Translational Medicine @ UniSa - ISSN 2239-9747 2019, Special Issue 1(49): 49

P29. GLUCOCORTICOID-INDUCED CHANGES IN TRANSCRIPTION AND LYMPHOCYTES FUNCTIONALITY IN ATAXIA-TELANGIECTASIA.

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Ataxia-Telangiectasia (A-T) is an incurable and rare hereditary syndrome. Treatment with glucocorticoids (GCs) leads to a variable improvement of the neurological and immunological phenotype. We wondered whether there was a correlation between the behavior of lymphocytes functionality and the neurological response to the GC administration. We found that the proliferative response to PHA or IL-7 showed a increase only in 2 of the 4 A-T patients, referred at a single Center. A correlation between the proliferative response to IL-7 and the percentage of CD3+CD127+ cells was found. A significant inverse relationship between the proliferative response to IL-7 and the behavior of the SARA score was found. Subcellular localization studies revealed that, only in the responders, IL-7Rα was localized into the early endosome (EEA1) vesicles and recycled back to the cell surface through the late endosomes (Rab-7). Using microarray analysis we have identified 4304 differently expressed genes (DEgenes), in PBMCs from the only A-T responder patient studied before or after GC treatment. Of these, 2933 transcripts decreased and 1371 transcripts exhibited an increased transcription. Interestingly, some DE-genes are implicated in pathways relevant for A-T pathogenesis, such as cell proliferation, regeneration and differentiation, endosomal/lysosomal trafficking and inflammation. In conclusion, our data indicate a tight correlation in A-T between the in vivo neurological response to GC and the in vitro lymphocyte behavior, and that in-vitro studies on lymphocyte functionality are an excellent cellular model to achieve a better understanding of the disease pathogenesis and of the mechanism of action of GC.