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Uncovering stem-cell heterogeneity in the microniche with label-free microfluidics[1]

LYDIA L. SOHN, University of California, Berkeley

Better suited for large number of cells from bulk tissue, traditional cell-screening techniques, such as fluorescence-activated cell sorting (FACS) and magnetic-activated cell sorting (MACS), cannot easily screen stem or progenitor cells from minute populations found in their physiological niches. Furthermore, they rely upon irreversible antibody binding, potentially altering cell properties, including gene expression and regenerative capacity. We have developed a label-free, single-cell analysis microfluidic platform capable of quantifying cell-surface marker expression of functional organ stem cells directly isolated from their micro-anatomical niche. With this platform, we have screened single quiescent muscle stem (satellite) cells derived from single myofibers, and we have uncovered an important heterogeneity in the surface-marker expression of these cells. By sorting the screened cells with our microfluidic device, we have determined what this heterogeneity means in terms of muscle stem-cell functionality. For instance, we show that the levels of beta1-integrin can predict the differentiation capacity of quiescent satellite cells, and in contrast to recent literature, that some CXCR4+ cells are not myogenic. Our results provide the first direct demonstration of a microniche-specific variation in gene expression in stem cells of the same lineage. Overall, our label-free, single-cell analysis and cell-sorting platform could be extended to other systems involving rare-cell subsets.

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