Friedrich-Alexander-Universität
Erlangen-Nürnberg

# Profile Center Immunomedicine

## Summer 2025

### CONTENT



**News and Updates p.9**

Participants of the RTG 2740 2nd International Conference "ImmunoMicroTope" at the Institute of Clinical Microbiology, Immunology and Hygiene in Erlangen from 9 – 11 April 2025.

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> *One of the latest dreadful examples is the appointment of Robert F. Kennedy, Jr., [...] as Secretary of the Department of Health and Human Services of the U.S. government."*

## *Dear colleagues and friends,*

In 1798, the British physician Edward Jenner published his clinical account on 27 patients, who were protected against smallpox by prior cowpox infection or inoculation of cowpox material. Together with several other pioneers in the field, he paved the way to the universal introduction of "vaccination" for the prevention of infectious diseases. Shortly after his study was published, anti-vaccinations movements started, mainly due to the fact that the new method of Edward Jenner on the prevention of a frequently deadly disease was propagated at a time when the decisive discoveries on the etiological cause of infectious diseases ("germ theory") had not yet been made. More than 200 years later, we have detailed insights into the pathogenesis of viral, bacterial, protozoan, fungal and helminthic infections and have safe and effective vaccines against many of them at hand. Nevertheless, there are still vaccine hesitancy or even active anti-vaccination movements within many societies including the Western World, which otherwise is very much oriented towards science and upholds the principles of the Enlightenment. One of the latest dreadful examples is the appointment of Robert F. Kennedy, Jr., a self-declared opponent of many vaccines and promotor of conspiracy theories, as Secretary of the Department of Health and Human Services of the U.S. government. However, not only in America, but also in Germany and other European countries skepticism or reluctance against vaccines, especially in early childhood, tends to spread, which results from false ideas about the mechanisms of action and side effects of vaccines or from poor knowledge of infectious diseases, their epidemiology and potential threat. Clearly, scientists need to be much more active also in the public to promote new results and scientific information.

In this context, it is good news that the Bavarian Ministry for Science and Arts recently approved the foundation and the funding of the *Bavarian Center for Preventive Infectious Disease Medicine (BZI),* which will be a joint venture of all six Bavarian Medical Faculties and University Hospitals. The BZI consist of two main columns of activities, i.e., the *Bavarian Surveillance Center (BaySurv)* and the *Bavarian Vaccine Center (BayVak).* The latter goes back to an initiative of our FAU I-MED member Prof. Klaus Überla. Besides carrying out clinical studies on vaccine effectiveness, BayVak also aims to improve the training of medical students in vaccinology and to implement measures of a better communication of the usefulness of vaccines to the public. In one of the forthcoming newsletters, the BZI will be presented in more detail.

I wish you all a relaxing summer break and look forward to see you in autumn, when the invited lectures of our FAU I-MED guest seminar series start again. Please also mark November 18 as the date for the next *Joachim Kalden Lecture* in your calendar.

**Prof. Christian Bogdan**

Spokesperson of the FAU Profile Center Immunomedicine

## Inflammation undermines vaccine T cell memory in treated HIV infection

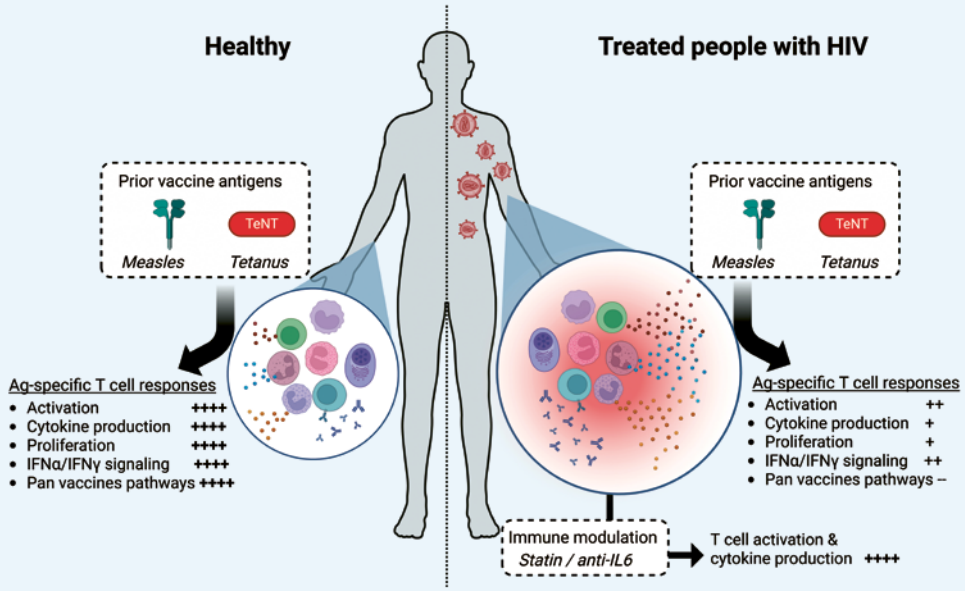
# This study highlights chronic inflammation as a determinant of vaccine-induced T cell immunity in people with HIV and suggests interventions to reduce inflammation as mitigation strategy

Krystelle Nganou-Makamdop

Department of Internal Medicine 3, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

This research focused on the persistence of chronic inflammation in antiretroviral (ART)-treated people with HIV and its potential to impair the functionality of CD4 T cells that were previously induced by vaccinations. Here, we hypothesized that sustained inflammatory responses leading to a state of immune exhaustion could reduce the effectiveness of vaccines administered before or during the course of treated HIV infection. To this end, we assessed recall T cell responses to measles virus (MV) and tetanus toxoid (TT) in participants with prior MV and TT vaccinations. Our key findings were that despite full virus suppression, chronic inflammation in ART-treated individuals was associated with diminished functionality of MV- and TT-specific CD4 T cells. This impairment was characterized by reduced cytokine production and proliferative capacity, which are critical for effective immune responses. Moreover, elevated levels of systemic inflammatory markers such as IL-6 or soluble CD14 – key predictors of morbidity – were found to correlate with the decreased functionality of CD4 T cells. Bulk RNA sequencing on sorted antigen-specific CD4 T cells to further unravel the molecular basis of impaired vaccine-induced immunity showed a significant downregulation of gene sets associated with protective immunity, particularly those involved in the IFN-α and IFN-γ response pathways. Altogether, these findings suggest that chronic inflammation in treated HIV infection leads to transcriptional alterations that compromise the functionality of memory CD4 T cells, thereby reducing the effectiveness of prior vaccinations. Proof of principle for the beneficial effects of anti-inflammatory interventions could be shown upon *in vitro* use of rosuvastatin and tocilizumab that enhanced memory T cell CD69 and IFN-γ responses. These finding underscores the importance of managing inflammation to maintain vaccine efficacy in people with HIV on ART.

M. Kießling, J. J. Cole, S. Kübel, P. Klein, K. Korn, A. R. Henry, F. Laboune, S. Fourati, E. Harrer, T. Harrer, D. C. Douek, K. Überla, K. Nganou-Makamdop. Chronic inflammation degrades CD4 T cell immunity to prior vaccines in treated HIV infection. *Nat Commun* 2024; 15(1):10200.




Despite antiretroviral therapy (ART) that suppresses but does not clear HIV, numerous factors including the virus reservoir contribute to uncontrolled and protracted activation of immune cells. The resulting state of chronic inflammation that impairs memory T cell immunity may be rescued by modulation with anti-inflammatory agents.

## Cell type-specific modulation of metabolic, immune-regulatory and anti-microbial pathways by CD101

# CD101 amplifies the immunosuppressive capacities of regulatory T lymphocytes (Tregs) and enhances the anti-bacterial functions of neutrophil granulocytes

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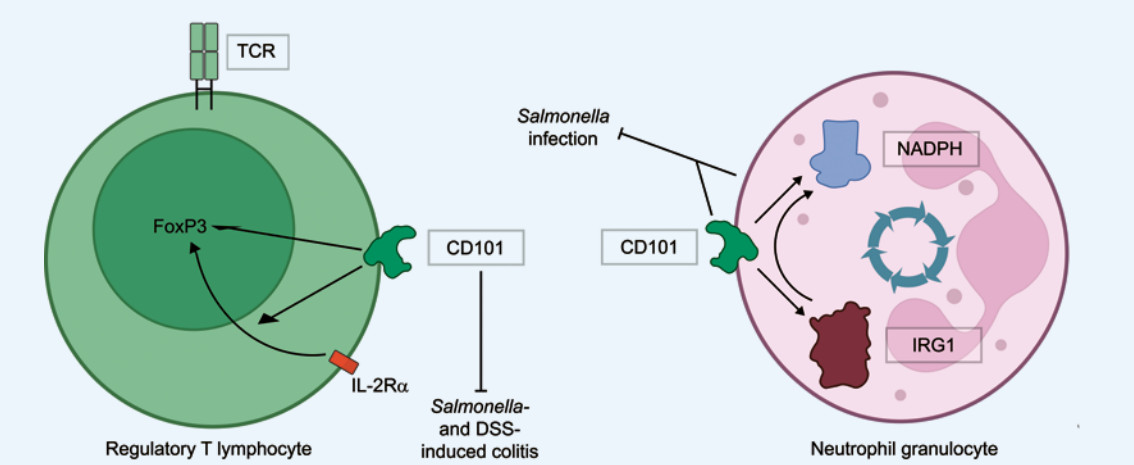
Disruptions of immune cell-specific metabolic networks and inter-cellular communication circuits accompany many immune-mediated and infectious diseases. So far, very few biomarkers have been identified that uncover tissue-specific disease activities or pathological changes within metabolic and molecular networks of individual immune cell subsets. We have observed that inflammatory and infectious stimuli prominently influence the expression of the immunoglobulin (Ig)-like molecule CD101 that is found on different lymphocyte and myeloid cell populations. Thus, CD101 is a promising marker molecule for cell-type specific alterations occurring in immune-mediated and infectious diseases. However, the metabolic and molecular targets of CD101 within individual cells have not been explored yet. To characterize the cell-specific functions of CD101, we compared the course of disease in conditional CD101 knockout mice before and after application of dextran sulfate sodium (DSS) or infection with *Salmonella enterica* Typhimurium (S. Tm). Regulatory T cells (Tregs) were sufficient for the CD101-mediated amelioration of colitis in both models. CD101 stabilized FoxP3 expression and promoted IL-2 signalling in Tregs. Moreover, neutrophil granulocytes required CD101 expression for improved anti-microbial and phagocytic activity. CD101 enhanced the expression of the immune responsive gene 1 (Irg-1) and of nicotinamide adenine dinucleotide phosphate oxidase (NADPH oxidase) and promoted the accumulation of itaconate and reactive oxygen species (ROS) in neutrophils. The concentrations of intestinal microbial antigens in the sera of patients with inflammatory bowel disease correlated inversely with CD101 expression on neutrophils, in line with the suppression of CD101 observed in mice following DSS application or S. Tm infection. In summary, CD101 acts as an immune-suppressive molecule, when expressed on Tregs, and exerts anti-microbial effects, when expressed on neutrophil granulocytes.

**M. Wrage, T. Holland, B. Nüse, J. Kaltwasser, J. Fröhlich, H. Arnold, C. Gießler, C. Flamann, H. Bruns, J. Berges, C. Daniel, M. H. Hoffmann, C. Anish, P. H. Seeberger, C. Bogdan, K. Dettmer, M. Rauh, J. Mattner.** Cell type-specific modulation of metabolic, immune-regulatory, and anti-microbial pathways by CD101. *Mucosal Immunol* 2024; 17(5):892-910.




CD101 expression of Tregs is necessary for the restriction of S. Tm- and DSS-driven colitis, while CD101 expression of neutrophils is pivotal for the control of S. Tm infection. When expressed on Tregs, CD101 promotes IL-2-signalling, the maintenance of FoxP3 expression and anti-colitogenic functions. When expressed on neutrophil granulocytes, CD101 enhances Irg-1 and NADPH oxidase expression, subsequently leading to increased phagocytosis and elimination of intracellular S. Tm.

## Therapeutic Tregs engineered to overexpress GPR15 improves functional fitness for *in vivo* gut homing

# Overexpression of the gut homing marker G-protein coupled receptor 15 on the surface of therapeutic, *ex vivo* expanded, regulatory T cells leads to an increased gut homing *in vivo* without affecting their immunosuppressive character

Tanja M. Müller,[1,2] Markus F. Neurath,[1,2] Caroline J. Voskens[2,3] and Sebastian Zundler[1,2]

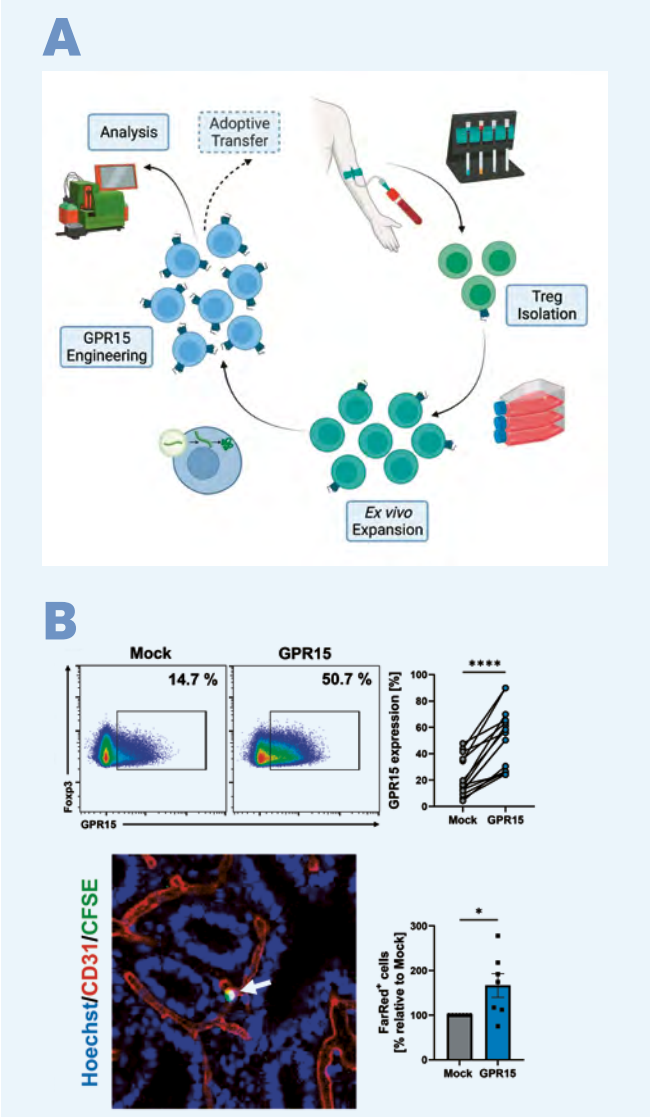
**1** Department of Medicine 1, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg
**2** Deutsches Zentrum für Immuntherapie (DZI), Universitätsklinikum Erlangen
**3** Department of Dermatology, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

Inflammatory bowel diseases (IBD), such as Crohn's disease and ulcerative colitis, are marked by an imbalance of pro- and anti-inflammatory T cells in the lamina propria of the intestinal tract. Only subgroups of patients respond to current therapeutic approaches designed to restrain pro-inflammatory cells or signalling. Adoptive transfer of autologous *ex vivo* expanded regulatory T cells (Tregs) has previously been suggested as a promising future therapeutic approach to resolve chronic intestinal inflammation by promoting anti-inflammatory pathways.

Using a previously established protocol for the *ex vivo* expansion of Tregs (Investigational Medicinal Product-Tregs; IMP-Tregs) we characterized the migration and homing capabilities as well as the immunosuppressive function of non-expanded and IMP-Tregs. Our data show that while the expansion protocol generates highly suppressive Tregs, only a fraction of them is equipped with surface molecules for gut homing. In order to overcome this limitation, we successfully engineered IMP-Tregs via electroporation of mRNA to express the gut homing marker G-protein coupled receptor 15 (GPR15). On a functional level, this led to improved adhesion to the cell adhesion molecules MAdCAM-1 and VCAM-1, which are expressed on the intestinal endothelium, as well as to increased gut homing in a humanized *in vivo* mouse model without affecting the immunosuppressive character of the engineered IMP-Tregs.

In conclusion, our data indicate superior functional fitness of GPR15-engineered IMP-Tregs for homing to the inflamed gut nominating them a promising further development of autologous Treg transfer therapy for IBD.

**T. M. Müller, L. J. Liu, M. Wiesinger, M. F. Neurath, C. J. Voskens, S. Zundler.** Engineering Therapeutic Regulatory T Cells to Overexpress G Protein-Coupled Receptor 15 Improves Functional Fitness for *In Vivo* Gut Homing. *Gastroenterology* 2025; 168(2):389-392.e384.




**A** Overview of the workflow.
**B** **UPPER PANEL** Flow cytometry data of GPR15 expression on IMP-Tregs engineered with GPR15 mRNA or receiving mock treatment. **LOWER PANEL** Humanized *in vivo* mouse model of intestinal cell trafficking.

## Acod1 – a key regulator of osteoclast metabolism and bone erosion in arthritis

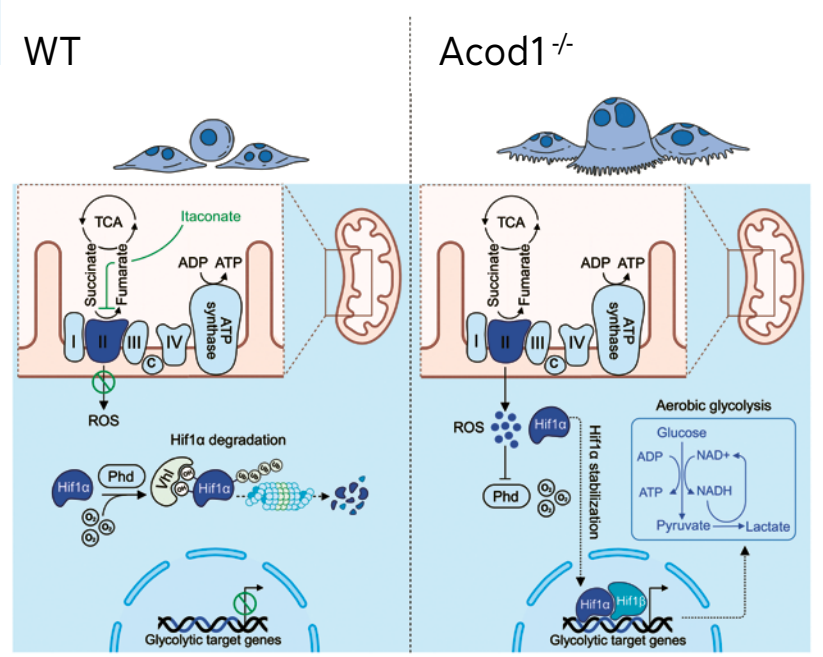
# Acod1 and its metabolite itaconate inhibit osteoclast differentiation and bone erosion in arthritis by suppressing aerobic glycolysis.

Katerina Kachler and Aline Bozec

Department of Internal Medicine 3 – Rheumatology and Immunology, FAU Erlangen-Nürnberg and Universitätsklinikum Erlangen
Deutsches Zentrum für Immuntherapie (DZI), FAU Erlangen-Nürnberg, Universitätsklinikum Erlangen

A prominent hallmark of rheumatoid arthritis (RA) is pathological bone erosion driven by increased osteoclast differentiation and activity. Recent evidence suggests that this disruption in bone homeostasis might be facilitated by metabolic dysregulation. Although osteoclastogenesis is known to involve bioenergetic reprogramming, the specific metabolic changes that osteoclasts and their precursors undergo in the context of RA remain poorly defined. The mitochondrial enzyme aconitate decarboxylase 1 (Acod1), which produces itaconate, has been implicated in regulating the metabolic state and cellular function of monocyte-derived macrophages. Given the shared lineage of osteoclasts and macrophages, we hypothesised a role for Acod1 and itaconate in osteoclast differentiation and arthritis-associated bone loss. Our study demonstrates that elevated osteoclast differentiation and bone resorption in arthritis are linked to enhanced hypoxia inducible factor (Hif)-1α-mediated induction of aerobic glycolysis – a process that is inhibited by Acod1 and its metabolic product itaconate. Acod1 interferes with the glycolytic shift by suppressing the activity of the electron transport chain enzyme succinate dehydrogenase (Sdh), resulting in limited formation of mitochondrial reactive oxygen species (ROS) and Hif-1α degradation. Acod1-deficient mice consequently exhibit enhanced osteoclast differentiation and exacerbated joint damage in an inflammatory arthritis model, while treatment with the itaconate analogue 4-octyl-itaconate (4-OI) ameliorates bone erosion *in vivo* and inhibits human and murine osteoclastogenesis *in vitro*. Together, these findings identify Acod1 and itaconate as crucial regulators of osteoclast differentiation and bone loss in inflammatory arthritis.

K. Kachler, D. Andreev, S. Thapa, D. Royzman, A. Gießl, S. Karuppusamy, M. Llerins Perez, M. Liu, J. Hofmann, A. Gessner, X. Meng, S. Rauber, A. Steinkasserer, M. Fromm, G. Schett, A. Bozec.
Acod1-mediated inhibition of aerobic glycolysis suppresses osteoclast differentiation and attenuates bone erosion in arthritis.
*Ann Rheum Dis* 2024; 83(12):1691-1706.




**Metabolic state of wildtype (WT) vs. Acod1-/- osteoclasts.**

**LEFT PANEL** Itaconate limits the activity of Sdh (complex II) within the respiratory chain, resulting in reduced ROS production. Under normoxic conditions and low ROS levels, Hif-1α is hydroxylated by prolyl hydroxylases (Phds), followed by interaction with von Hippel-Lindau protein (Vhl) and proteasomal degradation.

**RIGHT PANEL** In Acod1 deficiency, itaconate is absent, Sdh is overactivated, and ROS levels are increased, which inhibits Phd-mediated hydroxylation and degradation of Hif-1α. Stabilized Hif-1α translocates to the nucleus and induces the expression of glycolytic genes, thereby promoting upregulated aerobic glycolysis.

Created in BioRender. Bozec, A. (2025) https://BioRender.com/b3yxdsc

## ZEB1-mediated fibroblast polarization controls inflammation and sensitivity to immunotherapy in colorectal cancer

# Depletion of Zeb1 in cancer-associated fibroblasts restricts myofibroblastic myCAF function and modulates inflammatory iCAF features to collectively elevates immune cell infiltration

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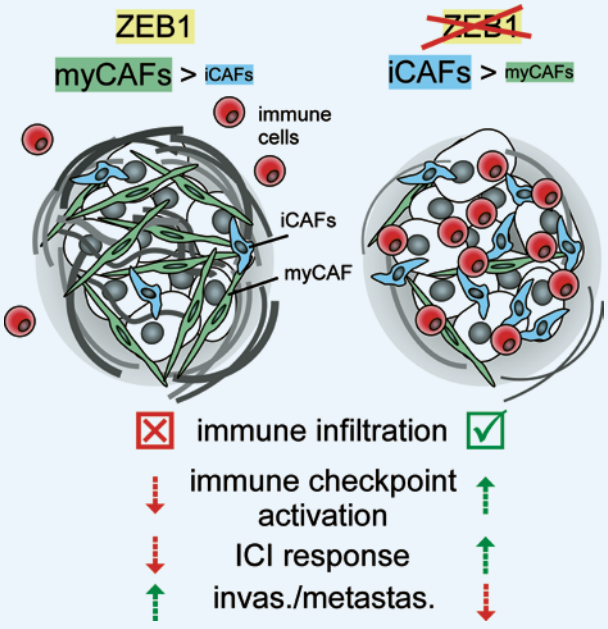
1 Georg-Speyer-Haus, Institute for Tumor Biology and Experimental Therapy, Frankfurt am Main
2 Frankfurt Cancer Institute, Goethe University Frankfurt
3 Department of Experimental Medicine 1, Nikolaus-Fiebiger Center for Molecular Medicine, FAU Erlangen-Nürnberg

The vast majority of colorectal cancer (CRC) tumors are refractory to immune checkpoint inhibition (ICI), partly due to limited generation of neoantigens and formation of an immunosuppressive tumor microenviroenment (TME). Cancer-associated fibroblasts (CAFs) represent a diverse cell population that critically contribute to the TME and are characterized by heterogenous activation of the EMT-transcription factor ZEB1. While ZEB1 in tumor cells regulates metastasis and therapy resistance, its role in CAFs is largely unknown.

To address the role of ZEB1 in CAFs, we analyzed the effect of fibroblast-specific Zeb1 deletion in various immunocompetent mouse models of CRC. We observed that inflammation-driven tumorigenesis was accelerated, whereas invasion and metastasis in sporadic cancers, induced by orthotopic transplantation of tumor organoids, was reduced. Single-cell transcriptomics, histological characterization and *in vitro* modelling revealed a crucial role of ZEB1 in CAF polarization, promoting myofibroblastic features by restricting inflammatory activation. Consequently, Zeb1 deficiency decreased collagen deposition and CAF barrier function but increased NFκB-associated cytokine production, jointly promoting lymphocyte recruitment and immune checkpoint activation. In the context of colitis-mediated tumorigenesis an increase in CD4+ T-cell and FoxP3+ Treg abundances together with elevated phospho-NFκB and CCL2 modulated the immune TME in favour of tumor growth, whereas in sporadic CRC increased cytotoxic CD8+ T cells limited tumor progression.

Strikingly, in all animal models the Zeb1-deficient CAF repertoire sensitized to ICI and restricted or blocked tumor growth. These findings offer a novel therapeutic opportunity of targeting ZEB1 in CAFs and introduce stromal ZEB1 as prognostic biomarker. Collectively, we demonstrate that ZEB1-dependent plasticity of CAFs suppresses anti-tumor immunity and promotes metastasis.

C. Menche, H. Schuhwerk, I. Armstark, P. Gupta, K. Fuchs, R. van Roey, M. H. Mosa, A. Hartebrodt, Y. Hajjaj, A. Clavel Ezquerra, M. K. Selvaraju, C. I. Geppert, S. Bärthel, D. Saur, F. R. Greten, S. Brabletz, D. B. Blumenthal, A. Weigert, T. Brabletz, H. F. Farin, M. P. Stemmler. ZEB1-mediated fibroblast polarization controls inflammation and sensitivity to immunotherapy in colorectal cancer. *EMBO Rep* 2024; 25(8):3406-3431.



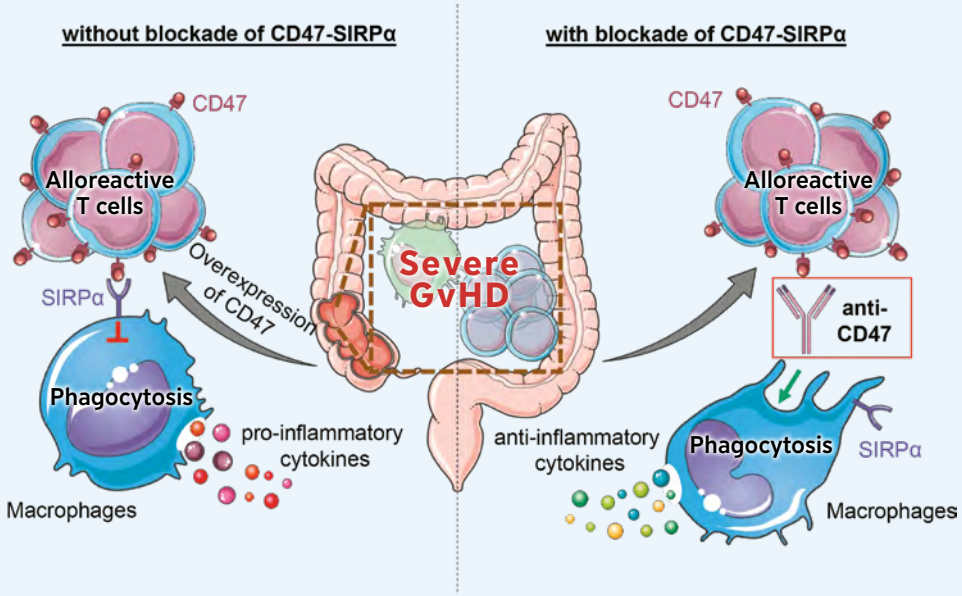

Fibroblast-specific Zeb1 knock-out in colorectal cancer models demonstrate a shift in myCAF and iCAF populations, which result in increased immune infiltration and immune checkpoint activation, rendering tumors susceptible to immune checkpoint inhibition (ICI).

## Augmented CD47 expression impairs alloreactive T cell clearance after allo-HCT

# Anti-CD47 treatment boosts phagocytosis of donor alloreactive T-cells, alleviates inflammation and improves survival after hematopoietic cell transplantation

Cindy Flamann and Heiko Bruns

Department of Internal Medicine 5 – Haematology and Oncology, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg




Alloreactive T cells from patients after allo-HSCT with severe GvHD inhibit phagocytosis by macrophages via CD47-SIRPα-signaling. Blocking CD47-SIRPα-axis by using an anti-CD47 antibody restores impaired phagocytosis of alloreactive T cells and mediates anti-inflammatory effects.

Graft-versus-Host Disease (GvHD) is a serious and often life-threatening complication that frequently arises following allogeneic hematopoietic stem cell transplantation (allo-HSCT). A key therapeutic goal in the management of GvHD is the resolution of inflammation. In this context, macrophage-mediated phagocytic clearance of apoptotic and inflammatory cells plays a critical role in terminating immune responses. However, the specific function of phagocytosis in the setting of allo-HSCT remains largely unexplored. In this study, we investigated the expression of the "don't eat me" signal CD47 on T cells from both GvHD patients and mice. We observed significantly elevated CD47 expression on intestinal T cells in patients with severe GvHD, which correlated with reduced phagocytosis by macrophages. Similar results were observed in GvHD mice, where intestinal T cells also displayed high CD47 levels after allo-HSCT. Functional experiments confirmed that activated T cells inhibit macrophage-mediated antibody-dependent phagocytosis in a CD47-dependent manner *in vitro*. Remarkably, application of an anti-CD47-IgG2σ antibody significantly restored phagocytosis of reactive T cells.

*In vivo*, anti-CD47 treatment led to enhanced phagocytic clearance of T cells in the gut and promoted immunosuppressive responses. This was accompanied by an expansion of the myeloid-derived suppressor cell population, systemic reduction in inflammatory cytokines responses and improved survival. Finally, transplantation of CD47-deficient donor T cells led to a significant improvement in clinical GvHD score and prolonged survival after allo-HCT.

Our study identifies CD47 as a potential therapeutic target, and proposes that anti-CD47 treatment may support the resolution of inflammation by enhancing the removal of pathogenic T cells in the context of GvHD.

The project was funded by the TRR221

**C. S. Flamann, H. Shaikh, C. Matos, M. Kreutz, H. Ali, M. A. Kern, M. Büttner-Herold, B. Jacobs, S. Völkl, C. Lischer, C. Kellner, J. Berges, K. Bitterer, D. Saul, M. Goel, C. Link-Rachner, A. Zernecke, D. A. Weber, D. Mougiakakos, A. Mackensen, A. Beilhack, H. Bruns.** Augmented CD47 expression impairs alloreactive T-cell clearance after allo-HCT. *Blood* 2025 May 7:blood.2023023056. doi: 10.1182/blood.2023023056. Epub ahead of print.

**Participants of the RTG 2740 2nd International Conference "ImmunoMicroTope" at the Institute of Clinical Microbiology, Immunology and Hygiene in Erlangen from 09–11 April 2025.**
Photo provided by Tim Holland, Institute of Clinical Microbiology, Immunology and Hygiene, Universitätsklinikum Erlangen.

## 2nd ImmunoMicroTope 2025

### Unlocking the Secrets of Infection Defense: Highlights from the 2nd International ImmunoMicroTope Conference in Erlangen

From April 9 – 11, 2025, the DFG-funded Research Training Group (RTG) 2740 (spokesman: Prof. Dr. C. Bogdan) hosted the *2nd International ImmunoMicroTope* Conference at the Institute of Clinical Microbiology, Immunology and Hygiene of the University Hospital Erlangen and the FAU. This meeting brought together approximately 100 scientists from 14 countries, who presented and discussed their latest results on the interplay between immune cells and pathogens within the tissue microenvironment.

Central to the symposium was the concept of the "Immunomicrotope" — a term coined by the researchers of the RTG 2740 to describe the complex network of cellular and soluble immune components, metabolites and other micromilieu factors at the site of infections.

A hallmark of the symposium was its emphasis on nurturing early-career researchers. PhD students from the RTG 2740 and selected external researchers presented short talks and posters, facilitating vibrant scientific exchanges and networking opportunities. Esteemed plenary speakers included Gordon Brown (Exeter, UK), Marco Colonna (St. Louis, USA), Mélanie Hamon (Paris, France), Paul Kaye (York, UK), Johanna Maria Kalucka (Aarhus, Denmark), Malcolm McConville (Melbourne, Australia), Monica Rolando (Paris, France), Gerald Späth (Paris, France), Thomas Weichhart (Vienna, Austria) among others.

The symposium concluded with a social evening at one of Bamberg's historic breweries, offering attendees a taste of local heritage and fostering informal interactions among participants.

For more information on RTG 2740 and future events visit: https://www.immunomicrotope.de/

## PUBLICATIONS

### Two "birds" with one stone: B cell-depleting CAR T cells in a patient with myasthenia gravis and rheumatoid arthritis

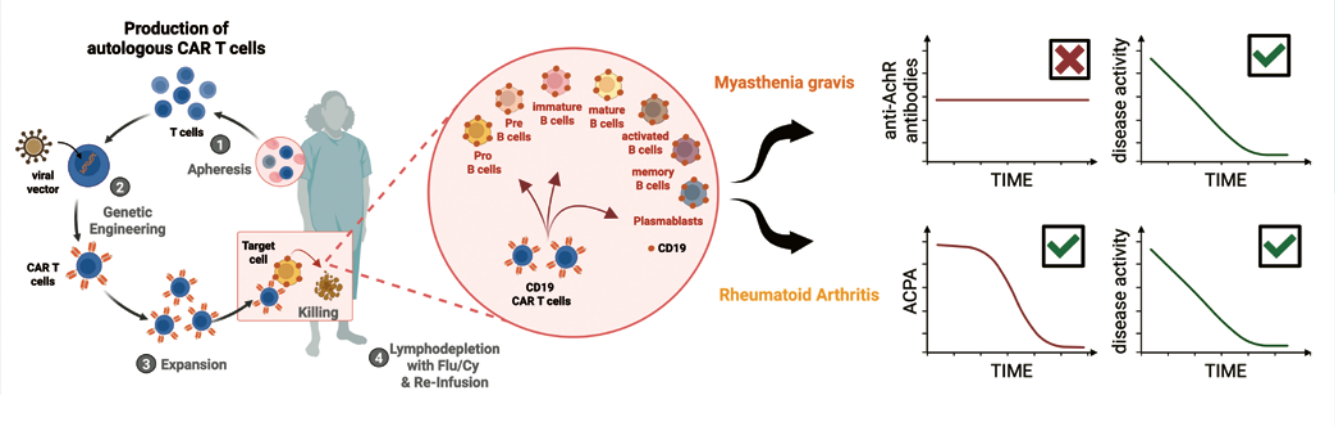
Published in Annals of the Rheumatic Diseases 2024 Nov

**Aiden Haghikia[1], Georg Schett[2,3], Dimitios Mougiakakos[4,5] et al.**

**1** Department of Neurology, Otto-von-Guericke-University Magdeburg
**2** Department of Internal Medicine 3 – Rheumatology and Immunology, FAU Erlangen-Nürnberg and Universitätsklinikum Erlangen
**3** Deutsches Zentrum für Immuntherapie (DZI), FAU Erlangen-Nürnberg, Universitätsklinikum Erlangen
**4** Health Campus Immunology, Infectiology, and Inflammation, Otto-von-Guericke-University Magdeburg
**5** Department of Haematology, Oncology, and Cell Therapy, Otto-von-Guericke-University Magdeburg

B-cell depleting CAR T cells may hold transformative potential in treating autoimmune diseases. The case described here is a 37-year-old female patient with anti-acetylcholine receptor (AchR) antibody-positive myasthenia gravis (MG) and anti-citrullinated protein antibody (ACPA)-positive rheumatoid arthritis (RA). As part of an individualized treatment approach ("Individueller Heilversuch"), the patient received autologous fully human second-generation anti-CD19 CAR T cells (KYV101). The therapy resulted in remission of both diseases: MG and RA activity decreased significantly and the patient regained muscle strength and joint function. Read more about these findings, that underscore the complex role of B cells in autoimmune diseases pathogenesis, beyond the production of autoantibodies.

**LINK** Clinical efficacy and autoantibody seroconversion with CD19-CAR T cell therapy in a patient with rheumatoid arthritis and coexisting myasthenia gravis - PubMed




The anti-CD19 CAR T cells were generated in a multi-step process. The first step was (1) (lymph) apheresis from the patient. Then (2) viral transduction with the CAR construct was performed and the cells were (3) expanded. After lymphodepletion with fludarabine (Flu) and cyclophosphamide (Cy), the cells were administered with the aim to eliminate all CD19+ target cells, i.e., B-cell populations. After treatment, the ACPA antibodies, but not the AchR antibodies, had completely disappeared. However, the patient was completely free of disease activity for both myasthenia and rheumatoid arthritis.

## PUBLICATIONS

### TGFα controls checkpoints in CNS resident and infiltrating immune cells to promote resolution of inflammation

Published in Nature Communications 2025 June

**Lena Löβlein,[1·2·3] Mathias Linnerbauer,[1·2] (...) Veit Rothhammer[1·2]**

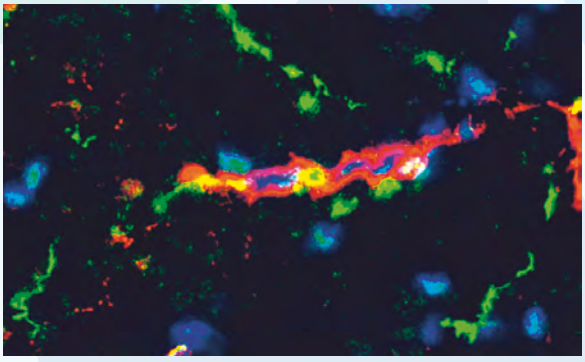
**1** Department of Neurology, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

**2** Deutsches Zentrum Immuntherapie (DZI), Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

**3** Center for Biotechnology, Khalifa University of Science and Technology, Abu Dhabi, United Arab Emirates

After central nervous system (CNS) injury, the extent of tissue repair versus progression to chronic damage is critically influenced by the interaction between infiltrating immune cells, microglia, and astrocytes. In this study, the authors analyzed cerebrospinal fluid (CSF) samples from patients with Multiple Sclerosis (MS) and CNS tissue from mice with experimental autoimmune encephalomyelitis (EAE), an animal model of MS. Their findings reveal that microglia secrete transforming growth factor alpha (TGFα), a molecule that substantially contributes to promoting neurodegeneration. The study further demonstrates that CNS-intrinsic TGFα expression is dynamically regulated across distinct cell types and brain regions over time. These insights highlight TGFα as a potential endogenous therapeutical modulator of recovery in autoimmune inflammatory CNS diseases.

**LINK** TGFα controls checkpoints in CNS resident and infiltrating immune cells to promote resolution of inflammation – PubMed



Immunofluorescence staining of TGFα (red) in microglia (green) in the CNS during autoimmune inflammation

## CLINICAL STUDIES

### CD19-targeting CAR T-cell therapy in patients with diffuse systemic sclerosis – a case series

Published in The Lancet Rheumatology 2025 Feb

**Janina Auth,[1·2] Fabian Müller,[2·3] Christina Bergmann[1·2] et al.**

**1** Department of Internal Medicine 3 – Rheumatology and Immunology, FAU Erlangen-Nürnberg and Universitätsklinikum Erlangen

**2** Deutsches Zentrum Immuntherapie (DZI), Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

**3** Department of Internal Medicine 5 – Haematology and Oncology, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

Systemic sclerosis (SSc) is an autoimmune-driven fibrotic model disease with a high case-related mortality. Many patients progress despite available treatments. CD19.CAR T therapy is a novel method of deep B-cell depletion. In extension to the available evidence, we provide the first detailed analysis of the effects of CD19.CAR T-cell therapy on fibrotic and vascular organ manifestations in 6 six patients with diffuse SSc who progressed despite several treatments. No serious adverse events (e.g., progression of lung fibrosis, cardiac or renal failure or treatment-intensification) occurred within the observational period. ACR-CRISS probability of having improved increased to 100% (IQR 99.95-100) at 6 months. mRSS decreased by 31% (median, IQR 29-38.3) within 100 days. Ground glass opacifications reduced on CT scan and the reticular pattern and forced vital capacity remained stable. Thus, CD19. CART therapy may be a novel option to modify disease activity in SSc and prevent further progression of the disease, however, longer follow-up studies are necessary.

**LINK** CD19-targeting CAR T-cell therapy in patients with diffuse systemic sclerosis: a case series - PubMed

# UPCOMING EVENTS

## Conferences and Events of Interest

**AUGUST 17–22** Vienna, Austria
IUIS2025: 19th International Congress of Immunology

**AUGUST 26–29** Basel, Switzerland
EMBO Workshop:
Adaptive Immunity in Barrier Tissues

**SEPTEMBER 16–18** Edinburgh, Scotland
EMDS 2025: The 38th European Macrophage and Dendritic Cell Society Meeting

**SEPTEMBER 29 – OCTOBER 1** Oxford, UK
Unravelling T cell recognition:
insights from immunology and AI

**OCTOBER 1** Erlangen, Germany
Dr. Andreas Strecker, DFG funding opportunities for early career researchers

**OCTOBER 1–2** Lausanne, Switzerland
2nd Symposium on the Immunobiology of Pattern Recognition Receptors

**OCTOBER 12–17** Chania, Crete, Greece
Aegean Conference: 4th International Conference on Oral Mucosal Immunity and Microbiome

**OCTOBER 12–17** Merseburg, Germany
DGfI Autumn School

**OCTOBER 14** Stockholm, Sweden
NK50 Symposium: 50 Years of NK Cell Research
Karolinska Institute

**OCTOBER 25** Erlangen – Fürth
Die Lange Nacht der Wissenschaften

## Immunological Colloquium FAU I-MED

**Winter 2025/26 Tuesdays, 05:15 pm**

**SEPTEMBER 17, 2025**
**Prof. Gerard C.L. Wong**
University of California, Los Angeles (UCLA)

**OCTOBER 14, 2025**
**Dr. Mercedes Gomez de Agüero**
Institut für Systemimmunologie,
Julius-Maximilians-Universität Würzburg

**OCTOBER 28, 2025**
**Prof. Dr. Dirk Bumann**
University of Basel

**NOVEMBER 18, 2025**
**JOACHIM KALDEN LECTURE**
**Prof. Dr. René E.M. Toes**
Leiden University Medical Center

**NOVEMBER 25, 2025**
**Prof. Dr. Uta Jappe**
Forschungszentrum Borstel, Leibniz Lungenzentrum

**DECEMBER 2, 2025**
**Prof. Dr. Sylvia Knapp**
Medizinische Universität Wien

**DECEMBER 16, 2025**
**Prof. Dr. Dr. Andreas Beilhack**
Universitätsklinikum Würzburg

# Profile Center Immunomedicine




**Publisher**
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Please note that the authors are responsible for the content of their contributions.

We are looking forward to suggestions for the next newsletter.
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