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Title: Bone marrow-derived MSCs from patients with COPD have abnormal functional capacity

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Body: Introduction: Chronic Obstructive Pulmonary Disease (COPD) is a major health problem. Bone marrow (BM)-derived MSCs have been shown to contribute to pulmonary repair and regeneration in experimental models. However, their role in COPD is unclear. Since COPD is also characterized by systemic inflammation, we hypothesize that BM-MSCs functional capacity and/or regenerative capability can be altered in these patients. Aims: To study the functional capacity of BM-MSCs from COPD patients (BM-COPD) compared to BM-MSCs from controls (BM-C). We have evaluated: 1) the cellular response of MSCs to both tobacco smoke (TS) and VEGF; and, 2) their differentiation capacity. Methods: MSCs were isolated from BM of sternum from subjects who underwent thoracic surgery. After treatments, MSCs were monitored with the xCELLigence system. This system measures real time changes in cellular impedance providing a value named cell index (CI). The differentiation protocol and cellular staining was carried out following R&D Systems instructions. Results: 1) After TS exposure BM-COPD respond in a dose/time dependent manner but are less sensitive than BM-C: on average the CI values goes down by a 75% in BM-C versus only a 40% in BM-COPD; 2) Both COPD and C cells react to VEGF also in a dose/time dependent manner, but at the higher doses and the longer times, BM-COPD are 4 times less sensitive than BM-C; and, 3) There is also a clear differentiation deficiency in BM-COPD, at least to adipocytes. Conclusions: BM-COPD have abnormal functional capacity compared with BM-C. However, whether BM-MSCs can be involved in the pathogenesis of COPD should be evaluated in further studies. Supported by FIS 10/00983 and SEPAR 2011.