POSTER 26 - EVALUATION OF PI3K/AKT/FOXO PATHWAY IN PATIENTS WITH COMMON VARIABLE IMMUNODEFICIENCY

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Objective: Common variable immunodeficiency (CVID) is the most frequent symptomatic primary immunodeficiency, characterized by hypogammaglobulinemia. PI3K/AKT/FOXO pathway has important role in survival and differentiation of B-cells. Since defect in this pathway could be involved in defective survival and differentiation of B-cells, we evaluated this pathway on B-cells from CVID patients.

Design and Methods: B-cells from 10 patients and 10 healthy individuals were purified by negative selection and were stimulated by anti-IgM and anti-CD40 antibody for 24 hours. We evaluated protein and gene expression of PI3K, AKT and Foxo molecules in B-cells by flowcytometry and real-time PCR, respectively. Moreover, the level of phosphorilated AKT in B-cells has also been measured by flowcytometry. Furthermore, spontaneous and induced apoptosis of B cells have been evaluated. Four-color flow cytometric immunophenotyping determinations of B-cell subsets were also performed using FACSCalibur.

Results: We have not identified significant difference between protein and gene expression of PI3K, AKT and Foxo molecules in B-cells from patients than controls. However, we surprisingly found phosphorylated Akt (p-AKT) levels are significantly lower in B-cells from patients compared with controls. Moreover, our results demonstrate increased spontaneous and induced apoptosis of B cells in patients. Furthermore, our patients presented a significant reduction in B-cell subset numbers than normal cases.

Conclusions: Our results suggest that impairment in phosphorilation of AKT leads to induction of apoptosis in B-cells from CVID patients. Thus, defective p-AKT and increased apoptosis leads to abnormality in B-cell subset numbers, as B cells could be unable to complete their maturation and differentiation.

Key words: Common Variable Immunodeficiency, Signaling, B-cells