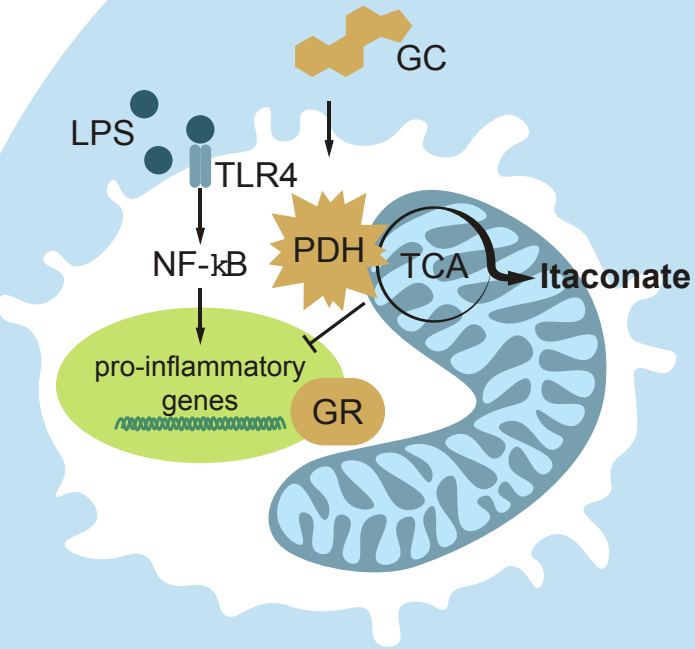
Friedrich-Alexander-Universität
Erlangen-Nürnberg

Profile Center Immunomedicine

Winter 2024

CONTENT



Scientific Highlight, p.7
Glucocorticoids reprogram the mitochondrial metabolism of inflammatory macrophages, potentiating itaconate production, which is critical for their anti-inflammatory effects

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A major task in the forthcoming years will be to define joint projects and fruitful cooperations between physicists, medical doctors and life science researchers.

Dear colleagues and friends,

On September 20, 2024, the new *Max Planck Center for Physics and Medicine* (MPZPM) next to the Departments of Internal Medicine and the four Translational Research Centers was officially opened. The festive event took place in the presence of the Bavarian Prime Minister Markus Söder and two of his cabinet members, Markus Blume (Minister for Science and Arts) and Hubert Aiwanger (Minister for Economic Affairs, Regional Development and Energy), the President of the FAU Joachim Hornegger, the Vice-President of the German Research Foundation Karin Jacobs, the Dean of the Medical Faculty Markus Neurath and the Medical Director of the Universitätsklinikum Erlangen, Heiner Iro. The ceremony also included well-selected keynote lectures by two Nobel Prize winners, Prof. Randy Schekman (University of California, Berkeley, who received the Nobel Prize in Physiology and Medicine 2013 for his work on membrane vesicle trafficking, and Prof. Stefan Hell (Max Planck Institute for Multidisciplinary Sciences in Göttingen), who was awarded the Nobel Prize for Chemistry in 2014 for developing super-resolved fluorescence microscopy.

The opening event represented the preliminary culmination of more than 10 years of efforts to establish this center. Prof. Vahid Sandoghdar, one of the directors of the Max Planck Institute for the Science of Light, was the initiator and the driving force behind the innovative concept of linking physics and medicine. In July 2017, the Max Planck Society, the FAU and the Universitätsklinikum Erlangen had signed a contract of cooperation for establishing a Center for Physics and Medicine and received a funding commitment of 60 million Euros by the Bavarian State Ministry for Economic Affairs, Energy and Technology. The MPZPM offers approximately 6,000 m^2 of research space for up to 180 scientists once all research groups have been established.

A major task in the forthcoming years will be to define joint projects and fruitful cooperations between physicists, medical doctors and life science researchers. The two-day scientific symposium, which preceded the MPZPM opening event, offered talks by excellent national and international scientists. This conference nicely highlighted potential fields of interactions across all major medical disciplines, illustrated the challenge of understanding each other's research language and way of thinking, and certainly would have deserved to be attended by many more members and researchers of the medical faculty.

Although the next newsletter of FAU I-MED is already in preparation, it will not arrive before the end of this year. I therefore wish you all a Merry Christmas and relaxing period of vaccination and all the best for 2025.

Prof. Christian Bogdan

Spokesperson of the FAU Profile Center Immunomedicine

Gene network-based and ensemble modeling-based selection of tumor-associated antigens with a predicted low risk of tissue damage for targeted immunotherapy

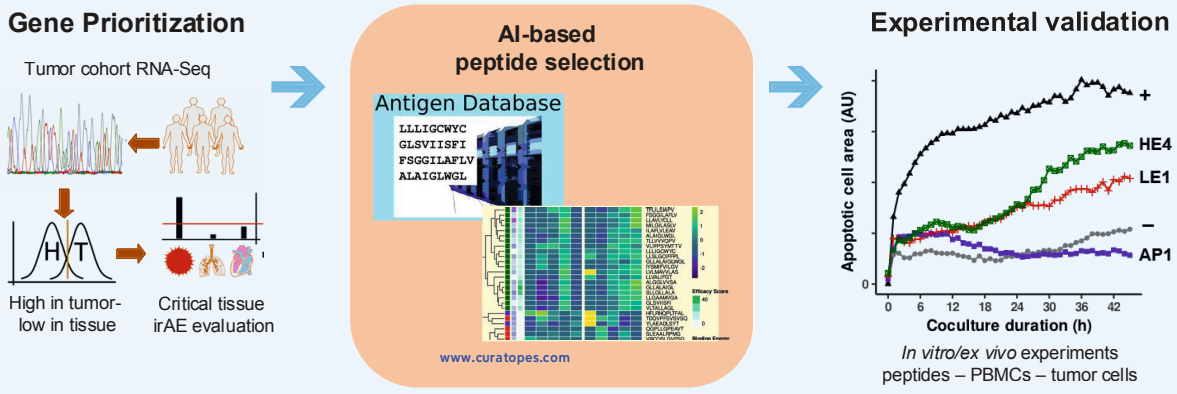
Selection of tumor-associated antigens for targeted immunotherapy with an artificial intelligence algorithm combining systems biology and machine learning

Julio Vera-González and Martin Eberhardt

Laboratory of Systems Tumor Immunology, Department of Dermatology, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

To develop cancer immunotherapy, one can select antigens from overly expressed proteins in cancer cells to stimulate an anticancer immune response. The challenge is to select broadly applicable antigens that induce robust anti-tumor responses and avoid immune-related adverse events. We recently presented an artificial intelligence-based method to select tumor peptides that (a) originate from highly expressed cancer-relevant genes, (b) are predicted to bind efficiently to MHC-I, and (c) are immunogenic. To predict the binding affinity to MHC and the immunogenicity, we utilized two ensembles of random forests, a robust machine-learning model, which in our approach learned from the physicochemical properties of the candidate peptides, like polarity or molecular weight as model input. We tested the AI-based methodology for uveal melanoma (UM), a rare and poorly treatable cancer of the anterior part of the eye. Using RNA-Seq profiles from UM patients, we found 22 genes highly expressed in the tumor that were expressed to a lower degree in a set of healthy body tissues. To avoid immune escape, simulations performed with a mechanistic computational model suggested focusing on genes in high-influence neighborhoods of a cancer importance gene network. To validate the efficacy of the selected tumor peptides, we conducted in vitro and ex vivo experiments with donor and UM patient material. The experiments showed that some of the 20 selected peptides were able to promote a robust immune response and efficient killing of uveal melanoma cells.

C. Lischer, M. Eberhardt, C. Flamann, J. Berges, E. Güse, A. Wessely, A. Weich, J. Retzlaff, J. Dörrie, N. Schaft, M. Wiesinger, J. März, B. Schuler-Thurner, H. Knorr, S. Gupta, K. P. Singh, G. Schuler, M. V. Heppt, E. A. T. Koch, N. D. van Kleef, J. J. Freen-van Heeren, A. W. Turksma, O. Wolkenhauer, B. Hohberger, C. Berking, H. Bruns, J. Vera. Gene network-based and ensemble modeling-based selection of tumor-associated antigens with a predicted low risk of tissue damage for targeted immunotherapy. *J Immunother Cancer* 2024; 12(5).



Sketch of the workflow to select and experimentally test tumor-associated peptides. It includes RNA-seq-based selection of candidate tumor antigens, AI-based prediction, ranking and selection of their derived peptides, and in vitro/ex vivo experimental validation. irAE: immune-related adverse events.

IL-20 controls resolution of experimental colitis by regulating epithelial IFN/STAT2 signalling

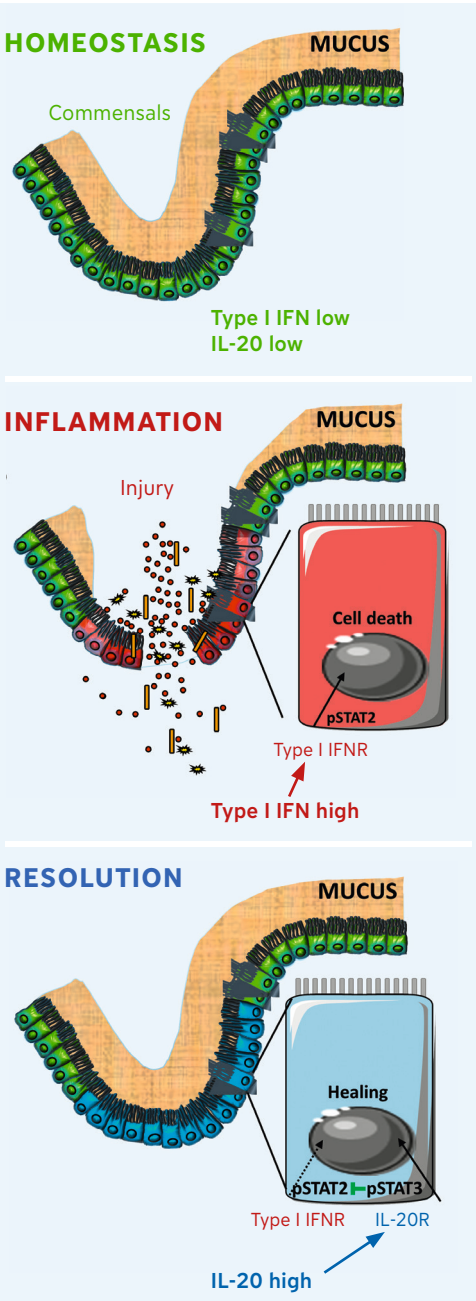
IL-20-dependent mechanisms counteract cell death and inflammation induced by IFN-STAT2 signals, thereby reducing inflammation and promoting mucosal healing in the gut

Mircea T. Chiriac, Markus F. Neurath

Department of Medicine 1, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

This study aimed to explore the role of interleukin (IL)-20 in inflammatory bowel disease (IBD) and experimental colitis. Mice deficient in IL-20 and STAT2 signaling components were subjected to experimental colitis. Intestinal epithelial cell-derived three-dimensional organoids were used to investigate the molecular mechanisms driving cell death and inflammation. We validated and further explored the relevance to the clinical context using samples from IBD patients and non-IBD controls. One of the main findings was that levels of IL-20 increased during remission and were significantly higher in patients with IBD who responded to anti-tumor necrosis factor therapy compared to those who did not. Functionally, IL-20 triggered the activation of STAT3, a well-known regulator of gut epithelial homeostasis. In murine colitis, intestinal epithelial cells were the primary producers of IL-20, and mice lacking IL20, IL20RA, and IL-20RB were more susceptible to experimental inflammation than wild-type control mice. Importantly, IL-20 deficiency was associated with increased IFN/STAT2 activity in these mice, while IL-20 effectively reduced IFN/STAT2-induced necroptotic cell death in intestinal epithelial cell-derived organoids. Results obtained from a newly generated mouse strain lacking STAT2 specifically in intestinal epithelial cells demonstrated reduced susceptibility to experimental colitis, further emphasizing the significance of our findings within the context of gut epithelium. Ultimately, administering IL-20 before the onset of experimental colitis delayed inflammation. These results suggest that IL-20 regulates colitis activity and healing by disrupting IFN/STAT2 death signaling in the context of gut inflammation. Modulating this interaction may offer therapeutic benefits for patients with IBD.

M. T. Chiriac, Z. Hracsko, C. Günther, M. Gonzalez-Acera, R. Atreya, I. Stolzer, L. Wittner, A. Dressel, L. Schickedanz, R. Gamez-Belmonte, L. Erkert, G. Hundorfean, S. Zundler, T. Rath, S. Vetrano, S. Danese, G. Sturm, Z. Trajanoski, A. A. Kühl, B. Siegmund, A. Hartmann, S. Wirtz, J. Siebler, S. Finotto, C. Becker, M. F. Neurath. IL-20 controls resolution of experimental colitis by regulating epithelial IFN/STAT2 signalling. *Gut* 2024; 73(2):282–297.



Schematic representation of potential interactions between IL-20 and type I IFN signals during homeostasis, active inflammation, and resolution phases of intestinal inflammation.

GLUT1-mediated glucose import in B cells is critical for anaplerotic balance and humoral immunity

Sweet-toothed plasma cells: Glucose transporter 1 controls germinal center B cells and humoral immunity

Theresa E.H. Bierling[1], Amelie Gumann[1], Shannon R. Ottmann[1],Sebastian R. Schulz[1], Leonie Weckwerth[1], Jana Thomas[1], Arne Gessner[2], Magdalena Wichert[1], Frederic Kuwert[1], Franziska Rost[1], Manuela Hauke[1], Tatjana Freudenreich[1], Dirk Mielenz[1], Hans-Martin Jäck[1], and Katharina Pracht[1]

1 Division of Molecular Immunology, Internal Medicine III, Universitätsklinikum Erlangen, FAU Erlangen-Nürnberg

2 Institute of Experimental and Clinical Pharmacology and Toxicology, FAU Erlangen-Nürnberg

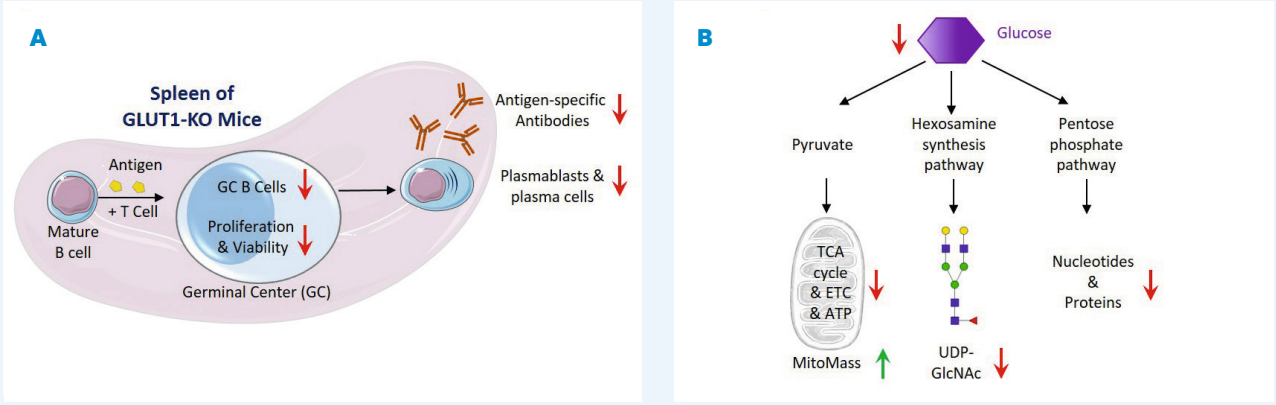
Glucose transporter 1 (GLUT1) is a cell membrane-bound protein that facilitates the import of glucose from the extracellular space into the cell cytoplasm to provide energy. Mutations in the GLUT1 *(Slc2a1)* gene result in reduced transporter production and cause the rare GLUT1 deficiency syndrome (DS).GLUT1-DS patients show severe developmental disorders, cognitive impairment and epileptic seizures.

We showed that the B cells of the murine adaptive immune system express *Slc2a1*. After pathogen contact (e.g., infection, vaccination), B cells differentiate into antibody-secreting plasma cells that are essential for efficient pathogen elimination during acute infections, but also allow long-lasting protection. To investigate the function of GLUT1 in B cells, we established a mouse model in which GLUT1 is deleted only in mature B cells (KO mice). These KO mice showed reduced B cell activation, which resulted in a severe drop in antigen-specific antibodies after immunization. This is most likely due to reduced proliferation and increased mortality of activated GLUT1-deficient B cells.

Analyses of GLUT1-deficient activated B cells and plasma cells by RNA sequencing and mass spectrometry showed changes in their metabolic profile. They were heavily dependent on oxidative phosphorylation in the mitochondria, whose activity was strongly reduced despite an increase in mass. They were also increasingly dependent on alternative energy sources such as fatty acids. Energy depletion and altered nucleotide and protein production explain the observed increased cell death and reduced proliferation of GLUT1-deficient activated B cells and decreased antibody production.

Our study shows that glucose deficiency in B cells affects many signalling pathways and processes that are not only used for energy production and that GLUT1 is essential for the humoral immune response.

T. E. H. Bierling, A. Gumann, S. R. Ottmann, S. R. Schulz, L. Weckwerth, J. Thomas, A. Gessner, M. Wichert, F. Kuwert, F. Rost, M. Hauke, T. Freudenreich, D. Mielenz, H. M. Jäck, K. Pracht. GLUT1-mediated glucose import in B cells is critical for anaplerotic balance and humoral immunity. *Cell Rep* 2024; 43(2):113739.



A GLUT1-deletion in mature B cells results in reduced splenic germinal center B cells, plasmablasts and plasma cells, and antigen-specific antibodies in the serum. **B** Glucose reduction in activated splenic B cells results in reduced mitochondrial activity despite increased mitochondrial mass, decreased abundance of activated glycans (UDP-GlcNAc) and reduced nucleotide and protein production. TCA= Citric acid cycle; ETC= Electron Transport Chain; ATP= Adenosine triphosphate. Figure partially created using SMART.

Tissue niche occupancy determines the contribution of yolk sac – versus bone marrow-derived macrophages to IgG effector functions

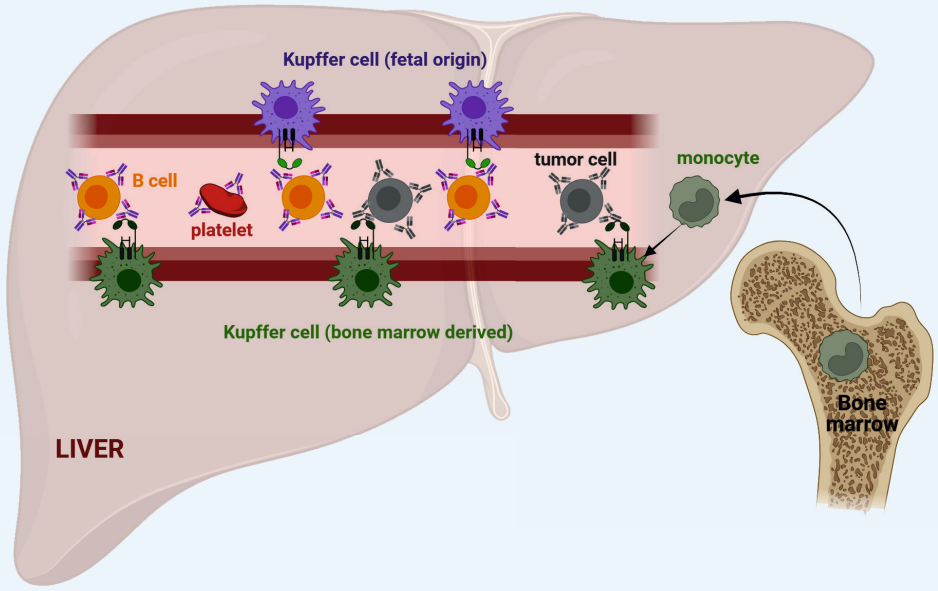
Cytotoxic antibodies targeting cells in the peripheral blood mediate their activity via liver resident Kupffer cells

Miriam Wöhner, Markus Biburger, Falk Nimmerjahn

Division of Genetics, Department of Biology, FAU Erlangen-Nürnberg

Understanding how cytotoxic immunoglobulin G (IgG) antibodies mediate their activity is critical for improving therapeutic IgG activity as well as for inhibiting the self-destructive effects of autoreactive antibodies. Several studies have highlighted the important role of the mononuclear phagocytic system as the major effector cell population responsible for removing opsonized target cells. It remains unclear, however, which monocyte or macrophage subsets, stemming either from primitive hematopoiesis in the yolk sac or fetal liver or from peri- or post-natal bone-marrow dependent definitive hematopoiesis, are involved in IgG-mediated target cell depletion. Moreover, it remains to be established to what extent the anatomical niche itself impacts effector cell activity. By using a titrated irradiation approach, we established conditions under which the contribution of bone marrow-derived monocytes versus yolk sac-derived liver resident macrophages can be studied. Our results demonstrate that liver resident macrophages play a central role for IgG-mediated depletion of B cells and platelets under steady state conditions. Of note, replacing the yolk sac-derived Kupffer cell population with bone marrow-derived macrophages as effector cells maintained IgG activity demonstrating that the tissue niche and not macrophage origin is critical to allow optimal macrophage mediated removal of opsonized tawrget cells from the blood.

M. Wöhner, S. Brechtelsbauer, N. Friedrich, C. Vorsatz, J. Bulang, C. Liang, L. Schorr, A. Beschin, M. Guilliams, J. Ravetch, F. Nimmerjahn, M. Biburger. Tissue niche occupancy determines the contribution of fetal- versus bone-marrow-derived macrophages to IgG effector functions. *Cell Rep* 2024; 43(2):113757.



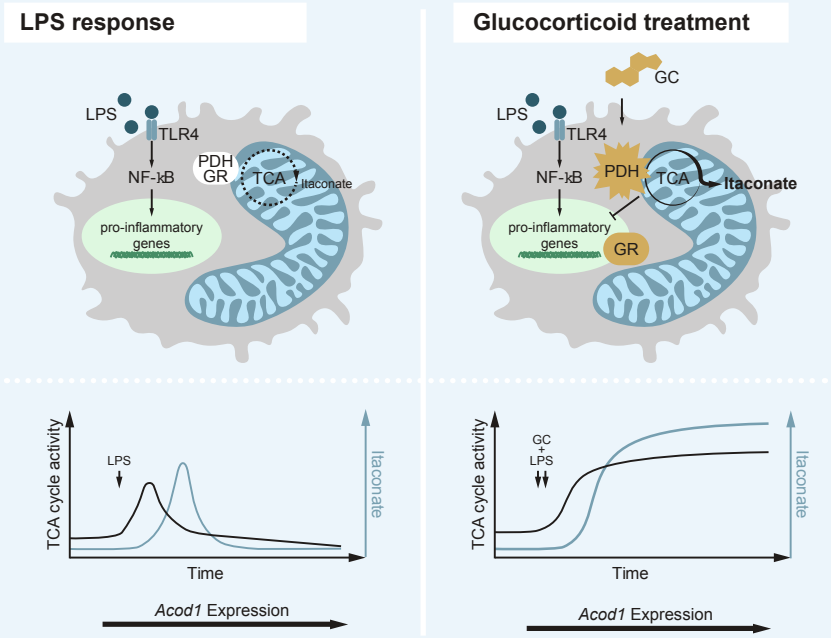
Cytotoxic IgG niches in the liver. Opsonized target cells (B cells, platelet, single disseminated tumour cells) are recognized by liver resident Kupffer cells, resulting in their depletion from the peripheral blood. Of note, the fetal derived Kupffer cell population can be replaced by bone marrow derived macrophages, which can functionally replace Kupffer cells.

Metabolic rewiring promotes the anti-inflammatory effects of glucocorticoids

Glucocorticoids reprogram the mitochondrial metabolism of inflammatory macrophages, potentiating itaconate production, which is critical for their anti-inflammatory effects

Jean-Philippe Auger[1] & Gerhard Krönke[1,2,3]

1 Department of Internal Medicine 3, FAU Erlangen-Nürnberg und Universitätsklinikum Erlangen
2 Department of Rheumatology and Clinical Immunology, Charité – Universitätsmedizin Berlin
3 Deutsches Rheuma-Forschungszentrum Berlin



During inflammation (eg., lipopolysaccharide, LPS), macrophage metabolism switches from oxidative phosphorylation to glycolysis following a break in the TCA cycle, which results in a rapid but unsustained production of the anti-inflammatory metabolite, itaconate (left). Binding of glucocorticoids (GC) to their receptor (GR) provokes increased pyruvate dehydrogenase (PDH) activity, which fuels the TCA cycle and induces accelerated TCA cycle functioning in pro-inflammatory macrophages. This metabolic rewiring by GCs potentiates and sustains itaconate production, which interferes with the production of pro-inflammatory cytokines, contributing to their well-known anti-inflammatory effects (right).

Glucocorticoids represent the mainstay of therapy for a broad spectrum of immune-mediated inflammatory diseases. However, the molecular mechanisms underlying their anti-inflammatory mode of action have remained incompletely understood. Recently, we demonstrated that the anti-inflammatory properties of glucocorticoids involve reprogramming of the mitochondrial metabolism of macrophages, which results in an increased and sustained production of the anti-inflammatory metabolite itaconate. This potentiated itaconate production causes inhibition of the inflammatory response. The glucocorticoid receptor, to which glucocorticoids bind, interacts with parts of the pyruvate dehydrogenase complex, which is central to cellular metabolism. This interaction provokes an increase in pyruvate dehydrogenase activity and allows for an accelerated and paradoxical flux of the tricarboxylic acid (TCA) cycle in otherwise pro-inflammatory macrophages. The glucocorticoid-mediated rewiring of mitochondrial metabolism potentiates TCA cycle-dependent production of itaconate throughout the inflammatory response, thereby interfering with the production of pro-inflammatory cytokines. In contrast, artificial block of the TCA cycle or genetic deficiency in aconitate decarboxylase 1, the rate-limiting enzyme of itaconate synthesis, interferes with the anti-inflammatory effects of glucocorticoids and accordingly abrogates their beneficial effects during a diverse range of preclinical models of immune-mediated inflammatory diseases. These findings provide important additional insights into the anti-inflammatory properties of glucocorticoids and have substantial implications for the future design of novel classes of anti-inflammatory drugs.

J. P. Auger, M. Zimmermann, M. Faas, U. Stifel, D. Chambers, B. Krishnacoumar, R. V. Taudte, C. Grund, G. Erdmann, C. Scholtysek, S. Uderhardt, O. Ben Brahim, M. Pascual Maté, C. Stoll, M. Böttcher, K. Palumbo-Zerr, M. S. J. Mangan, M. Dzamukova, M. Kieler, M. Hofmann, S. Blüml, G. Schabbauer, D. Mougiakakos, U. Sonnewald, F. Hartmann, D. Simon, A. Kleyer, A. Grüneboom, S. Finotto, E. Latz, J. Hofmann, G. Schett, J. Tuckermann, G. Krönke. Metabolic rewiring promotes anti-inflammatory effects of glucocorticoids. *Nature* 2024; 629(8010):184–192.

CD19 CAR T cells achieve lasting, treatment-free remission in refractory, systemic autoimmune diseases

Deep B cell reset is achieved by a single infusion of CD19 CAR T cells, which results in a rapid abrogation of disease-defining auto-antibodies and cessation of inflammation. Patients enter durable, treatment-free remission.

Fabian Müller, MD,[1·2·3] Andreas Mackensen, MD[1·2·3] and Georg Schett, MD[3·4]

1 Departments of Internal Medicine 5–Haematology and Oncology
2 Bavarian Center for Cancer Research (BZKF) – site of Erlangen
3 Deutsches Zentrum für Immuntherapie
4 Internal Medicine 3–Rheumatology and Immunology

The diagnosis of a severe systemic autoimmune disease (AD) carries the burden of life-long immunosuppressive therapy. Individuals with severe AD experience times of well-being under therapy followed by disease flairs, which, over time, lead to a gradually progressing end-organ damage and sequelae. Several AD including systemic lupus erythematosus (SLE), systemic sclerosis (SSc) and idiopathic inflammatory myositis (IIM) are characterized by disease defining auto-antibodies. Targeting autoantibody-producing B cells using therapeutic antibodies is a viable treatment option. Driven by a long-standing interest in cell therapy and supported by a visionary university, we acquired a cell manufacturing license to generate chimeric antigen receptor (CAR) T cells directed against the B cell surface antigen CD19. By nature, infused CAR T cells seek and destroy all cells that carry CD19. CD19 CAR T cells achieve durable remission in otherwise incurable B cell malignancies. Facilitated by in-house produced CD19 CAR T cells, the world-wide first patient with severe and refractory SLE was treated in Erlangen.[1] While treatment-related toxicity was remarkably low, the B cells vanished rapidly, the auto-antibody was abrogated and disease activity resolved rapidly. This remarkable remission of an entirely refractory SLE was unprecedented. Within 18 months from the first infusion, additional 7 SLE, 3 IIM, and 4 SSc patients were treated.[2] All 15 patients achieved a durable treatment-free state with only low-grade toxicity. In a first child treated with CAR T cells, terminal kidney failure was reverted, highlighting that tissue damage in AD may be partially reversible.[3] Despite a deep depletion and abrogation of most autoantibodies, B cells recurred on average around 3 months after CAR T cell infusion suggesting a deep reset. The CD19-directed therapy did not affect long-lasting plasma cells, which we consider as proof that many of the disease-defining auto-antibodies are derived from short-lived, CD19-positive plasma blasts. An important limitation today is the still short follow-up of a relatively small number of patients treated world-wide. Furthermore, the long-term effects of CAR T cell therapy are not yet well characterized. Despite these limitations, the unprecedented success of CAR T cells in severe, refractory B cell-driven AD has revolutionized the field. Emerging concepts entail off-the-shelf products for faster, less complex and less expensive access to similar therapies, which spurs hope for a brighter future of patients suffering from severe, previously incurable AD.

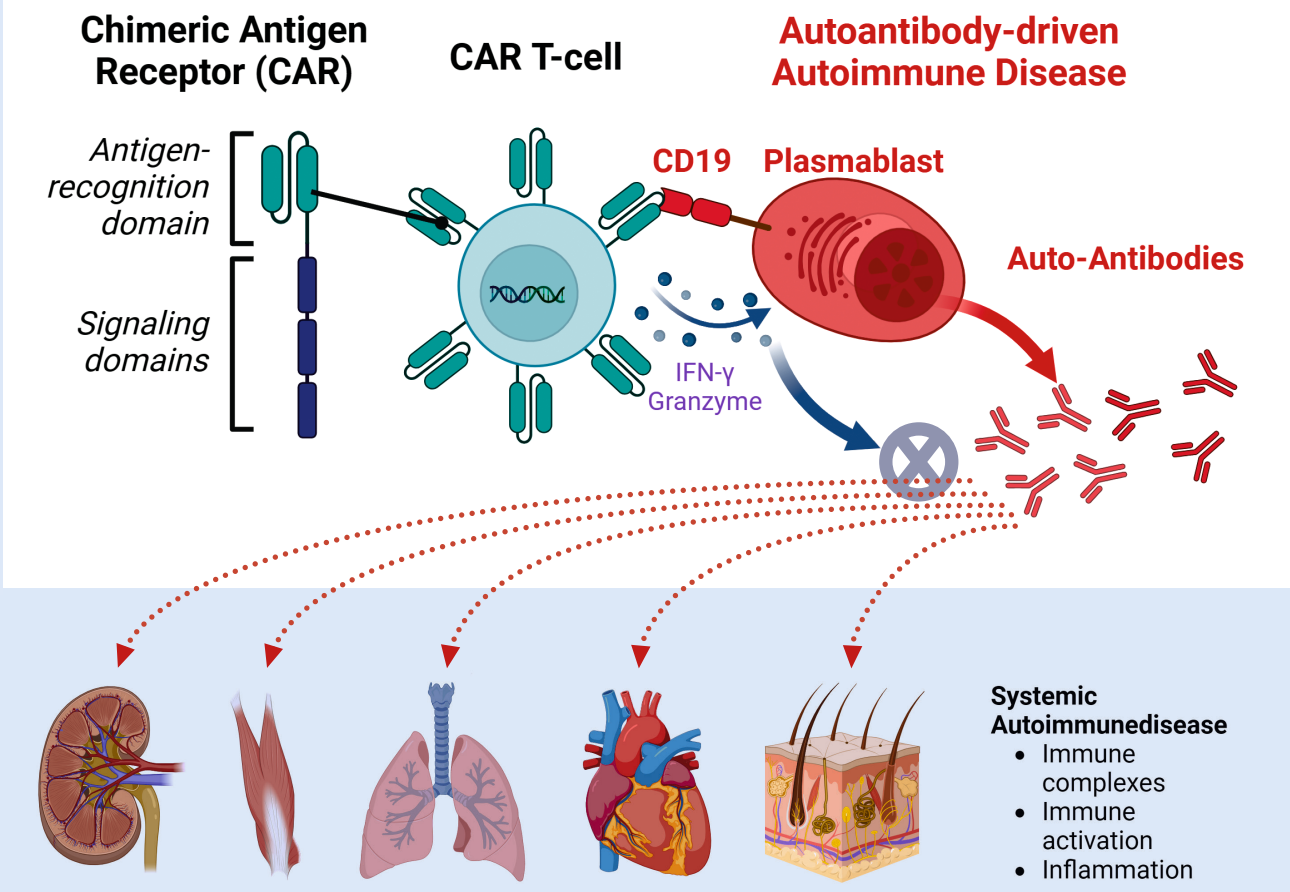
1 **D. Mougiakakos, G. Krönke, S. Völkl, S. Kretschmann, M. Aigner, S. Kharboutli, S. Böltz, B. Manger, A. Mackensen, G. Schett.** CD19-Targeted CAR T Cells in Refractory Systemic Lupus Erythematosus. *N Engl J Med* 2021; 385(6):567–569.

2 **F. Müller, J. Taubmann, L. Bucci, A. Wilhelm, C. Bergmann, S. Völkl, M. Aigner, T. Rothe, I. Minopoulou, C. Tur, J. Knitza, S. Kharboutli, S. Kretschmann, I. Vasova, S. Spoerl, H. Reimann, L. Munoz, R. G. Gerlach, S. Schäfer, R. Grieshaber-Bouyer, A. S. Korganow, D. Farge-Bancel, D. Mougiakakos, A. Bozec, T. Winkler, G. Krönke, A. Mackensen, G. Schett.** CD19 CAR T-Cell Therapy in Autoimmune Disease - A Case Series with Follow-up. *N Engl J Med* 2024; 390(8):687–700.

3 **T. Krickau, N. Naumann-Bartsch, M. Aigner, S. Kharboutli, S. Kretschmann, S. Spoerl, I. Vasova, S. Völkl, J. Woelfle, A. Mackensen, G. Schett, M. Metzler, F. Müller.** CAR T-cell therapy rescues adolescent with rapidly progressive lupus nephritis from haemodialysis. *Lancet* 2024; 403(10437):1627–1630.

CD19 CAR T cells achieve lasting, treatment-free remission in refractory, systemic autoimmune diseases

Deep B cell reset is achieved by a single infusion of CD19 CAR T cells, which results in a rapid abrogation of disease-defining auto-antibodies and cessation of inflammation. Patients enter durable, treatment-free remission.



Overview of CD19 CAR T cells in autoimmune diseases. The chimeric antigen receptor (CAR) is an artificial fusion protein consisting of an antibody fragment to target cell surface antigens and intracellular T cell signalling domain(s). The CAR is introduced into the patient's own T cells (autologous CAR T cells), which then find and eradicate CD19-positive B cells including plasma blasts upon CD19-CAR binding resulting in T cell activation. Among other effects, the CAR T cells abrogate most auto-antibodies and stop the inflammation in the specifically involved organs.

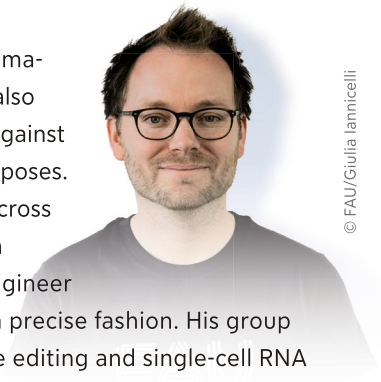
Graphic by F. Müller using BioRender.

PD Dr. rer. nat. Kilian Schober

FAU I-MED clinician scientist is one of the recipients of the 2024 Aventis Life Sciences Bridge Award

The activity of killer T cells in our immune system depends on the antigen they bind via their receptors. Novel therapeutic strategies against cancer, autoimmunity and infectious diseases require new insights into disease-specific antigens of T-cell receptors (TCRs), which are often still unknown.

Kilian Schober, a Clinician Scientist who spends a quarter of his time working as a medical microbiologist, heads the research group "Understanding & Engineering Human T Cell Immunity" at the Institute of Clinical Microbiology, Immunology, and Hygiene at the Universitätsklinikum Erlangen and FAU Erlangen-Nürnberg since 2021. To move into new dimensions of understanding and engineering human T cell immunity, his team investigates the composition and evolution of human antigen-specific T cell responses in well-defined model systems over space and time. The SARS-CoV-2 pandemic provided a unique research opportunity, as many people were rapidly and systematically vaccinated. The group also uses other vaccinations (e.g., against yellow fever virus) for such purposes. Based on findings that apply across various disease entities, Kilian Schober and his coworkers engineer TCRs to reprogram T cells in a precise fashion. His group also uses CRISPR-Cas genome editing and single-cell RNA sequencing to build libraries of TCRs with validated epitopes and to "deorphanize" TCRs with unknown specificity. This knowledge serves as a foundation for developing new cell-based immunotherapies by using functional and safe engineered therapeutic T cell products. In recognition of this work, the Aventis Foundation recently awarded Kilian Schober the prestigious Life Sciences Bridge Award, which is one of the most highly endowed research prizes for young scientists in Germany. Each awardee receives 100.000 €, ten percent of which can be used for personal purposes, while the rest is allocated to research funding.



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We sincerely congratulate Dr. Schober on this award and wish him much success for his future research!

Prof. Dr. med. Frederik Graw

RiseUp!-grant from the Boehringer-Ingelheim-Foundation

Prof. Dr. Frederik Graw (Department of Medicine 5 – Hematology and Oncology) received a RiseUp!-grant from the Boehringer-Ingelheim-Foundation to develop novel mathematical approaches for investigating immune cell dynamics. The project RETENTION aims at revealing the complex interplay between cell migration, proliferation and differentiation for the generation and maintenance of T cell responses within tissues. By developing novel mathematical methods and combining them with experimental data, his group aims to determine how single cell characteristics, such as receptor expression levels on individual cells, might allow us to infer and predict the dynamics of immune responses. Thereby, they will use methods from machine learning and data-driven modelling to disentangle the individual and intermingled processes governing T cell turnover and migration. The project is funded by the Boehringer-Ingelheim-Foundation with 470,000 € over a time period of 3 years within their RiseUp!-Program.

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Frederik Graw heads the research group "Modelling of Immune Processes" within the Department of Medicine 5 – Hematology and Oncology using mathematical modelling and data-analytical methods to study the spatio-temporal dynamics of immune processes in the context of inflammation, infection and malignant diseases.

We cordially congratulate Frederik Graw on this funding and look forward to receiving updates on this exciting project.

JOACHIM KALDEN LECTURE 2024

The FAU Profile Center Immunomedicine honors Prof. Dr. Carola Garcia de Vinuesa

The Joachim Kalden Lecture 2024, which took place on June 11, 2024, was delivered by Prof. Dr. Carola Garcia de Vinuesa from The Francis Crick Institute, London, United Kingdom.

Carola Vinuesa was born in Spain and earned her medical degree from the Universidad Autónoma de Madrid in 1993. After clinical training, she also received a PhD from the University of Birmingham, U.K., in 2000. As a Wellcome Trust International Travelling Prize Research Fellow, she conducted postdoctoral research at the John Curtin School of Medical Research of the Australian National University (ANU), where she became a Group Leader in 2006, Professor of Immunology in 2010, and Head of the Emerging Pathogens and Immunity Department in 2011. In 2014, she founded and co-directed the Centre for Personalised Immunology, an NHMRC Centre of Research Excellence, as well as a sister Centre in the Shanghai Renji Hospital (Jiaotong University, China), of which she became director in 2017. In 2021, Carol Vinuesa relocated to England where she accepted a position as principal group leader at the Francis Crick Institute in London.

Carola Vinuesa has made major contribution to the field of follicular helper T cells (Tfh) and follicular regulatory T cells (Tfr). She is one of the discoverers of Bcl6 as master regulator of Tfh differentiation. She has also unravelled mechanisms by which these cells control antibody responses and limit autoimmunity. Her recent work links genetic variation in humans to autoimmune diseases such as lupus, shedding light on disease pathogenesis.For her achievements, Prof. Vinuesa has received numerous accolades, including the Alfred Gottschalk Medal of the Australian Academy of Science (2009), the Lupus Insight Prize (2023) and the Johann Anton Merck Award (2023). Since 2022, she has been a fellow of the Royal Society.

Prof. Carola Garcia de Vinuesa together with Prof. Georg Schett (Vice President Research, FAU, and Director of the Medical Department 3, Universitätsklinikum Erlangen) and Prof. Christian Bogdan (Spokesperson of FAU I-MED and Director of the Institute of Clinical Microbiology, Immunology and Hygiene, Universitätsklinikum Erlangen).

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In her lecture, Carola Vinuesa first gave a detailed overview on the discovery and function of Tfh and Tfr, before she then outlined her excellent work on the genes and pathways that determine autoimmune diseases in humans and mice. She discussed diverse receptors and regulators in signalling cascades (e.g., TLR7, TREX1, UNC93B, P2RY8, SH2B3, TNIP1/ABIN-1), mutations of which will enhance proinflammatory immune responses and systemic autoimmune reactions.

Prof. Dr. rer. nat. Aline Bozec
Prof. Dr. rer. nat. Thomas Gramberg

Prof. Dr. rer. nat. Aline Bozec has been promoted to the position of W3 Professor in Experimental Immune Therapy at Friedrich-Alexander-University Erlangen-Nürnberg.

I'm also honored to take on the role of Head of Research at the Department of Internal Medicine 3 – Rheumatology and Immunology, Universitätsklinikum Erlangen, under Prof. Georg Schett. Looking forward to contributing further to this incredible team.

ALINE BOZEC

Prof. Dr. rer. nat. Thomas Gramberg has been appointed as W2 Professor.

I am excited to announce that Prof. Joachim Hornegger has appointed me W2 Professor for Antiviral Innate Immunity. I am very happy to continue my scientific journey amongst fantastic colleagues at the Institute of Virology and within the excellent research environment provided by the Medical Faculty at FAU.

THOMAS GRAMBERG

UPCOMING EVENTS

Conferences and Events of Interest
December 2024 – April 2025

DEC. 8–11, 2024 Whistler, British Columbia, USA
Keystone Symposium: Fibrosis: Inflammation, Drivers and Therapeutic Resolution

JAN. 23–24, 2025 Heidelberg, Germany
Innate Immune Checkpoints in Cancer and Tissue Damage – GRK2727

FEB. 11–12, 2025 Jena, Germany
8th German Mass Cytometry User Forum

FEB. 20–22, 2025 Paris, France
European Bronchiectasis Workshop – EBROW 2025

MARCH 4–7, 2025 Hamburg, Germany
Annual Meeting of the Society for Virology

MARCH 6–8, 2025 Venice, Italy
International Congress on Controversies in Rheumatology & Autoimmunity

MARCH 11–14, 2025 Würzburg, Germany
Joint Parasitology Spring Meeting

MARCH 12–15,2025 Davos, Switzerland
World Immune Regulation Meeting – WIRM

MARCH 26–28,2025 Weimar, Germany
Int. Symposium on Ticks and Tick-borne Diseases

APRIL 9–11, 2025 Erlangen, Germany
"ImmunoMicroTope": 2nd International Symposium of the DFG Research Training Group 2740 (RTG 2740)

APRIL 9–12, 2025 Freiburg, Germany
Int. Symposium on Perinatal and Early Life Immunity

APRIL 15–18, 2025 Paris, France
20e Congrès Francophone d'Allergologie

Immunological Colloquium FAU I-MED
Winter 2024/25 Tuesdays, 05:15 pm

JANUARY 7, 2025
Prof. Dr. Mikael Karlsson Karolinska Inst., Stockholm, Sweden

JANUARY 14, 2025
Dr. Claudine Blin Université Côte d'Azur, Nice, France

JANUARY 21, 2025
Prof. Dr. Johannes Huppa Med. Universität Wien

JANUARY 28, 2025
Dr. Effie Bastounis Universität Tübingen

FEBRUARY 4, 2025
Prof. Dr. Josef Penninger HZI Braunschweig

Profile Center Immunomedicine

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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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