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HUMAN ADIPOSE-DERIVED MESENCHYMAL STROMAL CELLS SUBPOPULATIONS THAT EXPRESS DIFFERENT SUBTYPES OF ADRENERGIC RECEPTORS ARE FUNCTIONALLY DISTINCT

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Catecholamines regulate differentiation and secretion of bone marrow mesenchymal stromal cells (MSCs). However, the expression of adrenergic receptors (AR) on adipose-derived MSCs (ADSCs) as well as their role on those cells remains poorly understood. Previously we showed that ADSC population exhibited functional heterogeneity. A variety of first messengers was capable of stimulating Ca2+ signaling in ADSCs, including specific agonists of various subtypes of ARs. Only a relatively small group of cells was nevertheless specifically responsive to the particular GPCR agonist (Biochim Biophys Acta, 2014, 1843(9), p1899).

Here, we explored the molecular mechanisms responsible for functional heterogeneity of ADSC. ADSC were isolated from subcutaneous fat tissue of healthy donors and analyzed at passages 2-3. Subpopulations of ADSCs expressing particular ARs were evaluated by flow cytometry and purified using FACS. ADSC phenotype characterized by flow cytometry was CD90+/CD73+/CD105+/CD45-/CD31- and cells were capable of adipogenic and osteogenic differentiation. We found that 3-5% of ADSC contained α1B, α2B or β2 ARs, using real-time PCR and immunofluorescence. ADSC subpopulations expressing α-ARs disappear during cultivation. ADSC functional analysis with Fluo8 Ca2+ indicator and specific antagonists showed that α1, α2 and β AR isoforms were functionally active in primary ADSC cultures. Proliferation, migration and secretory activity of isolated α1B and α2B ARs containing ADSC were determined. The motility and proliferation of α2B-expressing ADSC were 1,5-2 times lower as compared to other AR-positive subpopulations and non-adrenergic ADSC. The secretory activity

of the α1B and α2B expressing ADSC was dramatically increased as measured by the T-lymphocyte immunnosupression assay. Taken together, our data indicate that human ADSC contain distinct subpopulations of adrenergic cells. Remarkably, α1- and α2-AR expressing ADSCs can serve an immunosuppressive function. We further suggest that ADSC are functinally heterogenous and activities of distinct subpopulations depend on their hormonal sensitivity. This work was supported by RSF grant 14-15-00439.