The molecular characterization of 19 breast cancer cell lines by Sieuwerts et al. (1) and their subsequent classification according to breast cancer subtype is valuable information for those designing and evaluating preclinical research models. As developers and manufacturers of the CellSearch system and reagents, we would like to offer the following observations.

Epithelial cell adhesion molecule (EpCAM) has been the most frequently used receptor for capturing circulating tumor cells. However, it is widely recognized that EpCAM is not perfect in this regard. Unfortunately, suitable alternatives or additions to EpCAM have been difficult to identify. In our experience with samples from breast cancer patients, we have observed no gain in sensitivity by targeting other cell surface receptors such as MUC1. In fact, we have observed a decrease in specificity by targeting intracellular receptors such as cytokeratins. We were, however, able to increase CellSearch sensitivity by exploiting certain magnetic properties of our nanoparticles, thereby reducing the influence of the variability of EpCAM density on circulating tumor cells (2,3). More important, our studies showed that EpCAM expression on cell lines is relatively homogeneous and consequently does not reflect the broad range of EpCAM receptor levels seen on circulating tumor cells found in patients (2).

We were therefore disappointed by the study design pursued by Sieuwerts et al. who, by assuming that EpCAM levels on a cell line would equal those of circulating tumor cells from a patient, limited the investigation to cell lines that were added to normal donor blood and only tested the anti-EpCAM capture component of the CellSearch system. To support such broad conclusions about the suitability of EpCAM and CellSearch in breast cancer, patient samples representing all types of breast cancers should have been tested.

Last, it is the presence of elevated numbers of cells, as currently detected by the CellSearch system, and the failure to clear those cells with therapy that has defined the true clinical utility of circulating tumor cells. Whether alternative or additional targets will capture more cells in more patients, without compromising the demonstrated association of circulating tumor cell with clinical outcomes in patients with metastatic breast, colorectal, or prostate cancer (4,5,6), remains to be determined.

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Notes

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