

Project Title: Instruction and effector function of Th2/1 hybrid cells in parasite infections

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Project Description:

T-helper cell differentiation into Th2 cells is critical for the control of helminth infections, whereas Th1 responses are inadequate for the control of these parasites. However, we have previously shown that the differentiation of Th2/1 cells co-expressing the lineage specifying transcription factors of Th2 and Th1 cells (GATA-3 and T-bet) as well as Th2 and Th1 signature cytokines is a common phenomenon in murine helminth infections (Peine et al. *PLoS Biol* 2013, Bock et al. *Front Cell Infect Microbiol.* 2017). Up to 50% of all cells reacting to the parasite infections acquire the Th2/1 hybrid state and Th2/1 cells also occur in nematode-infected human patients (Bock et al. *Front Cell Infect Microbiol.* 2017). If the instruction of these cells is a way of preventing overt Th2 responses and hence protects the host from Th2-driven immunopathology or rather benefits the parasite by limiting the protective Th2 response is not clear.

A first focus of this project is on the origin and necessities for Th2/1 instruction. Secondly, the role of Th2/1 cells in the instruction of Th1-associated antibody subtypes contributing to protection against nematode challenge infections will be assessed. By tipping the balance between Th2 and Th2/1 cells in parasite infections the third aim of the project is to assess the contribution of Th2 and Th2/1 cells to parasite control and local immunopathology.

Hence this work will give insight into the instruction and effector functions of Th2/1 cells induced by parasites and their role in helminth infections affecting one third of the human global population and impacting significantly on health in life stock production.

References

Peine M, Rausch S, Helmstetter C, Fröhlich A, Hegazy AN, Kühl AA, Grevelding CG, Höfer T, Hartmann S, Löhning M. Stable T-bet+GATA-3+ Th1/Th2 hybrid cells arise in vivo, can develop directly from naive precursors, and limit immunopathologic inflammation. *PLoS Biol.* 2013;11(8):e1001633. doi: 10.1371/journal.pbio.1001633.

Bock CN, Babu S, Breloer M, Rajamanickam A, Boothra Y, Brunn ML, Kühl AA, Merle R, Löhning M7, Hartmann S, Rausch S. Th2/1 Hybrid Cells Occurring in Murine and Human Strongyloidiasis Share Effector Functions of Th1 Cells. *Front Cell Infect Microbiol.* 2017 7:261. doi: 10.3389/fcimb.2017.00261.