

BREAST CANCER

Mutations in breast cancer stem cells correlate with metastases

Breast cancer stem and progenitor cells (BCSCs) are thought to have a central role in the initiation, progression and clinical response of breast cancer. Mutations in the PI3K/AKT signalling pathway, which is frequently dysregulated in tumour cells, have been identified in BCSCs. Researchers, led by SuEllen J. Pommier, have now investigated the clinical implications of these mutations by assessing if PI3K/AKT mutations in BCSCs correlate with tumour aggressiveness, providing an early prognostic indicator in breast cancer.

The mutational status of genes in the PI3K/AKT signalling pathway were analysed in malignant and benign stem cells collected via cell sorting from 30 invasive ductal breast cancers (stage IA to IIIB cancers) and was correlated with the pathological features of the tumour as well as the patients' clinical outcomes. Tumours with BCSCs containing mutations in the PI3K/AKT signalling pathway were significantly more likely to

be associated with axillary lymph-node metastases. Mutations in *AKT1*, *HRAS* or *PIK3CA* were identified in BCSCs from 10 tumours. Of these, nine had associated lymph-node metastases compared with four tumours with BCSCs without mutations. These results were independent of size, grade and hormone status of the tumour.

As Pommier notes, "PIK/AKT signalling pathway defects have been reported in breast cancer, but reports vary with respect to incidence and clinical outcome. The results of this study help explain the heterogeneity we see among breast cancers and the variability in clinical response to treatment. It demonstrates the importance of independently testing the breast cancer's stem and progenitor cells."

Vanessa Marchesi

Original article Donovan, C. A. *et al.* Correlation of breast cancer axillary lymph node metastases with stem cell mutations. *JAMA Surg.* doi:10.1001/jamasurg.2013.3028