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Editorial:

LUNG AND BREAST CANCER RESEARCH: IMMUNOGLOBULIN KAPPA C HITS THE HEADLINES

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Recently, Schmidt and colleagues reported that immunoglobulin Kappa C (IGKC) predicts a favourable response to chemotherapy and better metastasis-free survival in breast cancer patients (Schmidt et al., 2012). The authors validated the prognostic and predictive role of IGKC in 1,810 breast cancer, 1,056 non-small cell lung cancer and 513 colorectal cancer patient samples. The identification of IGKC as a single and robust marker of the immune response represents a major progress in the field of clinical tumour immunology and biomarkers. During the past decades, the search for prognostic and predictive markers of human tumours represented a major research focus (Perou et al., 2000; Desmedt et al., 2007; Cadenas et al., 2010; Hellwig et al., 2010; Kammers et al., 2011; Hardelauf et al., 2011; Lee et al., 2010; Mariani et al., 2010). The prognostic relevance of proliferation-associated genes (Schmidt et al., 2009a, b, 2011) and – in breast cancer – gene signatures associated with steroid hormone receptors and ERBB2 has been consistently demonstrated (Desmedt et al., 2007; Brase et al., 2010; Petry et al., 2010). In contrast, the role of the immune system remained controversial. On the one hand, experimental and animal studies suggest that the humoral immune system may stimulate tumour growth, possibly by cytokine secretion (Tan and Coussens, 2008; Inoue et al., 2006; review: Schmidt et al., 2009a). However, several reports speculated that antibodies secreted after B-cell expansion may also control tumour growth by aiding destruction of tumour cells (review: Schmidt et al., 2010; 2011). Only as recently as 2008, was it finally made clear that a B-cell/plasma cell metagene, indicating infiltration of tumours with plasma cells, is associated with better prognosis in breast cancer (Schmidt et al., 2008). This effect is stronger in fast proliferating carcinomas. In this study, a metagene consisting of 60 individual genes was used to evaluate plasma cell infiltration. In the clinic however, routine determination of a 60-gene signature would be too laborious. Therefore, the major breakthrough of the large validation study is that the 60-gene B-cell/plasma cell metagene can be replaced by a single robust marker without loss of prognostic/predictive power: IGKC (Schmidt et al., 2012). The key messages of the study are:

- IGKC is associated with good prognosis in breast, lung and colon cancers
- IGKC indicates tumour-infiltrating plasma cells
- Besides its prognostic relevance in patients who did not receive systemic chemotherapy, IGKC also predicts favourable responses to anthracycline-based chemotherapy in breast cancer
- IGKC can be detected immunohistochemically in paraffin slides using commercially available antibodies. Al-

ternatively, it can be measured by qRT-PCR using RNA isolated from fresh frozen tumour tissue or from paraffin material. Immunostaining results and RNA expression levels correlate, and the high expression of IGKC obtained using both techniques is similarly associated with better prognosis.

Currently, there are no alternative markers available for the humoral immune system; therefore, IGKC is likely to play a central role as a prognostic and predictive factor of solid carcinomas.

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