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Title: Th17 clones in BOS evaluated by enzyme linked immunospot assay

Simona 12407 Miserere mukiss@libero.it [1], Dr. Rita 12408 Di Domenica didomenica.rita@gmail.com MD [1], Monica 12409 Morosini m.morosini@smatteo.pv.it [1], Anna Maria 12410 Grasso annamariag.grasso@gmail.com [1], Emanuela 12411 Cova e.cova@smatteo.pv.it [1] and Prof. Dr Federica 12430 Meloni f.meloni@smatteo.pv.it MD [1]. [1] Respiratory Diseases, Policlinico San Matteo and University of Pavia, Pavia, Italy, 27100 .

Body: IL-17- and Th17-associated cytokines have been linked to the development of acute and chronic rejection after lung transplantation in both animal models and humans. An increase in IL17 mRNA expression and of IL17 levels in BAL have been described in LTR with BOS and during AR episodes in comparison with Stables Recipients. On the other hand a decrease in IL10-producing clone number and in Treg cell frequency has been described in BOS patients. Aim of the present study was to assess with a feasible method the balance between IFN-gamma/IL17- producing clones and IL10-producing cells/Treg cells in the peripheral blood of 26 LTR (13 stable recipients, 13 BOSpatients). IFNgamma IL17 and IL10 producing clones were assessed by ELISPOT. $CD4^{+}CD25^{high}CD127^{dim}$ were assessed by flow-citometry. A significant increase of IL17 and IFN-gamma producing cells in the peripheral blood was observed in patients who developed BOS (p= 0,03 and 0,04 respectively) while Treg cell count decreased significantly (p= 0,002) and IL10 showed a non significant trend toward a decrease. Moreover the ratio between IL 17 and IL 10 or Treg cell count was significantly increased in BOS (0,85 vs 0,21; 10,4 vs 1,9 respectively) while IFNgamma/IL10 ratio did not significantly change. In conclusion detection of IL17/Treg ratio in the peripheral blood of LTR represents a feasible and useful tool in the identification of patients at higher risk of BOS development.By this way the role of Th17 axis in BOS pathogenesis is further confirmed.