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Current Fields of Research

The central research objective is to define disease relevant marker genes and to improve therapy and therapeutic stratification in patients with chronic inflammatory rheumatic disorders. The primary focus will lie on a patient centred approach for finding new strategies in innovative therapy. Molecular and cellular disease mechanisms lead to clinical manifestations that result in a comprehensive pattern of molecular and clinical profiles, which are essential for early diagnosis. Depending on these profiles, patients will receive either standard or more innovative therapies that include early use of biologics.

A main focus of the research center is the autoreactive immunological memory that drives chronic inflammation and maintains autoimmunity. This autoreactive memory is refractory to immunosuppressive therapies. So far, it can be only eliminated by unselective immunoablative regimens followed by autologous stem cell transplantation that may lead to long-term treatment-free remissions in refractory autoimmune diseases. Therefore, the research aims to identify targets for a specific depletion of the autoreactive memory such as long-lived plasma cells.

A customized cDNA array for diagnosis, prognosis and prediction of anti-TNF therapy was generated. This array will be extended with other cell and disease specific candidate genes and transferred to a commercial test system based on oligomers. Besides custom-microarrays the application of multiparametric flow cytometry offers an attractive alternative. This technology allows the monitoring of potential candidate genes in concert with an estimation of the cellular immune status of almost all major leukocyte populations on the single cell level in peripheral blood samples.

Another focus of our current research is to develop core technologies based on multidisciplinary knowledge for cell biology, cell culture and biocompatible delivery materials. This group is primarily working with cells from mesenchymal tissues and has extensive experience in 3D cell cultures and in the translation of research into therapies. Major focus is the development of tissue engineered cartilage and bone constructs for regenerative therapies and for in vitro models of inflammatory pathomechanisms and targeted therapies.

The research of the Epidemiology Unit aims at the long-term outcome of inflammatory rheumatic diseases in adults and children, the process and outcomes of health care, and the evaluation of the safety and effectiveness of new therapies in real-life settings. The epidemiologists also participate in investigator-driven randomized clinical trials of new therapies..

Selected Publications

1. Alexander, T., A. Thiel, O. Rosen, G. Massenkeil, A. Sattler, S. Kohler, H. Mei, H. Radtke, E. Gromnica-Ihle, G. R. Burmester, R. Arnold, A. Radbruch, and F. Hiepe. 2009. Depletion of autoreactive immunologic memory followed by autologous hematopoietic stem cell transplantation in patients with refractory SLE induces long-term remission through de novo generation of a juvenile and tolerant immune system. *Blood* 113:214-223.
IF=10,555

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IF = 7,332
3. Buttgereit, F., Doering, G., Schaeffler, A., Witte, S., Sierakowski, S., Gromnica-Ihle, E., Jeka, S., Krueger, K., Szechinski, J., Alten, R. (2008): Efficacy of modified-release versus standard prednisone to reduce duration of morning stiffness of the joints in rheumatoid arthritis (CAPRA-1): a double-blind, randomised controlled trial. *Lancet*, 371: 205-14.
IF = 30,758
4. Chu, V. T., A. Frohlich, G. Steinhauser, T. Scheel, T. Roch, S. Fillatreau, J. J. Lee, M. Lohning, and C. Berek. 2011. Eosinophils are required for the maintenance of plasma cells in the bone marrow. *Nat Immunol* 12:151-159.
IF=26,0
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IF = 10,555
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IF = 12,916
7. Hegazy, A. N., M. Peine, C. Helmstetter, I. Panse, A. Frohlich, A. Bergthaler, L. Flatz, D. D. Pinschewer, A. Radbruch, and M. Lohning. 2010. Interferons direct Th2 cell reprogramming to generate a stable GATA-3(+)T-bet(+) cell subset with combined Th2 and Th1 cell functions. *Immunity* 32:116-128.
IF= 20,589
8. Humrich, J. Y., H. Morbach, R. Undeutsch, P. Enghard, S. Rosenberger, O. Weigert, L. Kloke, J. Heimann, T. Gaber, S. Brandenburg, A. Scheffold, J. Huehn, A. Radbruch, G. R. Burmester, and G. Riemekasten. 2010. Homeostatic imbalance of regulatory and effector T cells due to IL-2 deprivation amplifies murine lupus. *Proc Natl Acad Sci U S A* 107:204-209.
IF=9,432
9. Mei, H. E., D. Frolich, C. Giesecke, C. Loddenkemper, K. Reiter, S. Schmidt, E. Feist, C. Daridon, H. P. Tony, A. Radbruch, and T. Dorner. 2010. Steady-state generation of mucosal IgA+ plasmablasts is not abrogated by B-cell depletion therapy with rituximab. *Blood* 116:5181-5190.
IF=10,555
10. Niesner, U., Albrecht, I., Janke, M., Doebis, C., Loddenkemper, C., Lexberg, MH., Eulenburg, K., Kreher, S., Koeck, J., Baumgrass, R., *et al.* (2008): Autoregulation of Th1-mediated inflammation by twist1. *J Exp Med*, 205 (8): 1889-901.
IF = 14,5051

11. Strangfeld, A., J. Listing, P. Herzer, A. Liebhaber, K. Rockwitz, C. Richter, and A. Zink. 2009. Risk of herpes zoster in patients with rheumatoid arthritis treated with anti-TNF-alpha agents. *JAMA* 301:737-744.
IF=28,899
12. Tokoyoda, K., S. Zehentmeier, A. N. Hegazy, I. Albrecht, J. R. Grün, M. Löhning, and A. Radbruch. 2009. Professional memory CD4+ T lymphocytes preferentially reside and rest in the bone marrow. *Immunity* 30:721-730.
IF=20,589

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WebPages

<http://rheumatologie.charite.de>

<http://www.drfz.de>