Title: PI3K and notch signal pathways coordinately regulate the activation and proliferation of T lymphocytes in asthma

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Body: Aims: In the present study, we determined whether Phosphoinositide 3-kinase (PI3K) and Notch signal pathways are involved in the expression of cyclinD1, cyclinA and p27kip1 which were key molecules in controlling cell cycling from CD4+ T lymphocyte in animal model of asthma. Main methods: Ovalbumin (OVA) sensitized murine model of asthma was used to investigate the expression of cyclin D1, cyclin A, and p27kip1 by splenic CD4+ T lymphocytes. We further observed the effect of specific inhibitor of PI3K(LY294002) and specific inhibitor of Notch(DAPT) on the proliferation of such CD4+ T lymphocytes. Key findings: We found that the expression of cyclinD1 and cyclinA was upregulated at both protein and mRNA levels in asthma group while p27kip1 was down-regulated. Both LY294002 and DAPT inhibit the proliferation of CD4+ T lymphocytes in a time- and dose-dependent manner. Furthermore, LY294002 and DAPT have additive effect in down-regulation of cylinD1 and upregulation of p27kip1. An upregulation of cyclinA, although not statistically significant, was also observed. Significance: These data suggested that PI3K signal pathway and Notch signal pathway may coordinately regulate the cell proliferation and differentiation processes through up-regulating cylinD1 and down-regulating p27kip1 of CD4+T lymphocytes.