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BREAST CANCER

Brain metastasis detectable in CTCs

The presence of radiologically detectable metastases often indicates a poor prognosis in patients with breast cancer, highlighting a need for earlier detection. Now, new research reveals the presence of circulating tumour cells (CTCs) with a distinctly different transcriptomic signature to that of other breast cancer CTCs in patients with breast cancer metastases to the brain (BCBM).

Researchers initially compared the transcriptomes of breast cancer CTCs with those of primary breast cancer cells, reporting the presence of a sizable subpopulation with transcriptomic signatures suggesting reduced metabolic activity, presumably enabling survival in the circulation.

Differences between breast cancer CTCs from those with BCBM and from those without were then explored. CTCs from patients with BCBM had higher levels of several proliferation-associated biomarkers, such as Ki67 and uPAR. Further transcriptomic investigations of samples from a small group of five patients with BCBM and five without revealed a 126-gene signature enabling the discrimination of BCBM-associated CTCs from those not associated with brain metastases. This signature included enrichment of several genes associated with activation of Notch signalling, or with novel immune-evasion pathways. The validity of transcriptomic data was confirmed by the immunocytochemical detection of Notch 1 in 72% of CTCs from patients with confirmed BCBM, versus only 16% in CTCs from patients without BCBM.

This proof-of-concept study demonstrates the potential of CTC-based analyses to identify metastatic disease in patients with breast cancer. The findings also demonstrate that CTCs in patients with breast cancer are a heterogeneous population. Collectively, these data provide some promise; however, further studies, including prospective evaluations of the performance of CTC-based classifiers for the early identification of metastatic disease, will be required prior to clinical implementation.

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