOC728613	programmed cell death 6 pseudogene	-1.3	-1.33	-1.28	-1.37
ITM2B	integral membrane protein 2B	-1.4	-1.37	1.19	1.16
TMEM37	transmembrane protein 37	-3.32	-3.24	-2.17	-2.14
TBX3	T-box 3	-4.06	-5.55	-1.48	-1.66
FAM228B	family with sequence similarity 228, member B	-2.99	-2.86	2	2.6
P2RX4	purinergic receptor P2X, ligand-gated ion channel, 4	-1.87	-1.82	1.08	1.32
MGAT4A	mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isozyme A	-3.35	-3.26	-1.06	1.1
SCML4	sex comb on midleg-like 4 (Drosophila)	-1.59	-1.61	1.81	1.91
HIST1H2BK	histone cluster 1, H2bk	-1.09	-2.11	-1.94	-1.86
BACE1	beta-site APP-cleaving enzyme 1	-2.8	-3	1.81	1.92
LOC100506358	uncharacterized LOC100506358	-5.97	-5.97	-3.17	-1.95
MBNL2	muscleblind-like splicing regulator 2	-4.87	-4.78	-1.16	-1.26
SOCS6	suppressor of cytokine signaling 6	-1.54	-1.67	-2.01	-2.51
TXNIP	thioredoxin interacting protein	-10.7	-10.48	1.39	1.62
MPP1	membrane protein, palmitoylated 1, 55kDa	-1.21	-1.26	-1.3	-1.2
APOLD1	apolipoprotein L domain containing 1	-2.04	-2.12	-1.76	-2.21
S100A16	S100 calcium binding protein A16	-2.59	-2.36	1.85	2.05
LOC145474	uncharacterized LOC145474	-2.66	-2.96	-2.33	-2.06
RAB24	RAB24, member RAS oncogene family	-2.26	-2.19	1.37	1.47
ABCG2	ATP-binding cassette, sub-family G (WHITE), member 2	-2.54	-3.18	-1.01	-1.13
PLEKHG1	pleckstrin homology domain containing, family G (with RhoGef domain) member 1	-2.7	-2.42	-1.68	-1.72
TNFAIP3	tumor necrosis factor, alpha-induced protein 3	-7.94	-7.38	2.82	2.34
SORBS1	sorbin and SH3 domain containing 1	-2.11	-2.05	-2.5	-2.43
SOWAHA	sosondowah ankyrin repeat domain family member A	-3.28	-3.07	2.41	2.39
MME	membrane metallo-endopeptidase	-3.24	-2.94	2.48	2.39
MGAM	maltase-glucoamylase (alpha-glucosidase)	-1.52	-1.53	-1.52	-1.42
NR2F2	nuclear receptor subfamily 2, group F, member 2	-6.76	-6.75	1.63	1.21
HIST1H2BF	histone cluster 1, H2bf	1.28	-1.05	-1.38	-1.37
ABHD12	abhydrolase domain containing 12	-1.38	-1.42	-1.47	-1.51
MORN1	MORN repeat containing 1	-2.56	-2.72	-2.43	-2.17
P4HA1	prolyl 4-hydroxylase, alpha polypeptide I	-2.73	-2.85	3.88	3.47
FAM89A	family with sequence similarity 89, member A	-1.19	-2.26	3.39	2.5
CD99	CD99 molecule	-2.72	-3.15	3.05	2.89
LIPA	lipase A, lysosomal acid, cholesterol esterase	-1.94	-2.1	-3.5	-3.06
FAM151A	family with sequence similarity 151, member A	-2.24	-2.1	1.45	1.34
SYTL5	synaptotagmin-like 5	-1.34	-1.25	1.68	1.6
ANXA4	annexin A4	-12.94	-14.13	-1.7	-1.8
OR7E14P	olfactory receptor, family 7, subfamily E, member 14 pseudogene	-1.39	-1.1	-1.85	-1.92
ATP7B	ATPase, Cu <sup>++</sup> transporting, beta polypeptide	-4.66	-4.96	4.87	3.68
RHOU	ras homolog family member U	-6.92	-7.39	2.73	2.7
GATA6-AS1	GATA6 antisense RNA 1 (head to head)	-1.8	-3.61	2.46	2.86
RHOBTB3	Rho-related BTB domain containing 3	-1.84	-3.93	2.83	2.23

MIR100HG	mir-100-let-7a-2 cluster host gene (non-protein coding)	-2.35	-2.49	-1.26	-1.67
COX7A1	cytochrome c oxidase subunit VIIa polypeptide 1 (muscle)	-2.46	-2.67	-2.83	-2.73
TMEM45B	transmembrane protein 45B	-3.65	-3.59	-2.28	-1.85
WNK4	WNK lysine deficient protein kinase 4	-1.16	-1.11	-1.11	1.03
TSPAN1	tetraspanin 1	-1.19	-1.15	-1.01	1.19
PPFIBP2	PTPRF interacting protein, binding protein 2 (liprin beta 2)	-9.3	-12.44	-4.44	-4.18
INPP1	inositol polyphosphate-1-phosphatase	-8.38	-8.48	-3.51	-3.41
KLF6	Kruppel-like factor 6	-7.28	-8.84	-2.37	-3.36
SLCO2B1	solute carrier organic anion transporter family, member 2B1	-7.03	-6.62	-3.22	-2.98
MPC2	mitochondrial pyruvate carrier 2	-15.67	-15.33	-4.85	-3.78
FUCA1	fucosidase, alpha-L- 1, tissue	-13.02	-14.11	-4.28	-3.98
ABHD15	abhydrolase domain containing 15	-7.95	-7.55	-3.32	-3.94
GSTK1	glutathione S-transferase kappa 1	-13.79	-15.08	-3.94	-3.58
ACYP2	acylphosphatase 2, muscle type	-7.48	-8.99	-4.58	-4.2
HDHD3	haloacid dehalogenase-like hydrolase domain containing 3	-9.05	-9.21	-4.73	-4.2
PCGF5	polycomb group ring finger 5	-9.79	-9.58	-4.09	-3.27
DTX3L	deltex 3-like (Drosophila)	-15.1	-13.16	-4.06	-4.92
APOE	apolipoprotein E	-12.21	-13.76	-3.88	-2.99
C10orf32	chromosome 10 open reading frame 32	-8.05	-8.11	-3.71	-4.4
PTGR1	prostaglandin reductase 1	-10.83	-15.02	-2.88	-2.8
CTBS	chitobiase, di-N-acetyl-	-14.75	-17.46	-2.39	-1.98
C4orf32	chromosome 4 open reading frame 32	-13.03	-11.64	-5.89	-5.97
SETD7	SET domain containing (lysine methyltransferase) 7	-8.03	-10.73	-3.07	-3.72
SLC22A18	solute carrier family 22, member 18	-10.74	-11.12	-2.66	-2.29
MEGF9	multiple EGF-like-domains 9	-10.2	-10.52	-6.69	-6.31
SLC23A1	solute carrier family 23 (ascorbic acid transporter), member 1	-10.45	-9.56	-3.47	-2.74
YPEL2	yippee-like 2 (Drosophila)	-10.52	-10.79	-2.79	-2.8
C2orf72	chromosome 2 open reading frame 72	-10.19	-10.53	-2.61	-2.45
RAB27A	RAB27A, member RAS oncogene family	-6.19	-7.63	-3.44	-2.92
REEP6	receptor accessory protein 6	-17.5	-17.3	-2.81	-2.4
COMMD3	COMM domain containing 3	-14.98	-15.78	-2.56	-2.8
IL6R	interleukin 6 receptor	-16.27	-15.62	-3.58	-3.88
CPQ	carboxypeptidase Q	-16.03	-15.47	-6.06	-5.38
AQP11	aquaporin 11	-6.31	-6	-3.59	-3.33
MST1	macrophage stimulating 1 (hepatocyte growth factor-like)	-12.47	-11.67	-5.48	-3.63
TSHZ1	teashirt zinc finger homeobox 1	-17.47	-17.62	-2.63	-3.43
PXDC1	PX domain containing 1	-16.95	-18.11	-3.24	-3.43
LURAP1L	leucine rich adaptor protein 1-like	-9.74	-8.94	-3.54	-4.42
TMEM120A	transmembrane protein 120A	-11.48	-12.28	-2.34	-1.89
ACAA1	acetyl-CoA acyltransferase 1	-15.24	-15.27	-7.89	-6.35
FAM8A1	family with sequence similarity 8, member A1	-9.99	-10.47	-2.67	-2.45
MGST2	microsomal glutathione S-transferase 2	-6.79	-9.23	-4.2	-4.63
C1orf115	chromosome 1 open reading frame 115	-18.46	-16.22	-3.51	-3.34



IFIT3	interferon-induced protein with tetratricopeptide repeats 3	-7.64	-8.06	-4.76	-4.39
CPEB4	cytoplasmic polyadenylation element binding protein 4	-11.15	-9.6	-2.97	-2.95
IL10RB	interleukin 10 receptor, beta	-9.74	-10.97	-2.55	-2.91
LAMP2	lysosomal-associated membrane protein 2	-8.16	-8.46	-2.68	-2.38
ZHX1	zinc fingers and homeoboxes 1	-24.57	-24.27	-3.04	-2.69
PID1	phosphotyrosine interaction domain containing 1	-6.69	-6.49	-5.05	-4.74
HMGCL	3-hydroxymethyl-3-methylglutaryl-CoA lyase	-12.66	-12.83	-4.08	-3.77
APOL6	apolipoprotein L, 6	-6.23	-6.1	-4.92	-5.17
HSDL2	hydroxysteroid dehydrogenase like 2	-14.85	-15.05	-2.97	-3.31
RCAN1	regulator of calcineurin 1	-15.13	-15.38	-3.85	-4
TMEM140	transmembrane protein 140	-7.42	-6.74	-3.55	-2.83
NFIL3	nuclear factor, interleukin 3 regulated	-9.63	-10.55	-3.14	-3.35
MXI1	MAX interactor 1, dimerization protein	-11.05	-12.6	-2.17	-2.45
SLC9B2	solute carrier family 9, subfamily B (NHA2, cation proton antiporter 2), member 2	-4.93	-4.77	-3.16	-2.76
CAMK2N1	calcium/calmodulin-dependent protein kinase II inhibitor 1	-19.83	-18.88	-2.62	-2.84
CTSZ	cathepsin Z	-8.31	-9.89	-4.66	-4.88
SAT2	spermidine/spermine N1-acetyltransferase family member 2	-10.29	-10.82	-4.23	-3.36
ABCC3	ATP-binding cassette, sub-family C (CFTR/MRP), member 3	-7.63	-7.36	-6.7	-6.01
PRRG4	proline rich Gla (G-carboxyglutamic acid) 4 (transmembrane)	-21.3	-20.32	-2.11	-2.48
C4orf19	chromosome 4 open reading frame 19	-12.07	-11.72	-7.09	-7.21
FAXDC2	fatty acid hydroxylase domain containing 2	-6.64	-6.45	-2.42	-2.5
STOM	stomatin	-17.36	-17.76	-3.03	-2.94
NFKBIA	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, alpha	-4.64	-6.64	-3.15	-2.93
SERPINE1	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	-6.71	-6.65	-2.41	-3.62
FAM134B	family with sequence similarity 134, member B	-19.94	-17.66	-7.16	-5.47
DEPDC7	DEP domain containing 7	-33.59	-37.49	-3.35	-2.67
SLC35D1	solute carrier family 35 (UDP-GlcA/UDP-GalNAc transporter), member D1	-15.85	-15.49	-5.54	-6.36
MAN1A1	mannosidase, alpha, class 1A, member 1	-15.76	-23.27	-1.85	-2.4
DNAJB9	DnaJ (Hsp40) homolog, subfamily B, member 9	-7.51	-8.11	-1.64	-1.42
C1RL	complement component 1, r subcomponent-like	-11.42	-10.82	-5.54	-5.01
HSD17B11	hydroxysteroid (17-beta) dehydrogenase 11	-29.22	-29.03	-4.43	-3.41
PPARA	peroxisome proliferator-activated receptor alpha	-13.84	-13.46	-5.06	-5.32
C11orf54	chromosome 11 open reading frame 54	-35.21	-35.99	-4.52	-3.4
INSIG2	insulin induced gene 2	-15.16	-14.69	-3.04	-3.21
ATP8B1	ATPase, aminophospholipid transporter, class I, type 8B, member 1	-11.09	-13.82	-2.21	-2.45
ETFB	electron-transfer-flavoprotein, beta polypeptide	-8.17	-10.14	-4.02	-4.55
AIG1	androgen-induced 1	-13.5	-10.22	-7.74	-7.17
EPS8	epidermal growth factor receptor pathway substrate 8	-10.73	-12.51	-1.68	-1.96

SLC31A2	solute carrier family 31 (copper transporter), member 2	-6.52	-6.73	-2.77	-2.49
AGPAT9	1-acylglycerol-3-phosphate O-acyltransferase 9	-12	-10.98	-7	-6.8
PNRC1	proline-rich nuclear receptor coactivator 1	-7.14	-8.09	-1.51	-1.63
C1orf53	chromosome 1 open reading frame 53	-5.36	-5.6	-4.4	-4.75
MAN2B2	mannosidase, alpha, class 2B, member 2	-7.78	-9	-2.59	-2.88
TBC1D8B	TBC1 domain family, member 8B (with GRAM domain)	-14.58	-14.58	-3.4	-3.13
B2M	beta-2-microglobulin	-12.09	-12.09	-1.78	-1.66
CTSH	cathepsin H	-11.74	-10.19	-1.38	1.11
CREG1	cellular repressor of E1A-stimulated genes 1	-8.08	-8.14	-1.73	-1.83
DGAT2	diacylglycerol O-acyltransferase 2	-11.43	-11.67	-5.93	-4.16
PPP1R16A	protein phosphatase 1, regulatory subunit 16A	-7.88	-8.69	-5.77	-4.59
PLA2G12B	phospholipase A2, group XIIB	-13.86	-14	-3.19	-2.09
ST3GAL1	ST3 beta-galactoside alpha-2,3-sialyltransferase 1	-7.79	-7.43	-1.94	-2.48
IRF9	interferon regulatory factor 9	-5.27	-4.91	-2.53	-2.68
ARSD	arylsulfatase D	-6.12	-6.29	-3.17	-3.52
SCML1	sex comb on midleg-like 1 (Drosophila)	-17.79	-17.31	-6.43	-4.15
AQP3	aquaporin 3 (Gill blood group)	-6.75	-6.76	-1.73	-1.8
EFHD1	EF-hand domain family, member D1	-7.89	-7.11	-1.64	-1.73
ARAP2	ArfGAP with RhoGAP domain, ankyrin repeat and PH domain 2	-6.82	-6.51	-1.67	-1.21
MAST4	microtubule associated serine/threonine kinase family member 4	-5.5	-5.35	-2.75	-2.63
NFKBIZ	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta	-16.31	-14.61	-7.37	-7.88
CASP4	caspase 4, apoptosis-related cysteine peptidase	-16.84	-16.5	-11.69	-10.96
---		-8.17	-8.22	-4.24	-4.67
PLIN2	perilipin 2	-14.74	-12.1	-1.76	-2.33
RNFT1	ring finger protein, transmembrane 1	-7.23	-7.56	-4.74	-4.78
SLC39A5	solute carrier family 39 (zinc transporter), member 5	-6.3	-6.27	-3.94	-3.3
DHRS3	dehydrogenase/reductase (SDR family) member 3	-13.63	-11.98	-3.58	-4.15
CRAT	carnitine O-acetyltransferase	-7.18	-7.78	-3.73	-3.48
IL1R2	interleukin 1 receptor, type II	-8.81	-8.94	-3.08	-1.7
ZFP36	ZFP36 ring finger protein	-10.82	-10.95	-3.89	-4.01
BCL6	B-cell CLL/lymphoma 6	-15.76	-15.48	-4.72	-4.37
GIPC2	GIPC PDZ domain containing family, member 2	-31.79	-30.29	-7.12	-7.9
JUNB	jun B proto-oncogene	-9.41	-9.23	-3.57	-5.22
RBKS	ribokinase	-12.46	-11.91	-7.68	-6.97
SLC2A10	solute carrier family 2 (facilitated glucose transporter), member 10	-13.01	-12.16	-1.84	-2.09
GDF15	growth differentiation factor 15	-25.28	-24.31	-3.66	-3.53
LTBP3	latent transforming growth factor beta binding protein 3	-8.46	-8.39	-3.59	-3.65
SLC25A20	solute carrier family 25 (carnitine/acylcarnitine translocase), member 20	-10.12	-10.38	-5.64	-4.95
FRMD4B	FERM domain containing 4B	-26.33	-23.43	-1.99	-2.16
RND1	Rho family GTPase 1	-9.48	-8.53	-5.5	-5.16
IFNAR1	interferon (alpha, beta and omega) receptor 1	-7.61	-7.29	-4.41	-5.09

KCNJ8	potassium inwardly-rectifying channel, subfamily J, member 8	-17.35	-16.99	-6.32	-3.9
TMEM27	transmembrane protein 27	-15.09	-29.44	-2.97	-2.13
HLA-E	major histocompatibility complex, class I, E	-7.08	-7.28	-1.66	-1.58
NRBP2	nuclear receptor binding protein 2	-22.03	-20.22	-7.94	-4.84
SUN2	Sad1 and UNC84 domain containing 2	-8.04	-7.58	-3.93	-4.28
SNTB1	syntrophin, beta 1 (dystrophin-associated protein A1, 59kDa, basic component 1)	-5.85	-5.65	-6.71	-6.09
ZBTB16	zinc finger and BTB domain containing 16	-9.33	-9.77	-2.26	-2.35
CTSB	cathepsin B	-37.29	-39.3	-2.02	-2.25
RETSAT	retinol saturase (all-trans-retinol 13,14-reductase)	-11.52	-11.4	-7.23	-7.17
CPM	carboxypeptidase M	-6.46	-6.38	-3.35	-3.36
MBNL3	muscleblind-like splicing regulator 3	-11.53	-12.01	-3.23	-3.07
IFIH1	interferon induced with helicase C domain 1	-28.67	-27.84	-9.41	-10.11
PARP9	poly (ADP-ribose) polymerase family, member 9	-5.4	-5.15	-3.33	-2.98
SCP2	sterol carrier protein 2	-8.78	-8.57	-4.48	-4.27
GPX3	glutathione peroxidase 3 (plasma)	-5.63	-6.58	-5.85	-4.63
SHC2	SHC (Src homology 2 domain containing) transforming protein 2	-6	-5.91	-2.41	-2.09
STARD10	StAR-related lipid transfer (START) domain containing 10	-21.63	-23.16	-5.84	-5.32
SLC7A9	solute carrier family 7 (amino acid transporter light chain, bo,+ system), member 9	-8.34	-7.7	-6.06	-5.13
LGSN	lensin, lens protein with glutamine synthetase domain	-12.07	-11.4	-8.37	-7.8
FAS	Fas cell surface death receptor	-9.74	-9.29	-6.8	-8.41
BHLHE40	basic helix-loop-helix family, member e40	-5.67	-6.91	-3.41	-4.58
SMPDL3A	sphingomyelin phosphodiesterase, acid-like 3A	-33.85	-40.13	-5.1	-4.39
IFI6	interferon, alpha-inducible protein 6	-14.27	-14.39	-2.25	-2.14
AKAP9	A kinase (PRKA) anchor protein 9	-10.49	-13.34	-6.94	-4.16
ID2	inhibitor of DNA binding 2, dominant negative helix-loop-helix protein	-3.43	-5.4	-2.24	-2.66
ACADVL	acyl-CoA dehydrogenase, very long chain	-16.22	-16.32	-4.85	-4.18
ABHD2	abhydrolase domain containing 2	-8.36	-8.49	-5.56	-5.99
IL8	interleukin 8	-5.42	-5.23	-5.64	-5.58
ERRFI1	ERBB receptor feedback inhibitor 1	-9.29	-10.14	-1.21	-1.5
DENND4A	DENN/MADD domain containing 4A	-10.29	-10.55	-6.32	-5.88
SMLR1	small leucine-rich protein 1	-17.74	-17.4	-7.09	-5.47
TP53TG1	TP53 target 1 (non-protein coding)	-9.03	-8.82	-2.36	-2.4
CEACAM1	carcinoembryonic antigen-related cell adhesion molecule 1 (biliary glycoprotein)	-5.21	-5.01	-3.98	-3.42
ACOT4	acyl-CoA thioesterase 4	-9.8	-9.1	-10.46	-9.82
TOB1	transducer of ERBB2, 1	-10.39	-10.28	-3.58	-4.54
FAM69A	family with sequence similarity 69, member A	-11.85	-11.61	-6.5	-4.93
FNIP2	folliculin interacting protein 2	-8.38	-8.39	-6.27	-6.12
EDEM1	ER degradation enhancer, mannosidase alpha-like 1	-6.31	-6.96	-2.89	-2.59
LGALS8	lectin, galactoside-binding, soluble, 8	-7.32	-7.3	-3.74	-3.43
TFPI	tissue factor pathway inhibitor (lipoprotein-associated coagulation inhibitor)	-32.9	-24.15	-1.68	-1.39

HERPUD1	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	-6.95	-7.88	-2.02	-2.6
RGCC	regulator of cell cycle	-7.55	-8.26	-2.14	-2.24
LINC00849	long intergenic non-protein coding RNA 849	-20.28	-18.35	-8.38	-8.22
SMIM14	small integral membrane protein 14	-12.65	-11.12	-5.54	-6.37
MT2A	metallothionein 2A	-18.04	-20.19	-3.45	-2.89
GDA	guanine deaminase	-49.16	-46.56	-4.68	-3.71
HSBP1L1	heat shock factor binding protein 1-like 1	-35.53	-39.24	-1.29	1.07
TST	thiosulfate sulfurtransferase (rhodanese)	-12.58	-14.08	-7.74	-6.14
GPR126	G protein-coupled receptor 126	-44.58	-35.01	-3.55	-4.24
KLB	klotho beta	-26.05	-25.47	-2.74	-2.05
AGMAT	agmatine ureohydrolase (agmatinase)	-13.73	-11.6	-11.82	-9.7
CNKSR3	CNKSR family member 3	-6.5	-7.42	-4.24	-4.33
ABCA1	ATP-binding cassette, sub-family A (ABC1), member 1	-21.35	-19.4	-1.58	-1.18
PTPN3	protein tyrosine phosphatase, non-receptor type 3	-8.96	-9.03	-6.48	-6.26
PIK3R1	phosphoinositide-3-kinase, regulatory subunit 1 (alpha)	-3.62	-4.35	-2.28	-2.44
CREB3L3	cAMP responsive element binding protein 3-like 3	-5.6	-5.67	-4.61	-4.95
MGLL	monoglyceride lipase	-15.29	-14.17	-5.59	-6.3
SLC15A1	solute carrier family 15 (oligopeptide transporter), member 1	-9.94	-8.66	-4.64	-3.28
COBLL1	cordon-bleu WH2 repeat protein-like 1	-10.13	-10.98	-1.46	-1.37
THRB	thyroid hormone receptor, beta	-9.96	-9.87	-1.46	-1.59
IRF8	interferon regulatory factor 8	-6.58	-6.22	-3.24	-3.56
GPR128	G protein-coupled receptor 128	-24.2	-22.64	-7.65	-6.76
TMEM14A	transmembrane protein 14A	-7.11	-7.73	-2.01	-1.95
ELF3	E74-like factor 3 (ets domain transcription factor, epithelial-specific )	-5.93	-5.77	-3.62	-4.23
PPARG	peroxisome proliferator-activated receptor gamma	-4.68	-4.59	-1.7	-1.4
MTUS1	microtubule associated tumor suppressor 1	-8.49	-10.08	-2.39	-1.92
BIRC3	baculoviral IAP repeat containing 3	-4.99	-4.71	-3.23	-2.65
FBXO8	F-box protein 8	-7.9	-8.67	-2.6	-2.98
IL13RA1	interleukin 13 receptor, alpha 1	-6.27	-8	-3.44	-4
TNFSF13B	tumor necrosis factor (ligand) superfamily, member 13b	-4.56	-4.57	-3.45	-2.73
G0S2	G0/G1switch 2	-36.59	-38.03	-2.6	1.11
CEBPA	CCAAT/enhancer binding protein (C/EBP), alpha	-17.94	-14.78	-5.98	-6.14
DCAF6	DDB1 and CUL4 associated factor 6	-6.37	-7.02	-2.08	-1.83
NR1H3	nuclear receptor subfamily 1, group H, member 3	-7.52	-7.23	-5.25	-3.93
MTCH2	mitochondrial carrier 2	-8.34	-7.61	-4.45	-4.38
POLD4	polymerase (DNA-directed), delta 4, accessory subunit	-5.72	-5.92	-3.61	-3.05
IL1R1	interleukin 1 receptor, type I	-7.99	-7.74	1.18	1.02
RDH10	retinol dehydrogenase 10 (all-trans)	-4.46	-5.01	-2.9	-3.07
HPGD	hydroxyprostaglandin dehydrogenase 15-(NAD)	-35.63	-38.49	-9	-5.43
GCHFR	GTP cyclohydrolase I feedback regulator	-7.3	-7.5	-5.68	-5.17
GADD45A	growth arrest and DNA-damage-inducible, alpha	-5.11	-5.34	-2.09	-2.57
NNT	nicotinamide nucleotide transhydrogenase	-11.91	-13.22	-2.48	-2.8

POLR3GL	polymerase (RNA) III (DNA directed) polypeptide G (32kD)-like	-8.04	-8.74	-2.63	-3.03
DNAJC22	DnaJ (Hsp40) homolog, subfamily C, member 22	-13.23	-12.86	-10.17	-9.25
ZG16	zymogen granule protein 16	-17.53	-15.45	-3.29	-1.58
GBP2	guanylate binding protein 2, interferon-inducible	-15.88	-16.11	1.23	1.54
DHRS1	dehydrogenase/reductase (SDR family) member 1	-12.91	-11.71	-7.57	-6.42
PARP14	poly (ADP-ribose) polymerase family, member 14	-7.28	-7.71	-3.67	-3.41
TPD52L1	tumor protein D52-like 1	-12.14	-11.32	-2.01	-1.79
DDX60L	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60-like	-10.27	-10.02	-8.6	-7.89
DMD	dystrophin	-4.86	-5.72	-5.43	-4.88
PLD1	phospholipase D1, phosphatidylcholine-specific	-4.71	-4.49	-1.95	-1.95
IDNK	idnK, gluconokinase homolog (E. coli)	-9.37	-8.97	-5.77	-5.93
DDC	dopa decarboxylase (aromatic L-amino acid decarboxylase)	-5.87	-6.11	-1.79	-1.31
FAM46A	family with sequence similarity 46, member A	-15.56	-16	1.33	1.34
CTAGE5	CTAGE family, member 5	-4.91	-5.07	-3.81	-3.09
OXSM	3-oxoacyl-ACP synthase, mitochondrial	-6.31	-6.97	-3.44	-3.16
NAAA	N-acylethanolamine acid amidase	-8.11	-7.57	-6.55	-6.11
FLJ22763	uncharacterized LOC401081	-24.89	-24.88	-2.16	-1.9
RASD1	RAS, dexamethasone-induced 1	-7.64	-7.64	-1.74	-1.16
IL6ST	interleukin 6 signal transducer (gp130, oncostatin M receptor)	-14.75	-17.2	1.42	1.32
KYNU	kynureninase	-14.01	-13.81	-9.79	-7.92
TMEM45A	transmembrane protein 45A	-9.31	-8.49	-1.43	-1.75
F10	coagulation factor X	-32.5	-32.62	-7.05	-5.19
DUSP1	dual specificity phosphatase 1	-13.63	-13.41	-4.6	-5.08
EPAS1	endothelial PAS domain protein 1	-10.84	-9.55	1.94	1.75
CST3	cystatin C	-6.43	-7.92	1.28	1.4
SQRDL	sulfide quinone reductase-like (yeast)	-25.14	-21.06	-6.43	-5.69
CMTM8	CKLF-like MARVEL transmembrane domain containing 8	-7.63	-7.93	-4.87	-4.83
SH3BGRL2	SH3 domain binding glutamic acid-rich protein like 2	-6.06	-5.69	-2.64	-2.5
ANKRD37	ankyrin repeat domain 37	-13.52	-11.67	-6.16	-9.12
CHI3L1	chitinase 3-like 1 (cartilage glycoprotein-39)	-17.11	-17.57	-4.41	-5.74
ZADH2	zinc binding alcohol dehydrogenase domain containing 2	-6.88	-7.18	-2.81	-3.4
TRIM4	tripartite motif containing 4	-16.69	-15.61	-13.13	-12.34
TBC1D9	TBC1 domain family, member 9 (with GRAM domain)	-3.07	-3.72	-1.54	-1.97
NBEAL1	neurobeachin-like 1	-7.56	-7.81	-5.18	-4.95
IFIT5	interferon-induced protein with tetratricopeptide repeats 5	-6.43	-6.2	-2.95	-3.35
NDRG1	N-myc downstream regulated 1	-10.73	-12.44	1.37	1.15
MST1L	macrophage stimulating 1-like	-6.42	-6.51	-5.95	-4.66
GALM	galactose mutarotase (aldose 1-epimerase)	-5.83	-5.93	-3.48	-3.45
SLC2A9	solute carrier family 2 (facilitated glucose transporter), member 9	-3.56	-3.11	-3.15	-2.46
PLA2G2A	phospholipase A2, group IIA (platelets, synovial fluid)	-9.43	-9.54	1.07	1.43

KIAA0895	KIAA0895	-8.21	-9.51	1.09	1.02
GBP3	guanylate binding protein 3	-40.45	-39.73	-5.56	-4.63
FOXA2	forkhead box A2	-1.89	-2.56	-4.1	-3.65
UNC5CL	unc-5 homolog C (C. elegans)-like	-5.84	-5.3	-2.35	-2.15
CRYL1	crystallin, lambda 1	-23.19	-22.83	-6.79	-5.19
SIL1	SIL1 nucleotide exchange factor	-5.29	-5.27	-2.72	-2.54
CNGA1	cyclic nucleotide gated channel alpha 1	-9.45	-8.96	-7.24	-7.26
LIPG	lipase, endothelial	-4.34	-6.18	-5.09	-6.74
MPC1	mitochondrial pyruvate carrier 1	-13.47	-12.69	-5.64	-4.55
NR3C1	nuclear receptor subfamily 3, group C, member 1 (glucocorticoid receptor)	-4	-4.96	-1.53	-1.73
LYRM1	LYR motif containing 1	-7.73	-7.09	-4.87	-4.55
ARRDC3	arrestin domain containing 3	-18.76	-17.24	-1.02	-1.43
SGK1	serum/glucocorticoid regulated kinase 1	-14.59	-11.54	-2.38	-2.74
FBXO6	F-box protein 6	-6.52	-6.3	-1.32	-1.04
CHST13	carbohydrate (chondroitin 4) sulfotransferase 13	-10.98	-9.91	-10.5	-8.95
ST3GAL6	ST3 beta-galactoside alpha-2,3-sialyltransferase 6	-16.44	-17.14	-4.18	-4.01
CIDEB	cell death-inducing DFFA-like effector b	-9.43	-8.59	-5.83	-4.7
CREBRF	CREB3 regulatory factor	-7.08	-7.22	-2.96	-2.55
CD68	CD68 molecule	-4.96	-5.03	-3.04	-2.77
SLC51A	solute carrier family 51, alpha subunit	-25.29	-22.52	-6.75	-4.56
CCDC68	coiled-coil domain containing 68	-10.99	-11.36	-5.13	-5.13
DEPTOR	DEP domain containing MTOR-interacting protein	-11.98	-12.74	-2.05	-2.68
LPIN2	lipin 2	-10.45	-11.76	-6.13	-7.11
HIST1H2BD	histone cluster 1, H2bd	-3.13	-3.71	-3.15	-3.69
EFNA1	ephrin-A1	-27.9	-26.83	-3.53	-2.92
FOXA1	forkhead box A1	-20.11	-25.51	-5.24	-4.81
CIB1	calcium and integrin binding 1 (calmyrin)	-5.5	-5.79	-2.32	-1.97
VCAM1	vascular cell adhesion molecule 1	-16.43	-16.84	-7.65	-4.51
ACP2	acid phosphatase 2, lysosomal	-4.32	-4.26	-4.46	-4.35
S100A9	S100 calcium binding protein A9	-6.07	-5.56	-2.59	-2.71
ATXN1	ataxin 1	-8.25	-8.81	-1.23	-1.46
SEPP1	selenoprotein P, plasma, 1	-55.4	-59.08	-1.16	-1.02
GPR137B	G protein-coupled receptor 137B	-11.66	-8.5	-3.7	-4.2
CEBPD	CCAAT/enhancer binding protein (C/EBP), delta	-68.4	-61.31	-1.07	-1.21
CYP4X1	cytochrome P450, family 4, subfamily X, polypeptide 1	-11.78	-11.89	-5.51	-6.43
GLCE	glucuronic acid epimerase	-6.64	-7.03	-5.56	-6.15
HLA-B	major histocompatibility complex, class I, B	-6.44	-6.78	-2.19	-2.03
SLC1A1	solute carrier family 1 (neuronal/epithelial high affinity glutamate transporter, system Xag), member 1	-3.91	-5.08	-1.75	-1.62
CYP1A1	cytochrome P450, family 1, subfamily A, polypeptide 1	-19.78	-20.07	-1.31	-2.3
TSPAN8	tetraspanin 8	-35.78	-36.39	-15.04	-11.31
GPRC5C	G protein-coupled receptor, family C, group 5, member C	-5.65	-5.26	-1.17	-1.11
LINC00341	long intergenic non-protein coding RNA 341	-8.3	-9.36	-1.53	-2.16
CCL20	chemokine (C-C motif) ligand 20	-6.14	-6.08	-4.38	-4.66



SLC3A1	solute carrier family 3 (amino acid transporter heavy chain), member 1	-29.75	-26.24	1.07	1.66
ALPK2	alpha-kinase 2	-7.16	-8.92	1.43	1.58
DIO1	deiodinase, iodothyronine, type I	-156.4	-152.7	-10.17	-6.41
RNASE4	ribonuclease, RNase A family, 4	-252.1	-247.3	-9.75	-7.29
SERPINA3	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 3	-133.5	-139.1	-12.96	-9.44
NNMT	nicotinamide N-methyltransferase	-207.2	-197.8	-11.65	-15.31
HGD	homogentisate 1,2-dioxygenase	-126.4	-110.5	-14.62	-8.84
GHR	growth hormone receptor	-125.4	-169.3	-10.42	-8.42
AGT	angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	-100.8	-95.13	-13.82	-7.65
HSD17B2	hydroxysteroid (17-beta) dehydrogenase 2	-105.2	-100.9	-21.84	-20.93
AHSG	alpha-2-HS-glycoprotein	-258	-234	-9.15	-3.6
VTN	vitronectin	-126.6	-126.5	-7.57	-4.73
C5	complement component 5	-280.2	-248	-33.66	-15.25
TNFSF10	tumor necrosis factor (ligand) superfamily, member 10	-115.6	-113.6	-6.79	-5.22
CFI	complement factor I	-260.7	-248.4	-57.9	-23.94
ALDH1A1	aldehyde dehydrogenase 1 family, member A1	-391.7	-374.9	-3.85	-2.62
A1CF	APOBEC1 complementation factor	-110.2	-103.7	-43.98	-27.9
SERPINA1	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 1	-305.6	-291.7	-13.35	-7.22
CFB	complement factor B	-374.8	-369.2	-34.86	-19.57
FABP1	fatty acid binding protein 1, liver	-585.4	-565.4	-9.08	-8.88
MTTP	microsomal triglyceride transfer protein	-235.9	-221.1	-4.64	-3.21
A2M	alpha-2-macroglobulin	-284.9	-353	-7.35	-3.02
ASGR2	asialoglycoprotein receptor 2	-77.99	-79.75	-19.94	-14.2
ACMSD	aminocarboxymuconate semialdehyde decarboxylase	-87.32	-87.31	-38.72	-23.78
AKR1D1	aldo-keto reductase family 1, member D1	-417.1	-417.6	-22.99	-22.51
PLG	plasminogen	-337.5	-340.8	-51.4	-26.98
TM4SF4	transmembrane 4 L six family member 4	-104.1	-92.88	-13.68	-7.65
LEAP2	liver expressed antimicrobial peptide 2	-116.4	-104	-11.38	-9.41
RBP4	retinol binding protein 4, plasma	-415.3	-438.9	-2.49	-1.71
HPX	hemopexin	-77.35	-74.01	-30.25	-17.88
F2	coagulation factor II (thrombin)	-76.8	-63.58	-30.71	-23.29
CXCL2	chemokine (C-X-C motif) ligand 2	-406.5	-376.2	-77.89	-48.89
GSTA1	glutathione S-transferase alpha 1	-371.9	-368.8	-2.82	-2.25
SULT2A1	sulfotransferase family, cytosolic, 2A, dehydroepiandrosterone (DHEA)-preferring, member 1	-203	-196.6	-37.86	-25.94
FGL1	fibrinogen-like 1	-130	-125.7	-45.52	-13.97
SLC40A1	solute carrier family 40 (iron-regulated transporter), member 1	-144.6	-267.3	-1.31	-1.57
MBL2	mannose-binding lectin (protein C) 2, soluble	-308.4	-285.3	-39.52	-38.76
AMBP	alpha-1-microglobulin/bikunin precursor	-315.2	-302.8	-55.25	-22.52
TF	transferrin	-532.6	-523.2	-94.37	-14.16
APOA1	apolipoprotein A-I	-283.1	-338.2	-1.92	-1.42
APOC3	apolipoprotein C-III	-501.8	-464.8	-3.05	-1.8

SLC10A1	solute carrier family 10 (sodium/bile acid cotransporter), member 1	-42.46	-41.19	-17.36	-10.04
RNF128	ring finger protein 128, E3 ubiquitin protein ligase	-223.4	-205	-6.75	-4.46
GBA3	glucosidase, beta, acid 3	-101.7	-94.98	-14.87	-9.02
FGA	fibrinogen alpha chain	-693.7	-656	-2.07	-1.51
APOA2	apolipoprotein A-II	-313.3	-794.5	-1.93	-1.76
C3	complement component 3	-131.7	-143.5	-42.21	-27.2
RGN	regucalcin	-76.61	-71.01	-10.43	-8.07
CPS1	carbamoyl-phosphate synthase 1, mitochondrial	-155.1	-116.4	-10.28	-10.72
GBP1	guanylate binding protein 1, interferon-inducible	-110.6	-108.8	-31.16	-44.59
C8orf4	chromosome 8 open reading frame 4	-170	-161.5	-1.28	-1.92
SERPIND1	serpin peptidase inhibitor, clade D (heparin cofactor), member 1	-242.2	-246.7	-57.47	-36.95
FGG	fibrinogen gamma chain	-747.8	-786.6	-1.21	-1
ASGR1	asialoglycoprotein receptor 1	-97.49	-90.45	-14.74	-9.04
TTR	transthyretin	-160.9	-152.5	-1.09	1.06
FGB	fibrinogen beta chain	-886.4	-866.6	-1.2	-1.03
PROS1	protein S (alpha)	-107.2	-120.7	-4.75	-4
SERPINA5	serpin peptidase inhibitor, clade A (alpha-1 antiproteinase, antitrypsin), member 5	-62.73	-62.83	-25.33	-19.02
CLRN3	clarin 3	-63.31	-56.18	-10.39	-7.44
AKR1C3	aldo-keto reductase family 1, member C3	-62.37	-63.58	-10.2	-5.54
LIPC	lipase, hepatic	-97.13	-94.46	-23.72	-15.04
ANG	angiogenin, ribonuclease, RNase A family, 5	-188.1	-171.8	-33.1	-21.22
APOB	apolipoprotein B	-49.47	-48.9	-4.9	-3.21
AKR1C1	aldo-keto reductase family 1, member C1	-192.7	-163.1	-23.84	-9.07
ALDOB	aldolase B, fructose-bisphosphate	-398.8	-411.6	-49.12	-21.89
GJB2	gap junction protein, beta 2, 26kDa	-52.34	-49.24	-9.59	-9.76
ANPEP	alanyl (membrane) aminopeptidase	-78.05	-64.1	-4.93	-3.64
H19	H19, imprinted maternally expressed transcript (non-protein coding)	-48.9	-47.23	-32.44	-28.54
FMO5	flavin containing monooxygenase 5	-47.97	-45.37	-13.99	-8.87
SLC46A3	solute carrier family 46, member 3	-35.48	-53.26	-16.55	-16.01
TMEM56	transmembrane protein 56	-76.94	-74.2	-17.63	-14.89
ACSL5	acyl-CoA synthetase long-chain family member 5	-34.63	-33.82	-11.56	-12.44
C8B	complement component 8, beta polypeptide	-178.4	-161.3	-16.76	-10.52
LBP	lipopolysaccharide binding protein	-29.95	-26.69	-17.98	-7.69
TMEM176B	transmembrane protein 176B	-48.02	-49.09	-32.06	-27.06

**Table 10 Cluster group II: Mature liver functions**

Total number of genes: 447

*The list of 447 genes represents a cluster group II that is responsible for mature liver functions as described in chapter 3.4.2, Fig. 18. Column 1(from left to right) represents the gene symbol and column 2 represents the corresponding gene description. Column 3 and 4*



contain the fold change values of hHEPs vs. hESCs. Column 5 and 6 contain fold change values of hHEPs vs. HLCs. HLCs-total: the heterogeneous population of hepatocyte like cells; HLCs-island: hepatocyte like islands extracted from the heterogeneous population; hESCs: human embryonic stem cells; hHEPs: freshly isolated adult hepatocytes; vs.: versus.

Symbol	Description	hESC1	hESC2	HLCs-total	HLCs-islands
LOC100505985	uncharacterized LOC100505985	-10.64	-10.08	-10.64	-9.89
APOL1	apolipoprotein L, 1	-12.62	-12.58	-12.75	-12.84
FCN2	ficolin (collagen/fibrinogen domain containing lectin) 2	-11	-11.04	-10.22	-9.7
IYD	iodotyrosine deiodinase	-16.32	-16.56	-13.23	-13.04
GIMAP2	GTPase, IMAP family member 2	-11.93	-11.49	-10.97	-10.74
BDH1	3-hydroxybutyrate dehydrogenase, type 1	-12.83	-12.34	-11.41	-9.84
C14orf105	chromosome 14 open reading frame 105	-15.22	-14.62	-14.62	-14.54
MLXIPL	MLX interacting protein-like	-13.37	-13.64	-13.27	-10.94
PALMD	palmdelphin	-12.06	-11.31	-8.35	-8.01
NDRG2	NDRG family member 2	-11.09	-10.92	-7.63	-7.94
ABCA9	ATP-binding cassette, sub-family A (ABC1), member 9	-12.14	-11.22	-12.46	-12.45
LYZ	lysozyme	-10.82	-10.62	-10.36	-9.58
GNE	glucosamine (UDP-N-acetyl)-2-epimerase/N-acetylmannosamine kinase	-13.18	-11.63	-8.8	-9.96
IFI27	interferon, alpha-inducible protein 27	-10.17	-10.39	-9.55	-9.25
PRODH2	proline dehydrogenase (oxidase) 2	-11.34	-10.61	-10.08	-9.91
CD163	CD163 molecule	-13.14	-12.49	-12.57	-12.73
GREM2	gremlin 2, DAN family BMP antagonist	-10.34	-11.34	-10.94	-11.2
DCXR	dicarbonyl/L-xylulose reductase	-14.59	-14.01	-8.41	-7.2
S100A8	S100 calcium binding protein A8	-9.12	-8.93	-8.35	-8.21
KHK	ketoheokinase (fructokinase)	-13.62	-13.27	-15.07	-14.27
LOC283587	uncharacterized LOC283587	-11.06	-10.67	-10.58	-10.16
TBX15	T-box 15	-9.14	-9.89	-8.82	-8.35
ADHFE1	alcohol dehydrogenase, iron containing, 1	-10.59	-9.93	-8.35	-7.19
CTSS	cathepsin S	-12.36	-11.96	-12.18	-11.51
SELENBP1	selenium binding protein 1	-21.01	-19.67	-7.4	-6.61
N4BP2L1	NEDD4 binding protein 2-like 1	-13.62	-12.65	-8.3	-7.77
NFIA	nuclear factor I/A	-14.43	-13.87	-15.96	-15.4
DNAJC12	DnaJ (Hsp40) homolog, subfamily C, member 12	-13.38	-12.7	-13.38	-12.33
DNASE1L3	deoxyribonuclease I-like 3	-11.7	-12.18	-9.16	-8.73
LOC145837	uncharacterized LOC145837	-8.52	-8.73	-8.57	-8.1
C1QB	complement component 1, q subcomponent, B chain	-8.26	-7.93	-8.34	-8.13
LDHD	lactate dehydrogenase D	-12.75	-12.15	-9.9	-9.89

PIK3C2G	phosphatidylinositol-4-phosphate 3-kinase, catalytic subunit type 2 gamma	-12.49	-12.04	-10.52	-10.73
ETFDH	electron-transferring-flavoprotein dehydrogenase	-20.53	-22.43	-17.22	-16.95
SGK2	serum/glucocorticoid regulated kinase 2	-12.43	-12.54	-10.21	-9.8
HLA-DRA	major histocompatibility complex, class II, DR alpha	-12.27	-11.64	-9.57	-9.43
ABCC6	ATP-binding cassette, sub-family C (CFTR/MRP), member 6	-15.14	-15.08	-13.03	-11.52
PXMP2	peroxisomal membrane protein 2, 22kDa	-16.74	-17.02	-21.86	-20.96
C11orf96	chromosome 11 open reading frame 96	-15.81	-16.16	-6.84	-9.37
LOC730102	quinone oxidoreductase-like protein 2 pseudogene	-18.99	-18.17	-20.3	-19.15
IFI44	interferon-induced protein 44	-8.17	-8.33	-7.47	-7.5
SELE	selectin E	-13.6	-13.04	-13.5	-13.03
DUSP10	dual specificity phosphatase 10	-7.73	-10.53	-11.22	-13.1
TRPM8	transient receptor potential cation channel, subfamily M, member 8	-10.72	-9.77	-10.63	-10.51
MYOM1	myomesin 1	-8.38	-8.09	-8.05	-8.97
CA5A	carbonic anhydrase VA, mitochondrial	-18.45	-18.41	-19.01	-17.16
SLC22A7	solute carrier family 22 (organic anion transporter), member 7	-12.91	-12.81	-7.97	-5.62
CSAD	cysteine sulfinic acid decarboxylase	-28.54	-30.69	-14.67	-12.12
XAF1	XIAP associated factor 1	-13.39	-13.03	-13.03	-12.53
ADRB2	adrenoceptor beta 2, surface	-7.65	-7.46	-9.92	-10.05
FMO4	flavin containing monooxygenase 4	-11.51	-10.94	-6.31	-6.39
CYP7B1	cytochrome P450, family 7, subfamily B, polypeptide 1	-9.07	-8.63	-9.33	-8.57
MARC2	mitochondrial amidoxime reducing component 2	-20.62	-20.25	-18.81	-16.39
PROZ	protein Z, vitamin K-dependent plasma glycoprotein	-17.67	-18.69	-14.97	-10.79
SYTL4	synaptotagmin-like 4	-20.27	-20.03	-18.66	-17.42
FAH	fumarylacetoacetate hydrolase (fumarylacetoacetase)	-30.52	-31.15	-9.12	-9.14
EPHX1	epoxide hydrolase 1, microsomal (xenobiotic)	-6.93	-7.59	-8.92	-8.67
GADD45B	growth arrest and DNA-damage-inducible, beta	-14.54	-17.68	-6.23	-8.55
CPEB3	cytoplasmic polyadenylation element binding protein 3	-28.03	-26.79	-14.53	-16.19
GPLD1	glycosylphosphatidylinositol specific phospholipase D1	-9.9	-8.95	-9.62	-9.57
SLC41A2	solute carrier family 41 (magnesium transporter), member 2	-16.03	-15.53	-13.58	-13.96
ENTPD5	ectonucleoside triphosphate diphosphohydrolase 5	-10.91	-11.08	-11.04	-8.51
ALAS1	aminolevulinate, delta-, synthase 1	-16.76	-17.26	-10.04	-9.86
RORC	RAR-related orphan receptor C	-13.48	-12.68	-12.15	-11.1
NADK2	NAD kinase 2, mitochondrial	-28.61	-27.65	-14.36	-14.51
ASB9	ankyrin repeat and SOCS box containing 9	-11.5	-10.2	-13.41	-12.45
SLC17A1	solute carrier family 17 (organic anion transporter), member 1	-8.28	-7.98	-7.86	-7.89
CYP4A11	cytochrome P450, family 4, subfamily A, polypeptide 11	-9.69	-10.74	-10.82	-10.68
RTP3	receptor (chemosensory) transporter protein 3	-8.31	-8.05	-8.46	-8.18

SLC6A12	solute carrier family 6 (neurotransmitter transporter), member 12	-7.27	-6.95	-6.75	-6.06
CYP2A7	cytochrome P450, family 2, subfamily A, polypeptide 7	-7.47	-6.41	-9.21	-7.13
CD1D	CD1d molecule	-5.19	-7.89	-10.38	-11.6
CYP27A1	cytochrome P450, family 27, subfamily A, polypeptide 1	-12.56	-12.51	-8.35	-8.23
ACTR3C	ARP3 actin-related protein 3 homolog C (yeast)	-12.23	-11.67	-11.93	-11.54
NR1I2	nuclear receptor subfamily 1, group I, member 2	-12.47	-12.57	-13.64	-13.24
F8	coagulation factor VIII, procoagulant component	-7.11	-6.95	-7.73	-7.78
ANO1	anoctamin 1, calcium activated chloride channel	-9.67	-9.58	-9.08	-9.14
CES2	carboxylesterase 2	-17.77	-17.96	-15.41	-16.25
PHYH	phytanoyl-CoA 2-hydroxylase	-22.22	-22.15	-11.08	-9.73
SHBG	sex hormone-binding globulin	-6.58	-6.25	-6.66	-6.17
XDH	xanthine dehydrogenase	-10.41	-9.59	-9.81	-9.02
METTL7A	methyltransferase like 7A	-21.88	-14.93	-7.49	-9.01
HBB	hemoglobin, beta	-8.47	-8.07	-6.77	-6
LOC150381	uncharacterized LOC150381	-13.57	-12.16	-15.77	-14.93
INHBB	inhibin, beta B	-18.21	-15.93	-5.52	-6.61
TPRG1	tumor protein p63 regulated 1	-7.95	-7.68	-7.45	-7.42
CLDN14	claudin 14	-8.83	-9.23	-10.01	-10.4
HRSP12	heat-responsive protein 12	-11.78	-11.34	-23.05	-19.72
LOC100507577	uncharacterized LOC100507577	-26.99	-26.95	-11.37	-10.17
PFKFB1	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 1	-7.37	-7.33	-7.02	-6.23
DAO	D-amino-acid oxidase	-7.56	-7.4	-10.08	-10.35
MUT	methylmalonyl CoA mutase	-15.4	-14.53	-9.8	-8.86
CYP2A6	cytochrome P450, family 2, subfamily A, polypeptide 6	-11.39	-11.78	-12.37	-11.49
PNPO	pyridoxamine 5'-phosphate oxidase	-8.69	-9.39	-8.09	-9.47
GCKR	glucokinase (hexokinase 4) regulator	-19.55	-18.31	-19.1	-13.86
ART4	ADP-ribosyltransferase 4 (Dombrock blood group)	-8.69	-8.34	-4.41	-4.92
C19orf80	chromosome 19 open reading frame 80	-15.57	-15.87	-11.93	-11.68
ATF5	activating transcription factor 5	-19.56	-21.11	-28.77	-27.05
FUOM	fucose mutarotase	-8.89	-10.51	-12.34	-10.23
C1QC	complement component 1, q subcomponent, C chain	-7.63	-7.12	-6.92	-6.4
TSLP	thymic stromal lymphopoietin	-16.11	-16.17	-15.81	-19.11
ADIRF	adipogenesis regulatory factor	-16.53	-17.02	-18.51	-16.48
ACADL	acyl-CoA dehydrogenase, long chain	-20.65	-20.12	-19.71	-18.87
HNMT	histamine N-methyltransferase	-11.3	-10.42	-10.29	-8.58
TTPA	tocopherol (alpha) transfer protein	-14.96	-14.91	-15.93	-14.71
CXCL13	chemokine (C-X-C motif) ligand 13	-10.94	-10.91	-8.19	-8.25
SDS	serine dehydratase	-14.72	-14.44	-13.87	-13.1
PC	pyruvate carboxylase	-13.89	-14.38	-9.1	-10.41
F7	coagulation factor VII (serum prothrombin conversion accelerator)	-13.77	-12.89	-5.05	-5.27
SORBS2	sorbin and SH3 domain containing 2	-27.49	-25.39	-10.25	-14.45
SLC22A3	solute carrier family 22 (organic cation transporter), member 3	-5.92	-9.97	-7.37	-5.24

MLIP	muscular LMNA-interacting protein	-16.06	-15.1	-13.86	-12.02
TMEM220	transmembrane protein 220	-13.43	-11.42	-21.28	-15.85
RARRES3	retinoic acid receptor responder (tazarotene induced) 3	-15.48	-13.32	-7.13	-7.48
CPED1	cadherin-like and PC-esterase domain containing 1	-10.3	-10.2	-3.32	-3.45
RBP5	retinol binding protein 5, cellular	-16.53	-16.2	-17.49	-16.43
ABCG8	ATP-binding cassette, sub-family G (WHITE), member 8	-5.97	-5.24	-6.69	-6.64
KAT2B	K(lysine) acetyltransferase 2B	-31.74	-31.49	-4.69	-5.5
NR0B2	nuclear receptor subfamily 0, group B, member 2	-14.56	-12.58	-14.53	-14.22
PECR	peroxisomal trans-2-enoyl-CoA reductase	-22.54	-18.35	-15.64	-11.24
FXYD1	FXYD domain containing ion transport regulator 1	-14.8	-13.58	-15.36	-16.25
OGDHL	oxoglutarate dehydrogenase-like	-11.95	-11.61	-15.79	-16.15
CTSO	cathepsin O	-11.73	-11.84	-6.88	-7.97
ZNF385B	zinc finger protein 385B	-17.54	-16.88	-17.22	-16.9
STEAP3	STEAP family member 3, metalloreductase	-7.44	-7.95	-12.95	-14.76
ALDH6A1	aldehyde dehydrogenase 6 family, member A1	-25.59	-25.96	-6.69	-5.97
CYP4F12	cytochrome P450, family 4, subfamily F, polypeptide 12	-14.94	-14.19	-13.05	-11.95
NFIC	nuclear factor I/C (CCAAT-binding transcription factor)	-7.7	-7.69	-6.47	-7.13
ABCC2	ATP-binding cassette, sub-family C (CFTR/MRP), member 2	-24.71	-25.69	-8.92	-5.47
C1orf168	chromosome 1 open reading frame 168	-30.02	-29.21	-5.93	-4.29
CYP4F11	cytochrome P450, family 4, subfamily F, polypeptide 11	-8.29	-7.97	-7.84	-7.7
MASP2	mannan-binding lectin serine peptidase 2	-14.94	-14.19	-13.54	-13.36
CPS1-IT1	CPS1 intronic transcript 1 (non-protein coding)	-8.68	-8.5	-8.28	-7.48
IGFALS	insulin-like growth factor binding protein, acid labile subunit	-7.57	-7.36	-7.32	-6.94
ASL	argininosuccinate lyase	-18.34	-20.28	-29.58	-21.36
S1PR1	sphingosine-1-phosphate receptor 1	-14.71	-14.12	-3.62	-4.37
SLC47A1	solute carrier family 47 (multidrug and toxin extrusion), member 1	-19.18	-19.68	-9.6	-11.1
TYROBP	TYRO protein tyrosine kinase binding protein	-10.39	-9.78	-6.83	-6.74
CAPN3	calpain 3, (p94)	-10.39	-10.39	-8.25	-7.58
ZBTB20	zinc finger and BTB domain containing 20	-22.83	-21.48	-10.93	-8.89
SKAP1	src kinase associated phosphoprotein 1	-16	-15.86	-13.43	-11.01
MFSD2A	major facilitator superfamily domain containing 2A	-6.5	-6.42	-9.99	-10.46
PDK4	pyruvate dehydrogenase kinase, isozyme 4	-31.23	-28.19	-10.87	-14.91
METTL7B	methyltransferase like 7B	-17.95	-17.95	-9.44	-7.63
UGT2B17	UDP glucuronosyltransferase 2 family, polypeptide B17	-7.3	-7.28	-6.09	-6.77
MAFB	v-maf avian musculoaponeurotic fibrosarcoma oncogene homolog B	-10.91	-12.64	-7.05	-9.78
CPN1	carboxypeptidase N, polypeptide 1	-19.51	-19.61	-10.85	-8.4
FCN3	ficolin (collagen/fibrinogen domain containing) 3	-6.64	-6.9	-3.71	-3.15
ALDH4A1	aldehyde dehydrogenase 4 family, member A1	-7.21	-6.75	-9.45	-9.71
ARL5B-AS1	ARL5B antisense RNA 1	-31.54	-31.4	-10.43	-8.54
ECHDC2	enoyl CoA hydratase domain containing 2	-46.29	-43.82	-11.71	-9.61

SERPINF2	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 2	-41.11	-42.46	-15.05	-12.13
ASS1	argininosuccinate synthase 1	-32.46	-33.67	-39.34	-29.9
NFIB	nuclear factor I/B	-9.03	-9.7	-19.34	-17.57
GADD45G	growth arrest and DNA-damage-inducible, gamma	-38.28	-40.04	-15.44	-12.48
GSAP	gamma-secretase activating protein	-38.85	-36.85	-27.63	-24.73
CNTN3	contactin 3 (plasmacytoma associated)	-32.69	-31.65	-11.38	-9.1
IFIT1	interferon-induced protein with tetratricopeptide repeats 1	-28.75	-25.56	-4.36	-3.96
SEC16B	SEC16 homolog B ( <i>S. cerevisiae</i> )	-6.52	-6.51	-6.76	-6.77
PLCG2	phospholipase C, gamma 2 (phosphatidylinositol-specific)	-6.53	-6.17	-7.47	-7.45
AR	androgen receptor	-9.48	-8.76	-16.01	-15.58
RCL1	RNA terminal phosphate cyclase-like 1	-6.57	-6.39	-15.84	-15.2
DEFB1	defensin, beta 1	-25.08	-25.81	-10.57	-7.3
EGR1	early growth response 1	-26.17	-13.45	-6.4	-23.5
FOSB	FBJ murine osteosarcoma viral oncogene homolog B	-6.19	-5.8	-5.72	-6.13
ABCB1	ATP-binding cassette, sub-family B (MDR/TAP), member 1	-15.19	-14.22	-14.09	-14.17
ASPA	aspartoacylase	-23.33	-22.63	-18.58	-17.16
SRD5A2	steroid-5-alpha-reductase, alpha polypeptide 2 (3-oxo-5 alpha-steroid delta 4-dehydrogenase alpha 2)	-18.38	-16.67	-17.82	-16.47
TTC38	tetratricopeptide repeat domain 38	-10.72	-11.09	-8.19	-7.18
ACSM3	acyl-CoA synthetase medium-chain family member 3	-27.98	-27.31	-16.98	-15.24
SMOC1	SPARC related modular calcium binding 1	-6.25	-5.96	-4.93	-5.06
DHODH	dihydroorotate dehydrogenase (quinone)	-8.7	-8.84	-12.16	-11.33
EGR2	early growth response 2	-16.57	-11.48	-6.11	-13.89
ACOX1	acyl-CoA oxidase 1, palmitoyl	-13.56	-13.96	-10.14	-11.13
AHR	aryl hydrocarbon receptor	-17.95	-16.93	-13.27	-16.13
HLA-DPA1	major histocompatibility complex, class II, DP alpha 1	-9.36	-8.92	-8.08	-6.96
MAOA	monoamine oxidase A	-28.67	-30.46	-6.04	-4.67
ONECUT2	one cut homeobox 2	-7.25	-7.67	-10.92	-9.79
APOC1	apolipoprotein C-I	-17.1	-21.55	-4.88	-3.64
LYSMD2	LysM, putative peptidoglycan-binding, domain containing 2	-6.51	-6.23	-12.72	-13.22
EPHX2	epoxide hydrolase 2, cytoplasmic	-47.58	-46.79	-16.71	-13.35
MT1G	metallothionein 1G	-22.5	-22.43	-24.8	-20.42
PAQR9	progesterin and adipoQ receptor family member IX	-8.53	-7.82	-18.28	-17.55
TRIM55	tripartite motif containing 55	-11.02	-10.84	-1.52	-1.7
GATM	glycine amidinotransferase (L-arginine:glycine amidinotransferase)	-24.45	-27.27	-11.11	-8.62
ALDH5A1	aldehyde dehydrogenase 5 family, member A1	-17.61	-16.52	-6.17	-6.81
CLU	clusterin	-31.58	-28.84	-17.16	-16.87
ABLIM3	actin binding LIM protein family, member 3	-8	-7.59	-6.1	-5.59
ST6GAL1	ST6 beta-galactosamide alpha-2,6-sialyltransferase 1	-7.77	-7.81	-13.1	-12.86
ANGPTL4	angiopoietin-like 4	-12.43	-13.04	-7.62	-9.56

ARSE	arylsulfatase E	-6.03	-8.67	-8.89	-7.57
ACOX2	acyl-CoA oxidase 2, branched chain	-27.21	-32.09	-23.58	-21.19
CLDN1	claudin 1	-30.85	-29.62	-19.2	-14.7
SHMT1	serine hydroxymethyltransferase 1 (soluble)	-6.68	-7.4	-15.64	-12.58
IL1RAP	interleukin 1 receptor accessory protein	-39.21	-38.71	-17.3	-15.66
TNFSF14	tumor necrosis factor (ligand) superfamily, member 14	-7.44	-6.93	-7.72	-7.84
ALDH2	aldehyde dehydrogenase 2 family (mitochondrial)	-17.16	-18.71	-7.31	-7.42
GLS2	glutaminase 2 (liver, mitochondrial)	-20.73	-18.09	-29.23	-27.49
ACADSB	acyl-CoA dehydrogenase, short/branched chain	-18.44	-23.26	-34.16	-26.39
JUN	jun proto-oncogene	-15.13	-15.68	-3.46	-4.17
NUPR1	nuclear protein, transcriptional regulator, 1	-29.44	-30.46	-17.77	-12.39
PLA1A	phospholipase A1 member A	-24.22	-22.57	-17.22	-16.17
PRAP1	proline-rich acidic protein 1	-30.05	-29.52	-17.4	-13.56
NSUN6	NOP2/Sun domain family, member 6	-10.54	-11.21	-12.86	-9.01
SLC17A3	solute carrier family 17 (organic anion transporter), member 3	-8.21	-7.26	-6.82	-6.81
BCO2	beta-carotene oxygenase 2	-27.26	-25.1	-2.33	-2.34
GOLT1A	golgi transport 1A	-21.61	-21.41	-16.56	-11.17
TMEM176A	transmembrane protein 176A	-23.74	-22.76	-10.25	-8.75
HYAL1	hyaluronoglucosaminidase 1	-25.17	-23.81	-23.3	-19.13
LGALS4	lectin, galactoside-binding, soluble, 4	-25.86	-24.28	-5.78	-4.96
ZMAT1	zinc finger, matrin-type 1	-9.64	-10.24	-11.35	-10.98
TM4SF5	transmembrane 4 L six family member 5	-30.39	-31.6	-8.14	-4.63
CUX2	cut-like homeobox 2	-11.68	-12.33	-45.71	-41.21
ABCA5	ATP-binding cassette, sub-family A (ABC1), member 5	-43.74	-34.48	-17.08	-12.85
ENPEP	glutamyl aminopeptidase (aminopeptidase A)	-39.39	-42.81	-5.82	-8.71
GPX2	glutathione peroxidase 2 (gastrointestinal)	-13.17	-14.96	-5.55	-5.2
OAS1	2'-5'-oligoadenylate synthetase 1, 40/46kDa	-8.2	-7.95	-7.71	-7.13
ABAT	4-aminobutyrate aminotransferase	-76.75	-72.14	-9.88	-9.47
SYBU	syntabulin (syntaxin-interacting)	-38.78	-36.76	-20.72	-22.5
KLF9	Kruppel-like factor 9	-22.5	-22.61	-3.37	-3.72
NR4A2	nuclear receptor subfamily 4, group A, member 2	-4.61	-5.83	-10.54	-10.23
CDO1	cysteine dioxygenase type 1	-27.54	-23.9	-29.56	-29.84
MT1F	metallothionein 1F	-9.7	-10.13	-12.11	-8.72
NMRK1	nicotinamide riboside kinase 1	-12.35	-14.95	-6.68	-6.28
UGT2A3	UDP glucuronosyltransferase 2 family, polypeptide A3	-28.01	-25.61	-24.06	-22.62
SULT1E1	sulfotransferase family 1E, estrogen-preferring, member 1	-29.4	-28.25	-12.04	-8.95
ABHD6	abhydrolase domain containing 6	-10.94	-14.99	-7.75	-8.08
GSDMB	gasdermin B	-16.3	-16.82	-8.13	-4.67
NEAT1	nuclear paraspeckle assembly transcript 1 (non-protein coding)	-26.59	-25.62	-11.82	-9.62
AGXT2	alanine--glyoxylate aminotransferase 2	-28.61	-27.27	-13.02	-9.74
HPN	hepsin	-29.59	-31.25	-12.39	-9.63
GRB14	growth factor receptor-bound protein 14	-8.95	-6.91	-86.97	-76.1
SLC27A2	solute carrier family 27 (fatty acid transporter), member 2	-65.05	-54.17	-17.61	-17.37

DECR1	2,4-dienoyl CoA reductase 1, mitochondrial	-11.76	-11.53	-6.65	-5.96
PBLD	phenazine biosynthesis-like protein domain containing	-45.2	-41.07	-20.61	-14.55
INHBE	inhibin, beta E	-5.48	-6.41	-45.62	-52.55
ECM2	extracellular matrix protein 2, female organ and adipocyte specific	-29.69	-30.23	-17.15	-10.37
SULT1A1	sulfotransferase family, cytosolic, 1A, phenol-preferring, member 1	-56.5	-51.54	-4.4	-3.73
SERPINF1	serpin peptidase inhibitor, clade F (alpha-2 antiplasmin, pigment epithelium derived factor), member 1	-56.78	-62.94	-1.51	-1.4
MAOB	monoamine oxidase B	-32.42	-31.09	-13.83	-12.96
UPB1	ureidopropionase, beta	-44.65	-45.9	-42.03	-35.24
ALDH1L1	aldehyde dehydrogenase 1 family, member L1	-42.39	-38.38	-37.03	-35.41
CYP2J2	cytochrome P450, family 2, subfamily J, polypeptide 2	-49.08	-46.64	-38.33	-34.11
PRG4	proteoglycan 4	-32.02	-31.66	-33.6	-32.06
CYP7A1	cytochrome P450, family 7, subfamily A, polypeptide 1	-34.61	-34.41	-35.66	-36.68
F11	coagulation factor XI	-34.68	-36.16	-36.41	-34.44
ITIH4	inter-alpha-trypsin inhibitor heavy chain family, member 4	-46.25	-43.49	-40.3	-32.75
CYP3A43	cytochrome P450, family 3, subfamily A, polypeptide 43	-29.05	-26.77	-29.48	-28.6
ACOT12	acyl-CoA thioesterase 12	-41.43	-37.4	-38.5	-35.3
CPN2	carboxypeptidase N, polypeptide 2	-39.94	-41.38	-37.92	-34.37
GRAMD1C	GRAM domain containing 1C	-55.14	-53.7	-29.74	-31.11
IDO2	indoleamine 2,3-dioxygenase 2	-30.84	-30.14	-29.02	-29.01
SERPINA4	serpin peptidase inhibitor, clade A (alpha-1 antitrypsin, antitrypsin), member 4	-38.04	-36.52	-32.08	-29.55
APOA5	apolipoprotein A-V	-27.65	-27.17	-21.23	-19.67
TTC36	tetratricopeptide repeat domain 36	-40.7	-38.97	-38.42	-34.77
SRGN	serglycin	-43.4	-39.59	-28.68	-42.7
TFR2	transferrin receptor 2	-47.93	-45.73	-50.45	-45.28
AKR7A3	aldo-keto reductase family 7, member A3 (aflatoxin aldehyde reductase)	-32.8	-33.57	-22.49	-22.64
GLYATL1	glycine-N-acyltransferase-like 1	-38.98	-37.86	-42.43	-36.09
CCL16	chemokine (C-C motif) ligand 16	-25.37	-24.71	-25.31	-23.29
GLYAT	glycine-N-acyltransferase	-30.97	-30.23	-30.28	-27.38
NR1I3	nuclear receptor subfamily 1, group I, member 3	-36.63	-36.06	-34.2	-28.88
CSTA	cystatin A (stefin A)	-51.15	-46.11	-48.71	-52.51
SLC25A47	solute carrier family 25, member 47	-30.79	-31.45	-34.26	-32.74
LEPR	leptin receptor	-40.24	-40.22	-18.96	-18.25
HAO2	hydroxyacid oxidase 2 (long chain)	-24.25	-22.93	-26.49	-25.19
C5orf27	chromosome 5 open reading frame 27	-30.01	-28.17	-28.22	-26.3
F12	coagulation factor XII (Hageman factor)	-74.08	-65.96	-57.3	-49.35
BLNK	B-cell linker	-55.56	-56.32	-27.65	-35.68
C8G	complement component 8, gamma polypeptide	-24.23	-23.44	-26.37	-28.37
G6PC	glucose-6-phosphatase, catalytic subunit	-43.9	-41.62	-34.97	-28.98
DMGDH	dimethylglycine dehydrogenase	-43.11	-46.65	-58.71	-58.29



CYP2B6	cytochrome P450, family 2, subfamily B, polypeptide 6	-24	-23	-25.77	-27.83
SLC17A2	solute carrier family 17, member 2	-60.09	-59.84	-58.11	-53.38
THRSP	thyroid hormone responsive	-38.7	-36.27	-38.45	-36.14
LOC100507389	uncharacterized LOC100507389	-21.52	-21.16	-20.78	-20.59
LRG1	leucine-rich alpha-2-glycoprotein 1	-70.56	-62.68	-51.37	-39.13
CYP1A2	cytochrome P450, family 1, subfamily A, polypeptide 2	-32.45	-31.79	-30.58	-29.74
HAL	histidine ammonia-lyase	-34.06	-31.1	-32.63	-30.39
CYP2C18	cytochrome P450, family 2, subfamily C, polypeptide 18	-65.91	-62.28	-60.54	-58.21
CYP4V2	cytochrome P450, family 4, subfamily V, polypeptide 2	-71.2	-69.39	-67.54	-70.36
LINC01018	long intergenic non-protein coding RNA 1018	-36	-34.19	-39.26	-36.29
HLF	hepatic leukemia factor	-42.57	-41.53	-38.56	-36.97
RUNDC3B	RUN domain containing 3B	-35.55	-32.72	-41.3	-40.41
NAT8	N-acetyltransferase 8 (GCN5-related, putative)	-29.16	-29.22	-26.02	-24.49
CNDP1	carnosine dipeptidase 1 (metallopeptidase M20 family)	-23.68	-20.26	-25.12	-22.46
RAPGEF4	Rap guanine nucleotide exchange factor (GEF) 4	-30.84	-31.25	-32.87	-33.76
AOX1	aldehyde oxidase 1	-67.79	-71.74	-55.84	-55.86
IGF1	insulin-like growth factor 1 (somatomedin C)	-21.12	-20.24	-16.4	-17.14
TCEA3	transcription elongation factor A (SII), 3	-54.19	-53.92	-43.9	-40.32
C1S	complement component 1, s subcomponent	-111.6	-101.7	-47.32	-41.83
RDH16	retinol dehydrogenase 16 (all-trans)	-43.99	-40.09	-41.6	-41.04
SERPINA6	serpin peptidase inhibitor, clade A (alpha-1 antitrypsin), member 6	-65.52	-62.57	-56.42	-40.21
FETUB	fetuin B	-62.95	-61.4	-62.91	-51.4
PGLYRP2	peptidoglycan recognition protein 2	-50.77	-53.06	-54.34	-52.74
ABCB4	ATP-binding cassette, sub-family B (MDR/TAP), member 4	-48.63	-44.07	-46.73	-48.59
HMGCS2	3-hydroxy-3-methylglutaryl-CoA synthase 2 (mitochondrial)	-78.79	-84.64	-36.11	-46.7
ETNPPL	ethanolamine-phosphate phospho-lyase	-26.61	-34.18	-79.52	-76.35
LPA	lipoprotein, Lp(a)	-78.35	-76.86	-68.75	-54.42
SLC25A18	solute carrier family 25 (glutamate carrier), member 18	-25.65	-25.43	-19.57	-14.5
HHEX	hematopoietically expressed homeobox	-11.86	-21.73	-52.19	-48.18
CAT	catalase	-78.84	-71.61	-75.08	-73.19
ADH6	alcohol dehydrogenase 6 (class V)	-58.36	-55.83	-54.27	-51.25
GPR88	G protein-coupled receptor 88	-20.41	-19.53	-22.6	-21.55
PPARGC1A	peroxisome proliferator-activated receptor gamma, coactivator 1 alpha	-34.42	-36.81	-42.25	-41.83
CYP2B7P1	cytochrome P450, family 2, subfamily B, polypeptide 7 pseudogene 1	-14.85	-14.1	-16.61	-14.82
GAS2	growth arrest-specific 2	-60.76	-57.41	-48.04	-47.08
HGFAC	HGF activator	-19.91	-18.9	-20.46	-19.39
KNG1	kininogen 1	-92.68	-93.46	-59.06	-33.49
HFE2	hemochromatosis type 2 (juvenile)	-75.3	-71.39	-86.12	-80.26
PROC	protein C (inactivator of coagulation factors Va and VIIIa)	-61.44	-58.48	-45.16	-34.7



CYP39A1	cytochrome P450, family 39, subfamily A, polypeptide 1	-33.3	-33.71	-32.17	-30.26
NAT2	N-acetyltransferase 2 (arylamine N-acetyltransferase)	-35.87	-31.58	-31.73	-31.44
MYRIP	myosin VIIA and Rab interacting protein	-18.06	-17.54	-30.61	-30.46
CYP4F2	cytochrome P450, family 4, subfamily F, polypeptide 2	-46.85	-50.44	-47.5	-46.39
FBP1	fructose-1,6-bisphosphatase 1	-71.81	-67.22	-53.45	-45.49
SLC27A5	solute carrier family 27 (fatty acid transporter), member 5	-22.43	-21.34	-35.48	-36.52
KMO	kynurenine 3-monooxygenase (kynurenine 3-hydroxylase)	-56.92	-54.99	-50.91	-51.25
C1R	complement component 1, r subcomponent	-161.9	-156.9	-56.33	-52.88
SERPINA10	serpin peptidase inhibitor, clade A (alpha-1 antitrypsin), member 10	-128.9	-129.7	-98.24	-58.88
MAT1A	methionine adenosyltransferase I, alpha	-66.33	-61.5	-23.5	-17.37
FTCD	formimidoyltransferase cyclodeaminase	-21.1	-20.66	-17.63	-14.41
NT5E	5'-nucleotidase, ecto (CD73)	-28.37	-26.09	-16.17	-23.18
CYP3A7	cytochrome P450, family 3, subfamily A, polypeptide 7	-65.22	-59.46	-21.87	-22.06
AGXT	alanine-glyoxylate aminotransferase	-60.04	-58.24	-64.87	-62.8
PLSCR4	phospholipid scramblase 4	-38.37	-56.4	-9.3	-10.52
HOGA1	4-hydroxy-2-oxoglutarate aldolase 1	-18.16	-17.67	-14.38	-13.65
EVA1A	eva-1 homolog A (C. elegans)	-36.71	-34.94	-12.54	-14.18
PPP1R3C	protein phosphatase 1, regulatory subunit 3C	-52.48	-49.48	-39.57	-40.23
PZP	pregnancy-zone protein	-16.39	-14.37	-14.61	-11
EHHADH	enoyl-CoA, hydratase/3-hydroxyacyl CoA dehydrogenase	-79.92	-82.83	-50.62	-45.68
C2	complement component 2	-21.36	-21.73	-22.49	-20.72
AKR1C2	aldo-keto reductase family 1, member C2	-30.54	-30.34	-19.12	-16.64
HABP2	hyaluronan binding protein 2	-24.45	-24.14	-21.28	-21.1
PROX1	prospero homeobox 1	-41.68	-40	-33.62	-33.18
BBOX1	butyrobetaine (gamma), 2-oxoglutarate dioxygenase (gamma-butyrobetaine hydroxylase) 1	-77.63	-78.25	-67.99	-68.24
SLC38A4	solute carrier family 38, member 4	-123.5	-113.7	-121.7	-122.64
SLC30A10	solute carrier family 30, member 10	-39	-37.35	-26.63	-21.94
CYP2C19	cytochrome P450, family 2, subfamily C, polypeptide 19	-48.24	-39.84	-49.26	-49.31
LOC100130232	LP2209	-76.69	-71.61	-71.02	-72.51
IGJ	immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	-20.26	-20.33	-20.32	-20.59
KLKB1	kallikrein B, plasma (Fletcher factor) 1	-17.91	-17.24	-103.9	-87.92
CYP3A5	cytochrome P450, family 3, subfamily A, polypeptide 5	-121.2	-117.6	-58.51	-40.2
A1BG	alpha-1-B glycoprotein	-122.1	-119.7	-34.12	-29.16
ECHDC3	enoyl CoA hydratase domain containing 3	-32.37	-31.36	-39.22	-36.69
RARRES2	retinoic acid receptor responder (tazarotene induced) 2	-47.82	-37.67	-27.22	-29.93
PIPOX	pipecolic acid oxidase	-19.21	-16.28	-107	-103.65

APOM	apolipoprotein M	-45.9	-40.42	-11.97	-9.31
FOLH1	folate hydrolase (prostate-specific membrane antigen) 1	-94.86	-91.66	-88.26	-87
NR1H4	nuclear receptor subfamily 1, group H, member 4	-41.79	-37.98	-36.35	-31.27
LOC201651	arylacetamide deacetylase (esterase) pseudogene	-19.58	-17.98	-19.2	-19.13
LCAT	lecithin-cholesterol acyltransferase	-27.88	-27.47	-22.81	-19.76
ACSL1	acyl-CoA synthetase long-chain family member 1	-54.65	-43.88	-12.03	-12.13
ZGPAT	zinc finger, CCCH-type with G patch domain	-25.64	-28.68	-37.2	-35.22
AGTR1	angiotensin II receptor, type 1	-30.7	-30.37	-15.06	-14.7
SERPINA7	serpin peptidase inhibitor, clade A (alpha-1 antitrypsin), member 7	-129.4	-136.9	-86.13	-38.43
SERPING1	serpin peptidase inhibitor, clade G (C1 inhibitor), member 1	-86.56	-77.48	-13.62	-11.71
FOS	FBJ murine osteosarcoma viral oncogene homolog	-33.18	-28.5	-9.66	-19.23
LINC00261	long intergenic non-protein coding RNA 261	-11.06	-20.92	-16.98	-11.56
SLC13A5	solute carrier family 13 (sodium-dependent citrate transporter), member 5	-63.96	-62.08	-14.1	-10.06
AKR1C4	aldo-keto reductase family 1, member C4	-276.2	-290.3	-256.2	-243.1
APCS	amyloid P component, serum	-212.6	-216	-192.7	- 189.68
GYS2	glycogen synthase 2 (liver)	-230.7	-213	-220.5	- 211.45
HRG	histidine-rich glycoprotein	-259.9	-255.4	-192.4	- 118.31
CYP2C9	cytochrome P450, family 2, subfamily C, polypeptide 9	-167	-155.5	-164.4	- 152.22
CRP	C-reactive protein, pentraxin-related	-177.8	-172.1	-183.5	- 172.22
CFHR2	complement factor H-related 2	-226.6	-226.2	-186.1	- 189.57
CD14	CD14 molecule	-169.4	-166.8	-152.9	- 145.14
HAO1	hydroxyacid oxidase (glycolate oxidase) 1	-172.1	-162	-173.3	- 164.23
ALDH8A1	aldehyde dehydrogenase 8 family, member A1	-390.7	-374.1	-235.9	-132.7
CFHR5	complement factor H-related 5	-201.8	-193.5	-199	- 195.11
APOF	apolipoprotein F	-269.8	-268.3	-266	- 255.78
ACSM5	acyl-CoA synthetase medium-chain family member 5	-130.7	-125.9	-115.7	- 118.74
CYP3A4	cytochrome P450, family 3, subfamily A, polypeptide 4	-127.5	-119.3	-101.7	-94.97
LINC00844	long intergenic non-protein coding RNA 844	-254.9	-255.4	-259	- 256.09
SLCO1B3	solute carrier organic anion transporter family, member 1B3	-131.8	-132.1	-125.4	- 120.19
C4BPA	complement component 4 binding protein, alpha	-119.8	-108	-111.6	- 106.78
VNN1	vanin 1	-149.4	-150.6	-157.3	- 152.04
DPYS	dihydropyrimidinase	-248	-251	-265.5	- 252.43

SLC22A1	solute carrier family 22 (organic cation transporter), member 1	-111.5	-122.1	-137.1	-
LECT2	leukocyte cell-derived chemotaxin 2	-97.66	-95.61	-104	-97.3
CFH	complement factor H	-385.7	-392.5	-403.6	-
AZGP1	alpha-2-glycoprotein 1, zinc-binding	-337.4	-319.6	-341	-
PON1	paraoxonase 1	-208.9	-210.8	-73.58	-50.57
AFM	afamin	-111.2	-109.3	-100.7	-89.27
HSD11B1	hydroxysteroid (11-beta) dehydrogenase 1	-198.8	-193.6	-213.6	-
ABCA8	ATP-binding cassette, sub-family A (ABC1), member 8	-151.6	-149.8	-75.09	-
ADH1C	alcohol dehydrogenase 1C (class I), gamma polypeptide	-285.3	-269.3	-260.4	-
FMO3	flavin containing monooxygenase 3	-332.2	-320.9	-290.2	-
ANXA10	annexin A10	-119.9	-117.1	-114.3	-
CYP2C8	cytochrome P450, family 2, subfamily C, polypeptide 8	-591.8	-644.4	-656	-
ADH4	alcohol dehydrogenase 4 (class II), pi polypeptide	-607.6	-590	-250.5	-
C3P1	complement component 3 precursor pseudogene	-91.91	-88.56	-102.8	-
CPB2	carboxypeptidase B2 (plasma)	-350.1	-337	-292.9	-
ITIH2	inter-alpha-trypsin inhibitor heavy chain 2	-191	-171	-102.9	-47.61
AMDHD1	amidohydrolase domain containing 1	-190.9	-196.9	-155.9	-
LINC01093	long intergenic non-protein coding RNA 1093	-90.55	-85.96	-91.73	-89.93
BAAT	bile acid CoA: amino acid N-acyltransferase (glycine N-choloyltransferase)	-121.9	-129.2	-103.7	-92.98
F9	coagulation factor IX	-520.4	-498.2	-521.2	-
C6	complement component 6	-144.8	-134.2	-104.2	-78.35
AADAC	arylacetamide deacetylase	-183.2	-167.3	-152.7	-
HSD17B6	hydroxysteroid (17-beta) dehydrogenase 6	-106.7	-109.7	-289.4	-
SLC6A1	solute carrier family 6 (neurotransmitter transporter), member 1	-94.42	-98.89	-111.2	-
ITIH3	inter-alpha-trypsin inhibitor heavy chain 3	-328.6	-365.8	-203.5	-
C9	complement component 9	-548.8	-539.7	-595.4	-
ADH1B	alcohol dehydrogenase 1B (class I), beta polypeptide	-448.3	-439.3	-472.3	-
BHMT2	betaine--homocysteine S-methyltransferase 2	-118.6	-120.3	-120.9	-122.4
CYP2E1	cytochrome P450, family 2, subfamily E, polypeptide 1	-426.2	-413.8	-376.3	-
UGT2B15	UDP glucuronosyltransferase 2 family, polypeptide B15	-184.4	-188.2	-181.7	-
ADH1A	alcohol dehydrogenase 1A (class I), alpha	-510.3	-508.2	-524	-

	polypeptide				<b>501.91</b>
PON3	paraoxonase 3	<b>-153.7</b>	<b>-151.7</b>	<b>-144.2</b>	- <b>143.04</b>
TDO2	tryptophan 2,3-dioxygenase	<b>-519.7</b>	<b>-470.7</b>	<b>-114.5</b>	<b>-80.77</b>
HAMP	hepcidin antimicrobial peptide	<b>-282.5</b>	<b>-286</b>	<b>-246</b>	- <b>228.01</b>
ARG1	arginase 1	<b>-395</b>	<b>-375.2</b>	<b>-323.2</b>	- <b>182.63</b>
TAT	tyrosine aminotransferase	<b>-96.27</b>	<b>-90.67</b>	<b>-98.94</b>	<b>-88.98</b>
SLCO1B1	solute carrier organic anion transporter family, member 1B1	<b>-109.1</b>	<b>-102.8</b>	<b>-109.7</b>	<b>-99.16</b>
UGT2B4	UDP glucuronosyltransferase 2 family, polypeptide B4	<b>-726.6</b>	<b>-678.5</b>	<b>-670.7</b>	- <b>506.34</b>
AQP9	aquaporin 9	<b>-59.76</b>	<b>-55.11</b>	<b>-54.02</b>	<b>-50.21</b>
CYP8B1	cytochrome P450, family 8, subfamily B, polypeptide 1	<b>-134.2</b>	<b>-129.4</b>	<b>-125.1</b>	- <b>109.76</b>
BCHE	butyrylcholinesterase	<b>-187</b>	<b>-189.7</b>	<b>-211.1</b>	- <b>236.46</b>
ORM2	orosomucoid 2	<b>-447.7</b>	<b>-435</b>	<b>-256.6</b>	<b>-98.94</b>
HPR	haptoglobin-related protein	<b>-195.5</b>	<b>-190.6</b>	<b>-141.7</b>	- <b>101.01</b>
C8A	complement component 8, alpha polypeptide	<b>-123.6</b>	<b>-113.1</b>	<b>-67.35</b>	<b>-52.88</b>
GC	group-specific component (vitamin D binding protein)	<b>-1396</b>	<b>-1332</b>	<b>-1425</b>	- <b>1374.7</b>
SLC2A2	solute carrier family 2 (facilitated glucose transporter), member 2	<b>-286.7</b>	<b>-280.6</b>	<b>-189.8</b>	- <b>116.47</b>
APOH	apolipoprotein H (beta-2-glycoprotein I)	<b>-737.7</b>	<b>-726.7</b>	<b>-532.6</b>	- <b>235.61</b>
PAH	phenylalanine hydroxylase	<b>-533.3</b>	<b>-487.2</b>	<b>-390</b>	- <b>300.18</b>
F5	coagulation factor V (proaccelerin, labile factor)	<b>-102.3</b>	<b>-101.2</b>	<b>-89.22</b>	<b>-71.43</b>
ANGPTL3	angiopoietin-like 3	<b>-302.2</b>	<b>-283.9</b>	<b>-247.3</b>	<b>-81.1</b>
GNMT	glycine N-methyltransferase	<b>-81.81</b>	<b>-73.2</b>	<b>-76.19</b>	<b>-68.07</b>
C4BPB	complement component 4 binding protein, beta	<b>-126.7</b>	<b>-126.6</b>	<b>-110.9</b>	<b>-67.87</b>
SERPINC1	serpin peptidase inhibitor, clade C (antithrombin), member 1	<b>-438.8</b>	<b>-424</b>	<b>-131.7</b>	<b>-67.33</b>
OTC	ornithine carbamoyltransferase	<b>-70.31</b>	<b>-66</b>	<b>-56.79</b>	<b>-49.85</b>
MT1M	metallothionein 1M	<b>-215.9</b>	<b>-222.7</b>	<b>-197.1</b>	- <b>155.47</b>
HPD	4-hydroxyphenylpyruvate dioxygenase	<b>-102.8</b>	<b>-95.26</b>	<b>-75.42</b>	<b>-79.18</b>
ITIH1	inter-alpha-trypsin inhibitor heavy chain 1	<b>-129.1</b>	<b>-123.3</b>	<b>-76.63</b>	<b>-49.16</b>
IGFBP1	insulin-like growth factor binding protein 1	<b>-305.5</b>	<b>-305.4</b>	<b>-295.1</b>	- <b>280.47</b>
ABCA6	ATP-binding cassette, sub-family A (ABC1), member 6	<b>-77.47</b>	<b>-73.43</b>	<b>-77.81</b>	<b>-70.96</b>
ABCG5	ATP-binding cassette, sub-family G (WHITE), member 5	<b>-66.08</b>	<b>-75.53</b>	<b>-72.64</b>	<b>-73.93</b>
SPP2	secreted phosphoprotein 2, 24kDa	<b>-71.22</b>	<b>-61.37</b>	<b>-57.74</b>	<b>-64.26</b>
F13B	coagulation factor XIII, B polypeptide	<b>-135.4</b>	<b>-132</b>	<b>-122.7</b>	<b>-76.5</b>
CP	ceruloplasmin (ferroxidase)	<b>-150.9</b>	<b>-146.5</b>	<b>-147.7</b>	- <b>111.99</b>
BHMT	betaine--homocysteine S-methyltransferase	<b>-107.7</b>	<b>-104</b>	<b>-75.49</b>	<b>-74.06</b>

ALB	albumin	-1744	-1738	-190.6	-38.11
PCK1	phosphoenolpyruvate carboxykinase 1 (soluble)	-999.4	-990	-22.61	-47.15
HP	haptoglobin	-613.4	-684.1	-150.3	-62.24
ORM1	orosomucoid 1	-1060	-978.4	-65.28	-14.19

**Table 11 Cluster group III: Proliferation process**

Total number of genes: 1,562

*The list of 1,562 genes represents a cluster group III that is responsible for proliferation process as described in chapter 3.4.3, Fig. 18. Column 1(from left to right) represents the gene symbol and column 2 represents the corresponding gene description. Column 3 and 4 contain the fold change values of hHEPs vs. hESCs. Column 5 and 6 contain fold change values of hHEPs vs. HLCs. HLCs-total: the heterogeneous population of hepatocyte like cells; HLCs-island: hepatocyte like islands extracted from the heterogeneous population; hESCs: human embryonic stem cells; hHEPs: freshly isolated adult hepatocytes; vs.: versus.*

Symbol	Description	hESC1	hESC2	HLCs-total	HLCs-islands
TDP1	tyrosyl-DNA phosphodiesterase 1	3.21	3.36	1.45	1.36
ZMYND8	zinc finger, MYND-type containing 8	3.13	3.22	1.34	1.38
DROSHA	drosha, ribonuclease type III	2.8	3	1.41	1.15
XPO5	exportin 5	3.08	3	1.21	1.22
NCL	nucleolin	3.29	3.39	1.2	1.19
IPO11	importin 11	2.97	3.06	1.16	1.11
CCNF	cyclin F	3.81	3.63	1.5	1.29
TTF1	transcription termination factor, RNA polymerase I	2.85	2.92	1.35	1.52
SSRP1	structure specific recognition protein 1	3.89	3.6	1.46	1.35
WDR75	WD repeat domain 75	3.52	3.12	1.02	1.05
SLIRP	SRA stem-loop interacting RNA binding protein	3.86	3.83	1.06	1.21
DIMT1	DIM1 dimethyladenosine transferase 1 homolog (S. cerevisiae)	3.33	3.2	1.35	1.3
MAK16	MAK16 homolog (S. cerevisiae)	3.84	3.8	1.2	1.26
KIF1A	kinesin family member 1A	3.96	3.52	1.13	1.13
ATIC	5-aminoimidazole-4-carboxamide ribonucleotide formyltransferase/IMP cyclohydrolase	3.41	3.59	1.11	1.21
CPSF3	cleavage and polyadenylation specific factor 3, 73kDa	3.67	3.83	1.15	1.19

POLD3	polymerase (DNA-directed), delta 3, accessory subunit	2.97	3.27	1.26	1.2
HNRNPC	heterogeneous nuclear ribonucleoprotein C (C1/C2)	3.35	3.75	-1.01	1.07
DSN1	DSN1, MIS12 kinetochore complex component	2.77	2.75	1.31	1.1
HENMT1	HEN1 methyltransferase homolog 1 (Arabidopsis)	2.52	3.02	1.24	1.25
CRLF3	cytokine receptor-like factor 3	3.83	3.75	1.35	1.14
NUP155	nucleoporin 155kDa	3.35	3.38	1.34	1.35
WDR12	WD repeat domain 12	3.93	4.07	1.14	1.15
TK1	thymidine kinase 1, soluble	4.18	3.99	1.49	1.51
FAM155A	family with sequence similarity 155, member A	3.63	4.06	1.32	1.26
LSM2	LSM2 homolog, U6 small nuclear RNA associated (S. cerevisiae)	2.9	2.59	1.34	1.29
MGME1	mitochondrial genome maintenance exonuclease 1	3.8	4.03	1.17	1.08
PSMC3IP	PSMC3 interacting protein	4.18	4.03	1.07	1.05
IPO5	importin 5	4.03	4.25	1.32	1.34
PAK1	p21 protein (Cdc42/Rac)-activated kinase 1	3.26	3.81	1.41	1.48
HEATR1	HEAT repeat containing 1	4.33	4.48	1.36	1.3
CENPN	centromere protein N	4.05	4.08	1.11	1.05
SNRNP40	small nuclear ribonucleoprotein 40kDa (U5)	3.89	3.73	1.45	1.44
MRPL47	mitochondrial ribosomal protein L47	3.02	2.96	1.11	1.26
C14orf169	chromosome 14 open reading frame 169	4.23	4.25	1.52	1.33
UBE3D	ubiquitin protein ligase E3D	3.24	2.96	1.05	1.16
NUDT21	nudix (nucleoside diphosphate linked moiety X)-type motif 21	3.46	3.34	1.53	1.58
TCF19	transcription factor 19	4.19	4.01	1.69	1.78
C17orf75	chromosome 17 open reading frame 75	2.98	3.18	-1.03	1.08
CAD	carbamoyl-phosphate synthetase 2, aspartate transcarbamylase, and dihydroorotase	2.88	2.88	1.16	1.21
GNL3	guanine nucleotide binding protein-like 3 (nucleolar)	3.22	2.97	1.56	1.8
XPO1	exportin 1 (CRM1 homolog, yeast)	4.34	4.46	1.5	1.25
NUP54	nucleoporin 54kDa	3.38	3.4	-1	1.05
RNPS1	RNA binding protein S1, serine-rich domain	3.63	3.79	1.55	1.51
GTF3C2	general transcription factor IIIC, polypeptide 2, beta 110kDa	3.35	3.4	1.56	1.53
USP10	ubiquitin specific peptidase 10	4.11	3.63	1.77	1.6
METTL21A	methyltransferase like 21A	3.08	3.43	-1.08	1.01
SRSF3	serine/arginine-rich splicing factor 3	3.19	3.35	1.11	-1.13
GGCT	gamma-glutamylcyclotransferase	2.63	2.93	1.26	1.31
SMARCAD1	SWI/SNF-related, matrix-associated actin-dependent regulator of chromatin, subfamily a, containing DEAD/H box 1	4.13	3.68	1.19	1.41
RAD51	RAD51 recombinase	3.46	3.53	1.85	1.77
TMEM178B	transmembrane protein 178B	3.48	4.03	1.49	1.48
LOC100289092	uncharacterized LOC100289092	2.75	3.02	1.07	1.11
ILF3	interleukin enhancer binding factor 3, 90kDa	3.64	3.54	1.37	1.22
EXOSC9	exosome component 9	4.9	5.12	1.22	1.37
CHCHD3	coiled-coil-helix-coiled-coil-helix domain containing 3	4.07	4.32	-1.01	-1.02
SNRPF	small nuclear ribonucleoprotein polypeptide F	4.39	4.39	1.12	1.04

DEK	DEK oncogene	4.21	4.23	-1.12	1.05
UBLCP1	ubiquitin-like domain containing CTD phosphatase 1	3.5	3.4	1.09	1.17
AEN	apoptosis enhancing nuclease	3.42	3.73	1.18	1.07
APEX1	APEX nuclease (multifunctional DNA repair enzyme) 1	3.82	3.82	1.45	1.54
GNL2	guanine nucleotide binding protein-like 2 (nucleolar)	3.9	4.01	1.58	1.9
NOLC1	nucleolar and coiled-body phosphoprotein 1	3.27	2.99	1.03	1.09
PPT1	palmitoyl-protein thioesterase 1	4.15	4.24	1.35	1.17
MTMR9	myotubularin related protein 9	2.66	2.86	1.44	1.26
RBBP4	retinoblastoma binding protein 4	2.65	2.7	1.11	1.14
UBR5	ubiquitin protein ligase E3 component n-recogin 5	2.23	2.4	1.19	1.13
BYSL	bystin-like	3.73	3.61	1.26	1.26
SIX4	SIX homeobox 4	2.84	3.08	1.75	1.61
DDX21	DEAD (Asp-Glu-Ala-Asp) box helicase 21	4.55	4.51	1	1.16
TCF3	transcription factor 3	3.94	4.09	1.82	1.66
ZNF551	zinc finger protein 551	2.93	3.28	1.17	1.09
CDC123	cell division cycle 123	4.5	4.36	1.28	1.33
YTHDF2	YTH domain family, member 2	3.69	3.71	1.29	1.07
QSER1	glutamine and serine rich 1	2.7	2.74	-1.02	-1.08
DDX20	DEAD (Asp-Glu-Ala-Asp) box polypeptide 20	4.06	4.16	1.11	-1.07
DTYMK	deoxythymidylate kinase (thymidylate kinase)	4.69	4.58	1.41	1.25
TGIF1	TGFB-induced factor homeobox 1	4.27	3.99	1.46	1.12
XPOT	exportin, tRNA	3.48	3.38	1.51	1.36
NUP107	nucleoporin 107kDa	4.33	4.4	-1.12	1.03
PSMD11	proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	2.83	2.89	1.14	1.25
YARS2	tyrosyl-tRNA synthetase 2, mitochondrial	2.98	3.03	1.01	-1.07
TCF7L1	transcription factor 7-like 1 (T-cell specific, HMG-box)	4.34	4.04	1.81	1.73
URB2	URB2 ribosome biogenesis 2 homolog (S. cerevisiae)	3.5	3.77	1.36	1.22
FAXC	failed axon connections homolog (Drosophila)	2.87	3.14	1.22	1.23
PNO1	partner of NOB1 homolog (S. cerevisiae)	3.37	3.4	-1.01	-1.15
R3HDM1	R3H domain containing 1	3.28	3.35	1.03	1.01
NME1	NME/NM23 nucleoside diphosphate kinase 1	4.15	4.13	-1.17	-1.21
KIAA0020	KIAA0020	3.44	3.05	-1.18	1.08
TCERG1	transcription elongation regulator 1	3.81	3.78	1.56	1.79
ZNF184	zinc finger protein 184	3	2.88	1.51	1.37
POLA2	polymerase (DNA directed), alpha 2, accessory subunit	3.8	3.7	1.47	1.41
MRPL3	mitochondrial ribosomal protein L3	3.3	3.4	1.23	1.3
ZNF567	zinc finger protein 567	2.6	2.59	1.52	1.79
RPA1	replication protein A1, 70kDa	2.81	2.77	1.65	1.49
NOP16	NOP16 nucleolar protein	4.73	4.68	1.17	1.19
ESCO2	establishment of sister chromatid cohesion N-acetyltransferase 2	4.52	4.37	1.3	1.31
ZNF286A	zinc finger protein 286A	3.02	3.15	1.55	1.5
MAD2L2	MAD2 mitotic arrest deficient-like 2 (yeast)	3.23	2.98	1.38	1.39



SAAL1	serum amyloid A-like 1	4.91	4.98	1.42	1.42
PARP1	poly (ADP-ribose) polymerase 1	3.96	4.29	1.03	-1.15
DNMT3A	DNA (cytosine-5-)-methyltransferase 3 alpha	4.32	4.66	1.47	1.4
UPF3B	UPF3 regulator of nonsense transcripts homolog B (yeast)	2.84	2.78	-1.21	-1.09
HSPH1	heat shock 105kDa/110kDa protein 1	4.29	3.58	1.06	1.09
ANP32A	acidic (leucine-rich) nuclear phosphoprotein 32 family, member A	3.54	3.51	1.47	1.28
HTATSF1	HIV-1 Tat specific factor 1	2.82	2.63	1.41	1.3
CCT7	chaperonin containing TCP1, subunit 7 (eta)	4.34	4.29	1.72	1.64
C1orf109	chromosome 1 open reading frame 109	3.7	4.06	2.13	1.93
LRR1	leucine rich repeat protein 1	4.74	4.84	-1.13	-1.12
CCDC88C	coiled-coil domain containing 88C	3.08	3.25	1.14	1.13
CPVL	carboxypeptidase, vitellogenic-like	3.08	2.98	1.26	1.31
NAA15	N(alpha)-acetyltransferase 15, NatA auxiliary subunit	4.3	4.19	-1.21	-1.08
SNN	stannin	3.4	3.57	1.85	1.64
TRIM28	tripartite motif containing 28	4.66	4.18	1.88	1.86
STRBP	spermatid perinuclear RNA binding protein	3.02	3.42	1.18	1.11
NARS	asparaginyI-tRNA synthetase	3.19	2.91	1.34	1.35
ACVR2B	activin A receptor, type IIB	3.14	3.24	2.16	1.93
SRM	spermidine synthase	4.46	4.13	1.09	1.17
SNRPB2	small nuclear ribonucleoprotein polypeptide B	3.49	3.53	1.59	1.64
GTF3C4	general transcription factor IIIC, polypeptide 4, 90kDa	3.96	4.44	1.98	1.87
HNRNPD	heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)	4.35	4.5	-1.16	-1.26
ABI2	abl-interactor 2	2.77	2.98	2.02	1.94
HNRNPM	heterogeneous nuclear ribonucleoprotein M	4.08	3.92	-1.29	-1.41
MATR3	matrin 3	3.26	3.16	1.49	1.41
PDSS1	prenyl (decaprenyl) diphosphate synthase, subunit 1	4.56	4.29	-1.05	1.18
C10orf137	chromosome 10 open reading frame 137	3.68	3.81	1.45	1.53
PWWP2A	PWWP domain containing 2A	2.22	2.27	1.27	1.21
CCT3	chaperonin containing TCP1, subunit 3 (gamma)	4.07	4.12	1.24	1.27
GRPEL2	GrpE-like 2, mitochondrial (E. coli)	3.26	3.32	1.76	1.69
SMNDC1	survival motor neuron domain containing 1	3.49	3.36	1.41	1.27
PRMT5	protein arginine methyltransferase 5	5.38	5.28	1.55	1.63
FAM213B	family with sequence similarity 213, member B	2.36	2.62	1.09	1.06
PHIP	pleckstrin homology domain interacting protein	3.1	2.98	1.35	1.78
WRN	Werner syndrome, RecQ helicase-like	2.4	2.49	-1.15	-1.08
KNSTRN	kinetochore-localized astrin/SPAG5 binding protein	3.94	3.6	1.48	1.38
NVL	nuclear VCP-like	3.14	3.23	1.34	1.5
PHF5A	PHD finger protein 5A	4.39	4.45	1.54	1.48
CPSF2	cleavage and polyadenylation specific factor 2, 100kDa	3.89	3.9	1.04	-1.11
GAR1	GAR1 ribonucleoprotein	4.34	4.33	1.15	1.13
LSM7	LSM7 homolog, U6 small nuclear RNA associated (S. cerevisiae)	2.69	2.45	1.29	1.46
NIF3L1	NIF3 NGG1 interacting factor 3-like 1 (S. cerevisiae)	2.65	2.62	-1.05	-1.08



TMEM35	transmembrane protein 35	3.23	3.48	1.6	1.53
PPAP2C	phosphatidic acid phosphatase type 2C	4.46	4.41	1.03	1.2
NOP56	NOP56 ribonucleoprotein	5.89	5.47	1.16	1.18
SAC3D1	SAC3 domain containing 1	2.39	2.69	1.62	1.39
RNASEH1-AS1	RNASEH1 antisense RNA 1	4.11	4.34	-1.11	-1.07
GIN54	GIN5 complex subunit 4 (Sld5 homolog)	3.81	4.13	1.38	1.39
CCDC137	coiled-coil domain containing 137	3.54	3.5	1.21	1.24
SLC6A15	solute carrier family 6 (neutral amino acid transporter), member 15	4.32	4.81	1.69	1.68
PFDN4	prefoldin subunit 4	3.97	4	1.91	1.86
NDC1	NDC1 transmembrane nucleoporin	4.68	4.87	-1.24	-1.26
RLN2	relaxin 2	2.71	3.27	1.41	1.48
HNRNPDL	heterogeneous nuclear ribonucleoprotein D-like	2.53	2.55	-1.06	-1.02
ZNF146	zinc finger protein 146	3	2.72	1.24	1.25
NIFK	nucleolar protein interacting with the FHA domain of MKI67	3.94	3.82	1.05	1.14
TAF5	TAF5 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 100kDa	3.23	3.18	1.11	1.05
CDC45	cell division cycle 45	4.42	4.8	1.33	1.49
DCAF12L1	DDB1 and CUL4 associated factor 12-like 1	3.77	4.17	1.44	1.68
RRAS2	related RAS viral (r-ras) oncogene homolog 2	3.07	2.78	1.09	1.04
LOC100996481	DNA primase large subunit-like	2.27	2.09	1.3	1.33
TARS	threonyl-tRNA synthetase	4.07	4.03	1.2	-1.01
AGPAT5	1-acylglycerol-3-phosphate O-acyltransferase 5	3.87	3.81	-1.35	-1.54
PRR11	proline rich 11	4.93	4.76	1.77	1.37
FANCG	Fanconi anemia, complementation group G	3.32	3.44	1.2	1.17
STX6	syntaxin 6	3.2	3.42	1.96	1.64
HNRNPR	heterogeneous nuclear ribonucleoprotein R	2.95	2.93	1.46	1.33
NIP7	NIP7, nucleolar pre-rRNA processing protein	3.4	3.86	1.07	-1.27
PAICS	phosphoribosylaminoimidazole carboxylase, phosphoribosylaminoimidazole succinocarboxamide synthetase	4.2	4.32	1.05	-1.12
ZNF678	zinc finger protein 678	3.1	3.02	1.22	1.37
RBBP8	retinoblastoma binding protein 8	3.67	3.37	-1.4	-1.26
NOL7	nucleolar protein 7, 27kDa	3.38	3.33	1.35	1.3
HAUS6	HAUS augmin-like complex, subunit 6	3.28	3.15	-1.24	-1.19
KCMF1	potassium channel modulatory factor 1	2.6	2.74	1.44	1.36
SART3	squamous cell carcinoma antigen recognized by T cells 3	2.5	2.44	1.05	-1.1
ZNF721	zinc finger protein 721	3.44	3.67	-1.34	-1.01
C4orf21	chromosome 4 open reading frame 21	2.91	2.67	-1.05	1.02
PRKD3	protein kinase D3	3.94	3.48	1.51	1.46
BRIP1	BRCA1 interacting protein C-terminal helicase 1	3.69	4.1	-1.05	1.01
CHAF1A	chromatin assembly factor 1, subunit A (p150)	5.6	5.18	1.01	-1.07
ACOT7	acyl-CoA thioesterase 7	2.43	2.36	-1.16	-1.23
HSPA4	heat shock 70kDa protein 4	3.8	3.53	1.15	1.2
JADE1	jade family PHD finger 1	3.17	3.5	1.14	-1.07
INA	internexin neuronal intermediate filament protein, alpha	3.85	4.06	1.73	1.48

G3BP1	GTPase activating protein (SH3 domain) binding protein 1	4.07	3.75	-1.12	-1.44
ZNF398	zinc finger protein 398	2.75	3.07	1.49	1.38
TSR1	TSR1, 20S rRNA accumulation, homolog (S. cerevisiae)	5.46	5.21	-1.26	-1.35
SUCLA2	succinate-CoA ligase, ADP-forming, beta subunit	3.77	3.42	1.29	1.36
CSNK1E	casein kinase 1, epsilon	2.41	2.5	1.64	1.46
ADNP2	ADNP homeobox 2	2.5	2.78	-1.04	-1.29
LSM4	LSM4 homolog, U6 small nuclear RNA associated (S. cerevisiae)	2.37	2.16	1.07	-1.05
USP1	ubiquitin specific peptidase 1	5.37	5.15	1.36	1.23
GABBR1	gamma-aminobutyric acid (GABA) B receptor, 1	3.53	3.21	1.87	2.15
TOP2B	topoisomerase (DNA) II beta 180kDa	3.29	3.25	1.22	1.36
RQCD1	RCD1 required for cell differentiation1 homolog (S. pombe)	3.21	3.21	1.56	1.45
BUB3	BUB3 mitotic checkpoint protein	2.87	2.84	1.46	1.33
MCM8	minichromosome maintenance complex component 8	2.61	2.54	-1.14	-1.11
DTD1	D-tyrosyl-tRNA deacylase 1	5.63	5.85	-1.2	-1.28
HNRNPAB	heterogeneous nuclear ribonucleoprotein A/B	6.17	6.11	1.14	1.01
RNF138	ring finger protein 138, E3 ubiquitin protein ligase	5.05	5.68	1.04	-1.08
ASUN	asunder spermatogenesis regulator	2.87	2.77	-1.21	-1.27
CASC5	cancer susceptibility candidate 5	2.96	2.63	1.38	1.31
NUDT1	nudix (nucleoside diphosphate linked moiety X)-type motif 1	5.18	4.98	-1.04	-1.18
ZNF589	zinc finger protein 589	2.92	3.05	1.54	1.66
DUT	deoxyuridine triphosphatase	4.67	4.84	1.18	-1.02
---		3.12	3.24	1.3	1.44
DCTPP1	dCTP pyrophosphatase 1	2.68	2.9	1.02	1.07
MYBL2	v-myb avian myeloblastosis viral oncogene homolog-like 2	3.64	3.58	-1.06	-1.09
LOC645321	uncharacterized LOC645321	2.96	2.82	1.15	1.24
BRCA1	breast cancer 1, early onset	2.43	2.52	-1.14	-1.16
ATAD5	ATPase family, AAA domain containing 5	2.83	2.38	1.49	1.74
PRPF38A	pre-mRNA processing factor 38A	2.61	2.64	-1.05	-1.19
TBC1D31	TBC1 domain family, member 31	3.17	2.94	-1.19	-1.26
APITD1	apoptosis-inducing, TAF9-like domain 1	4.36	4.43	-1.24	-1.31
CARM1	coactivator-associated arginine methyltransferase 1	2.79	2.99	1.37	1.32
DFFA	DNA fragmentation factor, 45kDa, alpha polypeptide	2.6	2.64	1.7	1.57
KIF21B	kinesin family member 21B	3.31	3.84	2.36	2.16
PTBP1	polypyrimidine tract binding protein 1	3.46	3.31	1.23	1.12
QTRTD1	queuine tRNA-ribosyltransferase domain containing 1	3.94	4.44	-1.42	-1.68
TOX	thymocyte selection-associated high mobility group box	2.14	2.73	1.15	-1.02
CCAR1	cell division cycle and apoptosis regulator 1	3.1	2.99	-1.29	-1.08
DDX39A	DEAD (Asp-Glu-Ala-Asp) box polypeptide 39A	6.01	5.81	-1.41	-1.22
WDR76	WD repeat domain 76	1.91	2.16	-1.04	-1.04
MRPS23	mitochondrial ribosomal protein S23	2.83	2.65	1.16	1.27

FBL	fibrillarlin	4.81	4.88	1.71	1.59
KIAA1586	KIAA1586	3.83	3.89	1.54	2.09
HMGAI	high mobility group AT-hook 1	3.06	3.05	1.32	1.32
NAA25	N(alpha)-acetyltransferase 25, NatB auxiliary subunit	2.41	2.45	1.3	1.36
CHRNAS	cholinergic receptor, nicotinic, alpha 5 (neuronal)	4.05	4.73	1.25	1.2
LARS	leucyl-tRNA synthetase	3.85	3.59	1.46	1.19
RFC2	replication factor C (activator 1) 2, 40kDa	2.7	2.66	-1.26	-1.4
PDCD2L	programmed cell death 2-like	5.01	5.15	1.21	1.3
SPRY1	sprouty homolog 1, antagonist of FGF signaling (Drosophila)	4.7	4.6	1.39	-1.07
POLD1	polymerase (DNA directed), delta 1, catalytic subunit	3.06	3.09	1.98	1.94
RBM15	RNA binding motif protein 15	2.87	2.95	1.08	-1.12
HMGXB4	HMG box domain containing 4	2.79	2.79	1.44	1.35
DENR	density-regulated protein	3.65	3.54	1.56	1.51
ARHGAP11A	Rho GTPase activating protein 11A	2.87	2.82	-1.08	-1.17
CDK4	cyclin-dependent kinase 4	4.13	3.89	1.84	1.89
CCDC77	coiled-coil domain containing 77	2.73	2.96	-1.2	-1.27
DRAXIN	dorsal inhibitory axon guidance protein	3.22	3.43	-1.11	-1.14
CELSR3	cadherin, EGF LAG seven-pass G-type receptor 3	2.3	2.61	1.84	1.91
RPRD1A	regulation of nuclear pre-mRNA domain containing 1A	2.44	2.09	1.08	1.09
TGS1	trimethylguanosine synthase 1	2.79	2.96	-1.03	-1.06
CEP68	centrosomal protein 68kDa	2.33	2.53	1.05	-1.1
HMGB3	high mobility group box 3	4.26	4.01	-1.19	-1.41
LRRTM4	leucine rich repeat transmembrane neuronal 4	1.93	2.19	1.39	1.36
SYT6	synaptotagmin VI	3.6	4.18	1.48	1.41
TRIM65	tripartite motif containing 65	2.75	2.47	1.57	1.4
C1QBP	complement component 1, q subcomponent binding protein	4.14	4	-1.3	-1.34
RRM1	ribonucleotide reductase M1	4	3.96	1.54	1.37
SFPQ	splicing factor proline/glutamine-rich	5.15	4.98	-1.08	-1.43
NUP43	nucleoporin 43kDa	2.17	2.13	1.28	1.16
TROAP	trophinin associated protein	2.94	2.69	1.6	1.65
YLP1	YLP motif containing 1	2.5	2.69	1.17	-1.03
GSG2	germ cell associated 2 (haspin)	3.36	3.34	1.37	1.51
PPRC1	peroxisome proliferator-activated receptor gamma, coactivator-related 1	3.45	3.76	-1.09	-1.25
ALMS1	Alstrom syndrome 1	4.12	4.31	-1.48	-1.65
CTDSPL2	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase like 2	3.18	3.16	1.64	1.56
PSMA4	proteasome (prosome, macropain) subunit, alpha type, 4	3.21	3.59	1.42	1.74
RUVBL1	RuvB-like AAA ATPase 1	5.25	5.38	-1.05	-1.07
NXPE3	neurexophilin and PC-esterase domain family, member 3	2.73	2.87	1.77	1.52
CEP152	centrosomal protein 152kDa	2.46	2.34	1.04	1.01
HSPA14	heat shock 70kDa protein 14	3.11	3.12	-1.4	-1.34
VBPI	von Hippel-Lindau binding protein 1	3.28	2.97	1.32	1.27

ACACA	acetyl-CoA carboxylase alpha	3.59	3.79	1.01	-1.07
UNG	uracil-DNA glycosylase	5.27	5.86	-1.3	-1.47
ZNF260	zinc finger protein 260	2.87	2.65	1.38	1.37
NRARP	NOTCH-regulated ankyrin repeat protein	2	2.49	1.6	1.47
MED22	mediator complex subunit 22	2.71	2.87	1.09	1.06
LPL	lipoprotein lipase	2.54	2.9	2.13	2.17
TNNI3	troponin I type 3 (cardiac)	2.58	2.63	1.72	1.9
USP28	ubiquitin specific peptidase 28	3.76	4.03	1.34	1.2
CMSS1	cms1 ribosomal small subunit homolog (yeast)	3.6	3.74	-1.56	-1.41
AQR	aquarius intron-binding spliceosomal factor	2.55	2.48	1.1	1.21
KIAA0947	KIAA0947	2.72	2.69	1.23	1.14
PSMD14	proteasome (prosome, macropain) 26S subunit, non-ATPase, 14	3.27	3.07	-1.04	1.05
RFX7	regulatory factor X, 7	4.46	4.16	1.73	1.27
LRRC8B	leucine rich repeat containing 8 family, member B	3.05	3.06	-1.45	-1.47
C11orf48	chromosome 11 open reading frame 48	3.04	2.84	-1.43	-1.11
MTF2	metal response element binding transcription factor 2	4.43	4.59	1.62	1.43
BRX1	BRX1, biogenesis of ribosomes, homolog (S. cerevisiae)	7.17	7.21	1.58	1.75
PELI1	pellino E3 ubiquitin protein ligase 1	2.65	2.38	1.27	1.42
RNF44	ring finger protein 44	4.78	4.95	1.72	1.38
COPS3	COP9 signalosome subunit 3	2.92	3.02	1.08	1.09
DKC1	dyskeratosis congenita 1, dyskerin	6.62	6.38	1.43	1.5
DHX15	DEAH (Asp-Glu-Ala-His) box helicase 15	4.25	4.24	1.84	1.87
MAGOHB	mago-nashi homolog B (Drosophila)	2.97	3.6	1.43	1.29
SEMG1	semenogelin I	4.32	4.39	1.15	1.29
PSME3	"proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; Ki)"	3.43	3.48	-1.06	-1.1
PTGES3	prostaglandin E synthase 3 (cytosolic)	2.84	2.91	1.21	1.12
COA1	cytochrome c oxidase assembly factor 1 homolog (S. cerevisiae)	2.2	2.06	1.22	1.3
RPF2	ribosome production factor 2 homolog (S. cerevisiae)	3.01	2.87	-1.28	1.02
CIRH1A	cirrhosis, autosomal recessive 1A (cirhin)	2.82	2.74	-1.18	-1.05
BRCA2	breast cancer 2, early onset	3.31	2.92	1.05	1.1
SH3GL2	SH3-domain GRB2-like 2	2.75	3.52	1.33	1.28
LYAR	Ly1 antibody reactive	5.21	5.02	-1.47	-1.44
SLC1A5	solute carrier family 1 (neutral amino acid transporter), member 5	3.17	2.79	1.91	1.91
FAM161A	family with sequence similarity 161, member A	2.4	2.49	1.21	1.41
E2F3	E2F transcription factor 3	4.34	4.33	1.51	1.43
SLC10A4	solute carrier family 10, member 4	2.48	2.26	1.02	1.01
EXOSC8	exosome component 8	3.09	2.9	-1.78	-1.57
GAP43	growth associated protein 43	6.38	6.3	1.29	1.21
PPP1R17	protein phosphatase 1, regulatory subunit 17	4.2	5.06	1.62	1.47
KIF26A	kinesin family member 26A	4.74	4.95	2.45	1.88
ANP32E	acidic (leucine-rich) nuclear phosphoprotein 32 family, member E	3.75	3.71	-1.31	-1.49
DNAAF2	dynein, axonemal, assembly factor 2	3.5	3.42	-1.33	-1.46

ZNF649	zinc finger protein 649	2.09	2.36	1.1	1.05
ME2	malic enzyme 2, NAD(+)-dependent, mitochondrial	2.14	1.88	1.15	1.32
MPP6	membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	4.32	4.23	-1.32	-1.23
BCL2L12	BCL2-like 12 (proline rich)	2.47	2.52	-1.15	-1.08
TTC9	tetratricopeptide repeat domain 9	4.74	4.64	1.71	1.37
DDX11	DEAD/H (Asp-Glu-Ala-Asp/His) box helicase 11	2.37	2.44	1.45	1.62
ZNF544	zinc finger protein 544	3.31	3.59	-1.51	-1.79
RAD1	RAD1 homolog (S. pombe)	2.7	2.82	1.6	1.5
SAP130	Sin3A-associated protein, 130kDa	3.28	3.38	1.97	1.75
GNA12	guanine nucleotide binding protein (G protein) alpha 12	2.75	2.7	1.97	1.68
POP1	processing of precursor 1, ribonuclease P/MRP subunit (S. cerevisiae)	2.7	2.95	1.57	1.4
INTS2	integrator complex subunit 2	2.07	2.27	1.21	1.14
ERCC6L	excision repair cross-complementing rodent repair deficiency, complementation group 6-like	5.99	6.79	1.24	1.21
PRMT3	protein arginine methyltransferase 3	6.05	6.36	1.26	1.23
C11orf73	chromosome 11 open reading frame 73	3.89	3.8	2.4	2.18
ST6GAL2	ST6 beta-galactosamide alpha-2,6-sialyltransferase 2	3.91	4.48	1.28	1.32
ARHGAP19	Rho GTPase activating protein 19	4.28	4.23	1.12	-1.06
ZBTB9	zinc finger and BTB domain containing 9	3.71	3.83	2.3	2.12
WDR77	WD repeat domain 77	3.64	3.33	1.3	1.26
FBXO45	F-box protein 45	2.09	2.1	-1.03	-1.21
ZNF35	zinc finger protein 35	3.26	3.48	1.1	1.14
PGD	phosphogluconate dehydrogenase	3.92	3.34	-1.06	-1.03
TAF1A	TATA box binding protein (TBP)-associated factor, RNA polymerase I, A, 48kDa	4.31	4.29	-1.01	1.02
CPSF6	cleavage and polyadenylation specific factor 6, 68kDa	4.4	4.43	1.72	1.89
TMEM108	transmembrane protein 108	2.35	2.51	1.57	1.65
ALYREF	Aly/REF export factor	5.77	5.36	1.15	1.07
RIF1	RAP1 interacting factor homolog (yeast)	2.39	2.43	-1.28	-1.09
SHISA9	shisa family member 9	6.2	5.95	1.44	1.44
SMARCC1	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 1	5.45	5.45	1.8	1.41
CCDC138	coiled-coil domain containing 138	5.85	5.85	1.12	1.44
HNRNPU	heterogeneous nuclear ribonucleoprotein U (scaffold attachment factor A)	1.91	1.97	-1.05	-1.18
PPM1G	protein phosphatase, Mg2+/Mn2+ dependent, 1G	2.74	2.65	-1.17	-1.07
VWDE	von Willebrand factor D and EGF domains	2.15	2.22	1.15	1.21
HNRNPA3	heterogeneous nuclear ribonucleoprotein A3	2.46	2.43	1.07	1.08
PALD1	phosphatase domain containing, paladin 1	5.19	5.63	1.21	1.17
METTL16	methyltransferase like 16	2.41	2.28	1.07	-1.08
ACTL6A	actin-like 6A	5.68	6	1.57	1.27
STK38L	serine/threonine kinase 38 like	2.42	2.62	1.25	1.16
RNF34	ring finger protein 34, E3 ubiquitin protein ligase	3.1	2.88	1.21	1.23
YWHAB	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, beta polypeptide	3.42	3.33	1.17	-1.21

ZBTB8A	zinc finger and BTB domain containing 8A	1.95	1.81	1.55	1.39
FEZ1	fasciculation and elongation protein zeta 1 (zygin I)	2.81	2.95	2.18	2.12
TACC3	transforming, acidic coiled-coil containing protein 3	4.64	4.34	1.13	-1.03
HES6	hes family bHLH transcription factor 6	7.18	6.9	1.14	1.16
STK33	serine/threonine kinase 33	4.28	4.41	1.84	2.09
TRIB2	tribbles pseudokinase 2	3.07	2.87	1.96	1.47
PA2G4	proliferation-associated 2G4, 38kDa	3.22	3	-1.28	-1.44
PAK1IP1	PAK1 interacting protein 1	4.21	4.36	-1.96	-1.8
ESPL1	extra spindle pole bodies homolog 1 ( <i>S. cerevisiae</i> )	3.34	3.35	1.28	1.22
FAM98B	family with sequence similarity 98, member B	5.86	5.57	1.45	1.09
POLR3F	polymerase (RNA) III (DNA directed) polypeptide F, 39 kDa	2.96	3.12	1.63	1.58
CCDC181	coiled-coil domain containing 181	2.21	2.51	1.06	1.19
MCM7	minichromosome maintenance complex component 7	6.37	6.54	-1.06	-1.16
CCDC86	coiled-coil domain containing 86	6.61	6.51	2.02	1.92
FGF13-AS1	FGF13 antisense RNA 1	4.81	4.5	1.44	1.39
CAPRIN1	cell cycle associated protein 1	3.28	3.36	1.8	1.64
IPO4	importin 4	4.92	4.69	-1.33	-1.52
KCNS3	potassium voltage-gated channel, delayed-rectifier, subfamily S, member 3	2.24	2.56	-1.25	-1.19
RIT2	Ras-like without CAAX 2	7.53	6.13	1.26	1.27
ZNF594	zinc finger protein 594	2.38	2.8	1.01	-1.06
SLC25A21	solute carrier family 25 (mitochondrial oxoadipate carrier), member 21	2.04	2.41	-1.06	-1.03
PRPF40A	PRP40 pre-mRNA processing factor 40 homolog A ( <i>S. cerevisiae</i> )	2.68	2.38	1.13	1.45
SALL3	spalt-like transcription factor 3	8.49	8.69	1.5	1.43
BRD7	bromodomain containing 7	2.8	2.7	1.43	1.32
METTL8	methyltransferase like 8	2.17	2.06	-1.31	-1.35
RBMX	RNA binding motif protein, X-linked	5.34	5.51	1.66	1.76
PRKDC	protein kinase, DNA-activated, catalytic polypeptide	3.92	4.15	1.18	1.02
ITGB3BP	integrin beta 3 binding protein (beta3-endonexin)	2.92	2.78	1.22	1.3
CIAPIN1	cytokine induced apoptosis inhibitor 1	3.66	3.68	1.8	1.7
CEBPZ	CCAAT/enhancer binding protein (C/EBP), zeta	2.97	3.05	-2	-1.39
NMRK2	nicotinamide riboside kinase 2	4.91	4.4	-1.23	-1.1
B3GNT7	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 7	4.57	4.12	1.38	1.3
PTBP2	polypyrimidine tract binding protein 2	3.43	3.29	-1.33	-1.28
TTC27	tetratricopeptide repeat domain 27	2.48	2.73	-1.03	1.05
HPDL	4-hydroxyphenylpyruvate dioxygenase-like	1.62	1.72	-1.01	1.03
PCNA	proliferating cell nuclear antigen	6.42	6.79	1.01	-1.25
NUDCD1	NudC domain containing 1	3.64	3.34	2.03	2.22
ZNF480	zinc finger protein 480	3.23	2.06	1.92	1.98
NOVA1	neuro-oncological ventral antigen 1	4.47	5.32	1.71	1.58
ANK2	ankyrin 2, neuronal	5.4	5.19	1.88	1.92
SUV39H2	suppressor of variegation 3-9 homolog 2 ( <i>Drosophila</i> )	5.71	5.72	1.16	1.16
MPHOSPH6	M-phase phosphoprotein 6	3.25	3.11	1.6	1.57



ADSL	adenylosuccinate lyase	5.62	5.88	1.83	1.95
PPM1E	protein phosphatase, Mg <sup>2+</sup> /Mn <sup>2+</sup> dependent, 1E	1.61	2.01	-1.09	-1.15
FBXL7	F-box and leucine-rich repeat protein 7	4.03	3.78	2.61	1.99
KNOP1	lysine-rich nucleolar protein 1	5.55	5.79	1.5	1.56
ZNF215	zinc finger protein 215	4.54	5.02	2.07	2.06
SRSF9	serine/arginine-rich splicing factor 9	3.26	3.18	1.77	1.57
SRSF2	serine/arginine-rich splicing factor 2	4.18	4.21	-1.43	-1.42
EMG1	EMG1 N1-specific pseudouridine methyltransferase	3.18	3.06	-1.22	-1.17
CEP78	centrosomal protein 78kDa	5.53	5.59	1.47	1.59
DNA2	DNA replication helicase/nuclease 2	4.7	5.01	-2.01	-1.82
MEGF10	multiple EGF-like-domains 10	2.29	3.12	-1.08	-1.03
CEP135	centrosomal protein 135kDa	4.54	3.98	-1.16	-1.07
OLFM1	olfactomedin 1	7.23	6.76	1.17	1.14
MAGEE1	melanoma antigen family E, 1	2.78	2.82	2.3	2.25
RRS1	RRS1 ribosome biogenesis regulator homolog (S. cerevisiae)	5.89	6.03	-1.6	-2.19
VPS72	vacuolar protein sorting 72 homolog (S. cerevisiae)	2.46	2.48	1.53	1.39
C2orf69	chromosome 2 open reading frame 69	2.52	2.75	-1.27	-1.35
NASP	nuclear autoantigenic sperm protein (histone-binding)	4.08	4.3	-1.95	-1.8
DESI2	desumoylating isopeptidase 2	3.74	3.49	2.15	1.92
FBXO30	F-box protein 30	4.28	4.62	1.79	1.51
YARS	tyrosyl-tRNA synthetase	3.9	3.5	1.67	1.55
TIGD1	tigger transposable element derived 1	2.21	2.68	1.4	1.81
CBX3	chromobox homolog 3	4.48	4.6	1.94	2.07
H2AFX	H2A histone family, member X	3.77	3.78	1.47	1.34
MCM4	minichromosome maintenance complex component 4	6.96	6.86	1.37	1.31
S100BPB	S100P binding protein	2.42	2.34	1.27	1.19
PARG	poly (ADP-ribose) glycohydrolase	2.85	2.71	1.68	1.4
GTF2E1	general transcription factor IIE, polypeptide 1, alpha 56kDa	5.75	5.6	1.63	1.28
PRKCQ-AS1	PRKCQ antisense RNA 1	3.39	3.88	1.1	1.16
NTM	neurotrimin	4.51	4.79	2.2	1.9
CCDC88A	coiled-coil domain containing 88A	2.26	2.32	-1.29	-1.01
WDR35	WD repeat domain 35	2.83	3.25	-1.14	-1.1
RTKN2	rhotekin 2	5.73	5.34	-1.05	1.01
SNHG4	small nucleolar RNA host gene 4 (non-protein coding)	3.31	3.54	2.42	2.47
MASTL	microtubule associated serine/threonine kinase-like	6.65	7.12	1.1	-1.07
SPATC1L	spermatogenesis and centriole associated 1-like	2.83	2.65	1.59	1.59
RASSF3	Ras association (RalGDS/AF-6) domain family member 3	2.91	2.64	1.83	1.55
FAM111B	family with sequence similarity 111, member B	7.48	5.18	1.54	1.5
SNRPA	small nuclear ribonucleoprotein polypeptide A	5.07	4.99	1.39	1.38
LOC100506098	uncharacterized LOC100506098	1.98	2.37	1.7	1.94
U2AF1	U2 small nuclear RNA auxiliary factor 1	4.3	4.08	1.47	1.53
ACBD6	acyl-CoA binding domain containing 6	2.58	2.68	1.63	1.74
ASF1A	anti-silencing function 1A histone chaperone	3.57	3.39	-1.24	-1.33
RFC3	replication factor C (activator 1) 3, 38kDa	5.78	6	1.59	1.48

HAUS3	HAUS augmin-like complex, subunit 3	3.14	3.01	1.15	1.43
POLQ	polymerase (DNA directed), theta	4.12	4.48	2.37	2.29
CCL26	chemokine (C-C motif) ligand 26	2.91	3.01	1.32	1.4
EPHX3	epoxide hydrolase 3	3.8	3.96	1.29	1.38
ANKRD32	ankyrin repeat domain 32	5.32	4.79	-1.09	-1.14
MYO5A	myosin VA (heavy chain 12, myosin)	2.03	2	1.33	1.17
ZNF814	zinc finger protein 814	5.16	6.04	-1.38	-1.45
KARS	lysyl-tRNA synthetase	2.77	2.74	1.6	1.66
CSE1L	CSE1 chromosome segregation 1-like (yeast)	7.12	7.13	1.09	1.2
EIF3M	eukaryotic translation initiation factor 3, subunit M	3.36	3.4	2.01	2.11
HAS3	hyaluronan synthase 3	4.36	5.15	1.17	1.06
RRP15	ribosomal RNA processing 15 homolog (S. cerevisiae)	2.91	3.07	-1.7	-1.51
MRPL50	mitochondrial ribosomal protein L50	3.24	3.23	1.01	-1
ZNF660	zinc finger protein 660	3.2	2.29	1.6	1.54
TIPIN	TIMELESS interacting protein	4.47	4.61	-2.27	-2.26
ZBED5	zinc finger, BED-type containing 5	3.5	3.43	2.02	1.87
ZNF138	zinc finger protein 138	2.24	1.79	-1.64	-1.25
CRMP1	collapsin response mediator protein 1	8.2	7.93	1.96	1.96
CABYR	calcium binding tyrosine-(Y)-phosphorylation regulated	2.67	3.08	1.72	1.98
YWHAH	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, eta polypeptide	4.57	4.3	1.45	1.23
SNHG3	small nucleolar RNA host gene 3 (non-protein coding)	4.7	4.56	1.49	1.74
SPRED1	sprouty-related, EVH1 domain containing 1	2.97	2.76	1.48	1.26
ERH	enhancer of rudimentary homolog (Drosophila)	2.93	2.94	1.44	1.51
SAPCD2	suppressor APC domain containing 2	3.71	3.52	1.75	1.67
FAM216A	family with sequence similarity 216, member A	4.1	4.68	1.82	1.77
SSB	Sjogren syndrome antigen B (autoantigen La)	5.22	4.98	1.3	1.88
EID2B	EP300 interacting inhibitor of differentiation 2B	1.74	1.76	1.25	1.26
FAM117B	family with sequence similarity 117, member B	5.25	5.71	2.55	2.21
FAM49B	family with sequence similarity 49, member B	4.36	4.5	1.64	1.44
ZNF304	zinc finger protein 304	1.81	2.08	1.44	1.12
SKIL	SKI-like oncogene	2.71	2.82	1.43	1.12
TMEM132D	transmembrane protein 132D	5.84	5.88	1.84	1.84
KIFC1	kinesin family member C1	3.68	3.49	1.73	1.59
FAM126A	family with sequence similarity 126, member A	3.67	3.53	1.72	1.87
ZNF607	zinc finger protein 607	2.76	2.69	1.97	1.91
---		1.74	1.94	-1.3	-1.55
FANCB	Fanconi anemia, complementation group B	2.05	1.83	1.05	1.05
AUNIP	aurora kinase A and ninein interacting protein	5.99	6.03	1.87	1.84
AIF1L	allograft inflammatory factor 1-like	7.2	7.76	2.27	2.07
MSH6	mutS homolog 6	4.7	4.49	2.15	2.14
EXOC2	exocyst complex component 2	1.75	1.8	1.18	1.1
TM6SF1	transmembrane 6 superfamily member 1	2.05	2.07	2.02	2.15
ZNF669	zinc finger protein 669	3.27	2.7	1.92	1.58
LRRCC1	leucine rich repeat and coiled-coil centrosomal protein 1	2.57	2.07	-1.5	-1.18
IQCB1	IQ motif containing B1	1.93	2.1	1.73	1.83



GDAP1	ganglioside induced differentiation associated protein 1	4.19	4.76	-1.01	-1
CIB2	calcium and integrin binding family member 2	2.79	2.9	2.08	2.58
SNHG15	small nucleolar RNA host gene 15 (non-protein coding)	2.77	2.84	1.63	2
UTP20	UTP20, small subunit (SSU) processome component, homolog (yeast)	5.36	5.24	-1.64	-1.61
TRIM24	tripartite motif containing 24	2.68	2.7	2.3	2.47
CCDC34	coiled-coil domain containing 34	2.39	2.51	1.14	1.37
GLI2	GLI family zinc finger 2	2.61	2.66	1.43	1.31
SMC2	structural maintenance of chromosomes 2	5.6	5.19	-1.13	1.02
PGAP1	post-GPI attachment to proteins 1	1.67	1.82	1.34	1.25
ZIK1	zinc finger protein interacting with K protein 1	6.09	6.69	1.93	2.06
SUSD5	sushi domain containing 5	5.4	5.36	3.52	2.44
AGO2	argonaute RISC catalytic component 2	2.57	2.46	-1.14	-1.51
RFX5	regulatory factor X, 5 (influences HLA class II expression)	2.28	2.35	1.41	1.54
RAP1GAP2	RAP1 GTPase activating protein 2	3.68	3.7	1.85	1.86
CDT1	chromatin licensing and DNA replication factor 1	5.61	5.94	1.49	1.6
UBE2N	ubiquitin-conjugating enzyme E2N	3.34	3.48	1.69	1.59
ZNF207	zinc finger protein 207	4.19	4.06	1.84	1.83
NUFIP1	nuclear fragile X mental retardation protein interacting protein 1	2.31	2.45	-1.07	-1.03
PSMD1	proteasome (prosome, macropain) 26S subunit, non-ATPase, 1	3.14	2.98	1.28	1.4
DIAPH3	diaphanous-related formin 3	4.06	3.7	2.46	2.39
---		2.03	1.72	1.25	1.31
ARL6IP6	ADP-ribosylation-like factor 6 interacting protein 6	3.19	3.17	2.16	2.02
RNFT2	ring finger protein, transmembrane 2	3.33	3.71	2.12	2.11
GMNN	geminin, DNA replication inhibitor	6.53	6.7	1.05	1.21
HS3ST3A1	heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1	5.5	4.41	1.47	1.41
HESX1	HESX homeobox 1	2.92	3.02	-1.05	-1.01
---		5.46	6.63	-2.03	-1.83
LINC00698	long intergenic non-protein coding RNA 698	3.03	3.07	1.58	1.69
MYB	v-myb avian myeloblastosis viral oncogene homolog	1.86	2.21	1.42	1.45
TMEM47	transmembrane protein 47	2.22	2.59	1.26	1.2
SKA2	spindle and kinetochore associated complex subunit 2	2.39	2.61	1.15	1.01
OTUD6B	OTU domain containing 6B	9.61	9.81	-1.14	-1.32
VSIG10	V-set and immunoglobulin domain containing 10	3.74	4.16	-2.1	-1.93
ARNT2	aryl-hydrocarbon receptor nuclear translocator 2	2.34	2.71	1.41	1.28
CTSC	cathepsin C	6.85	6.13	1.42	1.38
DHX9	DEAH (Asp-Glu-Ala-His) box helicase 9	4.46	3.21	1.02	-1.3
TRERF1	transcriptional regulating factor 1	2.3	2.55	1.94	1.87
CNOT7	CCR4-NOT transcription complex, subunit 7	3.37	3.18	1.24	1.22
ATP1A2	ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, alpha 2 polypeptide	1.78	2.35	1.19	1.24
LOC286467	family with sequence similarity 195, member A pseudogene	2.58	2.63	2.05	2.17

CRLF1	cytokine receptor-like factor 1	2.6	3.05	1.74	1.53
RBP1	retinol binding protein 1, cellular	4.38	3.59	1.99	1.38
ZFP37	ZFP37 zinc finger protein	2.43	2.51	1.66	1.89
ZSCAN10	zinc finger and SCAN domain containing 10	3.79	3.82	1.5	1.57
KCND2	potassium voltage-gated channel, Shal-related subfamily, member 2	6.44	6.41	1.65	1.36
PUS7	pseudouridylylase 7 homolog (S. cerevisiae)	5.24	5.26	-2.24	-2.12
BEND3	BEN domain containing 3	8.36	8.68	1.34	1.35
GPR63	G protein-coupled receptor 63	2.32	2.34	1.27	1.17
RIMS3	regulating synaptic membrane exocytosis 3	2.5	2.54	1.62	1.52
SYT14	synaptotagmin XIV	2.31	2.55	1.13	1.26
SLC4A7	solute carrier family 4, sodium bicarbonate cotransporter, member 7	2.63	2.51	1.72	1.67
EIF4A3	eukaryotic translation initiation factor 4A3	2.77	2.76	1.07	1.07
LINGO1	leucine rich repeat and Ig domain containing 1	5.1	7.88	1.18	1.3
DHX36	DEAH (Asp-Glu-Ala-His) box polypeptide 36	2.34	2.25	-1.09	-1.02
FANCF	Fanconi anemia, complementation group F	2.31	2.2	1.12	-1.01
SMC4	structural maintenance of chromosomes 4	4.81	4.57	1.76	2.22
ZNF101	zinc finger protein 101	2.38	2.31	1.14	1.19
DDIT4L	DNA-damage-inducible transcript 4-like	3.12	3.22	2.17	1.97
ARID2	AT rich interactive domain 2 (ARID, RFX-like)	2.21	2.38	1.48	1.47
ETF1	eukaryotic translation termination factor 1	3.06	3.03	1.45	1.35
ADNP	activity-dependent neuroprotector homeobox	3.08	3.13	2.14	1.57
KHDRBS1	KH domain containing, RNA binding, signal transduction associated 1	4.28	4.35	2.03	1.79
LOXL1-AS1	LOXL1 antisense RNA 1	1.83	2.02	1.96	1.64
GART	phosphoribosylglycinamide formyltransferase, phosphoribosylglycinamide synthetase, phosphoribosylaminoimidazole synthetase	2.74	2.71	-1.34	-1.37
LINC00545	long intergenic non-protein coding RNA 545	5.03	7.81	1.52	1.5
SEPW1	selenoprotein W, 1	2.98	2.86	2.61	2.68
PCDHB16	protocadherin beta 16	2.37	4.03	1.76	1.71
NUDT10	nudix (nucleoside diphosphate linked moiety X)-type motif 10	4.2	3.61	1.59	1.66
MEX3B	mex-3 RNA binding family member B	2.33	2.01	1.22	1.12
FDFT1	farnesyl-diphosphate farnesyltransferase 1	7.41	7.1	1.44	1.63
CPT1C	carnitine palmitoyltransferase 1C	1.24	1.62	1.07	1.11
POPDC3	popeye domain containing 3	4.62	5.02	2.59	3.16
AMD1	adenosylmethionine decarboxylase 1	4.27	4.55	1.36	1.53
ZNF74	zinc finger protein 74	2.81	2.72	1.47	1.48
NAT10	N-acetyltransferase 10 (GCN5-related)	2.99	3.18	-1.09	1.01
BBS9	Bardet-Biedl syndrome 9	2.65	3.33	1.34	1.19
CA14	carbonic anhydrase XIV	4.22	4.66	1.91	2.02
ZNF107	zinc finger protein 107	2.37	1.63	1.07	-1.02
TRMT6	tRNA methyltransferase 6 homolog (S. cerevisiae)	2.42	2.49	-1.31	-1.25
CDC25C	cell division cycle 25C	4.81	4.6	1.75	1.65
G3BP2	GTPase activating protein (SH3 domain) binding protein 2	3.92	3.89	1.39	1.24
CDCA8	cell division cycle associated 8	7.09	7.1	2.13	1.62

NOP2	NOP2 nucleolar protein	3.36	3.34	1.15	1.28
JAKMIP2-AS1	JAKMIP2 antisense RNA 1	2.72	4.12	1.09	1.23
PRKCQ	protein kinase C, theta	5.41	5.98	2.35	2.53
SSBP1	single-stranded DNA binding protein 1, mitochondrial	2.65	2.57	-1.5	-1.6
MITD1	MIT, microtubule interacting and transport, domain containing 1	2.13	2.12	1.08	1.07
ZFP69B	ZFP69 zinc finger protein B	6.08	5.6	1.07	1.03
PARP8	poly (ADP-ribose) polymerase family, member 8	2.24	2.25	1.84	2.06
ZNF331	zinc finger protein 331	1.71	1.73	1.58	1.74
CHST6	carbohydrate (N-acetylglucosamine 6-O) sulfotransferase 6	2.7	2.71	1.29	1.32
C2orf40	chromosome 2 open reading frame 40	2.44	2.85	2.57	3.13
IPO7	importin 7	2.21	2.16	1.14	1.22
KDM1A	lysine (K)-specific demethylase 1A	4.93	5.26	2.06	2.39
CLDN11	claudin 11	7.5	5.81	2.38	1.22
KDEL1C1	KDEL (Lys-Asp-Glu-Leu) containing 1	2.71	2.75	2.11	2.04
NPM1	nucleophosmin (nucleolar phosphoprotein B23, numatrin)	4.55	4.64	1.53	1.58
PRIM1	primase, DNA, polypeptide 1 (49kDa)	3.37	4.55	-1.71	-1.49
FAM124A	family with sequence similarity 124A	2.99	3.26	1.34	1.32
FLT1	fms-related tyrosine kinase 1	4.96	4.95	2.75	2.39
LSM5	LSM5 homolog, U6 small nuclear RNA associated (S. cerevisiae)	2.79	2.98	-1.1	-1.2
MED27	mediator complex subunit 27	4.04	4.12	2.12	2.24
METAP1	methionyl aminopeptidase 1	2.38	2.45	1.3	1.27
POLE2	polymerase (DNA directed), epsilon 2, accessory subunit	3.95	4.14	-1.47	-1.43
ZNF354A	zinc finger protein 354A	2.46	2.27	2.1	2.39
CSNK2A1	casein kinase 2, alpha 1 polypeptide	3.15	2.95	1.7	1.53
LCK	lymphocyte-specific protein tyrosine kinase	3.64	4.46	1.25	1.3
UCK2	uridine-cytidine kinase 2	2.69	2.59	1.19	1.13
THUMPD1	THUMP domain containing 1	2.88	2.75	1.12	-1.01
DNMT1	DNA (cytosine-5-)-methyltransferase 1	6.6	6.88	1.93	1.7
ZNF347	zinc finger protein 347	2.28	2.22	1.75	1.48
FAM200A	family with sequence similarity 200, member A	2.07	2.09	1.62	1.34
DCAF13	DDB1 and CUL4 associated factor 13	4.7	5.01	1.57	1.87
IRAK1BP1	interleukin-1 receptor-associated kinase 1 binding protein 1	2.64	3.42	1.58	1.56
CSTF2	cleavage stimulation factor, 3' pre-RNA, subunit 2, 64kDa	4.88	4.9	1.63	1.62
DCK	deoxycytidine kinase	3.3	3.27	1.77	1.41
SP4	Sp4 transcription factor	2.54	2.64	-1	1.02
MKI67	marker of proliferation Ki-67	5.63	4.81	1.81	1.65
NPF2R2	neuropeptide FF receptor 2	8.8	6.58	2.33	1.68
SCML2	sex comb on midleg-like 2 (Drosophila)	4.21	4.03	1.32	1.53
TRIML2	tripartite motif family-like 2	2.04	2.07	1.02	1.03
PACRGL	PARK2 co-regulated-like	2.84	2.76	1.89	1.55
ZNF280C	zinc finger protein 280C	3.02	2.81	-1.05	-1.17
CDK2AP1	cyclin-dependent kinase 2 associated protein 1	5.53	5.84	1.59	1.36

GEMIN5	gem (nuclear organelle) associated protein 5	2.94	2.99	-1.19	-1.2
UTP15	UTP15, U3 small nucleolar ribonucleoprotein, homolog (S. cerevisiae)	2.96	3.15	-1.65	-1.57
SNHG12	small nucleolar RNA host gene 12 (non-protein coding)	2.5	2.19	-1.05	2.01
PPP4R1	protein phosphatase 4, regulatory subunit 1	3.27	3.14	1.25	1.12
ZRANB2	zinc finger, RAN-binding domain containing 2	2.75	2.7	1.8	2.15
SLITRK5	SLIT and NTRK-like family, member 5	2.94	2.88	1.48	1.5
HEATR2	HEAT repeat containing 2	2.72	2.45	-1.06	-1.25
KNTC1	kinetochore associated 1	4.25	4.37	1.82	2.02
SRSF7	serine/arginine-rich splicing factor 7	2.29	2.74	-1.03	-1.33
SNORA64	small nucleolar RNA, H/ACA box 64	4.03	3.77	1.75	1.75
PVT1	Pvt1 oncogene (non-protein coding)	3.26	3.58	2.26	2.56
FOXH1	forkhead box H1	9.86	8.56	-1.05	-1.05
TTL12	tubulin tyrosine ligase-like family, member 12	3.16	3.08	1.08	1.07
EXOSC2	exosome component 2	2.39	2.35	-1.29	-1.31
MRE11A	MRE11 meiotic recombination 11 homolog A (S. cerevisiae)	1.92	1.68	-1.17	-1.18
NUP160	nucleoporin 160kDa	2.63	2.71	1.07	-1.03
C21orf59	chromosome 21 open reading frame 59	2.24	2.23	-1.39	-1.37
TRDMT1	tRNA aspartic acid methyltransferase 1	4.76	5.63	1.37	1.41
GNAS-AS1	GNAS antisense RNA 1	1.65	1.91	-1.23	-1.18
TBCB	tubulin folding cofactor B	2.44	2.16	1.09	1.04
MRAP2	melanocortin 2 receptor accessory protein 2	3.15	4.11	3.94	3.31
RAB39B	RAB39B, member RAS oncogene family	4.96	4.71	1.19	1.12
P2RY1	purinergic receptor P2Y, G-protein coupled, 1	3.9	2.92	1.12	1.18
IVNS1ABP	influenza virus NS1A binding protein	2.21	2.37	2.63	2.06
DIAPH2	diaphanous-related formin 2	8.42	9.08	-1.8	-1.61
MCM5	minichromosome maintenance complex component 5	6.56	6.9	-2.34	-2.38
CECR1	cat eye syndrome chromosome region, candidate 1	2.01	2.16	1.91	1.67
SNX16	sorting nexin 16	2.81	2.31	1.51	1.47
NUAK1	NUAK family, SNF1-like kinase, 1	4.19	3.71	2.12	1.22
FBN3	fibrillin 3	2.73	2.88	1.7	1.75
ZNF134	zinc finger protein 134	2.78	3.11	1.27	1.04
ZNF253	zinc finger protein 253	3.03	3.15	1.57	1.96
DDX25	DEAD (Asp-Glu-Ala-Asp) box helicase 25	2.34	2.94	-1.05	-1
C10orf2	chromosome 10 open reading frame 2	2.64	2.89	-1.3	-1.39
DANCR	differentiation antagonizing non-protein coding RNA	7.79	7.9	-1.11	-1.25
RBM12B	RNA binding motif protein 12B	2.37	2.68	2.29	1.73
SNAPC1	small nuclear RNA activating complex, polypeptide 1, 43kDa	1.63	1.56	-1	-1.07
KIF20B	kinesin family member 20B	7.38	6.85	1.46	1.75
CHAMP1	chromosome alignment maintaining phosphoprotein 1	2.99	3.23	1.15	-1.17
IDO1	indoleamine 2,3-dioxygenase 1	3.23	4.69	2.09	2.28
GPATCH4	G patch domain containing 4	5.13	4.47	-2.09	-2.06
PCYT1B	phosphate cytidylyltransferase 1, choline, beta	3.63	3.9	1.26	1.25
ZNF135	zinc finger protein 135	2.69	2.94	1.49	1.42

PRIMA1	proline rich membrane anchor 1	3.14	2.85	2.53	2.44
GINS3	GINS complex subunit 3 (Psf3 homolog)	8.34	8.75	1.12	1.03
TMX1	thioredoxin-related transmembrane protein 1	2.03	1.98	-1.01	-1.1
TMEFF2	transmembrane protein with EGF-like and two follistatin-like domains 2	2.23	2.22	1.28	1
C17orf104	chromosome 17 open reading frame 104	1.45	1.55	1.07	1.09
ZNF300	zinc finger protein 300	1.45	1.56	1.08	1.12
FARSB	phenylalanyl-tRNA synthetase, beta subunit	2.69	2.75	1.36	1.52
ADAMTS19	ADAM metalloproteinase with thrombospondin type 1 motif, 19	6.87	7.11	3.17	2.24
STIP1	stress-induced-phosphoprotein 1	2.04	1.57	-1.39	-1.45
TTL	tubulin tyrosine ligase	2.56	2.32	-1.31	-1.35
TPR	translocated promoter region, nuclear basket protein	1.83	1.61	1.04	1.44
PPAT	phosphoribosyl pyrophosphate amidotransferase	8.16	8.31	1.77	1.78
TIMP4	TIMP metalloproteinase inhibitor 4	6.95	6.29	2.21	2.25
TRBC2	T cell receptor beta constant 2	2.76	3.4	1.97	1.88
CDC25A	cell division cycle 25A	7.93	8.91	1.2	1.16
PFAS	phosphoribosylformylglycinamide synthase	7.64	8.61	-1.59	-1.98
SKA3	spindle and kinetochore associated complex subunit 3	7.34	8.77	2.31	2.25
RPRM	reprimin, TP53 dependent G2 arrest mediator candidate	8.21	5.08	1.74	1.58
SLITRK4	SLIT and NTRK-like family, member 4	2.1	1.95	1.63	1.93
LRAT	lecithin retinol acyltransferase (phosphatidylcholine--retinol O-acyltransferase)	2.21	2.44	1.02	1.04
CIT	citron (rho-interacting, serine/threonine kinase 21)	2.97	3.13	2.06	1.82
NAP1L2	nucleosome assembly protein 1-like 2	6.8	7.41	1.02	-1.14
PMS1	PMS1 postmeiotic segregation increased 1 (S. cerevisiae)	2.02	1.93	-1.57	-1.05
ZNF587B	zinc finger protein 587B	2.62	2.93	-2.42	-2.62
GTSE1	G-2 and S-phase expressed 1	7.27	6.16	1.66	1.32
POU5F1P4	POU class 5 homeobox 1 pseudogene 4	11.4	10.37	-1.85	-1.68
POLA1	polymerase (DNA directed), alpha 1, catalytic subunit	7.69	8.1	1.4	1.41
ACD	adrenocortical dysplasia homolog (mouse)	2.32	2.33	1.42	1.4
RRP36	ribosomal RNA processing 36 homolog (S. cerevisiae)	4.67	4.54	1.31	1.5
METTL3	methyltransferase like 3	1.78	1.61	-1.17	-1.11
TRIM45	tripartite motif containing 45	2.47	2.83	2.99	2.95
ADD2	adducin 2 (beta)	4.99	5.43	1.16	1.2
CPXM1	carboxypeptidase X (M14 family), member 1	4.82	4.41	3.01	3.2
RGS5	regulator of G-protein signaling 5	6.11	5.64	3.8	3.32
THY1	Thy-1 cell surface antigen	7.55	7.97	3.07	2.56
DAZL	deleted in azoospermia-like	1.68	1.98	1.43	1.42
C16orf59	chromosome 16 open reading frame 59	3.09	2.92	1.44	1.44
CCDC160	coiled-coil domain containing 160	3.49	2.51	1.08	1.13
ITGB5	integrin, beta 5	5.23	4.8	1.38	1.14
MIAT	myocardial infarction associated transcript (non-protein coding)	1.26	1.48	1.16	1.22
PTPRG	protein tyrosine phosphatase, receptor type, G	3.67	3.75	-2.14	-3.15

TCERG1L	transcription elongation regulator 1-like	3.88	3.65	1.75	1.67
STOX2	storkhead box 2	11.38	12.57	-1.47	-1.6
MGC57346	uncharacterized LOC401884	3.32	3.51	3.19	3.11
LOC100506392	uncharacterized LOC100506392	1.44	1.46	1.1	1.13
NPTX2	neuronal pentraxin II	3.3	5.24	1.27	1.43
FGD1	FYVE, RhoGEF and PH domain containing 1	2.99	3.27	3.1	2.67
JPH3	junctophilin 3	2.76	2.63	2.54	2.27
TLCD1	TLC domain containing 1	4.68	4.35	1.39	1.63
GTF2F2	general transcription factor IIF, polypeptide 2, 30kDa	2.52	2.44	1.15	1.16
INSM1	insulinoma-associated 1	1.66	2.12	1.43	1.43
PRMT6	protein arginine methyltransferase 6	3.35	3.19	-2.1	-3.11
GAS2L3	growth arrest-specific 2 like 3	2.62	2.24	1.67	1.42
NTPCR	nucleoside-triphosphatase, cancer-related	2.36	2.43	1.53	1.54
TEX9	testis expressed 9	4.24	3.8	-1.09	-1.1
KIAA1244	KIAA1244	1.5	1.59	-1.18	-1.16
FAM189A2	family with sequence similarity 189, member A2	5.05	4.34	1.69	1.63
PRPS1	phosphoribosyl pyrophosphate synthetase 1	2.96	2.73	1.09	-1
ZNF426	zinc finger protein 426	2.07	2.16	1.58	1.27
DYRK2	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 2	3.08	3.23	1.39	1.04
PIF1	PIF1 5'-to-3' DNA helicase	5.15	4.8	1.37	1.35
LRRC34	leucine rich repeat containing 34	1.07	1.08	-1.25	-1.2
VRTN	vertebrae development associated	3.41	3.56	-1.93	-1.81
FHOD3	formin homology 2 domain containing 3	1.64	1.93	2.4	2.1
PLA2G3	phospholipase A2, group III	7.95	8.55	1.01	1.04
TMEM132B	transmembrane protein 132B	3.34	4.14	2.05	1.35
DLAT	dihydrolipoamide S-acetyltransferase	3.6	3.31	1.41	1.48
TMEM69	transmembrane protein 69	2.72	2.88	1.84	1.67
SFR1	SWI5-dependent recombination repair 1	1.99	1.97	1.39	1.39
COL9A3	collagen, type IX, alpha 3	4.02	3.91	2.58	2.43
CNIH3	cornichon family AMPA receptor auxiliary protein 3	3.54	3.45	1.41	1.13
THBS2	thrombospondin 2	11.74	13.82	2.23	1.28
NUDT15	nudix (nucleoside diphosphate linked moiety X)-type motif 15	12.65	11.67	-1.06	-1.31
RABGAP1L	RAB GTPase activating protein 1-like	2.04	2.32	-1.59	-1.49
---		2.1	1.95	-1.32	-1.51
CHODL	chondrolectin	4.44	3.79	1.8	1.78
LOC100505946	uncharacterized LOC100505946	2.83	3.19	2.3	2.16
CHRDL1	chordin-like 1	4.76	6.24	1.28	1.34
PIM2	pim-2 oncogene	3.04	3.32	-1.45	-1.57
TDRP	testis development related protein	2.42	2.77	1.9	1.76
GNPTAB	N-acetylglucosamine-1-phosphate transferase, alpha and beta subunits	1.72	1.88	1.01	-1.12
PDCL	phosducin-like	2.78	2.85	1.84	1.72
G6PC3	glucose 6 phosphatase, catalytic, 3	3.47	3.66	2.22	2.14
ACTA1	actin, alpha 1, skeletal muscle	16.68	13.95	1.65	1.28
LDB2	LIM domain binding 2	8.63	8.32	1.36	1.07
HNRNPL	heterogeneous nuclear ribonucleoprotein L	3.86	3.86	1.3	1.16



CXCL6	chemokine (C-X-C motif) ligand 6	1.3	1.67	-1.51	-1.46
CCNA1	cyclin A1	1.85	2.08	1.32	1.42
CDKN2AIPNL	CDKN2A interacting protein N-terminal like	3.95	3.49	1.56	1.34
OGFOD1	2-oxoglutarate and iron-dependent oxygenase domain containing 1	2.55	2.69	1.26	1.25
ZCCHC3	zinc finger, CCHC domain containing 3	4.14	4.09	2.42	1.87
UST	uronyl-2-sulfotransferase	7.16	6.39	2.76	2.48
PCDHB15	protocadherin beta 15	1.7	1.94	1.68	1.92
LOC100506691	uncharacterized LOC100506691	1.42	1.65	1.71	1.64
NLGN1	neuroligin 1	4.42	4.12	1.27	1.35
CCDC14	coiled-coil domain containing 14	1.96	1.85	1.36	1.58
SNORA61	small nucleolar RNA, H/ACA box 61	2.29	1.79	-1.46	1.37
NEFH	neurofilament, heavy polypeptide	1.74	2.19	1.1	1.13
CDH13	cadherin 13	1.61	1.77	2.43	1.45
PIGW	phosphatidylinositol glycan anchor biosynthesis, class W	5.69	5.98	-2.88	-3.37
CYB5R2	cytochrome b5 reductase 2	2.05	2.25	3.67	3.61
UNC5A	unc-5 homolog A (C. elegans)	2.82	3.34	2.18	2.24
GLT8D2	glycosyltransferase 8 domain containing 2	1.53	1.96	3.54	3.71
DYX1C1	dyslexia susceptibility 1 candidate 1	1.44	1.4	1.06	1.11
MAGOH	mago-nashi homolog, proliferation-associated (Drosophila)	2.95	2.82	1.21	1.25
RFXAP	regulatory factor X-associated protein	1.67	1.6	1.16	1.1
RBBP7	retinoblastoma binding protein 7	2.55	3.06	2.29	2.26
FAM162B	family with sequence similarity 162, member B	1.34	1.75	2.07	2.09
GPR19	G protein-coupled receptor 19	6.5	8.25	1.47	1.58
MNS1	meiosis-specific nuclear structural 1	2.28	2.11	-1.13	-1.06
IFITM1	interferon induced transmembrane protein 1	9.81	8.13	3.69	4.23
NRK	Nik related kinase	1.58	1.85	1.95	1.9
CTTNBP2	cortactin binding protein 2	1.28	1.57	3.92	3.66
LOXL3	lysyl oxidase-like 3	3.26	3.48	2.15	2.28
LOC100996301	homeotic protein female sterile-like	6.83	6.17	-2.75	-2.77
HIP1	huntingtin interacting protein 1	2.31	2.29	2.04	1.52
WIF1	WNT inhibitory factor 1	1.67	2.25	-1.11	-1.13
MGC24103	uncharacterized MGC24103	1.21	1.29	2.75	3.62
CHD7	chromodomain helicase DNA binding protein 7	3.19	3.07	1.21	1.19
FGFR2	fibroblast growth factor receptor 2	1.95	2.17	3.71	2.86
LINC00664	long intergenic non-protein coding RNA 664	1.51	1.39	1.21	1.24
ST6GALNAC5	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 5	3.91	3.25	1.72	1.66
IRX1	iroquois homeobox 1	1.02	1.02	1.24	1.05
RGMA	RGM domain family, member A	3.41	3.75	2.18	2.32
GLB1L3	galactosidase, beta 1-like 3	8.42	9.89	-1.11	-1.08
CALCB	calcitonin-related polypeptide beta	3.38	4.07	1.3	1.3
NODAL	nodal growth differentiation factor	15.52	14.81	1.5	1.49
GDF3	growth differentiation factor 3	31.41	22.98	1.58	1.73
ABHD12B	abhydrolase domain containing 12B	4.09	4.15	-1.17	-1.15
FKBP1B	FK506 binding protein 1B, 12.6 kDa	3.59	3.69	2.68	2.6

HNRNPA1	heterogeneous nuclear ribonucleoprotein A1	4.18	4.27	3.22	2.99
ARMC9	armadillo repeat containing 9	3.47	3.78	2.82	2.32
RPL4	ribosomal protein L4	3.67	3.57	3.15	3.07
CDYL	chromodomain protein, Y-like	4.17	3.99	3.01	2.69
BZW2	basic leucine zipper and W2 domains 2	4.45	4.54	3.22	3.33
PAQR3	progesterin and adipoQ receptor family member III	4.76	4.73	2.23	2.23
LCMT1	leucine carboxyl methyltransferase 1	3.36	3.58	2.63	2.95
Sep-02	septin 2	4.44	4.21	3.45	3.27
MEX3C	mex-3 RNA binding family member C	4.02	4.04	3.51	2.56
CCDC43	coiled-coil domain containing 43	3.91	3.81	2.16	2.13
PPP1CC	protein phosphatase 1, catalytic subunit, gamma isozyme	4.65	4.78	2.35	2.2
PTPN14	protein tyrosine phosphatase, non-receptor type 14	4.24	4.55	3.53	2.87
SLC25A6	"solute carrier family 25 (mitochondrial carrier; adenine nucleotide translocator), member 6"	4.2	3.89	3.6	3.22
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LINC00094	long intergenic non-protein coding RNA 94	3.29	3.45	3.42	3.32
FNBP1L	formin binding protein 1-like	5.09	5.05	3.45	3.18
GTPBP4	GTP binding protein 4	4.9	5.08	2.25	2.1
NUPL1	nucleoporin like 1	3.55	3.54	3	2.31
IFT52	intraflagellar transport 52 homolog (Chlamydomonas)	3.07	3.27	3.28	3.47
DCP2	decapping mRNA 2	4.37	4.33	2.68	2.45
CAMSAP2	calmodulin regulated spectrin-associated protein family, member 2	3.24	3.25	3.82	3.39
CELF2	CUGBP, Elav-like family member 2	5.1	4.6	3.76	3.62
NEDD1	neural precursor cell expressed, developmentally down-regulated 1	4.03	3.65	2.35	2.35
ZNF827	zinc finger protein 827	4.41	5	2.99	2.71
COPG2	coatamer protein complex, subunit gamma 2	3.83	3.37	3.8	3.45
SLC7A1	solute carrier family 7 (cationic amino acid transporter, y+ system), member 1	5.16	4.92	3.17	2.47
PHACTR2	phosphatase and actin regulator 2	4.27	3.23	3.36	2.76
NAA40	N(alpha)-acetyltransferase 40, NatD catalytic subunit	4.65	4.48	2.85	2.79
TMEM206	transmembrane protein 206	4.38	4.59	2.23	2.2
YEATS2	YEATS domain containing 2	2.7	2.68	2.67	2.09
GNPDA1	glucosamine-6-phosphate deaminase 1	4.53	4.55	3.05	3.46
TPGS2	tubulin polyglutamylase complex subunit 2	4.54	4.23	3.02	2.46
PTPN12	protein tyrosine phosphatase, non-receptor type 12	4.05	3.31	2.28	2.06
KIAA1324L	KIAA1324-like	5.25	5.37	4.3	3.94
LDOC1L	leucine zipper, down-regulated in cancer 1-like	4.06	4.12	3.2	2.5
ZBED4	zinc finger, BED-type containing 4	6.33	5.74	3.38	2.4
RNF145	ring finger protein 145	4.44	4.01	2.94	2.63
CCT4	chaperonin containing TCP1, subunit 4 (delta)	4.92	4.92	2.7	2.62
KPNB1	karyopherin (importin) beta 1	6.09	6.04	2.3	2.16
ZNF14	zinc finger protein 14	2.54	2.49	2.69	2.7
DPY19L3	dpy-19-like 3 (C. elegans)	3.48	3.35	2.23	2.04
ADO	2-aminoethanethiol (cysteamine) dioxygenase	4.22	4.25	2.54	1.97
TRO	trophinin	3.15	3.01	3.08	3.67



MYL6B	myosin, light chain 6B, alkali, smooth muscle and non-muscle	3.41	3.62	2.8	2.94
CNIH4	cornichon family AMPA receptor auxiliary protein 4	3.11	3.29	2.51	2.73
TUBG1	tubulin, gamma 1	3.68	3.44	1.98	2.13
RAVER2	ribonucleoprotein, PTB-binding 2	3.62	3.69	3.51	3.1
UBE2D1	ubiquitin-conjugating enzyme E2D 1	5.65	5.01	2.37	1.95
HMGN4	high mobility group nucleosomal binding domain 4	2.9	2.87	3.44	3.17
SUPT3H	suppressor of Ty 3 homolog (S. cerevisiae)	4.2	4.06	3.97	4.17
AP3M2	adaptor-related protein complex 3, mu 2 subunit	3.88	4.01	3.2	3
TWSG1	twisted gastrulation BMP signaling modulator 1	3.46	3.2	4.26	3.86
RAP2A	RAP2A, member of RAS oncogene family	7.12	5.62	2.9	2.48
KRAS	Kirsten rat sarcoma viral oncogene homolog	3.4	3.11	2.3	1.86
RALA	v-ral simian leukemia viral oncogene homolog A (ras related)	3.78	3.75	1.97	1.94
LUZP1	leucine zipper protein 1	5.4	5.53	3.27	2.82
SMURF2	SMAD specific E3 ubiquitin protein ligase 2	5.42	5.27	3.45	2.57
UBAP2	ubiquitin associated protein 2	4.71	4.67	2.39	2.36
TMEM165	transmembrane protein 165	3.05	2.81	3.21	2.88
ANKRD27	ankyrin repeat domain 27 (VPS9 domain)	2.99	3.03	2.02	1.81
MYH10	myosin, heavy chain 10, non-muscle	5.01	5.3	4.59	4.05
RBM12	RNA binding motif protein 12	5.27	6.07	2.87	2.61
FLNA	filamin A, alpha	3.18	2.84	2.14	1.93
GYG1	glycogenin 1	3.19	3.11	3.3	3.29
EPRS	glutamyl-prolyl-tRNA synthetase	3.24	3.03	2.41	2.23
ENOPH1	enolase-phosphatase 1	4.98	5.22	1.97	2.02
TCEAL8	transcription elongation factor A (SII)-like 8	6.08	5.87	3.62	3.46
HSDL1	hydroxysteroid dehydrogenase like 1	3.41	3.6	2.03	1.83
MAPRE1	microtubule-associated protein, RP/EB family, member 1	3.25	2.79	1.8	1.76
KCNMB4	potassium large conductance calcium-activated channel, subfamily M, beta member 4	5.67	5.47	4.3	3.81
ZNF280B	zinc finger protein 280B	6.44	6.43	2.89	2.73
KIF3C	kinesin family member 3C	5.62	5.65	3.13	2.96
ABCC1	ATP-binding cassette, sub-family C (CFTR/MRP), member 1	4.36	4.6	3.88	3.7
EFCAB11	EF-hand calcium binding domain 11	3.49	3.29	2.05	1.84
CKAP5	cytoskeleton associated protein 5	3.82	3.51	2.15	2.11
SLC7A6OS	solute carrier family 7, member 6 opposite strand	3.34	3.41	2.51	2.47
SAE1	SUMO1 activating enzyme subunit 1	5.59	5.3	2.46	2.38
ZBTB34	zinc finger and BTB domain containing 34	2.79	2.99	4.28	3.57
GCA	grancalcin, EF-hand calcium binding protein	2.68	2.82	4.85	4.31
YWHAZ	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, zeta polypeptide	4.94	4.2	3.6	3.21
HNRNPLL	heterogeneous nuclear ribonucleoprotein L-like	3.85	3.83	2.72	2.32
SNRPB	small nuclear ribonucleoprotein polypeptides B and B1	4.08	3.74	1.6	1.78
BLVRA	biliverdin reductase A	4.35	4.26	4.43	5.46
ZNF85	zinc finger protein 85	5.59	5.8	2.8	3.35
GPRC5B	G protein-coupled receptor, family C, group 5,	5.39	5.91	2.45	2.38

	member B				
UNC119B	unc-119 homolog B ( <i>C. elegans</i> )	4.22	4.65	3.63	3.33
RNF2	ring finger protein 2	3.58	3.73	2.52	2.22
RBPJ	recombination signal binding protein for immunoglobulin kappa J region	3.99	4.25	2.12	2.23
GNG4	guanine nucleotide binding protein (G protein), gamma 4	5.7	6.08	3.69	3.34
PDE7A	phosphodiesterase 7A	4.68	4.67	4.07	3.85
CCT6A	chaperonin containing TCP1, subunit 6A (zeta 1)	5.62	5.66	1.69	1.76
CCT8	chaperonin containing TCP1, subunit 8 (theta)	3.85	3.79	2.01	2.13
RAB23	RAB23, member RAS oncogene family	3.42	3.35	4.88	4.75
SMARCA4	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 4	5.48	5.53	2.26	1.71
MARS	methionyl-tRNA synthetase	4.04	3.72	1.58	1.66
TMEM216	transmembrane protein 216	5.2	5.39	3.45	3.73
KIAA1549	KIAA1549	2.65	2.64	2.28	2.18
LRP12	low density lipoprotein receptor-related protein 12	3.62	3.65	5.2	3.7
PRKCI	protein kinase C, iota	5.2	5.07	3.34	3.18
HDCC2	HD domain containing 2	3.68	3.49	2.47	2.63
UBE2I	ubiquitin-conjugating enzyme E2I	3.48	3.41	2.33	2.21
ZNF267	zinc finger protein 267	5.38	5.08	1.65	2.69
TKT	transketolase	6.44	6.33	2.88	2.74
CCDC8	coiled-coil domain containing 8	3.5	3.08	3.44	2.81
BOD1	bioorientation of chromosomes in cell division 1	3.42	3.58	2.6	2.76
NCKAP1	NCK-associated protein 1	4.77	5.1	4.26	3.63
AKIRIN1	akirin 1	3.92	3.98	2.07	1.77
RAD21	RAD21 homolog ( <i>S. pombe</i> )	3.56	3.13	2.78	2.4
CTTNBP2NL	CTTNBP2 N-terminal like	3.74	3.92	3.98	3.21
FAM169A	family with sequence similarity 169, member A	6.49	5.66	2.17	2.09
RPS3	ribosomal protein S3	2.71	2.46	2.3	2.5
TPM2	tropomyosin 2 (beta)	4.43	4.32	4.07	2.95
DSE	dermatan sulfate epimerase	5.23	5.74	3.93	3.34
CNOT6	CCR4-NOT transcription complex, subunit 6	3.05	3.16	1.86	1.52
INPP5F	inositol polyphosphate-5-phosphatase F	4.12	4.21	3.61	3.41
USP22	ubiquitin specific peptidase 22	5.87	5.21	2.44	1.8
PHF19	PHD finger protein 19	2.64	2.77	2.44	2.34
MYO10	myosin X	3.38	3.58	3.44	2.32
AGPAT4	1-acylglycerol-3-phosphate O-acyltransferase 4	3.85	3.71	5.54	4.41
DNM1L	dynamamin 1-like	2.96	2.77	1.56	1.61
TUBB4B	tubulin, beta 4B class IVb	3.49	3.12	1.97	1.68
IMPDH2	IMP (inosine 5'-monophosphate) dehydrogenase 2	4.55	4.53	4.65	5.09
STAM	signal transducing adaptor molecule (SH3 domain and ITAM motif) 1	3.54	3.79	2.23	2.23
TCF4	transcription factor 4	5.13	5.5	3.98	3.58
CWC27	CWC27 spliceosome-associated protein homolog ( <i>S. cerevisiae</i> )	6.47	5.58	1.95	2.22
PPP1R9A	protein phosphatase 1, regulatory subunit 9A	3.14	3.17	1.8	1.83
RNF219	ring finger protein 219	2.61	2.66	2.33	2.19
LPHN1	latrophilin 1	4.88	5.09	2.39	2.11

CENPJ	centromere protein J	3.45	2.84	1.71	1.79
GBAS	glioblastoma amplified sequence	2.91	3.1	4.57	4.11
ZNF765	zinc finger protein 765	3.96	3.81	2.79	2.7
UBE2E1	ubiquitin-conjugating enzyme E2E 1	2.91	3.09	2.93	2.52
ANKRD33B	ankyrin repeat domain 33B	3.28	3.33	3.83	3.3
FSCN1	fascin homolog 1, actin-bundling protein (Strongylocentrotus purpuratus)	8.77	6.71	3.9	3.48
CENPQ	centromere protein Q	5.43	5.63	1.6	1.82
BEND5	BEN domain containing 5	3.57	3.69	4.83	4.07
ABCC5	ATP-binding cassette, sub-family C (CFTR/MRP), member 5	3.33	3.3	3.3	3.27
STMN3	stathmin-like 3	4.48	5.01	1.81	1.53
ENAH	enabled homolog (Drosophila)	4.35	5.02	3.42	3.1
CCNJL	cyclin J-like	3.28	3.59	1.92	2
KIF3A	kinesin family member 3A	3.35	3.35	3.76	3.25
GPSM2	G-protein signaling modulator 2	2.85	2.36	2.36	2
ALDOA	aldolase A, fructose-bisphosphate	4.7	4.3	4.95	4.03
HACE1	HECT domain and ankyrin repeat containing E3 ubiquitin protein ligase 1	3.31	3.54	5.02	4.74
SPIN1	spindlin 1	3.39	3.13	2.2	1.69
SLC22A15	solute carrier family 22, member 15	3.07	2.48	2.8	2.94
WDYHV1	WDYHV motif containing 1	2.92	2.92	2.73	2.98
TUBB	tubulin, beta class I	6.41	5.78	2.46	2.02
CDK7	cyclin-dependent kinase 7	2.5	2.32	2.41	2.99
CMTM7	CKLF-like MARVEL transmembrane domain containing 7	6.4	5.79	4.92	5.13
LARP6	La ribonucleoprotein domain family, member 6	2.88	2.73	2.81	3.27
BTF3L4	basic transcription factor 3-like 4	3.6	3.83	2.63	2.38
TMEM125	transmembrane protein 125	2.68	2.98	2.53	2.81
STXBP1	syntaxin binding protein 1	5.8	6.26	5.47	4.8
ZNF720	zinc finger protein 720	3.06	3.12	2.68	2.37
HIF1A	hypoxia inducible factor 1, alpha subunit (basic helix-loop-helix transcription factor)	4.14	4.09	4.5	4.38
BDNF	brain-derived neurotrophic factor	2.71	2.61	2.62	1.94
CHSY1	chondroitin sulfate synthase 1	5.36	5.72	4.02	2.5
UXS1	UDP-glucuronate decarboxylase 1	2.73	2.78	2.08	1.92
TMEM184B	transmembrane protein 184B	2.68	2.79	4.37	4
IGF2BP1	insulin-like growth factor 2 mRNA binding protein 1	7.57	7.91	3.45	3.2
GLMN	glomulin, FKBP associated protein	6.64	6.7	1.67	1.89
IARS	isoleucyl-tRNA synthetase	6.15	5.93	2.08	2.02
MTA3	metastasis associated 1 family, member 3	3.62	4.03	2.04	2.02
C18orf54	chromosome 18 open reading frame 54	4.84	4.63	2.58	2.65
CLDN6	claudin 6	6.67	6.23	3	2.71
FHDC1	FH2 domain containing 1	7.04	7.06	2.96	3.08
ERI1	exoribonuclease 1	2.98	2.95	1.75	1.54
SFT2D1	SFT2 domain containing 1	3.25	3.23	2.17	1.84
WASF1	WAS protein family, member 1	4.65	4.38	6.82	4.54
USP54	ubiquitin specific peptidase 54	3.47	3.37	1.39	1.72
PTK7	protein tyrosine kinase 7	4.32	3.74	6.66	5.94

CLSTN1	calsyntenin 1	3.03	2.93	2.81	2.52
NUP37	nucleoporin 37kDa	6.68	6.72	3.52	3.25
GRIP1	glutamate receptor interacting protein 1	3.36	3.44	4.57	4.16
PCYOX1L	prenylcysteine oxidase 1 like	4.38	5.21	5.79	5.73
SLC3A2	solute carrier family 3 (amino acid transporter heavy chain), member 2	3.94	3.27	2.56	2.49
AGTPBP1	ATP/GTP binding protein 1	5.11	5.4	2.2	2.82
CLMP	CXADR-like membrane protein	4.9	3.81	5.64	6.2
RPAP3	RNA polymerase II associated protein 3	3.21	2.5	1.52	2.18
MORF4L1	mortality factor 4 like 1	3.32	3.64	2.74	2.92
ABL1	c-abl oncogene 1, non-receptor tyrosine kinase	3.73	3.83	2.16	1.73
AMMECR1	Alport syndrome, mental retardation, midface hypoplasia and elliptocytosis chromosomal region gene 1	4.11	3.82	3.65	3.39
CBX5	chromobox homolog 5	4.39	4.6	2	1.57
CFL1	cofilin 1 (non-muscle)	4.49	3.59	2.23	1.82
UBXN2A	UBX domain protein 2A	2.88	2.36	2.63	1.96
STARD3NL	STARD3 N-terminal like	3.29	3.38	3.96	3.98
EPB41L2	erythrocyte membrane protein band 4.1-like 2	6.31	5.59	1.52	1.75
MSANTD3	Myb/SANT-like DNA-binding domain containing 3	3.12	3.1	2.96	2.83
RIMS2	regulating synaptic membrane exocytosis 2	6.97	6.13	5.49	5.01
ERC2	ELKS/RAB6-interacting/CAST family member 2	2.87	3.24	1.85	1.96
SYT13	synaptotagmin XIII	2.67	3.02	3.84	4.17
AFAP1	actin filament associated protein 1	2.94	2.83	3.21	2.07
RCBTB1	regulator of chromosome condensation (RCC1) and BTB (POZ) domain containing protein 1	2.87	2.96	1.86	1.92
SLC45A4	solute carrier family 45, member 4	3.64	3.71	1.72	1.71
SMARCA5	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 5	4.36	4.49	1.74	1.61
ARL2	ADP-ribosylation factor-like 2	4.83	4.51	3.52	3.68
TUBB3	tubulin, beta 3 class III	7.07	6.09	1.71	1.31
SP8	Sp8 transcription factor	4.24	3.9	1.7	1.75
PFN1	profilin 1	5.23	4.17	1.92	1.43
BTBD10	BTB (POZ) domain containing 10	3.02	2.62	2.18	2
RNF144A	ring finger protein 144A	5.44	6.18	3.19	2.79
PP1L1	peptidylprolyl isomerase (cyclophilin)-like 1	7.36	7.93	2.03	2.08
CERS5	ceramide synthase 5	3.05	2.9	3.13	3.06
GEMIN2	gem (nuclear organelle) associated protein 2	4.09	4.07	1.93	2.15
KDM5B	lysine (K)-specific demethylase 5B	4.56	5.08	5.21	3.75
PELI2	pellino E3 ubiquitin protein ligase family member 2	3.46	4.03	1.99	2.19
WARS	tryptophanyl-tRNA synthetase	5.61	4.65	1.59	1.57
SLBP	stem-loop binding protein	3.21	3.21	3.45	3.17
PAFAH1B3	platelet-activating factor acetylhydrolase 1b, catalytic subunit 3 (29kDa)	4.16	3.87	1.57	1.52
ZCCHC17	zinc finger, CCHC domain containing 17	3.7	3.59	2.32	2.32
ZNF682	zinc finger protein 682	3.53	3.41	2.25	2.94
SPINK5	serine peptidase inhibitor, Kazal type 5	5.15	4.53	4.45	5.28
GNAL	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type	6.84	4.96	1.58	1.55

TMEM237	transmembrane protein 237	6.64	7.81	3.47	3.19
ARHGAP28	Rho GTPase activating protein 28	7.9	6.89	6.23	5.64
BBS7	Bardet-Biedl syndrome 7	2.95	2.8	2.6	2.6
RAB8B	RAB8B, member RAS oncogene family	2.33	2.49	2.52	2.46
MARVELD1	MARVEL domain containing 1	6.9	6.65	5.82	5.06
NEK2	NIMA-related kinase 2	3.59	3.07	2.11	1.93
LOC100507507	uncharacterized LOC100507507	5.29	4.92	2.82	2.73
GNB4	guanine nucleotide binding protein (G protein), beta polypeptide 4	3.93	3.58	2.91	2.54
HSP90AB1	heat shock protein 90kDa alpha (cytosolic), class B member 1	7.63	6.76	4.39	4.01
LOC550643	uncharacterized LOC550643	3.53	3.36	4.37	4.85
VCL	vinculin	5.02	5.5	2.87	2.55
NAE1	NEDD8 activating enzyme E1 subunit 1	5.12	5.36	1.78	2.05
DGKZ	diacylglycerol kinase, zeta	6.9	6.83	3.78	3.42
C10orf118	chromosome 10 open reading frame 118	2.13	1.67	2.33	2.49
CKAP2L	cytoskeleton associated protein 2-like	7.66	6.76	2.75	2.93
HDAC2	histone deacetylase 2	7.53	7.45	2.61	2.48
SNHG1	small nucleolar RNA host gene 1 (non-protein coding)	6.37	6.77	2.74	3.62
SMC3	structural maintenance of chromosomes 3	4.09	3.23	1.18	1.7
OVOL2	ovo-like zinc finger 2	3.08	3.53	3.01	3.44
SPTLC2	serine palmitoyltransferase, long chain base subunit 2	2	2.07	2.93	2.58
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PJA1	praja ring finger 1, E3 ubiquitin protein ligase	4.32	4.33	7.61	7.26
MARK1	MAP/microtubule affinity-regulating kinase 1	4.61	4.64	2.97	2.65
ZNF608	zinc finger protein 608	4.71	4.29	2.29	2.13
MAGEL2	MAGE-like 2	2.97	3.14	6.04	4.73
TCTEX1D2	Tctex1 domain containing 2	2.9	3.04	3.52	3.4
HRASLS	HRAS-like suppressor	3.77	4.78	1.97	1.53
GTF2IRD1	GTF2I repeat domain containing 1	2.78	2.71	3.48	3.56
SQLE	squalene epoxidase	9.37	8.15	2.54	2.61
ANTXR1	anthrax toxin receptor 1	5.06	4.8	4.19	3.12
CCDC6	coiled-coil domain containing 6	2.93	3.16	2.11	2.14
UBTD2	ubiquitin domain containing 2	2.53	2.7	2.46	1.99
CSRP2	cysteine and glycine-rich protein 2	4.6	4.72	4.46	4
ASPHD2	aspartate beta-hydroxylase domain containing 2	6.48	6.28	2.52	2.28
FAM118B	family with sequence similarity 118, member B	4.01	4.04	1.33	1.47
ZFP82	ZFP82 zinc finger protein	6.12	6.13	3.23	3.57
FAT1	FAT atypical cadherin 1	3.52	3.61	2.07	1.62
GARS	glycyl-tRNA synthetase	7.37	6.74	3.58	3.25
LTA4H	leukotriene A4 hydrolase	2.62	2.84	2.46	2.49
FAM63B	family with sequence similarity 63, member B	1.88	1.66	2.11	1.56
HMGGA2	high mobility group AT-hook 2	7.07	7.6	5.86	5.63
PLEKHB2	pleckstrin homology domain containing, family B (evectins) member 2	3.32	3.17	2.33	1.86
RPL27A	ribosomal protein L27a	7.79	8.98	3.09	2.85
ACPL2	acid phosphatase-like 2	2.97	2.23	1.91	1.94
UBA2	ubiquitin-like modifier activating enzyme 2	4.13	4.31	2.43	2.41

SWAP70	SWAP switching B-cell complex 70kDa subunit	6.56	6.56	2.79	2.09
DNER	delta/notch-like EGF repeat containing	2.52	3.24	2.26	1.62
C6orf132	chromosome 6 open reading frame 132	2.78	3.2	2.01	1.75
ESCO1	establishment of sister chromatid cohesion N-acetyltransferase 1	3.04	2.11	1.26	1.68
RPGRIP1L	RPGRIP1-like	2.16	2.37	2.36	2.83
B4GALT6	UDP-Gal:betaGlcNAc beta 1,4-galactosyltransferase, polypeptide 6	7.4	7.57	4.25	3.77
LIN9	lin-9 homolog (C. elegans)	4.58	4.61	2.1	2.21
CDR2L	cerebellar degeneration-related protein 2-like	2.93	2.72	1.86	1.7
HIATL1	hippocampus abundant transcript-like 1	3.48	3.42	2.09	2.08
TMEM159	transmembrane protein 159	2.58	2.9	4.35	4.7
AP2B1	adaptor-related protein complex 2, beta 1 subunit	4	3.8	4.29	3.56
NCBP2	nuclear cap binding protein subunit 2, 20kDa	2.52	2.53	2.01	2.19
ADORA2B	adenosine A2b receptor	2.67	2.72	7.43	6.95
GPD2	glycerol-3-phosphate dehydrogenase 2 (mitochondrial)	3.42	3.19	1.65	1.45
CCT2	chaperonin containing TCP1, subunit 2 (beta)	5.85	5.23	1.64	1.58
RPL22L1	ribosomal protein L22-like 1	6.6	7.3	2.51	2.92
STMN1	stathmin 1	5.81	5.77	2.32	2.17
EML1	echinoderm microtubule associated protein like 1	4.69	5.03	4.68	4.32
MCM3AP-AS1	MCM3AP antisense RNA 1	4.22	4.09	1.74	2.15
JAG1	jagged 1	2.68	3.03	2.88	2.24
TUBB2A	tubulin, beta 2A class IIa	10.24	9.97	1.84	1.64
MAP4K5	mitogen-activated protein kinase kinase kinase 5	2.15	2.03	2.48	2.29
SLC39A6	solute carrier family 39 (zinc transporter), member 6	2.08	2.01	5.29	4.85
SLC27A6	solute carrier family 27 (fatty acid transporter), member 6	1.97	2.02	6.36	5.34
ARPC2	actin related protein 2/3 complex, subunit 2, 34kDa	3.07	2.9	3.29	3
FGD6	FYVE, RhoGEF and PH domain containing 6	2.44	2.29	1.81	2.05
PRKCDBP	protein kinase C, delta binding protein	8.87	6.93	3.89	3.43
FJX1	four jointed box 1 (Drosophila)	5.77	5.31	2.75	2.48
E2F7	E2F transcription factor 7	7.38	8.18	1.98	1.77
AP1M2	adaptor-related protein complex 1, mu 2 subunit	2.82	2.85	2.59	2.94
SUPT20H	suppressor of Ty 20 homolog (S. cerevisiae)	2.88	2.68	1.91	1.9
ZNF610	zinc finger protein 610	2.34	2.28	2.01	2.08
FAM65B	family with sequence similarity 65, member B	1.83	2.25	4.06	4.76
G2E3	G2/M-phase specific E3 ubiquitin protein ligase	5.55	4.93	2.39	2.56
PRICKLE1	prickle homolog 1 (Drosophila)	6.72	7.98	3.68	2.83
GLRX3	glutaredoxin 3	4.67	4.34	1.45	1.45
FAM19A4	family with sequence similarity 19 (chemokine (C-C motif)-like), member A4	2.89	3.76	4	6.57
RAD54L	RAD54-like (S. cerevisiae)	3.84	3.54	1.62	1.75
---		2.25	2.29	2.14	2.05
SMYD3	SET and MYND domain containing 3	2.15	2.09	5.75	5.13
EHD4	EH-domain containing 4	2.79	2.68	3.04	2.75
---		2.78	2.37	3.11	2.72



RHOQ	ras homolog family member Q	2.27	2.28	2.12	2.25
SPAG5	sperm associated antigen 5	4.33	4.12	1.57	1.9
BMPR1A	bone morphogenetic protein receptor, type IA	10.54	9.54	2.78	2.46
GPR143	G protein-coupled receptor 143	2.25	2.71	1.93	1.91
DCAF16	DDB1 and CUL4 associated factor 16	4.45	4.64	5.02	4.17
FAM175A	family with sequence similarity 175, member A	2.84	2.66	2.13	2.71
MICALL1	MICAL-like 1	3.79	3.7	2.47	2.02
ILF2	interleukin enhancer binding factor 2	6.51	6.16	2.3	2.32
SET	SET nuclear oncogene	7.31	7.36	1.86	1.75
SPOCK1	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 1	3.29	3.99	7.19	6.9
PRMT1	protein arginine methyltransferase 1	8.68	7.77	2.32	2.37
SKP2	S-phase kinase-associated protein 2, E3 ubiquitin protein ligase	3.62	3.64	5.13	5.02
KIAA1841	KIAA1841	2.24	1.94	1.24	1.46
MRS2	MRS2 magnesium transporter	5	5.47	1.62	1.83
ATL1	atlastin GTPase 1	2.59	3.37	2.46	2.03
RPL8	ribosomal protein L8	2.63	2.49	2.35	2.26
EIF2S3	eukaryotic translation initiation factor 2, subunit 3 gamma, 52kDa	3.46	3.61	2.75	2.41
EFS	embryonal Fyn-associated substrate	5.5	5.27	6.35	5.61
TSHZ3	teashirt zinc finger homeobox 3	2.67	3.39	5.14	4.33
ACTG2	actin, gamma 2, smooth muscle, enteric	3.66	4.41	6.3	3.75
MAP3K7	mitogen-activated protein kinase kinase kinase 7	2.65	2.49	1.89	2.05
SPATS2	spermatogenesis associated, serine-rich 2	3.4	3.06	4.2	4.22
SGCE	sarcoglycan, epsilon	2.62	2.56	3.9	3.95
PIAS3	protein inhibitor of activated STAT, 3	2.41	2.38	3.37	3.34
MBOAT2	membrane bound O-acyltransferase domain containing 2	5.32	5.4	6.15	5.21
TMEM55A	transmembrane protein 55A	8.39	8.54	3.82	3.37
TFAP2C	transcription factor AP-2 gamma (activating enhancer binding protein 2 gamma)	4.25	4.27	4.98	4.44
FXYD5	FXYD domain containing ion transport regulator 5	3.31	3.03	2.79	2.9
CCDC109B	coiled-coil domain containing 109B	5.69	6.49	4.12	3.58
TAF1B	TATA box binding protein (TBP)-associated factor, RNA polymerase I, B, 63kDa	3.25	3.06	1.73	1.63
INTU	inturned planar cell polarity protein	2.11	2.08	2.15	2.21
SNHG16	small nucleolar RNA host gene 16 (non-protein coding)	2.66	2.98	2.51	2.6
C3orf14	chromosome 3 open reading frame 14	4.43	4.38	1.43	1.15
FUBP1	far upstream element (FUSE) binding protein 1	5.23	4.89	2.05	1.88
MFAP2	microfibrillar-associated protein 2	4.46	4.08	4.45	4.06
HDHD1	haloacid dehalogenase-like hydrolase domain containing 1	2.57	2.54	2.02	1.88
ZNF670	zinc finger protein 670	5.71	5.83	1.09	1.05
LDOC1	leucine zipper, down-regulated in cancer 1	5.73	5.64	7.25	7.35
FAM102B	family with sequence similarity 102, member B	2.63	2.56	1.88	1.82
LOC100506548	uncharacterized LOC100506548	1.71	1.65	5	5.9
ADRBK2	adrenergic, beta, receptor kinase 2	3.13	3.16	2.36	2.29
ZNF124	zinc finger protein 124	3.87	3.7	4.53	4.25

C5orf54	chromosome 5 open reading frame 54	1.87	2.09	2.62	2.85
ACLY	ATP citrate lyase	9.98	8.97	2.17	2.39
NAT14	N-acetyltransferase 14 (GCN5-related, putative)	2.46	2.36	2.57	2.35
CASP3	caspace 3, apoptosis-related cysteine peptidase	7.31	7.55	1.8	1.8
ASAP1	ArfGAP with SH3 domain, ankyrin repeat and PH domain 1	2.67	2.56	2.97	2.91
ABRACL	ABRA C-terminal like	5.16	5.27	1.35	1.19
SCG2	secretogranin II	1.86	2.15	3.97	3.43
STC1	stanniocalcin 1	3.28	3.07	3.77	3.05
HNRNPA0	heterogeneous nuclear ribonucleoprotein A0	4	3.99	1.99	1.48
TEAD4	TEA domain family member 4	7.45	6.9	1.9	1.74
CDCA4	cell division cycle associated 4	4.64	4.43	2.38	2.25
NT5DC2	5'-nucleotidase domain containing 2	6.1	5.86	7.2	7.39
PROSER1	proline and serine rich 1	3.97	4.09	1.55	1.47
SV2A	synaptic vesicle glycoprotein 2A	7.99	8.18	3.93	4.41
GLI3	GLI family zinc finger 3	2.74	3.15	4.14	3.41
NES	nestin	7.52	7.17	1.95	1.65
TEX10	testis expressed 10	8.1	8.42	2.81	2.9
API2	adaptor-related protein complex 1, sigma 2 subunit	6.67	6.84	4.21	4.08
DNAJC18	DnaJ (Hsp40) homolog, subfamily C, member 18	2.76	3.1	2.88	2.8
LOC100505501	uncharacterized LOC100505501	6.65	8.66	1.37	1.27
JPH1	junctophilin 1	6.22	6.71	3.55	3.19
FOCAD	focadhesin	4.83	4.93	4.86	4.6
PPIH	peptidylprolyl isomerase H (cyclophilin H)	4.12	4.11	1.88	1.98
OSBPL10	oxysterol binding protein-like 10	2.61	2.92	2.45	2.32
TNPO1	transportin 1	3.99	4	2.3	2.09
C14orf166	chromosome 14 open reading frame 166	3.49	3.53	1.99	2.24
ZNF195	zinc finger protein 195	5.57	4.95	1.01	1.28
RUNX1T1	"runt-related transcription factor 1; translocated to, 1 (cyclin D-related)"	4.84	4.43	6.08	4.96
NUP205	nucleoporin 205kDa	7.57	7.6	2.64	2.45
NEO1	neogenin 1	2.73	2.67	3.47	3.34
LRRC49	leucine rich repeat containing 49	4.65	5.01	2.13	2.46
ZNF256	zinc finger protein 256	4.57	5.39	2.12	1.81
SPA17	sperm autoantigenic protein 17	6.7	6.46	2.28	1.75
CMTM4	CKLF-like MARVEL transmembrane domain containing 4	2.4	2.39	3.58	3.33
PRKD1	protein kinase D1	3.09	3.06	4.48	4.23
SNRPD1	small nuclear ribonucleoprotein D1 polypeptide 16kDa	6.08	6.04	1.42	1.59
CENPL	centromere protein L	6.37	7.19	3.27	2.77
HSPA13	heat shock protein 70kDa family, member 13	1.94	2	2.5	3.32
GSKIP	GSK3B interacting protein	2.73	2.48	1.86	2.18
TMEM147	transmembrane protein 147	3.01	2.85	2.04	1.83
INTS9	integrator complex subunit 9	3.07	3.16	1.55	1.46
ALDH1A3	aldehyde dehydrogenase 1 family, member A3	4.04	3.46	2.91	1.87
NSG1	neuron specific gene family member 1	2.84	3.83	7.76	7.78
LHFPL2	lipoma HMGIC fusion partner-like 2	3.5	3.33	3.64	4.03
PEA15	phosphoprotein enriched in astrocytes 15	4.15	3.72	4.13	3.7



SLC35F1	solute carrier family 35, member F1	4.81	5.22	2.55	2.5
MYL9	myosin, light chain 9, regulatory	5.96	5.26	7.54	6.04
CCDC113	coiled-coil domain containing 113	1.72	1.96	1.67	1.42
SNRPD2	small nuclear ribonucleoprotein D2 polypeptide 16.5kDa	3.52	3.31	2.5	2.7
SASS6	spindle assembly 6 homolog (C. elegans)	4.21	4.65	1.03	1.29
PLK4	polo-like kinase 4	5.89	6.16	1.56	1.58
PLCB4	phospholipase C, beta 4	4.91	4.87	2.55	2.55
MID1	midline 1 (Opitz/BBB syndrome)	4.01	4.47	4.39	3.15
WFDC2	WAP four-disulfide core domain 2	3.26	2.68	3.04	3.07
USP14	ubiquitin specific peptidase 14 (tRNA-guanine transglycosylase)	3.04	3.09	1.68	1.54
PPIA	peptidylprolyl isomerase A (cyclophilin A)	3.77	4.12	1.71	1.66
ZNF708	zinc finger protein 708	3.67	4.1	-1.06	1.26
CRABP2	cellular retinoic acid binding protein 2	2.37	2.51	7.17	6.68
KCNG1	potassium voltage-gated channel, subfamily G, member 1	7.57	5.82	4.24	3.84
ATP8B2	ATPase, aminophospholipid transporter, class I, type 8B, member 2	2.64	2.72	2.11	2.02
ZNF100	zinc finger protein 100	4.27	4.62	1.13	1.48
OSBPL3	oxysterol binding protein-like 3	3.54	3.12	2.99	3.3
EEF1E1	eukaryotic translation elongation factor 1 epsilon 1	5.52	5.6	1.32	1.63
SNHG6	small nucleolar RNA host gene 6 (non-protein coding)	2.4	2.39	1.97	2.26
TC2N	tandem C2 domains, nuclear	1.79	1.95	1.44	1.77
EGLN3	egl-9 family hypoxia-inducible factor 3	3.48	3.48	4.78	3.11
EPHA4	EPH receptor A4	6.17	4.75	2.58	2.37
ANXA5	annexin A5	2.8	2.86	3.8	3.91
BIK	BCL2-interacting killer (apoptosis-inducing)	2.16	2.54	3.78	3.48
NHS	Nance-Horan syndrome (congenital cataracts and dental anomalies)	2.78	2.75	1.36	1.44
PLEKHH1	pleckstrin homology domain containing, family H (with MyTH4 domain) member 1	2.15	2.22	3.69	3.54
RAB11FIP4	RAB11 family interacting protein 4 (class II)	1.76	1.8	2.31	1.97
FLVCR1-AS1	FLVCR1 antisense RNA 1 (head to head)	5.54	5.76	2.97	3.52
NGFRAP1	nerve growth factor receptor (TNFRSF16) associated protein 1	3.76	3.77	2.39	2.34
WWC3	WWC family member 3	4.86	4.54	4.76	3.56
PABPC3	poly(A) binding protein, cytoplasmic 3	5.29	5.51	4.36	3.58
FBLN1	fibulin 1	3.67	3.38	9.39	8.72
RPL39L	ribosomal protein L39-like	6.88	7.16	2.99	3.29
RASGEF1A	RasGEF domain family, member 1A	6.03	7.13	2.71	3.2
SPG20	spastic paraplegia 20 (Troyer syndrome)	3.38	3.09	4.08	4.29
FUNDC1	FUN14 domain containing 1	2.14	2.1	1.67	1.6
ISYNA1	inositol-3-phosphate synthase 1	2.6	2.75	4.03	3.92
BLMH	bleomycin hydrolase	3.44	3.28	2.04	2.09
FGFR1	fibroblast growth factor receptor 1	7.12	7.28	2.77	2.75
RGS17	regulator of G-protein signaling 17	4.43	4.59	1.64	1.76
NEIL3	nei endonuclease VIII-like 3 (E. coli)	7.15	7.03	2.5	2.51
CENPM	centromere protein M	8.63	7.76	1.99	1.7

MZT1	mitotic spindle organizing protein 1	7.66	6.75	2.51	2.52
LOC646903	uncharacterized LOC646903	2.66	2.86	2.43	2.31
FRAS1	Fraser syndrome 1	6.76	6.98	6.64	5.83
ZNF165	zinc finger protein 165	4.75	4.74	1.19	1.3
ZNF185	zinc finger protein 185 (LIM domain)	2.19	2.12	6.91	6.28
TYRO3	TYRO3 protein tyrosine kinase	2.27	2.22	2.85	2.65
RNF24	ring finger protein 24	3.63	3.62	2.94	2.89
RASGRF2	Ras protein-specific guanine nucleotide-releasing factor 2	4.57	5.23	2.22	1.75
MIF	macrophage migration inhibitory factor (glycosylation-inhibiting factor)	2.91	2.72	3.26	3.11
ZNF93	zinc finger protein 93	10.9	10.31	4.03	4.7
---		2.88	2.57	2.81	2.54
MTRFR2	mitochondrial fission regulator 2	5.31	6.54	1.48	1.39
ABHD17C	abhydrolase domain containing 17C	2.86	2.92	2.04	1.91
GMFB	glia maturation factor, beta	3.53	3.47	1.46	1.54
C7orf49	chromosome 7 open reading frame 49	2.88	2.71	2.47	2.5
NMNAT2	nicotinamide nucleotide adenylyltransferase 2	2.53	2.79	3.21	2.73
SYNGR3	synaptogyrin 3	2.6	2.98	1.81	1.93
SRI	sorcin	2	2.35	1.8	1.74
ZNF137P	zinc finger protein 137, pseudogene	1.82	1.66	1.63	1.75
ADAMTS3	ADAM metalloproteinase with thrombospondin type 1 motif, 3	2.32	2.14	2.84	2.79
CAV1	caveolin 1, caveolae protein, 22kDa	16.14	12.89	4.33	2.84
FERMT1	fermitin family member 1	4.42	6.24	7.18	5.32
LOC728392	uncharacterized LOC728392	3.12	3.61	7.73	6.55
SERPINB9	serpin peptidase inhibitor, clade B (ovalbumin), member 9	6.71	3.95	6.45	4.89
C1orf198	chromosome 1 open reading frame 198	4.1	4.12	7.25	5.8
TLDC1	TBC/LysM-associated domain containing 1	1.97	2.05	3.63	3.32
RNF150	ring finger protein 150	3.06	3.7	4.07	3.75
RECQL	RecQ protein-like (DNA helicase Q1-like)	2.62	2.47	1.68	1.85
ENO2	enolase 2 (gamma, neuronal)	2.89	3.19	2.77	2.23
ZC2HC1A	zinc finger, C2HC-type containing 1A	6.12	6.21	6.88	7.09
RPS6KA6	ribosomal protein S6 kinase, 90kDa, polypeptide 6	2.82	2.65	1.61	1.73
KIF2A	kinesin heavy chain member 2A	8.08	7.75	2.59	2.7
TYMS	thymidylate synthetase	7.54	7.15	3.27	2.56
CTGF	connective tissue growth factor	4.27	5.63	5.45	1.38
RUSC1	RUN and SH3 domain containing 1	2.95	2.84	1.76	1.98
PCDH18	protocadherin 18	6.53	8.33	7.1	5.8
GUCA1A	guanylate cyclase activator 1A (retina)	2.58	3.49	6.99	6.47
NPM3	nucleophosmin/nucleoplasmin 3	14.9	14.38	2.77	2.69
STRAP	serine/threonine kinase receptor associated protein	3.59	3.7	2.49	2.56
ADAM17	ADAM metalloproteinase domain 17	2.31	2.22	3.52	3.1
LOC100288637	OTU domain containing 7A pseudogene	4.36	4.62	2.16	1.81
BNC2	basonuclin 2	2.05	2.65	5.76	5.17
EOGT	EGF domain-specific O-linked N-acetylglucosamine (GlcNAc) transferase	17.02	15.39	1.28	1.19
ACY1	acylphosphatase 1, erythrocyte (common) type	2.03	1.69	1.18	1.15

HMGCR	3-hydroxy-3-methylglutaryl-CoA reductase	10.11	9.74	1.38	1.7
CACNA2D3	calcium channel, voltage-dependent, alpha 2/delta subunit 3	2.01	2.14	2.71	2.83
CTPS2	CTP synthase 2	2.9	3.3	2.21	2.18
TMA16	translation machinery associated 16 homolog (S. cerevisiae)	11.49	11.19	3.15	2.87
PTBP3	polypyrimidine tract binding protein 3	2.14	1.95	1.87	1.57
DNAJB6	DnaJ (Hsp40) homolog, subfamily B, member 6	10.36	10.06	1.52	1.12
DOK5	docking protein 5	5.18	4.47	4.42	3.86
RCAN2	regulator of calcineurin 2	7.86	6.17	2.17	1.48
CETN3	centrin, EF-hand protein, 3	1.99	2.09	2.35	2.08
DNAJC10	DnaJ (Hsp40) homolog, subfamily C, member 10	3.11	2.98	1.25	1.37
FREM2	FRAS1 related extracellular matrix protein 2	1.71	1.93	11.76	8.47
HIST1H4C	histone cluster 1, H4c	7.58	7.82	2.57	2.27
PPP2R3A	protein phosphatase 2, regulatory subunit B", alpha	2.83	2.9	3.89	4.1
PGM2L1	phosphoglucomutase 2-like 1	3.66	4.26	2.11	2.07
SH3PXD2B	SH3 and PX domains 2B	3.8	3.54	2.96	2.38
EIF4EBP1	eukaryotic translation initiation factor 4E binding protein 1	2.43	1.85	3.82	4.03
PAK6	p21 protein (Cdc42/Rac)-activated kinase 6	2.68	2.97	9.71	7.54
TNNT1	troponin T type 1 (skeletal, slow)	4.46	4.28	5.89	8.23
ADD3	adducin 3 (gamma)	2.01	1.94	2.55	2.61
SLC16A9	solute carrier family 16, member 9	3.69	5.51	2.56	2.24
MACC1	metastasis associated in colon cancer 1	1.69	1.86	1.71	1.88
NOX4	NADPH oxidase 4	2.28	3.23	13.34	10.25
SYCP2L	synaptonemal complex protein 2-like	2.04	2.13	2.39	2.83
ZFAS1	ZNFX1 antisense RNA 1	2.37	2.33	5.15	6.25
PDE9A	phosphodiesterase 9A	3.58	3.15	2.07	2.25
SOX8	SRY (sex determining region Y)-box 8	3.33	3.72	2.83	2.74
ALPK3	alpha-kinase 3	2.95	2.92	2.44	2.56
B3GALNT1	beta-1,3-N-acetylgalactosaminyltransferase 1 (globoside blood group)	5.16	4.54	4.22	3.87
WDR54	WD repeat domain 54	5.51	5.98	6.6	5.36
STON1	stonin 1	1.98	2.07	9.11	7.78
ZNF239	zinc finger protein 239	8.7	9.3	2.24	2.33
KISS1R	KISS1 receptor	1.43	1.74	1.94	1.65
PMEPA1	prostate transmembrane protein, androgen induced 1	9.7	8.84	2.33	2.13
PIFO	primary cilia formation	2.94	2.95	5.85	6.6
SEL1L3	sel-1 suppressor of lin-12-like 3 (C. elegans)	2.42	2.64	1.06	-1.18
PSMD10	proteasome (prosome, macropain) 26S subunit, non-ATPase, 10	1.85	1.93	1.93	1.91
NFE2L3	nuclear factor, erythroid 2-like 3	5.33	5.64	1.5	1.9
RNF175	ring finger protein 175	4.98	6.01	1.35	1.38
LMO3	LIM domain only 3 (rhombotin-like 2)	2	2.32	4.99	4.49
SH2D3A	SH2 domain containing 3A	2.64	2.89	1.52	1.52
TP53I3	tumor protein p53 inducible protein 3	4.09	3.83	2.34	1.78
NPEPPS	aminopeptidase puromycin sensitive	2.31	2.16	3.35	2.94
PCDH10	protocadherin 10	11.37	8.48	6.02	4.34

RGS10	regulator of G-protein signaling 10	1.67	2.16	7.65	7.01
CLDN10	claudin 10	3.33	4.5	7.39	8.29
BAX	BCL2-associated X protein	2.92	2.42	1.01	-1.1
ZNF57	zinc finger protein 57	1.81	2	1.38	1.29
DOCK11	dedicator of cytokinesis 11	1.11	1.23	2.22	2.3
SH3GL3	SH3-domain GRB2-like 3	8.15	8.59	9.4	8.92
CAPG	capping protein (actin filament), gelsolin-like	1.84	1.73	3.29	3.54
TMTC2	transmembrane and tetratricopeptide repeat containing 2	2.59	1.97	7.35	4.98
ZNF114	zinc finger protein 114	5.16	6.23	1.29	1.3
ODC1	ornithine decarboxylase 1	4.58	4.16	3.91	6.52
SLIT2	slit homolog 2 (Drosophila)	7.4	6.28	10.74	7.64
MMP2	matrix metalloproteinase 2 (gelatinase A, 72kDa gelatinase, 72kDa type IV collagenase)	11.56	10.14	16.58	14.37
CLGN	calmegin	2.4	2.41	3.11	5.73
IFT80	intraflagellar transport 80 homolog (Chlamydomonas)	1.65	1.68	2.62	3.31
IGDCC3	immunoglobulin superfamily, DCC subclass, member 3	7.73	7.73	11.95	9.88
TAC1	tachykinin, precursor 1	15.09	12.96	1.05	-1.01
FAM150B	family with sequence similarity 150, member B	2.33	2.29	14.47	15.75
GPR64	G protein-coupled receptor 64	12.82	8.58	1.24	1.37
FZD2	frizzled family receptor 2	5.65	5.65	8.8	8.04
MEST	mesoderm specific transcript	1.49	1.7	9.32	7.69
MIR205HG	MIR205 host gene (non-protein coding)	1.18	1.1	6.21	6.93
HJURP	Holliday junction recognition protein	15.43	15.69	3.75	3.13
C4orf46	chromosome 4 open reading frame 46	13.45	13.82	2.83	1.99
TRIP13	thyroid hormone receptor interactor 13	21.07	21.92	3.05	2.8
IPW	imprinted in Prader-Willi syndrome (non-protein coding)	13.92	15.04	2.31	2.07
BLM	Bloom syndrome, RecQ helicase-like	18.43	19.19	3.05	3.31
CHEK1	checkpoint kinase 1	21.88	22.73	2.43	2.15
CENPW	centromere protein W	20.73	20.07	4.02	3.32
DEPDC1	DEP domain containing 1	16.21	15.08	3.95	3.21
NUSAP1	nucleolar and spindle associated protein 1	15.88	14.12	3.22	2.44
BIRC5	baculoviral IAP repeat containing 5	15.65	14.9	3.68	3.06
STIL	SCL/TAL1 interrupting locus	23.52	23.86	2.18	1.78
RMI2	RecQ mediated genome instability 2	15.76	16.83	2.48	2.29
ZWILCH	zwilch kinetochore protein	11.48	11.48	1.88	1.86
MSH2	mutS homolog 2	19.88	21.27	2.09	2.25
KIAA0101	KIAA0101	14.34	15.11	2.4	2.04
KIF14	kinesin family member 14	15.06	14.71	1.8	1.69
CENPA	centromere protein A	11.97	11.52	4.13	3.04
PRKX	protein kinase, X-linked	13.83	12.48	2.81	1.96
FANCI	Fanconi anemia, complementation group I	10.14	10.58	2.8	2.62
CEP55	centrosomal protein 55kDa	28.08	21.73	2.85	2.12
PSRC1	proline/serine-rich coiled-coil 1	15	14.95	4.04	3.54
BUB1	BUB1 mitotic checkpoint serine/threonine kinase	11.76	11.01	2.36	2.01
CENPE	centromere protein E, 312kDa	19.59	14.62	2.48	3.39
DBF4	DBF4 homolog (S. cerevisiae)	22.16	22.81	1.79	1.9

HOMER1	homer homolog 1 (Drosophila)	19.53	20.24	4.33	3.98
PARPBP	PARP1 binding protein	16.82	16.26	1.35	1.27
KIF5C	kinesin family member 5C	14	13.36	2.07	2.21
OXCT1	3-oxoacid CoA transferase 1	13.26	14.99	3.58	3.09
EZH2	enhancer of zeste homolog 2 (Drosophila)	17.54	18.78	1.73	1.73
FBXO5	F-box protein 5	11.65	11.18	1.97	1.76
CDC6	cell division cycle 6	25.82	24.27	1.68	1.57
WDHD1	WD repeat and HMG-box DNA binding protein 1	10.56	11.06	1.78	1.82
RCC2	regulator of chromosome condensation 2	37.22	37.39	3.67	3.1
GJC1	gap junction protein, gamma 1, 45kDa	15.96	15.72	4.98	4.05
MIS18BP1	MIS18 binding protein 1	10.44	8.7	1.4	1.77
CENPF	centromere protein F, 350/400kDa	19.13	19.93	2.7	2.64
OIP5	Opa interacting protein 5	33.95	33.66	3.44	2.53
VRK1	vaccinia related kinase 1	10.9	11.2	1.5	1.46
CCDC112	coiled-coil domain containing 112	9.52	10.68	2.57	2.91
TPX2	TPX2, microtubule-associated	11.86	10.64	2.96	2.09
DSCC1	DNA replication and sister chromatid cohesion 1	15.14	15.12	1.62	1.45
DTL	denticleless E3 ubiquitin protein ligase homolog (Drosophila)	29.61	34.56	2.43	2.42
MCM10	minichromosome maintenance complex component 10	16.19	17.43	1.58	1.48
RASL11B	RAS-like, family 11, member B	13.65	14.67	3.2	2.59
CD200	CD200 molecule	24.1	19.9	5.54	5.44
TTF2	transcription termination factor, RNA polymerase II	24.02	25.13	3.42	2.7
MND1	meiotic nuclear divisions 1 homolog (S. cerevisiae)	16.31	15.86	1.31	1.23
SHCBP1	SHC SH2-domain binding protein 1	11.72	13.72	2.51	1.96
SPC25	SPC25, NDC80 kinetochore complex component	27.12	26.06	1.68	1.44
KIF15	kinesin family member 15	14.6	15.36	1.49	1.64
IRX2	iroquois homeobox 2	16.74	19.55	5.21	3.9
LRP8	low density lipoprotein receptor-related protein 8, apolipoprotein e receptor	23.98	19.74	1.64	1.7
ASPM	asp (abnormal spindle) homolog, microcephaly associated (Drosophila)	13.92	12.35	1.71	1.53
SOX2	SRY (sex determining region Y)-box 2	15.59	14.05	1.65	1.48
ZNF423	zinc finger protein 423	23.57	25.74	4.38	3.7
JARID2	jumonji, AT rich interactive domain 2	10.74	11.85	2.11	1.62
VANGL2	VANGL planar cell polarity protein 2	12.02	10.66	4.41	4.16
SPDL1	spindle apparatus coiled-coil protein 1	16.77	15.93	4.03	4.4
BORA	bora, aurora kinase A activator	9.89	9.49	3.21	2.79
BCL11A	B-cell CLL/lymphoma 11A (zinc finger protein)	18.92	20.7	4.02	4.03
IL17RD	interleukin 17 receptor D	14.33	14.58	1.56	1.52
HELLS	helicase, lymphoid-specific	37.71	37.52	1.76	1.73
RNF182	ring finger protein 182	8.31	9.62	3.08	2.08
KIF2C	kinesin family member 2C	10.19	9.79	3.07	2.59
PSIP1	PC4 and SFRS1 interacting protein 1	12.56	12.69	1.55	1.59
CKAP2	cytoskeleton associated protein 2	17.74	15.57	4.84	4.62
NDC80	NDC80 kinetochore complex component	28.16	27.01	2.23	1.7
NELL2	NEL-like 2 (chicken)	14.66	15.71	2.26	1.85
HMGB2	high mobility group box 2	19.01	18.24	5.82	3.95

SUPT16H	suppressor of Ty 16 homolog ( <i>S. cerevisiae</i> )	10.16	7.88	3.37	2.65
MLF1	myeloid leukemia factor 1	8.78	10.05	4.94	5.23
FANCD2	Fanconi anemia, complementation group D2	10.81	11.85	2.51	2.36
NEFM	neurofilament, medium polypeptide	21.41	11.93	1.85	1.57
NBEA	neurobeachin	9.57	8.7	2.74	2.43
RAD51AP1	RAD51 associated protein 1	33.91	36.23	4.38	3.86
CYYR1	cysteine/tyrosine-rich 1	21.37	19.71	3.85	2.88
PTTG3P	pituitary tumor-transforming 3, pseudogene	15.38	17.52	4.69	3.51
NUDT11	nudix (nucleoside diphosphate linked moiety X)- type motif 11	21.75	22.61	6.49	6.36
TERF1	telomeric repeat binding factor (NIMA-interacting) 1	14.61	15.86	1.8	1.86
SEMA6A	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6A	15.31	13.95	2.8	2.59
LMNB1	lamin B1	61.12	41.09	3	1.94
ZFP42	ZFP42 zinc finger protein	25.99	26.45	5.9	4.61
MIS18A	MIS18 kinetochore protein homolog A ( <i>S. pombe</i> )	11.62	11.46	1.85	1.81
RIMKLB	ribosomal modification protein rimK-like family member B	11.12	10.55	1.87	1.94
CKS2	CDC28 protein kinase regulatory subunit 2	11.48	11.04	2.55	1.95
NUF2	NUF2, NDC80 kinetochore complex component	29.06	25.82	4.07	3.51
PTTG1	pituitary tumor-transforming 1	26.11	27.28	7.53	5.8
AURKB	aurora kinase B	36.75	33.23	3.79	3.03
NUP93	nucleoporin 93kDa	9.74	9.45	2.57	2.8
NCAPD2	non-SMC condensin I complex, subunit D2	10.05	9.29	3.38	2.73
TRIM59	tripartite motif containing 59	28.27	25.23	5.78	4.77
FOXM1	forkhead box M1	12.11	11.64	2.27	2.18
AURKA	aurora kinase A	23.47	23.32	4.9	3.71
KIF4A	kinesin family member 4A	39.48	37.68	4.94	3.5
KIF18B	kinesin family member 18B	10.93	11.49	2.32	1.94
VAT1L	vesicle amine transport 1-like	27.38	28.63	4.66	3.47
HMMR	hyaluronan-mediated motility receptor (RHAMM)	41.9	41.11	3.23	2.98
COCH	cochlin	12.71	9.38	1.55	1.62
SYT1	synaptotagmin I	20.13	18.92	4.94	3.87
MYEF2	myelin expression factor 2	23.91	26.4	5.23	5.08
CDCA5	cell division cycle associated 5	12.18	12.28	2.31	2.14
RHNO1	RAD9-HUS1-RAD1 interacting nuclear orphan 1	9.84	9.93	4.11	3.38
CALB1	calbindin 1, 28kDa	50.39	37.71	1.15	1.19
UBE2T	ubiquitin-conjugating enzyme E2T (putative)	7.32	6.86	1.78	1.71
OTX2	orthodenticle homeobox 2	64.2	50.05	2.25	1.89
NETO2	neuropilin (NRP) and tolloid (TLL)-like 2	22.34	19.99	2.84	2.56
NLGN4X	neuroligin 4, X-linked	34.12	32.98	3.99	3.19
SLC7A3	solute carrier family 7 (cationic amino acid transporter, y <sup>+</sup> system), member 3	35.75	38.32	2.82	2.57
ZWINT	ZW10 interacting kinetochore protein	35.35	35.81	3.95	3.01
TMEM158	transmembrane protein 158 (gene/pseudogene)	22.06	16.02	4.87	3.91
FAM46B	family with sequence similarity 46, member B	11.31	12.84	5.47	5.41
EXO1	exonuclease 1	10.06	11.6	2.06	2.16
ZNF788	zinc finger family member 788	8.64	9.52	2.23	1.93
CDKN3	cyclin-dependent kinase inhibitor 3	43.45	37.24	4.65	3.63



SGOL2	shugoshin-like 2 (S. pombe)	24.76	22.28	2.33	2.9
CDC7	cell division cycle 7	33.01	34.18	4.16	4.32
ZIC3	Zic family member 3	19.86	18.49	1.54	1.36
FAM64A	family with sequence similarity 64, member A	12.48	13.19	1.13	-1.1
FAT3	FAT atypical cadherin 3	15.7	15.14	2.31	1.67
TCEAL2	transcription elongation factor A (SII)-like 2	6.83	11.4	1.4	1.68
FGF2	fibroblast growth factor 2 (basic)	13.21	15.37	1.59	1.66
RNASEH2A	ribonuclease H2, subunit A	8.37	8.34	2.16	1.98
FGFBP3	fibroblast growth factor binding protein 3	40.13	40.77	1.12	1.14
CDCA7L	cell division cycle associated 7-like	12.04	15.19	1.07	-1.17
C11orf82	chromosome 11 open reading frame 82	13.32	12.04	1.41	1.48
ELAVL2	ELAV like neuron-specific RNA binding protein 2	7.52	10.87	2.28	1.86
ROR1	receptor tyrosine kinase-like orphan receptor 1	10.71	11.35	4.05	4.58
MELK	maternal embryonic leucine zipper kinase	20.76	19.1	5.15	5.19
PLP1	proteolipid protein 1	36.9	56.89	1.76	1.59
LOC100127983	uncharacterized LOC100127983	10.93	11.57	6.27	6.19
BARD1	BRCA1 associated RING domain 1	7.83	8.47	3.24	3.52
KAL1	Kallmann syndrome 1 sequence	47.35	42.3	1.75	1.48
GINS2	GINS complex subunit 2 (Psf2 homolog)	12.26	12.55	1.21	1.15
ZNF273	zinc finger protein 273	9.15	8.42	1.88	2.5
SALL2	spalt-like transcription factor 2	45.72	49.71	6.02	5.21
TRAF5	TNF receptor-associated factor 5	6.41	5.73	3.1	3.26
MCM3	minichromosome maintenance complex component 3	11.37	11.65	1.24	1.17
BUB1B	BUB1 mitotic checkpoint serine/threonine kinase B	48.47	49.37	4.54	3.02
KIF11	kinesin family member 11	48.78	49.8	5.22	3.88
SCG3	secretogranin III	30.21	30.22	1.13	1.09
SALL4	spalt-like transcription factor 4	14.65	13.97	1.82	1.93
FAM83D	family with sequence similarity 83, member D	14.04	14.26	1.52	1.15
HAUS1	HAUS augmin-like complex, subunit 1	8.25	8.46	3.41	3.76
RFWD3	ring finger and WD repeat domain 3	9.29	9	1.82	1.44
MCM2	minichromosome maintenance complex component 2	9.62	9.91	1.35	1.31
TCEAL7	transcription elongation factor A (SII)-like 7	7.13	13.43	4.8	4.7
PWAR5	Prader Willi/Angelman region RNA 5	5.71	6.31	1.06	1.03
PRKAR2B	protein kinase, cAMP-dependent, regulatory, type II, beta	22.33	30.31	8.54	5.55
RFC4	replication factor C (activator 1) 4, 37kDa	7.45	7.42	2.27	2.55
C5orf34	chromosome 5 open reading frame 34	5.23	5.05	2.4	2.75
MICB	MHC class I polypeptide-related sequence B	17.53	16.84	1.11	1.62
LMNB2	lamin B2	11.62	10.86	3.03	2.53
GPM6B	glycoprotein M6B	31.61	40.77	2.24	2.21
E2F5	E2F transcription factor 5, p130-binding	18.16	14.96	4.9	4.76
CTBP2	C-terminal binding protein 2	24.5	25.24	6.94	6.87
PRTFDC1	phosphoribosyl transferase domain containing 1	12.85	14.99	2.11	2.01
SHISA2	shisa family member 2	23.41	17.92	15.57	8.37
CRABP1	cellular retinoic acid binding protein 1	7.57	7.06	1.48	1.59
CACHD1	cache domain containing 1	19.86	19.47	2.59	2.13
CENPK	centromere protein K	35.28	34.66	4.6	4.17

H2AFZ	H2A histone family, member Z	12.81	12.82	3.78	3.42
NMU	neuromedin U	19.27	18.06	2.06	1.96
GPC4	glypican 4	68.23	66.25	7.38	5.76
KLHL7	kelch-like family member 7	8.22	8.71	1.94	2.31
MCM6	minichromosome maintenance complex component 6	8.98	9.99	1.91	2.06
SFRP2	secreted frizzled-related protein 2	59.18	63.81	11.62	7.54
VASH2	vasohibin 2	78.7	80.16	1.59	1.53
ITM2A	integral membrane protein 2A	10.66	14.09	5.12	6
KIF18A	kinesin family member 18A	7.63	6.64	1.43	1.65
E2F8	E2F transcription factor 8	15.52	15.77	1.7	1.59
MIR17HG	miR-17-92 cluster host gene (non-protein coding)	8.36	7.8	1.38	1.07
DEPDC1B	DEP domain containing 1B	60.79	65.07	3.62	2.62
DBN1	drebrin 1	11.94	11.53	4.4	4.11
GABRB3	gamma-aminobutyric acid (GABA) A receptor, beta 3	32.65	26.61	-1.23	-1.35
RBPM5	RNA binding protein with multiple splicing 2	20.33	20.8	2.26	2.24
CDCA3	cell division cycle associated 3	10.47	10.1	2.82	2.4
BEND4	BEN domain containing 4	13.5	19.52	1.09	1.1
NCAPG	non-SMC condensin I complex, subunit G	35.9	30.66	3.02	2.54
KPNA2	karyopherin alpha 2 (RAG cohort 1, importin alpha 1)	16.68	17.33	8	6.47
CCNA2	cyclin A2	56.5	53.01	7.03	4.82
C9orf135	chromosome 9 open reading frame 135	58.42	47.8	-1.12	-1.05
DNMT3B	DNA (cytosine-5-)-methyltransferase 3 beta	87.44	100.68	2.73	2.4
CHN1	chimerin 1	12.19	12.07	12.6	11.79
SLC38A1	solute carrier family 38, member 1	16.29	14.96	6.73	6.17
MAMDC2	MAM domain containing 2	5.3	6.65	4.25	1.98
PPP2R2B	protein phosphatase 2, regulatory subunit B, beta	14.88	17.03	3.42	2.34
USP44	ubiquitin specific peptidase 44	59.3	69.45	1.23	1.13
LECT1	leukocyte cell derived chemotaxin 1	8.87	13.67	1.14	1.17
KIT	v-kit Hardy-Zuckerman 4 feline sarcoma viral oncogene homolog	9.23	6.76	3.2	2.53
NEFL	neurofilament, light polypeptide	10.62	6.97	1.24	1.17
CDCA2	cell division cycle associated 2	14.9	12.91	3.08	2.89
PBX1	pre-B-cell leukemia homeobox 1	8.46	8.93	6.29	5.5
L1TD1	LINE-1 type transposase domain containing 1	129.02	128.61	2.59	2.9
KBTBD8	kelch repeat and BTB (POZ) domain containing 8	13.66	14.23	1.53	1.39
DCLK1	doublecortin-like kinase 1	14.75	12.61	1.11	1.1
FEN1	flap structure-specific endonuclease 1	10.42	9.76	1.33	1.18
NCAPG2	non-SMC condensin II complex, subunit G2	7.92	8.53	1.63	1.49
CENPH	centromere protein H	25.81	28.49	5.61	4.32
GFPT2	glutamine-fructose-6-phosphate transaminase 2	14.31	13.85	7.47	6.71
SKA1	spindle and kinetochore associated complex subunit 1	9.2	7.05	1.31	1.2
SFRP1	secreted frizzled-related protein 1	22.82	19.47	15.64	10.48
CNTNAP2	contactin associated protein-like 2	30.05	20.59	1.7	1.63
POU5F1P3	POU class 5 homeobox 1 pseudogene 3	94.83	89.47	1.46	1.35
KIF23	kinesin family member 23	65.1	64.96	6.33	3.63
PRC1	protein regulator of cytokinesis 1	21.63	20.46	7.91	6.07



CHML	choroideremia-like (Rab escort protein 2)	6.66	7.37	2.82	3.54
LPAR4	lysophosphatidic acid receptor 4	5.08	7.41	1.13	1.21
SBK1	SH3 domain binding kinase 1	9.32	9.93	3.13	2.38
ZNF738	zinc finger protein 738	23.49	26.24	7.19	6.1
NTS	neurotensin	252.33	173.69	1.36	1.39
ZNF681	zinc finger protein 681	4.8	5.01	1.94	2.62
CCNJ	cyclin J	11.57	11.43	4.37	3.58
UBE2C	ubiquitin-conjugating enzyme E2C	48.61	43.49	9.19	6.67
ZNF883	zinc finger protein 883	3.21	3.41	1.76	1.89
TMSB15A	thymosin beta 15a	43.97	55.28	4.14	3.16
DPPA4	developmental pluripotency associated 4	82.17	90.28	5.34	5.38
LINC00458	long intergenic non-protein coding RNA 458	147.3	89	1.38	1.42
LPHN3	latrophilin 3	7.85	7.6	2.73	2.22
FAR2	fatty acyl CoA reductase 2	17.66	13.67	2.86	3.14
MTMR2	myotubularin related protein 2	9.77	9.66	4.1	3.81
SPP1	secreted phosphoprotein 1	11.38	12.65	27.89	12.35
GAL	galanin/GMAP prepropeptide	184.47	132.03	4.47	3.12
SEMA3A	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	11.44	10.01	3.13	2.49
SEPHS1	selenophosphate synthetase 1	16.16	17.81	-1.42	-1.7
DZIP1	DAZ interacting zinc finger protein 1	9.84	8.83	9.99	8.7
ORC1	origin recognition complex, subunit 1	11.18	12.57	1.18	1.24
DACT1	dishevelled-binding antagonist of beta-catenin 1	27.74	32.11	14.78	11.89
AKR1B1	aldo-keto reductase family 1, member B1 (aldose reductase)	23.27	21.9	18.82	20.55
POLR3G	polymerase (RNA) III (DNA directed) polypeptide G (32kD)	16.02	15.4	-1.69	-1.72
NAPIL1	nucleosome assembly protein 1-like 1	7.18	7.15	4.27	4.02
MLF1IP	MLF1 interacting protein	9.87	10.24	1.06	1.11
LINC00617	long intergenic non-protein coding RNA 617	13.21	10.68	1.44	1.48
NCAPH	non-SMC condensin I complex, subunit H	9.51	9.8	2.23	2.16
PRDM14	PR domain containing 14	10.53	10.81	1.94	1.93
ZNF850	zinc finger protein 850	7.6	9.06	2.49	1.46
FABP7	fatty acid binding protein 7, brain	12.59	13.49	1.32	1.31
TAF4B	TAF4b RNA polymerase II, TATA box binding protein (TBP)-associated factor, 105kDa	6.88	6.62	1.82	1.76
KIAA1524	KIAA1524	9.61	8.76	1.42	1.41
HAS2	hyaluronan synthase 2	79.44	31.32	10.09	6.16
BRINP1	bone morphogenetic protein/retinoic acid inducible neural-specific 1	13.89	17.31	1.89	1.54
FAM101B	family with sequence similarity 101, member B	5.7	7.24	8.73	7.53
ESRG	embryonic stem cell related (non-protein coding)	287.72	303.39	1.34	1.33
ERVMER34-1	endogenous retrovirus group MER34, member 1	8.42	9.11	1.54	1.67
SCGB3A2	secretoglobin, family 3A, member 2	14.73	15.61	3.74	3.75
LOC100131138	uncharacterized LOC100131138	9.75	9.97	3.96	2.75
LOC100996702	uncharacterized LOC100996702	23.71	15.39	6.49	5.29
PKIA	protein kinase (cAMP-dependent, catalytic) inhibitor alpha	6.97	7.18	10.09	8.01

ST6GALNAC3	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 3	5.67	6.84	14.12	11.23
LEFTY1	left-right determination factor 1	81.51	75.24	1.17	1.25
LRFN5	leucine rich repeat and fibronectin type III domain containing 5	15.51	11.36	5	4.73

**Table 12 Cluster group IV: Proliferation process**

Total number of genes: 101

*The list of 101 genes represents a cluster group IV that is responsible proliferation process as described in chapter 3.4.4, Fig. 18. Column 1(from left to right) represents the gene symbol and column 2 represents the corresponding gene description. Column 3 and 4 contain the fold change values of hHEPs vs. hESCs. Column 5 and 6 contain fold change values of hHEPs vs. HLCs. HLCs-total: the heterogeneous population of hepatocyte like cells; HLCs-island: hepatocyte like islands extracted from the heterogeneous population; hESCs: human embryonic stem cells; hHEPs: freshly isolated adult hepatocytes; vs.: versus.*

Symbol	Description	hESC1	hESC2	HLCs-total	HLCs-islands
CRISPLD1	cysteine-rich secretory protein LCCL domain containing 1	45.31	49.08	22.7	18.38
LDHB	lactate dehydrogenase B	37.39	37.57	19.9	20.66
RAB34	RAB34, member RAS oncogene family	45.95	47.3	34.95	36.02
BCAT1	branched chain amino-acid transaminase 1, cytosolic	52.24	50.59	20.82	16.16
ARMCX2	armadillo repeat containing, X-linked 2	39.14	41.94	30.45	27.19
ATP1B3	ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, beta 3 polypeptide	41.87	42.6	20.23	20.16
SLC39A10	solute carrier family 39 (zinc transporter), member 10	42.79	46.17	20.66	18.06
MLLT11	"myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila); translocated to, 11"	72.73	66.23	41.66	40.18
GALNT7	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 7 (GalNAc-T7)	63.46	62.13	34.75	28.83
ESRP1	epithelial splicing regulatory protein 1	48.43	54.82	19.9	18.72
MAP1B	microtubule-associated protein 1B	34.3	29.79	17.3	11.53
SCRN1	secernin 1	28.22	31.15	22.23	21.71

GULP1	GULP, engulfment adaptor PTB domain containing 1	64.83	63.68	53.1	57.15
ROBO1	roundabout, axon guidance receptor, homolog 1 (Drosophila)	29.88	27.15	21.46	16.03
ZNF462	zinc finger protein 462	37.69	43.13	12.24	8.31
ANLN	anillin, actin binding protein	57.2	46.26	14.45	12.05
GPX8	glutathione peroxidase 8 (putative)	34.56	31.12	81.19	70.66
SLC25A36	solute carrier family 25 (pyrimidine nucleotide carrier ), member 36	18.29	18.52	21.34	23.86
TPM4	tropomyosin 4	40.61	34.4	42.82	24.32
TUBA1A	tubulin, alpha 1a	130.56	138.57	44.32	27.78
ARMCX1	armadillo repeat containing, X-linked 1	17.84	18.83	22.43	22
SLC25A24	"solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 24"	30.27	29.23	26.02	21.61
OLFML3	olfactomedin-like 3	25.14	24.06	39.52	34.71
SLC2A3	solute carrier family 2 (facilitated glucose transporter), member 3	49.64	40	82.56	55.25
TUBB6	tubulin, beta 6 class V	25.5	26.37	18.1	14.18
ORC6	origin recognition complex, subunit 6	47.07	50.38	12	9.7
CDK1	cyclin-dependent kinase 1	66.44	61.11	15.31	11.37
STK39	serine threonine kinase 39	41.18	45.04	48.3	43.8
GSTP1	glutathione S-transferase pi 1	26.79	24.18	20.27	21.48
PTPN13	protein tyrosine phosphatase, non-receptor type 13 (APO-1/CD95 (Fas)-associated phosphatase)	18.56	18.32	16.75	12.15
VCAN	versican	40.66	47.37	19.36	13.68
TPBG	trophoblast glycoprotein	21.04	21.12	14.25	12.8
CCNB1	cyclin B1	77.57	80.26	10.72	6.77
PMAIP1	phorbol-12-myristate-13-acetate-induced protein 1	92.76	109.28	8.36	6.42
BEX2	brain expressed X-linked 2	65.6	74.76	10.06	11.01
TMEM200A	transmembrane protein 200A	33.76	42.8	59.23	63.09
TOP2A	topoisomerase (DNA) II alpha 170kDa	136.26	123.63	27.44	20.4
IGF2BP3	insulin-like growth factor 2 mRNA binding protein 3	93.98	119.63	82.4	84.22
HDGFRP3	hepatoma-derived growth factor, related protein 3	46.46	43.7	15.26	14.99
FGF13	fibroblast growth factor 13	127.62	111.4	6.49	5.45
ASNS	asparagine synthetase (glutamine-hydrolyzing)	171.4	141.14	70.22	51.2
MTHFD2	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2, methenyltetrahydrofolate cyclohydrolase	169.24	168.72	74.36	50.11
FZD7	frizzled family receptor 7	76.61	90.01	13.2	8.53
LRRN1	leucine rich repeat neuronal 1	132.36	146.27	29.16	16.38
CCNB2	cyclin B2	62.33	60.73	11.45	7.95
LIN28B	lin-28 homolog B (C. elegans)	210.7	219.75	68.89	69.17
C12orf75	chromosome 12 open reading frame 75	24.53	27.62	66.44	64.83
PODXL	podocalyxin-like	150.11	162.84	121.81	88.51
FBN2	fibrillin 2	32.58	25.27	76.09	39.12
UCHL1	ubiquitin carboxyl-terminal esterase L1 (ubiquitin thiolesterase)	91.54	78.85	9.32	6.48
BEX1	brain expressed, X-linked 1	30.02	37.37	12.45	14.4
SPINT2	serine peptidase inhibitor, Kunitz type, 2	17.32	16.62	34.9	34.36

MAD2L1	MAD2 mitotic arrest deficient-like 1 (yeast)	70.18	68.16	12.48	9.78
NDN	neccin, melanoma antigen (MAGE) family member	16.56	15.73	29.48	28.05
CDCA7	cell division cycle associated 7	88.2	99.74	14.46	13.02
PROM1	prominin 1	74.29	84.96	78.17	86.63
ANXA3	annexin A3	44.54	33.67	86.45	89.08
DLGAP5	discs, large (Drosophila) homolog-associated protein 5	196.14	186.34	9.79	6.51
PFKP	phosphofructokinase, platelet	10.39	10.9	37.24	35.55
PNMAL1	paraneoplastic Ma antigen family-like 1	15.96	17.84	13.5	11.56
KIF20A	kinesin family member 20A	65.97	62.32	11.71	6.66
LAMA1	laminin, alpha 1	11.77	12.36	40.28	37.81
TUBB2B	tubulin, beta 2B class IIb	520.97	480.79	46.91	33.21
COL1A2	collagen, type I, alpha 2	35.92	37.83	366.26	303.88
ECT2	epithelial cell transforming sequence 2 oncogene	38.76	36.97	6.11	5.87
SOX11	SRY (sex determining region Y)-box 11	37.38	38.36	15.14	12.11
BEX4	brain expressed, X-linked 4	22.2	20.48	16.57	14.03
TET1	tet methylcytosine dioxygenase 1	33.93	40.1	20.19	21.51
RRM2	ribonucleotide reductase M2	84.08	83.58	4.62	3.08
CDC20	cell division cycle 20	86.22	87.08	6.89	4.41
SERPINE2	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 2	562.4	455.04	250.58	213.5
NAPIL3	nucleosome assembly protein 1-like 3	185.73	182.37	59.82	66.29
TRIM6	tripartite motif containing 6	11.82	13.15	17.4	17.96
GINS1	GINS complex subunit 1 (Psf1 homolog)	54.1	59.43	5.48	4.89
HEPH	hephaestin	26.59	30.33	117.42	137.47
MARCKSL1	MARCKS-like 1	44.39	43.1	11.08	8.58
EPCAM	epithelial cell adhesion molecule	212.55	226.35	282.3	295.41
PTPLA	protein tyrosine phosphatase-like (proline instead of catalytic arginine), member A	17.4	15.86	15.92	16.71
KRT19	keratin 19	60.73	43.74	424.71	405.28
PTN	pleiotrophin	12.24	14.84	186.97	197.5
LRRC1	leucine rich repeat containing 1	7.6	7.41	61.81	60.09
GJA1	gap junction protein, alpha 1, 43kDa	769.53	727.24	461.87	401.33
SPARC	secreted protein, acidic, cysteine-rich (osteonectin)	11.47	11.36	125.16	124.77
TTK	TTK protein kinase	68.59	68.37	5.75	5.49
FAR1	fatty acyl CoA reductase 1	17.63	16.56	8.43	9.56
LIN28A	lin-28 homolog A (C. elegans)	569.99	593.31	14.62	7.94
CTHRC1	collagen triple helix repeat containing 1	3.44	6.21	36	41.32
VIM	vimentin	18.72	16.02	24.75	22.57
RACGAP1	Rac GTPase activating protein 1	28.97	26.95	10.3	7.6
SACS	spastic ataxia of Charlevoix-Saguenay (sacsin)	20.85	20.93	5.1	4.25
DPYSL3	dihydropyrimidinase-like 3	12.86	16.14	10.44	6.74
LAMB1	laminin, beta 1	9	9.63	105.09	105.77
PKIB	protein kinase (cAMP-dependent, catalytic) inhibitor beta	11.47	11.58	10.65	10.99
LOC100506013	uncharacterized LOC100506013	57.47	68.39	5.09	6.4
PTPRZ1	protein tyrosine phosphatase, receptor-type, Z polypeptide 1	149.56	159.77	3.58	4.42
HK1	hexokinase 1	19.14	17.64	15.08	14.92

ACTC1	actin, alpha, cardiac muscle 1	39.83	47.6	151.73	125.86
GPC3	glypican 3	3.39	4.48	44.9	63.52
PITX2	paired-like homeodomain 2	40.84	36.35	103.41	93.1
ZIC2	Zic family member 2	300.65	264.28	1.89	1.66
DLK1	delta-like 1 homolog (Drosophila)	3.11	3.93	684.86	644

**Table 13 Cluster group V: ECM and Migration**

Total number of genes: 505

*The list of 505 genes represents a cluster group V that is responsible for proliferation process as described in chapter 3.4.5, Fig. 18. Column 1 (from left to right) represents the gene symbol and column 2 represents the corresponding gene description. Column 3 and 4 contain the fold change values of hHEPs vs. hESCs. Column 5 and 6 contain fold change values of hHEPs vs. HLCs. HLCs-total: the heterogeneous population of hepatocyte like cells; HLCs-island: hepatocyte like islands extracted from the heterogeneous population; hESCs: human embryonic stem cells; hHEPs: freshly isolated adult hepatocytes; vs.: versus.*

Symbol	Description	hESC1	hESC2	HLCs-total	HLCs-islands
ELF4	E74-like factor 4 (ets domain transcription factor)	1.37	1.41	6.26	5.78
PCDH7	protocadherin 7	2.08	1.98	3.81	4.3
ATP1A1	ATPase, Na <sup>+</sup> /K <sup>+</sup> transporting, alpha 1 polypeptide	1.82	1.78	4.88	4.69
TMEM87B	transmembrane protein 87B	1.22	1.14	3.61	3.55
TMEM51	transmembrane protein 51	1.89	1.81	5.06	4.91
SBSPON	somatomedin B and thrombospondin, type 1 domain containing	1.07	1.14	7.18	6.76
PLCE1	phospholipase C, epsilon 1	1.2	-1.02	3.66	3.75
SUSD1	sushi domain containing 1	1.49	1.45	2.8	2.87
CLDN4	claudin 4	-1.1	-1.16	5.17	5.13
TSPAN13	tetraspanin 13	1.14	1.18	3.22	3.57
ENDOD1	endonuclease domain containing 1	1.27	1.35	3.85	3.38
ITGAV	integrin, alpha V	2.62	2.36	7.43	5.86
ADAM9	ADAM metalloproteinase domain 9	1	-1.07	7.87	8.11
DFNA5	deafness, autosomal dominant 5	-1.35	-1.16	5.76	5.05
KLF5	Kruppel-like factor 5 (intestinal)	1.81	1.4	5.32	3.37
PRICKLE2	prickle homolog 2 (Drosophila)	1.2	1.3	7.12	5.78
UPK3A	uroplakin 3A	-1.08	-1.14	4.01	6.5

ADAMTS9	ADAM metalloproteinase with thrombospondin type 1 motif, 9	1.17	1.06	9.21	7.53
CCNG2	cyclin G2	1.71	1.58	6.25	5.69
TMC4	transmembrane channel-like 4	1.45	1.66	3.89	4.62
IGFBP6	insulin-like growth factor binding protein 6	2.24	2.2	8.23	7.58
---		1.19	1.14	3.7	4.92
S100A6	S100 calcium binding protein A6	-1.18	-1.14	5.49	7.79
NEU1	sialidase 1 (lysosomal sialidase)	1.55	1.25	2.31	3.01
GABRB1	gamma-aminobutyric acid (GABA) A receptor, beta 1	1.17	1.23	4.79	4.82
C1orf116	chromosome 1 open reading frame 116	1.62	1.75	2.68	2.79
CLDN7	claudin 7	1.96	1.93	2.96	3.06
HSPA12A	heat shock 70kDa protein 12A	1.89	1.96	3.19	2.95
WIPF1	WAS/WASL interacting protein family, member 1	-1.01	-1.09	11.02	8.91
CDX2	caudal type homeobox 2	1.2	1.17	2.53	2.42
ITGB6	integrin, beta 6	1.43	1.51	10.28	9.05
SLC2A5	solute carrier family 2 (facilitated glucose/fructose transporter), member 5	1.74	1.78	5.83	9.12
NDNF	neuron-derived neurotrophic factor	2.19	2.31	6.63	6.56
SLCO2A1	solute carrier organic anion transporter family, member 2A1	1.99	1.57	5.57	5.04
DPEP1	dipeptidase 1 (renal)	-1.09	-1.05	6.85	9.92
GABRA2	gamma-aminobutyric acid (GABA) A receptor, alpha 2	-1.08	-1.02	3.41	2.64
PAPPA	pregnancy-associated plasma protein A, pappalysin 1	1.25	1.23	13.73	8.29
LIFR	leukemia inhibitory factor receptor alpha	1.27	-1.09	15.31	14.77
CPE	carboxypeptidase E	1.38	1.05	6.28	4.64
SH3YL1	SH3 and SYLF domain containing 1	-1.49	-1.45	3.9	4.34
DAB2	Dab, mitogen-responsive phosphoprotein, homolog 2 (Drosophila)	1.14	1.02	5.06	4.34
SLC1A3	solute carrier family 1 (glial high affinity glutamate transporter), member 3	1.6	1.46	3.82	4.27
ME1	malic enzyme 1, NADP(+)-dependent, cytosolic	2.81	2.37	2.77	2.33
TNFSF4	tumor necrosis factor (ligand) superfamily, member 4	1.47	1.43	4.34	3.99
SFXN3	sideroflexin 3	-1.14	-1.14	3.28	3.58
TMEM255A	transmembrane protein 255A	1.77	1.26	10.12	8.81
BAMBI	BMP and activin membrane-bound inhibitor	2.09	1.49	7.61	6.54
SLC7A6	solute carrier family 7 (amino acid transporter light chain, y+L system), member 6	2.27	2.05	2.52	2.67
OLR1	oxidized low density lipoprotein (lectin-like) receptor 1	1.24	1.27	4.65	2.6
USH1C	Usher syndrome 1C (autosomal recessive, severe)	1.81	1.84	2.63	3.41
SESN3	sestrin 3	1.79	2.04	6.74	4.56
LYPD1	LY6/PLAUR domain containing 1	2.43	2.54	3.02	3.18
HEG1	heart development protein with EGF-like domains 1	2.06	1.75	4.57	2.7
LIMA1	LIM domain and actin binding 1	1.88	2.01	3.81	3.61
TACSTD2	tumor-associated calcium signal transducer 2	-1.34	-1.19	3.28	3.03

MFI2	antigen p97 (melanoma associated) identified by monoclonal antibodies 133.2 and 96.5	1.52	1.56	3.29	3.5
PNLIPRP2	pancreatic lipase-related protein 2	1.13	1.15	2.43	4.57
LOC100129550	uncharacterized LOC100129550	1.05	-1.02	2.25	2.04
CD3D	CD3d molecule, delta (CD3-TCR complex)	-1.24	-1.27	3.15	5.25
KCNJ16	potassium inwardly-rectifying channel, subfamily J, member 16	1.18	1.24	1.87	2.08
LMCD1	LIM and cysteine-rich domains 1	1.05	1.09	11.62	11.72
UBASH3B	ubiquitin associated and SH3 domain containing B	1.55	1.4	8.62	6.94
TMEM144	transmembrane protein 144	1.29	1.32	2.15	1.88
STX3	syntaxin 3	2.26	2.09	3.38	3.81
IGSF1	immunoglobulin superfamily, member 1	1.49	1.52	3.26	4.92
TSPAN3	tetraspanin 3	2.02	2.18	3.21	3.66
ABCC4	ATP-binding cassette, sub-family C (CFTR/MRP), member 4	2.14	2.09	2.88	2.7
REEP1	receptor accessory protein 1	1.2	1.34	5.52	11.55
PRSS8	protease, serine, 8	2.27	2.05	3.46	3.82
RAB11FIP1	RAB11 family interacting protein 1 (class I)	2.2	2.3	6.51	4.96
XKRX	XK, Kell blood group complex subunit-related, X-linked	2	2.1	2.14	2.34
TIMP2	TIMP metalloproteinase inhibitor 2	2.28	2.39	5.92	5.26
WNT5A	wingless-type MMTV integration site family, member 5A	-1.32	-1.27	10.77	8.97
FXYD3	FXYD domain containing ion transport regulator 3	1.74	1.84	2.43	2.52
MSX2	msh homeobox 2	2.88	1.69	14	11.3
OSR2	odd-skipped related transcription factor 2	1.09	1.04	2.42	1.83
FMO1	flavin containing monooxygenase 1	1.13	1.24	9.33	11.2
TFF1	trefoil factor 1	1.18	1.27	4.56	8.38
COL12A1	collagen, type XII, alpha 1	1.55	1.54	6.5	6.1
FAM3B	family with sequence similarity 3, member B	1.41	1.42	3.25	3.56
S100A10	S100 calcium binding protein A10	1.85	2.02	9.53	9.38
PLP2	proteolipid protein 2 (colonic epithelium-enriched)	1.53	1.68	4.14	4.54
MSX1	msh homeobox 1	2.02	1.34	16.98	12.78
THBD	thrombomodulin	-1.17	-1.24	10.81	8.42
GATA3	GATA binding protein 3	1.86	1.43	24.77	18.79
FBLN5	fibulin 5	1.56	1.65	15.93	15.47
GALNT10	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 10 (GalNAc-T10)	2.77	2.44	11.5	10.07
MAP7D2	MAP7 domain containing 2	1.09	1.23	1.58	1.89
PRR15L	proline rich 15-like	-1.2	-1.09	3.48	4.1
EGF	epidermal growth factor	2.98	2.4	3.59	4.87
PALLD	palladin, cytoskeletal associated protein	1.36	1.42	11.58	9.66
FLNC	filamin C, gamma	3.01	2.74	9.16	8.51
NPPB	natriuretic peptide B	2.21	1.93	9.3	5.84
SEMA3C	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3C	1.68	1.84	13.18	9.6
EPS8L3	EPS8-like 3	1.5	1.56	2.37	3.14
GCNT3	glucosaminyl (N-acetyl) transferase 3, mucin type	1.05	1.11	2.16	2.64
GPR87	G protein-coupled receptor 87	1.25	1.32	20.4	18.85



DUSP9	dual specificity phosphatase 9	-1.76	-1.67	2.12	2.65
LRP2	low density lipoprotein receptor-related protein 2	1.11	1.16	13.64	13.92
GXYLT2	glucoside xylosyltransferase 2	2.23	2.02	10.61	10.95
GPRC5A	G protein-coupled receptor, family C, group 5, member A	1.3	1.34	7.17	5.21
RRAS	related RAS viral (r-ras) oncogene homolog	-1.17	-1.1	4.32	4.74
KLHL13	kelch-like family member 13	-1.59	-1.22	3.25	3.95
C7orf60	chromosome 7 open reading frame 60	-1.01	1.13	5.9	5.23
TNNC1	troponin C type 1 (slow)	1.3	1.12	2.69	3.34
ANXA2P2	annexin A2 pseudogene 2	2.44	2.46	8.07	7.01
BMP2	bone morphogenetic protein 2	5.9	2.31	7.74	7.75
P4HA2	prolyl 4-hydroxylase, alpha polypeptide II	-2.73	-3.03	12.15	10.77
ISX	intestine-specific homeobox	1.44	1.46	1.98	2.37
MFSD6	major facilitator superfamily domain containing 6	1.52	1.69	2.6	2.21
GALNT6	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 6 (GalNAc-T6)	1.47	1.5	4.69	4.67
KRT7	keratin 7	-1.03	-1.02	10.65	8.5
CNTN4	contactin 4	1.4	1.35	8.2	8.55
SLC16A3	solute carrier family 16 (monocarboxylate transporter), member 3	1.07	-1.01	33.72	28.34
PLA2G10	phospholipase A2, group X	1.73	1.88	4.49	5.52
TMEM65	transmembrane protein 65	1.62	1.65	2.72	2.21
ERMP1	endoplasmic reticulum metalloproteinase 1	1	1.02	3.17	2.68
CSGALNACT1	chondroitin sulfate N-acetylgalactosaminyltransferase 1	-1.04	-1.02	4.1	4.28
CD44	CD44 molecule (Indian blood group)	1.48	1.55	4.14	3.44
CYBA	cytochrome b-245, alpha polypeptide	1.72	1.59	3.49	3.43
TDP2	tyrosyl-DNA phosphodiesterase 2	1.42	1.32	1.91	2.31
TIMP1	TIMP metalloproteinase inhibitor 1	-1.79	-1.94	7.71	7.15
GLS	glutaminase	4.11	3.26	5.42	4.63
PMP22	peripheral myelin protein 22	2.06	1.76	28.66	25.04
FILIP1L	filamin A interacting protein 1-like	1.19	1.21	3.63	3.49
APPL2	adaptor protein, phosphotyrosine interaction, PH domain and leucine zipper containing 2	1.27	1.02	2.4	2.01
F2RL1	coagulation factor II (thrombin) receptor-like 1	1.92	2.06	5.18	5.59
TUFT1	tuftelin 1	1.6	1.73	2.74	2.43
CD109	CD109 molecule	1.82	2.01	2.69	2.9
LGALS2	lectin, galactoside-binding, soluble, 2	-1.96	-2.13	1.87	3.08
GATA5	GATA binding protein 5	-1.01	1.07	3.9	3.76
FHL2	four and a half LIM domains 2	2.36	3.23	4.31	3.01
GUCY2C	guanylate cyclase 2C (heat stable enterotoxin receptor)	1.25	1.18	5.36	9.01
GNRH2	gonadotropin-releasing hormone 2	-1.16	-1.1	25.36	32.29
TYRP1	tyrosinase-related protein 1	1.36	1.47	25.63	12.91
TMEM164	transmembrane protein 164	2.68	2.59	2.95	2.9
SLC51B	solute carrier family 51, beta subunit	1.41	1.47	5.18	4.67
FMOD	fibromodulin	-1.06	1.01	25.34	24.2
SLC44A3	solute carrier family 44, member 3	-2.56	-2.3	3.37	3.98
LAYN	layilin	1.83	2.08	11.16	10.21
MXRA7	matrix-remodelling associated 7	-1.36	-1.32	3.79	3.26



MPZL1	myelin protein zero-like 1	2.45	2.38	4.16	4.31
MFGE8	milk fat globule-EGF factor 8 protein	1.64	1.97	5.83	6.41
DUOX2	dual oxidase 2	1.02	1.03	10.67	15.22
GOLGA8A	golgin A8 family, member A	-1.11	-1.3	2.26	3.7
CIDEC	cell death-inducing DFFA-like effector c	1.67	1.75	3.23	4.85
FZD6	frizzled family receptor 6	1.45	1.44	9.64	9.65
BBS12	Bardet-Biedl syndrome 12	1.75	1.59	5.37	8.06
DCDC2	doublecortin domain containing 2	-1.33	-1.27	1.21	1.72
SRPX2	sushi-repeat containing protein, X-linked 2	1.44	1.51	2.49	2.15
DSC2	desmocollin 2	3.65	3.03	6.15	4.37
OGFRL1	opioid growth factor receptor-like 1	2.14	2.13	11.22	12.56
CA8	carbonic anhydrase VIII	1.12	1.15	7.19	5.76
CDH6	cadherin 6, type 2, K-cadherin (fetal kidney)	1.57	1.75	1.76	1.64
PHGR1	proline/histidine/glycine-rich 1	1.44	1.56	3.12	4.17
XPR1	xenotropic and polytropic retrovirus receptor 1	1.76	1.82	2.76	2.58
EPHX4	epoxide hydrolase 4	1.5	1.63	1.41	1.62
LOC400043	uncharacterized LOC400043	1.54	1.57	50.89	50.16
SLC10A2	solute carrier family 10 (sodium/bile acid cotransporter), member 2	1.31	1.33	1.58	1.59
ANKS1A	ankyrin repeat and sterile alpha motif domain containing 1A	2.08	2.19	10.67	8.81
ALDH18A1	aldehyde dehydrogenase 18 family, member A1	2.19	2.28	3.46	4.05
GNPDA2	glucosamine-6-phosphate deaminase 2	1.43	1.48	2.82	2.84
QSOX1	quiescin Q6 sulfhydryl oxidase 1	1.67	1.6	4.02	4.08
LPAR1	lysophosphatidic acid receptor 1	1.75	1.64	3.54	3.52
RECK	reversion-inducing-cysteine-rich protein with kazal motifs	1.67	1.34	5.7	4.27
ITGA3	integrin, alpha 3 (antigen CD49C, alpha 3 subunit of VLA-3 receptor)	1.52	1.47	2	2.01
TTC39A	tetratricopeptide repeat domain 39A	1.9	1.94	1.98	2.33
LCT	lactase	1.48	1.57	8.98	9.6
ASAP2	ArfGAP with SH3 domain, ankyrin repeat and PH domain 2	-1.07	1.72	6.74	6.56
AGR2	anterior gradient 2	1.67	1.76	4.81	7.39
MXRA5	matrix-remodelling associated 5	3.18	2.72	12.65	9.32
RBP2	retinol binding protein 2, cellular	1.04	1.04	12.37	18.33
NOG	noggin	1.59	1.59	10.18	6.46
MOSPD1	motile sperm domain containing 1	2.47	2.13	3.22	3.39
LOX	lysyl oxidase	1.1	1.25	59.72	39.8
WLS	wntless Wnt ligand secretion mediator	2.17	1.51	5.93	4.71
LGALS3	lectin, galactoside-binding, soluble, 3	-1.93	-1.66	16.68	19.64
ARHGEF3	Rho guanine nucleotide exchange factor (GEF) 3	1.89	1.99	25.17	20.18
PLAC8	placenta-specific 8	-2.22	-2.09	5.92	6
ARL14	ADP-ribosylation factor-like 14	-1.05	-1.08	1.25	1.69
FBN1	fibrillin 1	2.57	2.64	17.9	11.19
TGFB111	transforming growth factor beta 1 induced transcript 1	2.91	3.7	10.49	9.98
ZNF518B	zinc finger protein 518B	3.37	2.89	3.46	2.63
PLIN3	perilipin 3	2.59	2.61	4.04	3.71

CAPN2	calpain 2, (m/II) large subunit	-1.27	-1.24	4.52	4.44
FOXQ1	forkhead box Q1	4.41	2.91	2.18	1.71
MYZAP	myocardial zonula adherens protein	1.35	1.36	1.95	1.95
KDEL3	KDEL (Lys-Asp-Glu-Leu) endoplasmic reticulum protein retention receptor 3	-1.36	-1.32	5.19	5.91
MUM1L1	melanoma associated antigen (mutated) 1-like 1	-1.5	-1.54	24.33	35.81
LAMC1	laminin, gamma 1 (formerly LAMB2)	2.82	2.74	7.87	6.97
PGF	placental growth factor	1.05	1.14	3.5	4.2
AMOTL2	angiomin like 2	4.6	4.18	5.04	3.11
UGCG	UDP-glucose ceramide glucosyltransferase	1.19	1.08	3.07	2.87
LAMA5	laminin, alpha 5	1.19	1.18	3.41	3.05
CASK	calcium/calmodulin-dependent serine protein kinase (MAGUK family)	1.74	1.54	2.33	2
ST6GALNAC2	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 2	1.15	1.03	3.61	3.52
IKBIP	IKBKB interacting protein	2.07	2.02	5.33	6.22
S100A14	S100 calcium binding protein A14	-2.51	-2.48	14.3	17.37
RSPO3	R-spondin 3	1.64	1.82	14.66	8.89
SYTL2	synaptotagmin-like 2	2.08	2.4	2.54	2.83
SCGN	secretagogin, EF-hand calcium binding protein	-1.11	-1.09	6.86	8.89
NEDD4L	neural precursor cell expressed, developmentally down-regulated 4-like, E3 ubiquitin protein ligase	1.83	2.01	3.37	3.62
LYPD6B	LY6/PLAUR domain containing 6B	2.36	2.48	6.94	6.61
RHOBTB1	Rho-related BTB domain containing 1	1.49	1.8	4.78	3.63
TANC2	tetratricopeptide repeat, ankyrin repeat and coiled-coil containing 2	2.42	2.31	10.67	8.01
AGR3	anterior gradient 3	1.1	1.08	1.27	1.3
FBXL2	F-box and leucine-rich repeat protein 2	2.77	2.98	6.61	6.13
SLC7A7	solute carrier family 7 (amino acid transporter light chain, y+L system), member 7	-1.06	-1.1	22.85	25.26
CRYAB	crystallin, alpha B	2.39	2.65	4.28	4.31
CKAP4	cytoskeleton-associated protein 4	2.23	2.15	4.59	4.13
FKBP10	FK506 binding protein 10, 65 kDa	1.87	1.86	5.42	5.12
CACNB3	calcium channel, voltage-dependent, beta 3 subunit	2.3	2.15	4.86	5.14
MYLIP	myosin regulatory light chain interacting protein	1.55	1.7	9.78	8.93
LAMB3	laminin, beta 3	-2.12	-2.06	1.87	3.71
TWIST1	twist family bHLH transcription factor 1	2.21	1.77	5.39	4.19
RHOC	ras homolog family member C	-1.26	-1.59	2.73	3
SMAD7	SMAD family member 7	3.08	2.79	3.39	2.39
TMCO3	transmembrane and coiled-coil domains 3	2.18	2.2	6.45	6.24
KRT6A	keratin 6A	1.07	1.07	2.87	2.53
MCOLN3	mucolipin 3	1.9	2.19	3.63	4.27
PIGZ	phosphatidylinositol glycan anchor biosynthesis, class Z	-1.06	-1.01	1.93	2.48
MYOF	myoferlin	2.15	1.87	37.45	30.45
PRDM1	PR domain containing 1, with ZNF domain	3.43	2.22	2.21	2.37
MMD	monocyte to macrophage differentiation-associated	1.43	1.54	4.08	4.32
ITGA2	integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	1.83	1.88	6.52	5.74

PLAGL1	pleiomorphic adenoma gene-like 1	1.26	1.2	32.43	24.05
B3GNT5	UDP-GlcNAc:betaGal beta-1,3-N-acetylglucosaminyltransferase 5	3.34	2.8	4.48	4.6
METRNL	meteorin, glial cell differentiation regulator-like	1.11	1.19	4.54	3.9
LIPH	lipase, member H	-1.15	-1.15	1.79	2.31
GPR124	G protein-coupled receptor 124	1.36	1.41	13.62	8.45
ARL4C	ADP-ribosylation factor-like 4C	2.06	2.13	5.3	3.35
HILPDA	hypoxia inducible lipid droplet-associated	1.55	1.68	4.68	3.24
AMOT	angiominin	1.2	1.4	11.52	11.14
ST6GALNAC1	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)-N-acetylgalactosaminide alpha-2,6-sialyltransferase 1	-1.15	-1.19	1.84	2.83
FKBP14	FK506 binding protein 14, 22 kDa	1.76	1.7	5.25	4.52
LOXL1	lysyl oxidase-like 1	2.06	2.19	27.21	19.02
CMTM3	CKLF-like MARVEL transmembrane domain containing 3	3.2	2.98	4.71	4.11
ERP27	endoplasmic reticulum protein 27	1.88	1.99	19.5	20.04
FKBP11	FK506 binding protein 11, 19 kDa	-1.23	-1.15	4.41	5.42
HOXC6	homeobox C6	1.76	1.89	25.24	22.72
NPNT	nephronectin	-1.22	-1.1	82	70.71
HSD3B1	hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 1	1.33	1.27	10.13	7.94
STXBP6	syntaxin binding protein 6 (amisyn)	-1.26	-1.05	3.23	3
LAMP3	lysosomal-associated membrane protein 3	1.74	1.74	2.18	2.28
CYP1B1	cytochrome P450, family 1, subfamily B, polypeptide 1	-1.09	-1.1	4.11	2.27
SLN	sarcolipin	1.7	1.73	47.49	57.27
SH3BGRL3	SH3 domain binding glutamic acid-rich protein like 3	1.64	1.4	2.24	1.85
MMP1	matrix metalloproteinase 1 (interstitial collagenase)	2.16	5.16	13.57	8.49
C19orf69	chromosome 19 open reading frame 69	1.26	1.32	2.28	2.65
PRSS23	protease, serine, 23	1.78	2.03	25.11	18.51
PLD5	phospholipase D family, member 5	1.85	1.98	3.2	2.87
EGFL6	EGF-like-domain, multiple 6	1.07	1.25	38.34	29.34
FLRT2	fibronectin leucine rich transmembrane protein 2	5.28	3.49	8.23	5.51
PLA2G4A	phospholipase A2, group IVA (cytosolic, calcium-dependent)	-1.31	-1.26	7.53	5.92
S100A4	S100 calcium binding protein A4	-1.29	-1.08	8.34	9.14
SLC26A3	solute carrier family 26 (anion exchanger), member 3	-1.31	-1.3	8.54	9.81
TFAP2A	transcription factor AP-2 alpha (activating enhancer binding protein 2 alpha)	1.36	1.4	8.97	8.16
PTPRM	protein tyrosine phosphatase, receptor type, M	-1.68	-2.64	2.68	2.4
COL4A5	collagen, type IV, alpha 5	1.98	1.88	3.6	3.11
C19orf33	chromosome 19 open reading frame 33	1.39	1.41	2.34	2.52
LOC100132735	uncharacterized LOC100132735	1.07	1.13	16.45	20.97
MUC13	mucin 13, cell surface associated	-1.17	-1.17	1.29	1.33
LOC100506718	uncharacterized LOC100506718	3.24	2.47	13.26	11.41
GEM	GTP binding protein overexpressed in skeletal muscle	2	2.1	2.36	2.33
COL5A1	collagen, type V, alpha 1	4.61	3.46	75.47	48.97

DCN	decorin	1.01	1.05	34.38	38.09
CDH17	cadherin 17, LI cadherin (liver-intestine)	1.65	1.76	15.9	16.55
MAGED2	melanoma antigen family D, 2	2.57	2.29	4.72	5.06
ISL1	ISL LIM homeobox 1	2.94	2.26	16.82	14.98
BNC1	basonuclin 1	-1.1	-1.07	66.82	61.54
MECOM	MDS1 and EVI1 complex locus	1.36	1.39	2.18	2.4
CGA	glycoprotein hormones, alpha polypeptide	1.52	1.63	13.72	36.81
KRT6C	keratin 6C	1.36	1.44	1.42	1.45
CCDC80	coiled-coil domain containing 80	1.07	1.18	9.31	5.98
HEY1	hes-related family bHLH transcription factor with YRPW motif 1	2.14	2.77	21.98	15.19
RASGRP1	RAS guanyl releasing protein 1 (calcium and DAG-regulated)	1.09	-1.01	1.48	1.3
C15orf48	chromosome 15 open reading frame 48	-1.85	-1.72	1.66	2.26
TSPAN2	tetraspanin 2	2.09	2.3	3.37	3.02
FOXF1	forkhead box F1	1.52	1.65	9.7	6.49
TMEM98	transmembrane protein 98	2.44	2.35	11.16	10.21
SFN	stratifin	3.59	3.61	5.04	3.83
IGFBP3	insulin-like growth factor binding protein 3	-2.38	-2.08	43.85	31.24
CEACAM6	carcinoembryonic antigen-related cell adhesion molecule 6 (non-specific cross reacting antigen)	1.22	1.23	1.24	1.28
H2AFY	H2A histone family, member Y	2.58	2.27	2.39	2.44
CA4	carbonic anhydrase IV	1.1	1.22	4.08	4.19
COL15A1	collagen, type XV, alpha 1	1.21	1.22	93.05	57.56
OXTR	oxytocin receptor	2.13	1.93	2.27	2.18
INPP4B	inositol polyphosphate-4-phosphatase, type II, 105kDa	-1.05	1.03	1.12	1.2
ACTA2	actin, alpha 2, smooth muscle, aorta	-1.91	-1.87	10.71	4.63
MEP1A	mepirin A, alpha (PABA peptide hydrolase)	1.28	1.31	29.65	45.18
CRISPLD2	cysteine-rich secretory protein LCCL domain containing 2	2.04	2.19	82.66	68.64
PDCD4	programmed cell death 4 (neoplastic transformation inhibitor)	-3.31	-3.71	6.12	5.15
SHISA6	shisa family member 6	2.95	2.52	2.93	1.95
RAB31	RAB31, member RAS oncogene family	6.4	6.33	12.54	11.53
WBP5	WW domain binding protein 5	6.84	6.94	12.37	13.2
TMSB10	thymosin beta 10	7.75	6.63	6.9	6.68
NCK2	NCK adaptor protein 2	7.14	7.12	6.82	6.3
ARID3A	AT rich interactive domain 3A (BRIGHT-like)	7.02	6.37	14.37	10.92
MAP9	microtubule-associated protein 9	5.99	5.12	4.94	6.56
RAB38	RAB38, member RAS oncogene family	10.38	8.92	8.36	7.9
IGF1R	insulin-like growth factor 1 receptor	7.9	8.47	6.95	5.23
PAPSS1	3'-phosphoadenosine 5'-phosphosulfate synthase 1	7.9	7.96	13.43	11.4
IQGAP1	IQ motif containing GTPase activating protein 1	7.96	6.91	13.58	12.15
ZNF816	zinc finger protein 816	7.07	6.59	6.22	7.2
LRP4	low density lipoprotein receptor-related protein 4	6.86	8.05	6.47	5.42
ZNF415	zinc finger protein 415	4.69	4.42	6.62	7.85
PLAG1	pleiomorphic adenoma gene 1	5.67	5.84	9.62	8.78
S100A11	S100 calcium binding protein A11	6.3	5.01	14.08	10.16

TRPC1	transient receptor potential cation channel, subfamily C, member 1	5.23	5.26	12.75	11.57
GLIS2	GLIS family zinc finger 2	4.46	5.13	8.75	6.82
VGLL3	vestigial like 3 (Drosophila)	5.77	5.71	10.89	9.51
LINC00960	long intergenic non-protein coding RNA 960	6.18	5.7	10.15	11.52
ZNF430	zinc finger protein 430	7.35	7.65	6.4	8.8
FSTL1	follistatin-like 1	10.29	10.45	18.47	15.65
MARCKS	myristoylated alanine-rich protein kinase C substrate	11.29	11.18	10.07	7.92
ZDHHC13	zinc finger, DHHC-type containing 13	7.62	7.25	5.34	5.37
ANK3	ankyrin 3, node of Ranvier (ankyrin G)	4.63	4.71	6.12	5.86
DSG2	desmoglein 2	4.72	4.52	7.73	6.86
SGK223	homolog of rat pragma of Rnd2	9.75	9.71	8.66	6.36
HK2	hexokinase 2	7.63	8.06	6.54	4.99
PDZRN3	PDZ domain containing ring finger 3	4.92	5.02	20.43	15.21
UBE2Q2	ubiquitin-conjugating enzyme E2Q family member 2	4.61	5.21	10.2	12.42
SSBP2	single-stranded DNA binding protein 2	3.71	3.48	12.17	11.58
EZR	ezrin	6.57	5.91	11.31	9.38
C3orf52	chromosome 3 open reading frame 52	8.44	9.3	9.63	8.16
TPM1	tropomyosin 1 (alpha)	5.85	5.8	15	13.45
TUSC3	tumor suppressor candidate 3	9.72	9.74	13	10.75
TNFAIP8	tumor necrosis factor, alpha-induced protein 8	3.32	3.18	10.11	9.11
PEG10	paternally expressed 10	5.69	5.5	6.41	4.14
FAM217B	family with sequence similarity 217, member B	10.65	10.06	4.8	4.06
SPINT1	serine peptidase inhibitor, Kunitz type 1	4.4	4.31	7.41	6.99
NEXN	nexilin (F actin binding protein)	6.76	6.29	6.54	6.68
CRIM1	cysteine rich transmembrane BMP regulator 1 (chordin-like)	4.94	4.46	11.43	5.93
STC2	stanniocalcin 2	5.43	4.35	7.52	4.75
ID3	inhibitor of DNA binding 3, dominant negative helix-loop-helix protein	13.96	11.71	8.65	6.16
FAM57A	family with sequence similarity 57, member A	4.81	5.13	6.89	7.06
TAGLN	transgelin	15.46	11.42	12.65	6.79
ZNF711	zinc finger protein 711	6.36	6.24	5.6	5.58
DDX26B	DEAD/H (Asp-Glu-Ala-Asp/His) box polypeptide 26B	5.7	5.18	6.52	6.44
CORO2A	coronin, actin binding protein, 2A	6.32	6.18	5.36	4.78
FUT8	fucosyltransferase 8 (alpha (1,6) fucosyltransferase)	5.59	4.76	16.78	14.46
LPCAT1	lysophosphatidylcholine acyltransferase 1	11.23	11.06	8.87	7.42
TES	testis derived transcript (3 LIM domains)	8.01	7.06	7.3	5.47
ID4	inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	5.92	4.93	13.85	12.26
ZNF83	zinc finger protein 83	2.73	2.32	12.62	18.7
ZNF468	zinc finger protein 468	13.62	13.1	19.75	16.11
DKK3	dickkopf WNT signaling pathway inhibitor 3	9.74	8.41	19.05	14.99
IGF2BP2	insulin-like growth factor 2 mRNA binding protein 2	8.88	9.44	9.11	7.07
LXN	latexin	3.62	3.89	4.66	4.45
PHLDA2	pleckstrin homology-like domain, family A,	6.66	6.61	4.33	4.35

	member 2				
GALNT12	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 12 (GalNAc-T12)	4.65	4.95	6.14	7.23
CDS1	CDP-diacylglycerol synthase (phosphatidate cytidylyltransferase) 1	5.39	6.51	11.29	11.23
GOLM1	golgi membrane protein 1	3.52	3.98	4.78	4.8
DLG5	discs, large homolog 5 (Drosophila)	7.85	7.49	4.45	3.96
TNFRSF21	tumor necrosis factor receptor superfamily, member 21	10.08	8.37	19.95	14.03
METTL9	methyltransferase like 9	4.37	4.82	7.94	7.76
PFKM	phosphofructokinase, muscle	7.7	8.33	9.98	9.39
PRSS16	protease, serine, 16 (thymus)	4.09	3.86	5.47	5.04
COL4A1	collagen, type IV, alpha 1	6.83	6.37	35.58	25.43
C5orf30	chromosome 5 open reading frame 30	6.84	7.07	36.89	31.41
PXDN	peroxidasin homolog (Drosophila)	11.72	11.54	10.53	7.95
SUCO	SUN domain containing ossification factor	3.69	3.69	10.25	11.26
RAB25	RAB25, member RAS oncogene family	3.95	4.54	13.77	15.12
SLC7A11	solute carrier family 7 (anionic amino acid transporter light chain, xc- system), member 11	14.84	12.25	8.73	9.46
TRNP1	TMF1-regulated nuclear protein 1	8.06	8.22	15.68	16.6
COL4A2	collagen, type IV, alpha 2	3.1	3.02	22.61	14.52
ITM2C	integral membrane protein 2C	6.74	6.17	7.01	6.62
TSPAN5	tetraspanin 5	3.8	3.86	14.54	11.66
EFNB2	ephrin-B2	7.34	7.86	26.67	17.68
LHFP	lipoma HMGIC fusion partner	2.65	4.13	28.09	17.07
CRNDE	colorectal neoplasia differentially expressed (non-protein coding)	6.95	5.51	4.43	3.43
ASRGL1	asparaginase like 1	3.54	3.41	3.64	4.68
F2R	coagulation factor II (thrombin) receptor	6.07	6.37	7.54	5.25
SERPINH1	serpin peptidase inhibitor, clade H (heat shock protein 47), member 1, (collagen binding protein 1)	5.75	4.85	11.48	10.36
APOBEC3B	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3B	4.65	4.82	5.09	4.87
TMED3	transmembrane emp24 protein transport domain containing 3	3.75	4.12	11.79	14.36
PFN2	profilin 2	6.47	6.97	8.06	6.91
CDC42EP3	CDC42 effector protein (Rho GTPase binding) 3	5.53	5.51	9.22	4.85
EFEMP1	EGF containing fibulin-like extracellular matrix protein 1	2.85	3.22	9.8	6.92
SLC35F2	solute carrier family 35, member F2	9.24	8.76	36.26	32.88
RAB3B	RAB3B, member RAS oncogene family	5.58	5.57	3.57	4.3
DPP10-AS1	DPP10 antisense RNA 1	11.05	10.15	4.48	4.31
PIP5K1B	phosphatidylinositol-4-phosphate 5-kinase, type I, beta	3.4	2.85	4.73	4.57
TMEM243	transmembrane protein 243, mitochondrial	2.88	2.93	5.1	6.37
EPB41L3	erythrocyte membrane protein band 4.1-like 3	8.12	4.73	10.9	8.92
SLC6A8	solute carrier family 6 (neurotransmitter transporter), member 8	4.98	6.57	3.16	3.01
NXN	nucleoredoxin	15.94	13.98	11.19	8.85



UGT8	UDP glycosyltransferase 8	3.79	3.66	2.89	3.59
LEPREL4	leprecan-like 4	3.85	3.58	10.09	8.93
MST4	serine/threonine protein kinase MST4	8.7	8.32	12.57	10.98
AMIGO2	adhesion molecule with Ig-like domain 2	10.85	9.08	27.45	19.82
COTL1	coactosin-like 1 (Dictyostelium)	7.71	8.36	6.48	5.34
CCNE1	cyclin E1	8.81	8.86	6.75	7.32
TUBA1C	tubulin, alpha 1c	11.76	10.65	5.22	4.55
C12orf5	chromosome 12 open reading frame 5	6.68	6.45	3.58	2.62
MB21D2	Mab-21 domain containing 2	10.67	10.45	4.41	3.93
PKM	pyruvate kinase, muscle	7.85	7.05	5.52	3.77
CLIC1	chloride intracellular channel 1	7.38	6.79	5.81	5.8
KIAA1211	KIAA1211	8.29	8.61	11.23	9.01
EPPK1	epiplakin 1	4.31	5.41	6.94	5.16
CTSV	cathepsin V	9.4	8.85	9.57	9.23
CKB	creatine kinase, brain	3.39	3.26	14.97	17.43
AKAP12	A kinase (PRKA) anchor protein 12	5.12	6.81	7.37	5.36
IGDCC4	immunoglobulin superfamily, DCC subclass, member 4	9.82	9.46	24.92	20.44
LAPTM4B	lysosomal protein transmembrane 4 beta	15.36	12.55	9.84	7.74
SMIM3	small integral membrane protein 3	14.39	16.96	24.19	22.51
VLDLR	very low density lipoprotein receptor	15.83	13.12	27.61	18.94
ZNF320	zinc finger protein 320	15.22	15.22	7.82	6.25
SOGA2	SOGA family member 2	16.33	14.59	5.89	4.03
DPYSL2	dihydropyrimidinase-like 2	8.61	10.63	6.6	4.69
FAM129A	family with sequence similarity 129, member A	3.98	3.74	4.8	4.62
ELOVL7	ELOVL fatty acid elongase 7	2.27	2.63	2.83	3.16
DMKN	dermokine	14.38	12.37	5.7	6.6
PCSK5	proprotein convertase subtilisin/kexin type 5	2.24	2.75	22.3	21.76
COL4A6	collagen, type IV, alpha 6	4.57	4.03	7.36	5.43
LOC100288911	uncharacterized LOC100288911	4.95	4.95	4.69	4.22
TFPI2	tissue factor pathway inhibitor 2	4.36	4.51	22.43	10.05
PNMA1	paraneoplastic Ma antigen 1	14.06	14.44	6.25	4.63
DPP10	dipeptidyl-peptidase 10 (non-functional)	5.43	5.04	3.06	2.33
DUSP4	dual specificity phosphatase 4	8.4	5.78	4.81	3.01
PABPC4L	poly(A) binding protein, cytoplasmic 4-like	2.87	2.54	13.35	9.94
PAM	peptidylglycine alpha-amidating monooxygenase	5.17	6.15	23.65	20.21
COL5A2	collagen, type V, alpha 2	8.99	5.18	37.78	27.96
ENPP5	ectonucleotide pyrophosphatase/phosphodiesterase 5 (putative)	2.72	2.71	3.63	3.81
ZNF614	zinc finger protein 614	5.5	5.75	3.84	4.36
SOX4	SRY (sex determining region Y)-box 4	16.58	15.89	7.95	5.96
PRSS35	protease, serine, 35	2.45	2.16	38.35	26.26
ZNF43	zinc finger protein 43	8.05	6.01	2.78	3.86
LRCH2	leucine-rich repeats and calponin homology (CH) domain containing 2	4.16	4.6	27.14	22.99
STMN2	stathmin-like 2	3.31	2.77	34.35	20.26
COLEC12	collectin sub-family member 12	7.95	3.64	44.89	30.97
YBX3	Y box binding protein 3	13.06	12.72	8.91	7.56
FMNL2	formin-like 2	6.65	5.94	2.85	2.7

COL21A1	collagen, type XXI, alpha 1	3.53	4.28	32.61	25.26
MATN3	matrilin 3	19.36	12.68	12.5	10.29
HS6ST2	heparan sulfate 6-O-sulfotransferase 2	4.8	5.06	29.91	25.33
ANXA1	annexin A1	3.37	3.25	34.41	29.07
SLC7A5	solute carrier family 7 (amino acid transporter light chain, L system), member 5	32.63	28	9.98	6.1
COL1A1	collagen, type I, alpha 1	6.98	8.52	85.17	68.58
PAQR8	progesterin and adipoQ receptor family member VIII	2.27	2.53	8.86	8.18
CCND2	cyclin D2	16.6	15.8	25.94	18.36
GPX7	glutathione peroxidase 7	2.2	2.05	6.85	7.4
NQO1	NAD(P)H dehydrogenase, quinone 1	19.85	17.68	11.32	11.84
ZNF204P	zinc finger protein 204, pseudogene	10.11	6.61	3.8	6.83
SPIN4	spindlin family, member 4	12.76	15.55	25.89	22.13
GPR160	G protein-coupled receptor 160	6.63	7.72	4.84	5.61
PDGFA	platelet-derived growth factor alpha polypeptide	18.8	17.54	14.29	12.51
GRHL2	grainyhead-like 2 (Drosophila)	5.85	6.95	10.03	8.29
COL11A1	collagen, type XI, alpha 1	4.72	4.29	42.48	25.22
SRPX	sushi-repeat containing protein, X-linked	1.66	2.18	20.99	24.04
ANXA2	annexin A2	3.95	3.5	10.54	9.82
NANOS1	nanos homolog 1 (Drosophila)	14.46	14.01	10.52	7.65
EDNRB	endothelin receptor type B	5.14	4.41	10.41	9.49
DDR1	discoidin domain receptor tyrosine kinase 1	4.67	4.74	6.32	5.69
CDH11	cadherin 11, type 2, OB-cadherin (osteoblast)	5.91	6.08	25.53	20.22
ARG2	arginase 2	3.77	4.07	10.43	10.33
HSPB8	heat shock 22kDa protein 8	3.79	2.72	18.56	17.34
SELM	selenoprotein M	1.53	1.71	27.48	31.59
USP46	ubiquitin specific peptidase 46	7.18	7.11	3.8	3.68
BASP1	brain abundant, membrane attached signal protein 1	18.23	18.79	15.5	15.07
MTHFD1L	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1-like	12.3	11.94	5.41	4.85
SLC26A2	solute carrier family 26 (anion exchanger), member 2	4.01	3.72	10.84	11
RCN2	reticulocalbin 2, EF-hand calcium binding domain	11.64	13.68	6.12	7.08
C4orf48	chromosome 4 open reading frame 48	3.35	3.15	9.38	8.62
FLVCR1	feline leukemia virus subgroup C cellular receptor 1	13.08	14.2	3.94	3.62
PBK	PDZ binding kinase	9.39	9.3	7.8	5.56
GALNT3	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3)	4.96	5.5	3.5	3.29
IMPDH1	IMP (inosine 5'-monophosphate) dehydrogenase 1	6.65	6.69	5.15	4.92
AACS	acetoacetyl-CoA synthetase	8.92	10.32	3.02	3.19
PSPH	phosphoserine phosphatase	4.28	3.83	2.27	1.79
CDH3	cadherin 3, type 1, P-cadherin (placental)	13.13	13.79	30.49	28.28
ARHGEF10	Rho guanine nucleotide exchange factor (GEF) 10	7.24	7.09	6.13	6.19
BTBD3	BTB (POZ) domain containing 3	6.84	6.16	7.72	6.69
HN1	hematological and neurological expressed 1	14.01	15.2	3.7	3.36
PKDCC	protein kinase domain containing, cytoplasmic	1.98	1.77	7.34	6.31
TUBA1B	tubulin, alpha 1b	8.63	8.75	4.81	4.31
ELOVL4	ELOVL fatty acid elongase 4	4.21	5.03	3.84	4.8
LBH	limb bud and heart development	12.32	10.22	48.77	38.69



F3	coagulation factor III (thromboplastin, tissue factor)	3.6	2.99	61.05	57.05
PCDHB2	protocadherin beta 2	23.16	25.23	14.57	9.8
MOB3B	MOB kinase activator 3B	2.97	3.39	4.8	5.18
FZD3	frizzled family receptor 3	6.74	6.91	4.68	4.64
PRR15	proline rich 15	3.53	3.57	19.59	17.78
ITGA6	integrin, alpha 6	2.92	3.38	2.6	1.9
NSUN7	NOP2/Sun domain family, member 7	2.12	2.46	2.71	3.51
CDKN1C	cyclin-dependent kinase inhibitor 1C (p57, Kip2)	2.04	1.68	41.98	43.81
PARM1	prostate androgen-regulated mucin-like protein 1	1.93	2.12	29.63	30.34
MN1	meningioma (disrupted in balanced translocation) 1	3.75	3.31	6.37	4.66
PDP1	pyruvate dehydrogenase phosphatase catalytic subunit 1	3.1	3.05	2.7	2.22
TMSB15B	thymosin beta 15B	6.32	6.86	3.83	3.63
BTG3	BTG family, member 3	2.47	2.43	10.58	10.48
GCNT1	glucosaminyl (N-acetyl) transferase 1, core 2	4.52	3.57	5.64	5.8
SLC2A1	solute carrier family 2 (facilitated glucose transporter), member 1	4.12	4.64	16.63	12.79
PDPN	podoplanin	6.19	6.63	47.83	43.22
PLXDC2	plexin domain containing 2	7.61	6.85	15.89	18.53
NAALAD2	N-acetylated alpha-linked acidic dipeptidase 2	1.21	1.4	16.12	15.54
PRTG	protogenin	2.75	2.94	26.69	24.12
NLRP2	NLR family, pyrin domain containing 2	36.58	41.46	12.51	13.75
DKK1	dickkopf WNT signaling pathway inhibitor 1	43.01	19.91	10.07	6.92
PTX3	pentraxin 3, long	1.75	1.96	8.7	8.53
NID2	nidogen 2 (osteonidogen)	1.59	2.01	230.76	174.9
GREM1	gremlin 1, DAN family BMP antagonist	8.94	8.73	5.7	1.61
CXCL5	chemokine (C-X-C motif) ligand 5	2.85	3.2	1.31	2.27
COL6A3	collagen, type VI, alpha 3	7.45	9.96	232.63	149.56
ANKRD1	ankyrin repeat domain 1 (cardiac muscle)	2.62	2.16	31.63	21.14

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