

Report in English

1. Name of group

Intestinal Immune Regulation

2. Key sentence

We are investigating the role of T-helper (Th) cells in immune-mediated diseases. Using novel approaches for the direct analysis of antigen-reactive Th cells, we try to understand why tolerance mechanisms of the immune system fail in patients with chronic inflammatory diseases.

3. Keywords

Immune tolerance, Antigen-specific T cells, Inflammatory bowel diseases, Commensal microbiota, Immunogenetics, Allergy, Regulatory T cells

4. Please list all group members including titles and position

- Group leader: Prof. Dr. rer. nat. Petra Bacher
- Technical Assistance: Sandra Ussat, Alejandro Urritia
- PhD Student: N.N.

5. Scientific Profile

Our main focus is the role of antigen-specific Th cells in human immune responses. T helper (Th) cells are central organizers of immune responses. Via their T cell receptor, they are able to recognize a specific antigen. By releasing different effector cytokines, they can initiate a immune response appropriate to the antigen. However, inappropriate or too strong immune reactions can lead to immune pathologies, such autoimmunity, chronic inflammation or allergies. A specialized Th cell subpopulation, the regulatory T cells (Tregs) on the other hand, have suppressive properties. This enables them to dampen or even prevent the immune response against a certain antigen.

However, which T cells react against a particular antigen, which antigens are at all recognized and how protective immunity and tolerance is maintained or disrupted is in many clinically situations not known. Using novel approaches to analyze antigen-reactive Th cells directly ex vivo from human samples, we are conducting studies to understand why in patients with chronic inflammatory diseases, such as inflammatory bowel disease or allergies, tolerance mechanisms fail. Antigen-reactive Th cell analysis can be combined with powerful state-of-the-art analytical technologies, such as multidimensional flow cytometry, (single cell) transcriptomics, TCR sequencing and proteomics, to provide single cell information at high resolution. We aim to elucidate the interaction between

environmental factors and microbial and inflammatory processes that lead to dysfunctions and inflammation. The analysis of these fundamental processes directly in cells from the human immune system will significantly advance our understanding of basic mechanisms underlying human immune-mediated diseases and speed up the development of new diagnostic as well as therapeutic strategies for chronic inflammatory diseases, autoimmunity or allergy.

List of scientific projects

- Human T cell responses against intestinal microbiota
- Characterization of food-reactive T cells
- Antigen-specific CD4+ T cells as specific diagnostic sensors in cystic fibrosis patients
- Functional and molecular characterization of human Th17 subsets

6. Selected publications

1. **Bacher P**, Heinrich F, Stervbo U, Nienen M, Vahldieck M, Iwert C, Vogt K, Kollet J, Babel N, Sawitzki B, Schwarz C, Bereswill S, Heimesaat MM, Heine G, Gadermaier G, Asam C, Assenmacher M, Kniemeyer O, Brakhage AA, Ferreira F, Wallner M, Worm M, Scheffold A. Regulatory T Cell Specificity Directs Tolerance versus Allergy against Aeroantigens in Humans. *Cell*. (2016) 167(4):1067-1078.
2. **Bacher P**, Steinbach A, Kniemeyer O, Hamprecht A, Assenmacher M, Vehreschild MJGT, Vehreschild JJ, Brakhage AA, Cornely OA, Scheffold A. Fungus-specific CD4+ T cells for rapid identification of invasive pulmonary mold infection. *Am J Respir Crit Care Med*. (2015) 191(3):348-52.
3. **Bacher P**, Kniemeyer O, Schoenbrunn A, Sawitzki B, Assenmacher M, Rietschel E, Steinbach A, Cornely OA, Brakhage AA, Thiel A, Scheffold A. Antigen-specific expansion of human regulatory T cells as a major tolerance mechanism against mucosal fungi. *Mucosal Immunology*. (2014) Jul;7(4):916-28.
4. **Bacher P**, Kniemeyer O, Teutschbein J, Thoen M, Vödisch M, Wartenberg D, Scharf DH, Köster-Eiserfunke N, Schütte M, Dübel S, Assenmacher M, Brakhage AA, Scheffold A. Identification of immunogenic antigens from *Aspergillus fumigatus* by direct multi-parameter characterization of specific conventional and regulatory CD4+ T cells. *J Immunol*. (2014) Oct 1;193(7):3332-43.
5. **Bacher P**, Schink C, Teutschbein J, Kniemeyer O, Assenmacher M, Brakhage AA, Scheffold A. Antigen-reactive T cell enrichment for direct, high-resolution analysis of the human naive and memory Th cell repertoire. *J Immunol*. (2013) Apr 15;190(8):3967-76.

6. Third party funding

Others

ECCO Grant 2019: The immune repertoire of microbe-reactive T cells in blood and tissue of IBD patients

Christiane Herzog Foundation “Antigen-specific CD4+ T cells as specific diagnostic sensors for high-resolution pathogen diagnostics in CF patients”

8. List of cooperation partners in alphabetical order

- Dr. Mario Assenmacher, Marco Vahldieck, Jennifer Pankratz; Miltenyi Biotec GmbH, Bergisch Gladbach, Germany
- Prof. Nina Babel, Dr. Ulrik Stervbo; Marien Hospital Herne, Universitätsklinikum der Ruhr-Universität Bochum, Germany
- Prof. Axel Brakhage, Dr. Olaf Kniemeyer; Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie (HKI), Jena, Germany
- Prof. Oliver Cornely, Angela Steinbach; Klinik I für Innere Medizin, Uniklinik Köln, Köln, Germany
- Prof. Andre Franke, Elisa Rosati; Institut für Klinische Molekularbiologie, CAU Kiel, Germany
- Prof. Bernhard Hube, Dr. Sascha Brunke; Leibniz-Institut für Naturstoff-Forschung und Infektionsbiologie (HKI), Jena, Germany
- Dr. Jochen Maul, Medizinische Klinik für Gastroenterologie, Infektiologie und Rheumatologie CBF, Charité – Universitätsmedizin Berlin, Berlin, Germany
- Prof. Birgit Sawitzki, Katrin Vogt; Berlin-Brandenburg Center for Regenerative Therapies, Charité - University Medicine Berlin, Germany
- Prof. Alexander Scheffold; Institut für Immunologie, CAU Kiel, Germany
- Dr. Carsten Schwarz, Svenja Kaufmann, Jobst Röhmel; Klinik für Pädiatrie m.S. Pneumologie und Immunologie, Charité – Universitätsmedizin Berlin, Berlin, Germany
- Prof. Margitta Worm, Dr. Guido Heine, Klinik für Dermatologie, Venerologie und Allergologie, Charité – Universitätsmedizin Berlin, Berlin, Germany