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Title: Study of CD44 expression in fibroblastoid cells isolated from BAL of LTR

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Body: Progressive and irreversible fibroproliferative process leads to BOS. The presence of mesenchymal cells, the primary source of fibrotic cells, has been described in BAL fluid of LTR as predictive of BOS onset (Badri et al, 2011). CD44 cell surface glycoprotein has been found increasingly expressed by graft infiltrating lymphocytes, macrophages and AR fibroblasts with active OB. CD44 has been also associated to an invasive fibroblast phenotype. Inhibition of mTOR, responsible of cell over-proliferation has been found effective in treating fibrotic process. Aim of this work is to assay CD44 expression in fibroblastoid cells derived from colony-forming units (CFU) of mesenchymal cells isolated from BAL of LTR patients with BOS 0p, 1 and 2 to evaluate its implication in fibrotic process. In addition, in the same cells expression of the active form of mTOR has been assayed to specifically target pharmacological treatment. Methods: Mesenchymal CFUs from BAL were isolated from two patients with BOS 0p, two with BOS 1 and one with BOS 2, respectively. Proliferation rate was evaluated at 24, 48 and 72 h. CD44 and mTOR expression was assayed by immunocystochemistry. Results: BOS 1 and 2 patients showed moderate to strong expression of both CD44 and mTOR in 80% cells and weak in 20% cells. BOS 0P subjects displayed moderate to high expression in 5% cells, weak signal in 60% and no detection in 35% cells. We also found that cells isolated from BOS 0p had a significantly ($P<0.01$, ANOVA) lower proliferation rate compared to other cultured fibroblastoid cells. Conclusion: These results open new perspectives in the identification of a specific fibroblastoid phenotype linked to BOS grades and to target a therapeutic treatment.