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Editorial:

APOPTOSIS IN TOXICOLOGICAL RESEARCH

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Toxicological research on apoptosis addresses the questions if and by which mechanisms certain chemicals induce apoptosis and to which degree this contributes to adverse effects. Recent studies have shown that benzene upregulates pro-apoptotic genes in the bone marrow, uranium induces apoptosis in lung epithelial cells and fluoride causes apoptosis in osteoblasts. The elucidation of these mechanisms is highly important, but unfortunately knowledge of their in vivo relevance remains scarce. For example it would be interesting to know if long term excessive fluoride causes skeletal disease because of apoptosis induction. Or does benzene induced apoptosis in bone marrow contribute to its carcinogenic effect by inducing replacement proliferation? Although much has been published addressing apoptosis in vitro it remains important to learn whether this translates in vivo or rather represents a specific situation that only occurs under specific in vitro conditions. The table summarizes the conclusions of recently published articles on apoptosis in toxicological research.

Table 1: Studies on apoptosis

Key message	Reference
Brevetoxins are known to induce neurotoxicity by interaction with sodium channels. However, they also induce apoptosis in Jurkat cells, as evidenced by caspase activation and PARP clearage.	Murrell and Gibson, 2009
Arsenic induces apoptosis in a human hepatocyte cell line through the mitochondrial pathway dependent on the generation of reactive oxygen species.	Wang et al., 2009
Propyl gallate, which is used in processed food and cosmetics induced apoptosis in Hela cells by depletion of intracellular glutathione levels and generation of oxidative stress.	Han et al., 2009
Benzene transcriptionally upregulates caspase 4 and caspase 12 in mouse bone marrow cells. However, no apoptosis is induced in absence of functional P53.	Yi et al., 2009
Lactational exposure to the phytoestrogen coumestrol caused apoptosis in the ovaries of rats.	Moon et al., 2009
Uranium induces apoptosis in lung epithelial cells by activation of caspase 3 and 8.	Periyakaruppan et al., 2009
Long term excessive fluoride intake may cause skeletal disease. This study shows that fluoride induces apoptosis in osteoblasts in vitro.	Yan et al., 2009
Fluoride treatment of rat exocrine pancreas cells causes autophagy. This study describes the turning point, when cells switch from autophagy to apoptosis.	Ito et al., 2009
Calmidazolium causes apoptosis by Ca^{2+} release from the endoplasmic reticulum in a protein kinase C dependent manner.	Liao et al., 2009

REFERENCES

Han YH, Moon HJ, You BR, Park WH. The anti-apoptotic effects of caspase inhibitors on propyl gallate-treated HeLa cells in relation to reactive oxygen species and glutathione levels. Arch Toxicol 2009;83:825-33.

Ito M, Nakagawa H, Okada T, Miyazaki S, Matsuo S. ER-stress caused by accumulated intracistanal granules activates autophagy through a different signal pathway from unfolded protein response in exocrine pancreas cells of rats exposed to fluoride. Arch Toxicol 2009;83:151-9.

Liao WC, Huang CC, Cheng HH, Wang JL, Lin KL, Cheng JS et al. Effect of calmidazolium on [Ca2+] and viability in human hepatoma cells. Arch Toxicol 2009;83:61-8.

Moon HJ, Seok JH, Kim SS, Rhee GS, Lee RD et al. Lactational coumestrol exposure increases ovarian apoptosis in adult rats. Arch Toxicol 2009;83:601-8.

Murrell RN, Gibson JE. Brevetoxins 2, 3, 6, and 9 show variability in potency and cause significant induction of DNA damage and apoptosis in Jurkat E6-1 cells. Arch Toxicol 2009;83:1009-19.

Periyakaruppan A, Sarkar S, Ravichandran P, Sadanandan B, Sharma CS, Ramesh V et al. Uranium induces apoptosis in lung epithelial cells. Arch Toxicol 2009;83:595-600.

Wang Y, Xu Y, Wang H, Xue P, Li X, Li B et al. Arsenic induces mitochondria-dependent apoptosis by reactive oxygen species generation rather than glutathione depletion in Chang human hepatocytes. Arch Toxicol 2009;83:899-908.

Yan X, Feng C, Chen Q, Li W, Wang H, Lv L et al. Effects of sodium fluoride treatment in vitro on cell proliferation, apoptosis and caspase-3 and caspase-9 mRNA expression by neonatal rat osteoblasts. Arch Toxicol 2009;83:451-8.

Yi JY, Hirabayashi Y, Choi YK, Kodama Y, Kanno J, Han JH et al. Benzene activates caspase-4 and -12 at the transcription level, without an association with apoptosis, in mouse bone marrow cells lacking the p53 gene. Arch Toxicol 2009;83:795-803.