Current Research Interests:

Our team is mainly interested in the role of glucocorticoids (GC) on development and function of T cells. In particular, we focus on a CD4+ T cell subset that negatively regulates immune responses and prevents the development of autoimmune diseases, i.e. regulatory T cells expressing the transcription factor Foxp3 (Fig.1).As GC are potent negative regulators of immune and inflammatory responses, they are successfully used in the treatment of autoimmune and inflammatory diseases. We currently pursue the idea that the effectiveness of GC may, among other mechanisms, be due to potentiationof the development and/or function ofFoxp3+ Tcells by these hormones.

To directly investigate the impact of GC on these cells we generated mice specifically lacking the glucocorticoid receptor (GR) in these regulatory T cells. The aim of this project is to examine whether these mice show signs of autoimmunity and display changes in regulatory T cell homeostasis and function. If it turns out that GC indeed potentiateTreg cell function then this may build a basis for developing strategies to improve the currenttherapy of autoimmune diseases with GC. In a second line of research, we explore whether GC can be directly produced by the murine thymus and act in a paracrine or autocrine manner (Fig. 2).

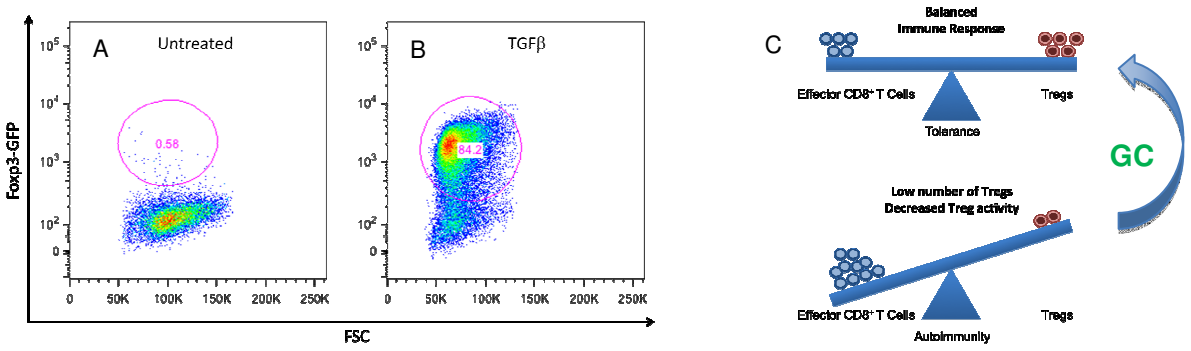

Fig. 1: In vitro generation of (induced) Foxp3+ iTreg cells. Naïve CD4+ T cells were activated in the absence (A) or presence (B) of TGF-beta for 3 days and Foxp3 expression analyzed. These so-called iTregcells can be used to study the function of Treg cells. (C) GC may improve the effectiveness, or increase the number of Treg cells, thus contributing to restoring immune homeostasis.

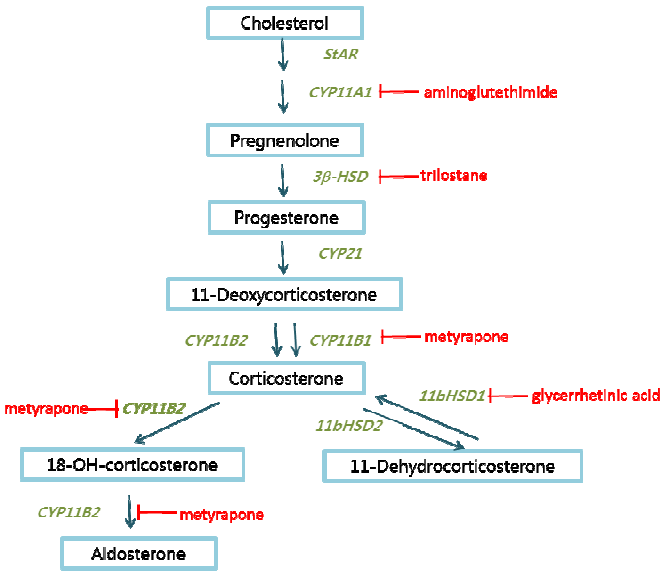

Fig. 2: Pathways of glucocorticoid biosynthesis (i.e. corticosterone in mice). The figure depicts the steps in the steroidogenesis of glucocorticoids from the precursor cholesterol, the enzymes involved, and the sites of action of enzyme inhibitors such as metyrapone. Most of the enzymes(except CYP11B1 and CYP11B2) are expressed by the murine thymus.