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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.