Lack of Glucocorticoid-induced leucine zipper (GILZ) in T cell results in autoimmunity

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CD4+CD25+FoxP3+ T regulatory (Treg) cells modulate immune responses by suppressing the proliferation and cytokine production in different types of immune cells. Reduced functional activity of Tregs results in an increased susceptibility to autoimmune diseases, such as multiple sclerosis, rheumatoid arthritis or type-I diabetes.
We have recently generated a conditional knock out (cKO) mice where gilz gene was selectively deleted in T cells. Young GILZ cKO mice (8-12 weeks old) showed a predisposition to develop a proinflammatory condition associated with a decreased frequency and number of T regulatory (Treg) cells subset.
In order to investigate whether defective Treg production in GILZ cKO mice promotes autoimmunity, we searched for signs of autoimmunity in 10-12 month old wt and GILZ cKO mice. We found a statistically significant increase in serum levels of total IgG1 as well as IgE in GILZ cKO mice compared to age-matched wild-type controls, indicating for the abnormal antibody production by B cells. To check for the accumulation of auto-reactive antibodies, we performed Western Blot analysis using protein extracts from various tissues and seri from wt or GILZ cKO mice of same age and same IgG concentration. We found autoreactive serum Ab that react most pronouncedly with autoantigens in digestive tract tissues (such as stomack, pancreas, intestine and salivary glands). We also measured the serum levels of anti-nuclear antigens (ANA), another marker for autoimmunity by ELISA. We found a tendency of increase in ANA levels in GILZ KO mice. Moreover, GILZ cKO mice showed an increase of spontaneous colitis as indicated by clinical score, weight/length colon ratio.
Altogether, these results suggest that defective Treg cells function, in the absence of GILZ, predisposes to autoimmunity and suggest a physiological role of GILZ as mediator of endogenous GC-mediated control of autoimmunity and inflammation.