Novel markers of mesenchymal stem cells defined by genome-wide gene expression analysis of stromal cells from different sources.

Mesenchymal stem cells (MSC) represent a mixture of different cell types, of which only a minority is therapeutically relevant. Surface markers specifically identifying non-differentiated MSC from their differentiated progeny have not been described in sufficient detail. We here compare the gene expression profile of the in vivo bone-forming bone marrow-derived MSC (BM-MSC) with non-bone-forming umbilical vein stromal cells (UVSC) and other non-MSC. Clustering analysis shows that UVSC are a lineage homogeneous cell population, clearly distinct from MSC, other mesenchymal lineages and hematopoietic cells. We find that 89 transcripts of membrane-associated proteins are represented more in cultured BM-MSC than in UVSC. These include previously identified molecules, but also novel markers like NOTCH3, JAG1, and ITGA11. We show that the latter three molecules are also expressed on fibroblast colony-forming units (CFU-F). Both NOTCH3 and ITGA11, but not JAG1, further enrich for CFU-F when combined with CD146, a known marker of cells with MSC activity in vivo. Differentiation studies show that NOTCH3+ and CD146+ NOTCH3+ cells sorted from cultured BM-MSC are capable of adipogenic and osteogenic progeny, while ITGA11-expressing cells mainly show...
an osteogenic differentiation profile with limited adipogenic differentiation. Our observations may facilitate the study of lineage relationships in MSC as well as facilitate the development of more homogeneous cell populations for mesenchymal cell therapy.