The Team:
Head of Department: G. von Wichert (temporary)
Head of Division of Endocrinology and Diabetes: B. O. Böhm
Head of the Laboratory of Mucosal Immunology and Inflammatory Bowel Disease: J. H. Niess
Professor: R. Schirmbeck
Group Leaders/Postdocs: S. Merger, S. Rosinger, A. Spyrantis
PhD Students: U. Chinaka, Z. Fang, C. Manta, K. Radulovic, V. Rossini, N. Schäfer
Additional Members of Thesis Advisory Committees: P. Gierschik (Ulm), S. Kochanek (Ulm), D. Leslie (London, GB), P. Pozzilli (Rome, I), H.-C. Reinecker (Boston, USA)

Department of Internal Medicine I

Division of Endocrinology and Diabetes

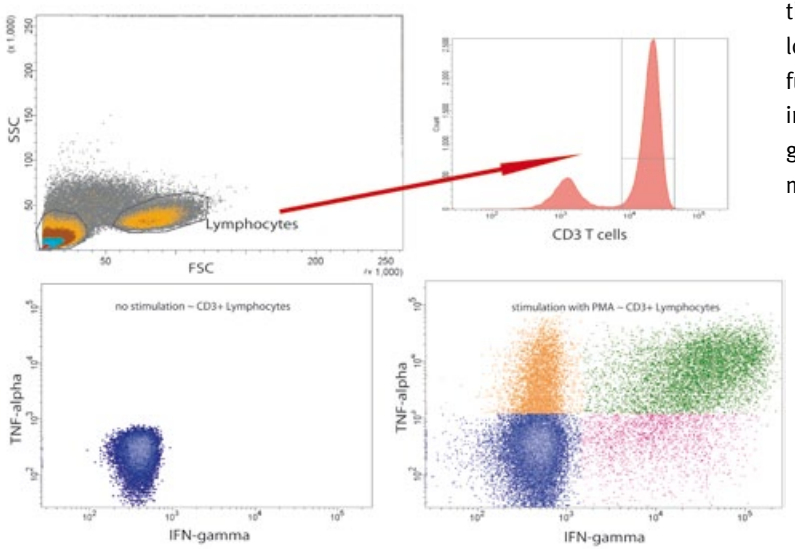
Head: Bernhard O. Böhm

Auto Reactive T-cells in Type 1 Diabetes

Type 1 diabetes is the result of a progressive immune-mediated destruction of insulin-producing ß-cells in the pancreatic islets of Langerhans. Type 1 diabetes is a model disease for studying the progression of autoimmunity. Preservation of ß-cell function is a central goal in type 1 diabetes (type 1 DM) immune intervention. Our group studies T cell responses in type 1 diabetes in humans and in various animal models. In clinical trials, we modulate ß-cell specific autoimmunity with the use of immunomodulatory drugs.

Genetic Basis of Diabetes Mellitus

By employing genome-wide association studies, we try to unravel the genetic basis of type 1 and type 2 diabetes. We recently identified novel signals for type 1 (adult-onset autoimmune diabetes) and type 2 diabetes in cohorts of European descent. The genetic loci identified in type 2 diabetes overlap those loci implicated in monogenic and multifactorial forms of diabetes. In addition, T2D-associated signals also show evidence of the enrichment of genes involved in cell cycle regulation. To understand in greater detail the impact of identified risk loci, we make use of extended functional studies of the ß-cell in humans and have also generated novel ko-mouse models.



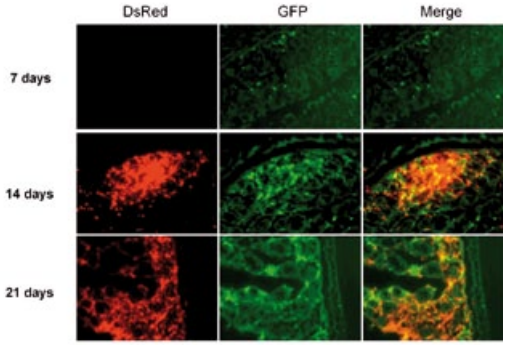
Functional analysis and profiling of PBMC: 6hr mitogen-stimulated PBMC are screened for TNF-alpha and IFN-gamma secretion using intracellular multicolour FACS staining. RNA profiling is applied performing Real-Time PCR array analysis.

Ulm University
Department of Internal Medicine I
Goetz von Wichert
Albert-Einstein-Allee 23
89081 Ulm, Germany
Tel. +49 (0)731 500 44501
Fax +49 (0)731 500 44502
almuth.stein@uniklinik-ulm.de
www.uniklinik-ulm.de/innere1

Laboratory of Mucosal Immunology and Inflammatory Bowel Disease

Head: Jan Hendrik Niess

The mucosal immune system is continuously exposed to challenges provided by the intestinal microflora. We are interested in studying mechanisms by means of which the mucosal immune system has adapted to challenges provided by the intestinal microflora. The focus of our research is the identification of host factors that are involved in maintaining mucosal homeostasis and in regulating intestinal inflammation, such as that found in Crohn´s disease and ulcerative colitis. Within this context, we investigate pathways by which the host recognizes constituents of the intestinal pathway. We have identified a major cell in the intestinal lamina propria involved by taking samples of the intestinal microflora and initiating innate and adaptive immune responses. Intestinal mononuclear phagocytes are reduced in the LP of germ-free animals. As a consequence, IL-17-producing Th17 cells are greatly reduced in germ-free animals. Finally, we have recently identified the activation antigen CD69 as a key regulator of mucosal immune responses. In particular, the activation antigen CD69 is involved in the development of oral tolerance, a key mechanism for preventing potentially harmful mucosal immune responses.



CX3CR1-GFP/RAG$^{-/-}$ animals were reconstituted with CD45RB(high) CD4 T cells from DsRed–transgenic mice, in which cells express the red fluorescent protein under the control of chicken *Actb* promoter. Colonic tissues were taken from transplanted CX3CR1-GFP/RAG$^{-/-}$ animals in the first, second or third week after reconstitution with CD4 T cells and then fixed and analyzed using fluorescent microscopy.

Selected Publications:

- *Burster T, Böhm BO (2010) Processing and presentation of (pro)-insulin in the MHC class II pathway: the generation of antigen-based immunomodulators in the context of type 1 diabetes mellitus, Diabetes Metab Res Rev 26, 227-38.*
- *Voight BF et al. (2010) Twelve type 2 diabetes susceptibility loci identified through large-scale association analysis, Nat Genet 42, 579-89.*
- *Rajasalu T, Brosi H, Schuster C, Spyrantis A, Böhm BO, Chen L, Reimann J, Schirmbeck R (2010) Deficiency in B7-H1 (PD-L1)/PD-1 coinhibition triggers pancreatic beta-cell destruction by insulin-specific, murine CD8 T-cells, Diabetes 59, 1966-73.*
- *Diegelmann J, Seiderer J, Niess JH, Haller D, Göke B, Reinecker HC and Brand S (2010) Expression and regulation of the chemokine CXCL16 in Crohn's disease and models of intestinal inflammation, Inflamm Bowel Dis 16, 1871-81.*
- *Preising J, Philippe D, Gleinser M, Wei H, Blum S, Eikmanns BJ, Niess JH and Riedel CU (2010) Selection of bifidobacteria for amelioration of murine colitis based on adhesion and anti-inflammatory capacity in vitro, Appl Environ Microbiol 76, 3048-51.*
- *Niess JH and Adler G (2010) The Enteric Flora Selectively Expand Gut Lamina Propria CX3CR1+ Dendritic Cells Supporting Inflammatory Immune Responses under normal and inflammatory conditions, J Immunol 15, 2026-37.*