We are looking for two Ph.D. students for our project on the **functional heterogeneity of developmental Foxp3$^+$ regulatory (Treg) cell subsets**. Candidates should have a strong interest in immune regulation, a background in immunobiology and experience in molecular and cell biology.

CD4$^+$CD25$^+$ Treg cells expressing the transcription factor Foxp3 develop in the thymus (tTreg) and in peripheral lymphoid tissues (pTreg), and are thought to synergistically act to prevent catastrophic autoimmunity in mice and humans (Schallenberg et al. J Exp Med. 2010; Petzold et al., Eur J Immunol. 2014). The important role of Foxp3$^+$ Treg cells in constraining organ-specific autoimmune disease is exemplified by our recent observation that transient diphtheria toxin (DT)-mediated ablation of all Foxp3$^+$ Treg cells in the NOD mouse model for human type 1 diabetes is sufficient to unleash an aggressive autoimmune response directed against insulin-producing beta cells, in the absence of other severe autoimmune symptoms (Watts *et al.*, Front Immunol. 2021). Foxp3$^+$ Treg cells have also been implicated in functions beyond dominant immune suppression, such as the control of adipose tissue metabolism or promoting regeneration of non-lymphoid tissues, such as the nervous system or brain. However, although of considerable clinical interest, the developmental origin and functional specialization of Treg cells involved in the control of autoimmune disease, metabolic homeostasis and tissue regeneration have remained largely unknown. This has recently encouraged us to establish novel and unique mouse genetic tools (Simonetti et al., Methods Mol Biol. In Press) that have allowed us to provide first insights into the molecular and cellular mechanisms underlying the functional specialization of both Foxp3$^+$ tTreg and pTreg cell subsets.

Key questions relevant to the proposed Ph.D. projects:

(1) How exactly do Foxp3$^+$ tTreg and pTreg cells exert their specialized effector functions in the control of autoimmunity and tissue homeostasis/regeneration?
(2) Can the functional heterogeneity of tTreg and pTreg cells be exploited for their selective (*i.e.*, tTreg/pTreg-cell-specific) therapeutic manipulation *in vivo*?