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The role of TGF-β in the development of thyrocyte hyperplasia in NOD.H2h4 mice

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Wild type (WT) NOD.H-2h4 mice develop lymphocytic spontaneous autoimmune thyroiditis (L-SAT) and IFN-γ-/- NOD.H-2h4 mice develop severe thyroid epithelial cell (TEC) hyperplasia when given 0.05% NaI water. Since hyperplastic TEC in IFN-γ-/- mice strongly express TGF-β, transgenic NOD.H-2h4 mice expressing TGF-β on TEC were generated to test the hypothesis that overexpression of TGF-β on TEC would promote earlier and/or more severe TEC hyperplasia. Consistent with this hypothesis, all IFN-γ-/- NOD.H-2h4 mice developed severe thyrocyte hyperplasia, and compared to WT Tg- mice with L-SAT, all WT Tg+ mice developed thyrocyte hyperplasia with minimal lymphocyte infiltration 2 months after NaI water. The goal of this study was to compare lymphocyte activation in WT transgenic and nontransgenic mice to determine the mechanisms by which overexpression of TGF-β in thyroids inhibits L-SAT in TGF-β transgenic WT mice. Flow cytometry indicated that CD4 and CD8 splenic T-cells from WT Tg- mice with L-SAT and WT Tg+ mice with severe hyperplasia were similarly activated. By RT-PCR, splenocytes of WT Tg+ mice expressed slightly higher levels of TGF-β compared to WT Tg- mice. However, other cytokines did not differ significantly between WT Tg+ and WT Tg- mice, suggesting lymphocytes in both groups were activated to a similar extent. Splenocytes from both WT Tg+ and WT Tg- mice induced L-SAT after transfer to NOD.H-2h4 SCID recipients, suggesting splenocytes from Tg+ mice were activated and could induce L-SAT in Tg- recipients. RT-PCR and immunohistochemical staining showed that thyroids of WT Tg+ mice expressed more TGF-β and less IFN-γ than WT Tg- thyroids. These results suggest that overexpression of TGF-β on thyrocytes inhibits L-SAT and promotes thyrocyte hyperplasia in NOD.H-2h4 mice. Further research is needed to determine the mechanism by which TGF-β mediates these effects.