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Title: Immunosuppressive properties of bronchial epithelial cells are altered in lung transplant recipients: “ex-vivo” model of T cell-allogeneic response

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Body: Introduction: Obliterative bronchiolitis (OB) remains the major cause of death in lung transplant recipients (LTxR). Despite evidence that adaptive T-cell responses play an important role in OB, the T-cell effector mechanisms remain poorly understood. Aims and objectives: To evaluate the T-cells-bronchial epithelial cells (BEC) interaction both in stable LTxR and with OB. An “Ex-vivo” model of T cell-mediated allogeneic response against primary cultures of BEC from human LTxR was developed. T cells allogeneic response (measured by lymphocyte proliferation) against BEC, or in combination with a professional Antigen presenting-cell (APC) was assessed. Methods: 17 LTxR [in stable condition (n=9), or with OB (n=8)] were included. For each LTxR, a “mixed reaction” was performed between peripheral mononuclear (PMN) cells and BEC from the same LTxR, in the absence and in the presence of APC. BEC and PMN cells from non-transplant individuals were used as controls (n=4). Results: A marked inhibition of T-cell alloproliferation in mixed reaction with BEC and APC was observed in all groups (stable, OB, controls), but this response was significantly reduced in LTxR, as compared to controls, mostly in LTxR with OB. Expression of co-stimulatory (CD40,CD80,CD83,CD86,HLA-DR) and tolerogenic (HLA-G) molecules was similar in BEC from all groups (stable,OB,Controls) except for CD83 and HLA-G, which were found only in BEC from LTxR. Conclusion: T cell proliferation seems more potently inhibited by BEC from LTxR, as compared to controls, mostly in those with OB. This mechanism may be important in the initiation of T cell-dependent immune responses in LTxR.