Medical Immunology Campus Erlangen

MICE Letter *Summer 2010*

CONTENT

EDITORIAL

Dear colleagues and friends,

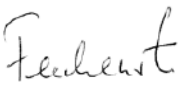
… 70 university teachers and two associated members

… welcome to our new members

This is now the second issue of the MICE letter that should serve as a bulletin to report on recent scientific developments on the Medical Immunology Campus Erlangen (MICE) – an interdisciplinary research center of the University that was founded in March 2009 by scientists of the Medical School and the Department of Biology. The group now consists of 70 university teachers and two associated members. We are especially pleased to welcome our new members who have recently accepted professor positions in Erlangen. David Vöhringer has taken responsibility as Chairman of the newly created Division of Immune Defense and Tolerance of the Medical School. Rainer Böckmann and Achim Gerbitz were appointed as Professor (W2) of Computational Biology at the Department of Biology and Professor (W2) for Hematology with focus on Cellular Immunotherapy, respectively. Jochen Mattner took a position as Professor (W2) in the Department of Clinical Microbiology, Immunology and Hygiene, Christoph Becker in the Department of Internal Medicine 1 (Gastroenterology), and Olaf Prante in the Department of Nuclear Medicine. Kai Hildner was appointed to a Junior Professor position (W1) in the Department of Internal Medicine 1 (Gastroenterology). We wish to thank the Board of the University Hospital (Klinikumsvorstand) for a highly successful negotiation strategy that led to attract outstanding colleagues who will substantially support our research field.

… a proposal for a MICE Center of Excellence initiative

During the past few months, we have intensively worked on a proposal for a MICE Center of Excellence initiative whose vision is to develop into a Cluster of Excellence that translates innovative immunological research into new and personalized immunotherapeutic strategies for the prevention, diagnosis, and treatment of infectious, inflammatory, autoimmune, and neoplastic diseases. The research proposal will be submitted, according to the rules of the national Exellence Initiative, prior to 1 September 2010. We were particularly pleased to see that more than half of the key scientists in MICE have been appointed by our Medical School during the past four years only. Though we cannot expect a positive funding decision prior to spring 2012, we want to join forces to intensify the academic life in the field, whatever the final outcome of the proposal will be. We wish to invite all our colleagues in the field, professors as well as junior faculty, to join our forces in improving academic life and research infrastructure.



Prof. Bernhard Fleckenstein
Coordinator

SCIENTIFIC HIGHLIGHTS

Click for PET

Radiotracer development by click chemistry for molecular imaging in small animals

Molecular imaging by using positron emission tomography (PET) has emerged as an imaging technology with excellent sensitivity for studying intact biological systems. PET chemistry is challenging since short-lived positron-emitting isotopes such as ^{18}F (half-life: 110 min) are used as labeling agents for the synthesis of radiopharmaceuticals. Bioactive peptides that specifically address molecular targets *in vivo* represent an important class of PET tracers to facilitate predictive imaging and PET-guided therapy. Following the concept of click chemistry introduced by Nobel laureate Barry Sharpless in 2001, Huisgen's azide-alkyne cycloaddition has been adapted to ^{18}F-radiosynthetic methods, taking advantage of its selectivity, reliability, and speed under aqueous mild Cu(I)-promoted reaction conditions.

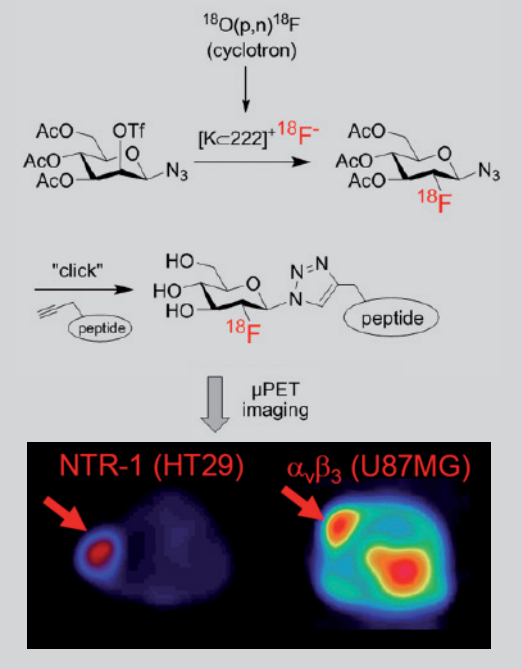
… PET chemistry is challenging since short-lived positron-emitting isotopes are used

Based on previous work on click chemistry in drug discovery in the laboratory of Peter Gmeiner, Department of Chemistry and Pharmacy, and carbohydrate syntheses, the laboratory of Olaf Prante, Department of Nuclear Medicine (Molecular Imaging and Radiochemistry), developed an efficient strategy toward ^{18}F-labeling with concomitant glycosylation for the synthesis of ^{18}F-glycopeptides as imaging agents for PET. The mild conditions and general applicability of this reliable reaction gave access to a new class of ^{18}F-glycopeptide radiopharmaceuticals with improved biokinetic properties for *in vivo* imaging studies by PET. As a proof of concept, two ^{18}F-glycopeptides derived from neurotensin (8–13) and a cyclic RGD-containing peptide, respectively, were extensively studied for their biological properties *in vitro* and *in vivo*, providing evidence for excellent receptor affinity, metabolic stability, and rapid biodistribution. The laboratory of Olaf Prante successfully applied the newly-designed PET tracers to biodistribution studies and small-animal PET (μPET) for imaging neurotensin receptor expression and $\alpha_v\beta_3$-integrin expression of tumors *in vivo* using xenograft nude mice models.

… an efficient strategy toward ^{18}F-labeling with concomitant glycosylation for the synthesis of ^{18}F-glycopeptides as imaging agents for PET

It is anticipated that the "click"-ligation of ^{18}F-labeled glycosyl azides and alkyne-bearing substrates is generally applicable to the modular design of a wide variety of PET tracers. The new procedure is highly amenable to automation using micro-reactor systems and therefore could facilitate the further evaluation of new tracers in longitudinal PET imaging studies on animal models. Future efforts also aim at the development of a Cu-free "click chemistry"-based labeling strategy for cells as a prerequisite for cell trafficking studies in living subjects by PET.

Maschauer S, Einsiedel J, Haubner R, Hocke C, Ocker M, Hübner H, Gmeiner P, Kuwert T, Prante O. Labeling and Glycosylation of Peptides using Click Chemistry: A General Approach to ^{18}F-Glycopeptides as Effective Positron Emission Tomographic Imaging Probes. Angew Chem Int Ed Engl. 2010; 49(5): 976-9.

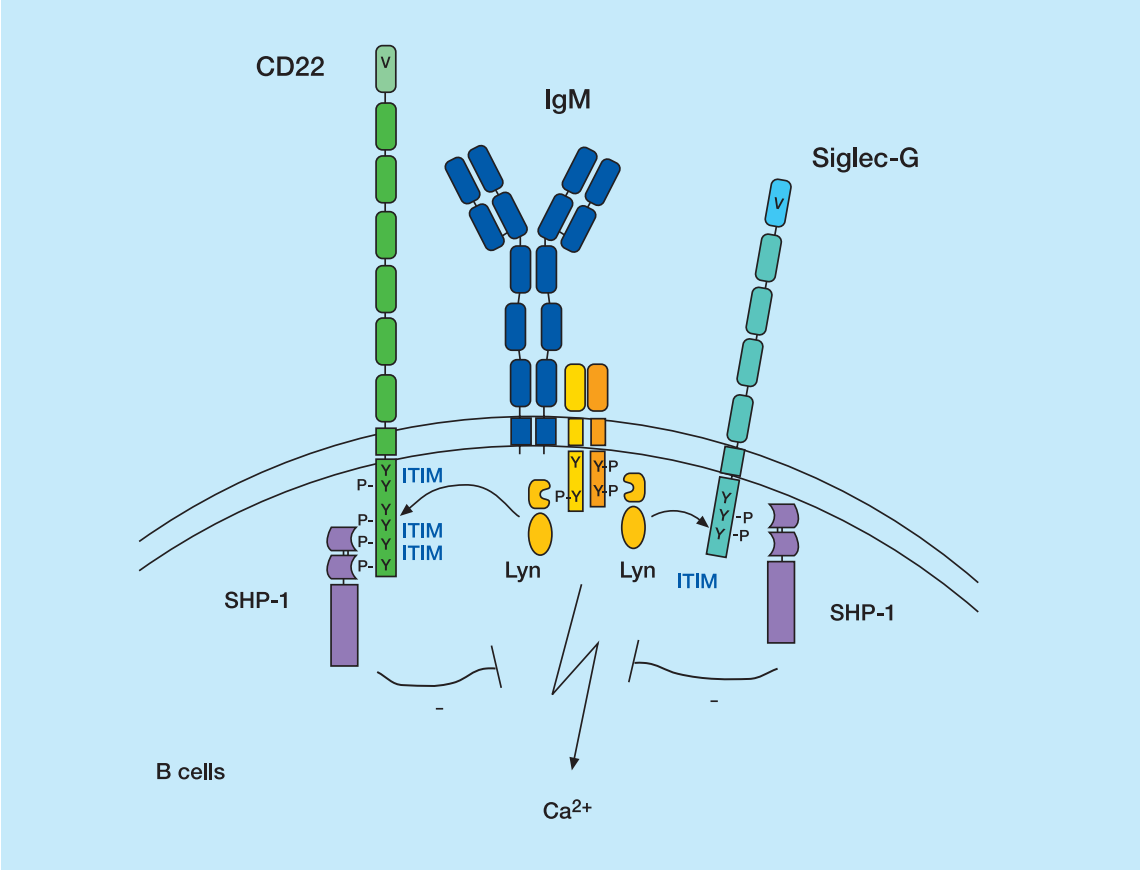


Strategy toward ^{18}F-labeling with concomitant glycosylation for the synthesis of ^{18}F-glycopeptides for small-animal PET (μPET) imaging

CD22 x Siglec-G double knockout

CD 22 x Siglec-G double-deficient mice have massively increased B1 cell numbers and develop systemic autoimmunity.

CD22 (Siglec-2) and Siglec-G are inhibitory co-receptors for B cell receptor mediated signaling. These co-receptors control the signaling threshold of B cell activation. Both proteins belong to the same protein family, which inhibits signaling in several types of immune cells. Both CD22-deficient mice and Siglec-G deficient mice, which were generated in the group of Lars Nitschke, Chair of Genetics, Department of Biology, show increased calcium signaling in B cells. While the deficiency of CD22 leads to higher signaling in conventional B cells, the deficiency of Siglec-G mainly affects B1 cells, a subpopulation of B cells, which is greatly



CD22 and Siglec-G are inhibitory co-receptors on B cells. BCR signals on B cells are inhibited by the BCR-associated co-receptors CD22 (Siglec-2) and Siglec-G. Both inhibitory receptors are phosphorylated on inhibitory ITIM motifs by the tyrosine kinase Lyn and recruit the inhibitory tyrosine phosphatase SHP-1 to the BCR signalosome. Recruited SHP-1 inhibits intracellular Ca^{2+} signaling. CD22 and Siglec-G together prevent development of systemic autoimmunity.

expanded in numbers in Siglec-G-deficient mice. Many inhibitory receptors on lymphocytes control immunological tolerance and are thought to prevent overstimulation of lymphocytes potentially leading to autoimmunity. However, neither CD22-deficient nor Siglec-G-deficient mice develop autoimmunity. Siglec-G x CD22 double-deficient mice were generated and analysed together with the groups of Thomas Winkler, Chair of Genetics and Kerstin Amann, Department of Pathology. Siglec-G x CD22 double-deficient mice showed elevated BCR-induced calcium responses in both B1 cells and conventional B cells. Also, Siglec-G x CD22 double-deficient B cells exhibited a hyperproliferative response to stimulation with several TLR ligands. Aged Siglec-G x CD22 double deficient mice spontaneously developed anti-DNA and anti-nuclear autoantibodies resulting in a moderate form of immune complex glomerulonephritis. These results show that Siglec-G and CD22 have partly compensatory functions and together are crucial in maintaining B cell tolerance and preventing systemic autoimmunity.

Jellusova J, Wellmann U, Amann K, Winkler TH, Nitschke L. CD22 x Siglec-G Double-Deficient Mice Have Massively Increased B1 Cell Numbers and Develop Systemic Autoimmunity. J Immunol. 2010 Apr 1;184(7):3618-27.

Hoffmann A, Kerr S, Jellusova J, Zhang J, Weisel F, Wellmann U, Winkler TH, Kneitz B, Crocker PR, Nitschke L. Siglec-G is a B1 cell-inhibitory receptor that controls expansion and calcium signaling of the B1 cell population. Nat Immunol. 2007 Jul; 8(7): 695-704.

Hsp 70 gene locus linked to SLE

Polymorphisms in the Hsp 70 gene locus are associated with systemic lupus erythematosus

Systemic lupus erythematosus (SLE) is a prototypic autoimmune disease. The disease manifestation depends on genetic as well as on environmental factors. In addition to HLA, alleles of Fcgamma RIIIA, molecules involved in type I interferon signaling, and others were found to be associated with SLE. In a collaborative effort with researchers from the Oklahoma research foundation, Barbara Fürnrohr from the research group of Reinhard Voll, Department of Internal Medicine 3, identified in her PhD thesis an association of allelic variants in the heat shock protein 70 gene locus with SLE. This work was recently published online ahead of print in the Annals of the Rheumatic Diseases.

… an association of allelic variants in the heat shock protein 70 gene locus with SLE

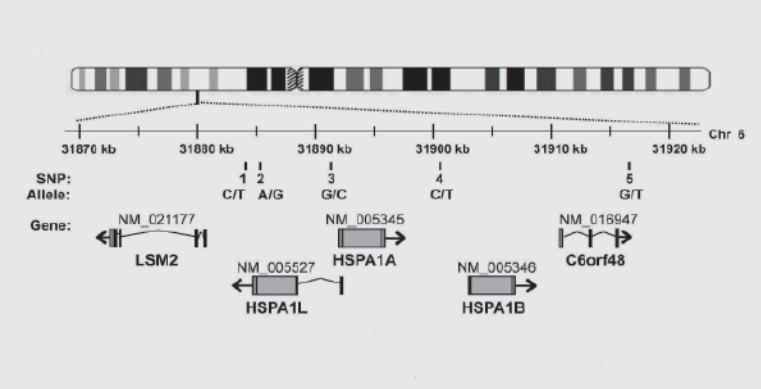
Heat shock proteins (Hsps) have been discovered due to their inducible expression in response to endogenous and exogenous stimuli. Most of them act as molecular chaperones by selectively recognizing and binding misfolded proteins, thereby preventing irreversible aggregation under physiological and stress conditions. By virtue of their peptide binding ability, this protein family modulates antigen processing and presentation and also contributes to immune responses against pathogens.

... the haplotype T-G was significantly associated with SLE

In a haplotype-tagging single nucleotide polymorphism (SNP) approach the group examined the Hsp70 locus on chromosome 6p21.33 in patients with SLE. In two independent Caucasian case-control studies common variants of cytosolic Hsp70 genes, namely Hsp70A1L, Hsp70A1A, and Hsp70A1B were genotyped and one haplotype was found to be significantly associated with SLE. In both cohorts, the Erlangen-SLE cohort and the OMRF (Oklahoma Medical Research Foundation) cohort, the haplotype T-G was significantly associated with SLE. Depending on the cohort, odds ratios were ranging from 1.43 to 1.88 and 2.64 to 3.16 for individuals heterozygous and homozygous for the associated haplotype, respectively. Relative quantification of mRNA unraveled that donors carrying the potential risk haplotype have higher HspA1A mRNA levels compared to donors with the protective haplotype. Conditional regression analysis demonstrated that allelic variants in Hsp70 act independently of HLA-DR3. In addition, patients carrying the risk haplotype or the risk allele displayed more frequently anti-Ro and -La autoantibodies in both cohorts. In healthy controls bearing this haplotype, the amount of HspA1A mRNA was significantly increased, whereas total Hsp70 protein concentration was not markedly altered, at least not in peripheral blood lymphocytes.

... allelic variants of the Hsp70 genes are significantly associated with SLE in Caucasians

In summary, allelic variants of the Hsp70 genes are significantly associated with SLE in Caucasians, they act independently of HLA-DR3, and correlate with the presence of autoantibodies to Ro and La. Hence, the Hsp70 gene locus appears to be involved in SLE pathogenesis.



The Hsp70 gene locus

Fürnrohr BG, Wach S, Kelly JA, Haslbeck M, Weber CK, Stach CM, Hueber AJ, Graef D, Spriewald BM, Manger K, Herrmann M, Kaufman KM, Frank SG, Goodmon E, James JA, Schett G, Winkler TH, Harley JB, Voll RE.
Polymorphisms in the Hsp70 gene locus are genetically associated with systemic lupus erythematosus. Ann Rheum Dis. 2010 May 24 [epub ahead of print].

PEOPLE

Prof. Dr. Stephan Ensminger awarded Ernst-Derra-Preis of the German Society for Thoracic and Cardiovascular Surgery

Prof. Dr. Stephan Ensminger, Department of Cardiac Surgery, has been honored by the German Society for Thoracic and Cardiovascular Surgery for his work on transplant arteriosclerosis. The renowned prize worth 5,000 € was awarded at the annual conference of the Society in Stuttgart in February 2010.

Prof. Dr. Armin Gerbitz W2 Professor for Hematology with focus on Celluar Immunotherapy

Armin Gerbitz was born in 1968 in Konstanz. He studied medicine at the Ludwigs-Maximilian-University (LMU) in Munich, where he received his doctoral degree on “Deregulation of the proto-oncogene c-myc through t(8;22) translocation in Burkitt’s-lymphoma” in 1996. He joined the Department of Hematology at the LMU in 1996 where he received his training in internal medicine with focus on allogeneic stem cell transplantation. After having spent 2 years as a postdoctoral fellow at the Dana Farber Cancer Institute in Boston from 1997 to 1999 he continued his education at the University of Regensburg and again in Munich. In 2007 he was asked to join the Department of Hematology at the Charité Berlin from where he moved to Erlangen in 2010. His clinical and research interests reside in allogeneic stem cell transplantation and the development of cellular therapy strategies for cancer, especially for B-cell-lymphomas. In murine models he currently develops strategies to target lymphomas by CD19 and CD22 specific T-cells. In addition, he is developing clinical study protocols for GMP conform T-cell production to target foreign antigens derived from EBV and CMV in patients after allogeneic stem cell transplantation.

Prof. Dr. Rainer Böckmann
W2 Professor for Computational Biology

Rainer Böckmann joined the Biology Department at the Friedrich-Alexander University (FAU) Erlangen-Nuremberg as Professor for Computational Biology in November 2009.

Rainer Böckmann studied physics at the University of Cologne, the Niels-Bohr Institute in Copenhagen and the Research Center Jülich with a specialization on theoretical nuclear physics. After his PhD in theoretical biophysics at the University of Göttingen in 2002 and postdoc stays at the Max Planck Institute for Biophysical Chemistry, Göttingen and the University of Zurich, he set up a young research group for Theoretical and Computational Membrane Biology at the Center for Bioinformatics at the Saarland University in 2005.

One research focus of the Computational Biology Group is on the structure-dynamics-function relationship of proteins and the membrane-protein interaction using the method of molecular dynamics simulations. For the latter, the aim is to elucidate e.g. the role of lipid-peptide interactions in synaptic vesicle membrane fusion. A second focus is put on the in silico design of protein binding sites with predefined properties. Here, a main project is the prediction of structural and dynamical properties of MHC:peptide complexes as well as the prediction of the peptide binding strength to MHC and its relation to T cell recognition.

Prof. Dr. Jochen Mattner
W2 Professor for Molecular Microbiology and Infection Immunology

Jochen Mattner obtained his MD (*summa cum laude*) at the Friedrich-Alexander University (FAU) Erlangen-Nuremberg. During his postdoctoral fellowship at the University of Chicago he could identify self and microbial glycosphingolipid (GSL) ligands that trigger NKT cell activation. These observations led to the characterization of the dual self/foreign recognition model for NKT cell activation during microbial infection. One of these identified pathways involves the direct recognition of microbial GSLs, the LPS substitutes in Sphingomonas and related alphaproteobacteria suggesting that NKT cells represent a major innate recognition pathway for this class of bacteria.

Based on recent compelling evidence that patients with primary biliary cirrhosis (PBC) are seropositive for Sphingomonas and exhibit NKT cell redistribution to the liver, his laboratory at the Cincinnati Children's Hospital Medical Center could establish a mouse model of infection-triggered autoimmunity of the liver. These studies, funded by the NIH and the Lupus Research Institute, were extended to the analyses of genetic susceptibility and are continued now at the FAU, where Dr. Mattner has been promoted to Associate Professor. As induction of autoimmunity in this model is directly associated with bacterial infection, genetic susceptibility may be interpreted not only as aberrant immune responses against self antigens, but also as susceptibility of an individual to develop an infection and/or the development of an inappropriate immune response causing collateral autoimmune tissue damage.

The major focus of his laboratory is now to explore the intriguing possibility that some forms of autoimmune PBC may be triggered by infection with Sphingomonas or related bacteria.

Prof. Dr. Diana Dudziak
member of the Förderkolleg of the Bavarian Academy of Sciences and Humanities

Prof. Dr. Diana Dudziak, Nikolaus Fiebiger Center for Molecular Medicine and Department of Dermatology, has been affiliated to the Förderkolleg of the Bavarian Academy of Sciences and Humanities. Her research project "Generation of Troyan Antibodies for the Targeted Therapy of Immune Responses" will be supported by a stipend of 12,000 Euro per year for three years. The Förderkolleg was installed in 2010 to promote outstanding young scientists and to support innovative projects, especially at the interface between conventional scientific disciplines.

NEWS AND UPDATES

ON THE FAST TRACK

From bachelor to PhD in 4.5 years

A new PhD training program in immunology has been granted by the German Research Foundation (DFG) for initially 4.5 years. The Research Training Group 1660 "Key Signals in the Adaptive Immune Response", coordinated by Prof. Hans-Martin Jäck, Division of Molecular Immunology at the Department of Internal Medicine 3, is the first fast-track PhD training grant nationwide and offers the unique possibility for life science students with a bachelor's degree of directly joining a PhD training program. The Research Training Group 1660 involves 20 research groups from the Medical School and the Department of Biology of the Friedrich-Alexander University Erlangen-Nuremberg and will investigate the role of dendritic cells, B lymphocytes, and T lymphocytes in the defense against infectious agents and tumor cells as well as during autoimmune and chronic inflammatory diseases.

WOMEN IN SCIENCE

Minisymposium on career paths and challenges for female researchers

On 09 July 2010, the "Women in Science" minisymposium was hosted by the Research Training Group 1071 "Viruses of the Immune System" and organized by PhD students Sarah Jill de Jong and Kristin Katsch. Speakers were Prof. Ulrike Protzer, Munich, PD Dr. Barbara Müller, Heidelberg, and Prof. Martina de Zwaan, Erlangen. Prof. Protzer and PD Dr. Müller presented their scientific education and career paths and talked about tackling the challenges of e.g. a double career at two institutions, the compatibility of science, teaching and family, and the importance of taking the right opportunities at the right time as well as the necessity of networking. Prof. de Zwaan, Women's Representative at the Friedrich Alexander University (FAU) Erlangen-Nuremberg, gave an overview on the situation of women in science today, considering aspects of publication efficiency, the proportion of female researchers in decision making positions, work load, salaries, and the working status of parents. Furthermore, Prof. de Zwaan presented the various measures taken at the FAU to challenge the loss of highly qualified female scientists, e.g. offering career support by the ARIADNE mentoring and "Fit-for-Science" programs, presenting role models in the seminar series "Gender Lectures", implementing stipends, awards, and a fund for equal opportunity initiatives, and providing family services. Lively discussions confirmed the relevance of the topic "women in science".

A forum for vivid discussions: the "Women in Science" minisymposium

UPCOMING EVENTS

14 December 2010

Joachim-Kalden-Lecture 2010

The Joachim Kalden Lecture 2010 will be given by Prof. Charles A. Dinarello, University of Colorado, Aurora, USA. The "founding father of cytokine biology" received the Paul Ehrlich and Ludwig Darmstaedter Prize in March 2010 for his fundamental achievements in cytokine research and will talk about

Interleukin-1β and the treatment of auto-inflammatory diseases

Chronic inflammatory diseases fall into two categories: either "autoimmune" or "auto-inflammatory". Although nearly all autoimmune diseases have an inflammatory component as in rheumatoid arthritis, in autoimmune diseases, the auto-reactive T-cell is dysfunctional. The cytokines to block are TNFα, IFNγ and similar Th1 cytokines as well as IL-12/23 and IL-17. The "Auto-inflammatory Diseases" encompass several local and systemic diseases due to monocyte dysfunction, each responsive to blocking interleukin-beta (IL-1β)[1]. "Auto-inflammatory Diseases" include type 2 diabetes and gout and new data suggest heart failure. The best example is Familial Mediterranean Fever since the manifestations of this disease include fever, inflamed serosal and synovial tissues, biochemical markers of systemic inflammation and hematological responses of leukocytosis. The co-cytokine in auto-inflammatory diseases is IL-6 as this cytokine drives CRP, thrombocytosis and polyclonal B-cell activation. Some of the syndromes have mutations in the protein "cryopyrin" and are called "cryopyrinopathies"; the same syndromes are also termed "Cryopyrin Associated Periodic Syndromes" (CAPS); however, identical biochemical, hematological and clinical disease is also observed in patients without mutations. What is the common link? The common link is dysregulation of the tight control over the processing and secretion of IL-1β from the activated monocyte. The processing and secretion of IL-1β is a function of the IL-1β/caspase-1 "inflammasome", a complex of intracellular proteins that results in the secretion of IL-1β. Despite the highly consistent clinical response to blocking the activity of IL-1β in these diseases, circulating IL-1β is difficult to detect. The measurement of IL-6 in the circulation is the preferred method for assessing the severity of the inflammation in auto-inflammatory diseases and the fall in serum IL-6 reveals the effectiveness of anti-IL-1β treatment. The auto-inflammatory diseases are examples in cytokine biology that reveal a causative role of a specifc cytokine in a disease process. In addition to treating CAPS with anti-IL-1β, several trials of anti-IL-1β are currently underway including type 1 and 2 diabetes[2], post-myocardial infarction heart failure[3], osteoarthritis, gout[4] and smoldering myeloma[5,6].

[1] Dinarello CA. Ann Rev Immunol. 2009; 27: 519-550.

[2] Donath MY, et al. Diabetes. 2009; 58: A30.

[3] Abbate A, et al. Am. J. Cardiology. 2010; 105:1371-1377.

[4] Terkeltaub R, et al. Rheum Dis. 2009; 68: 1613-1617.

[5] Lust JA, et al. Mayo Clin Proc. 2009; 84: 114-122.

[6] Dinarello CA. Mayo Clin Proc. 2009; 84: 105-107.

MICE Immunological Colloquium – Preview Autumn/Winter 2010/2011

The weekly seminar series of MICE has been well established as a discussion forum for current topics in immunology by presenting distinguished speakers from all over the world. The lectures take place in the seminar room of the Institute of Clinical Microbiology, Immunology and Hygiene, Wasserturmstr. 3–5, 1st floor, Erlangen, at 5.15 p.m. Please have a look at our homepage for a regular update of the seminar program:

www.mice.uni-erlangen.de/events/immunological-seminar.shtml

MICE Preview Autumn/Winter 2010/2011

26.10.2010
Dirk Busch
Munich
Primary T cells: A source for novel immunotherapies?

27.10.2010
Manolis Pasparakis
Cologne
Title to be announced

02.11.2010
Ulrich Koszinowski
Munich
Much ado about almost nothing: A random approach to herpesvirus morphogenesis

09.11.2010
Gernot Achatz
Salzburg, Austria
The biology of IgE: Molecular mechanisms restraining potentially dangerous high serum IgE titres in vivo

16.11.2010
Hansjörg Schild
Mainz
Title to be announced

23.11.2010
To be announced

30.11.2010
Silvia Bulfone-Paus
Borstel
Title to be announced

07.12.2010
Eicke Latz
Bonn
Mechanisms of inflammasome activation

14.12.2010
Joachim-Kalden-Lecture
Charles Dinarello
Aurora, USA
Interleukin-1β and the treatment of auto-inflammatory diseases

21.12.2010
Ari Waisman
Mainz

Title & synopsis
New murine models to study inflammatory cytokines

Experimental autoimmune encephalomyelitis (EAE) is the animal model for multiple sclerosis (MS). EAE can be induced in susceptible mice by the immunization with peptides derived from myelin oligodendrocytes glycoprotein (MOG). Immunization with the MOG peptide results in the activation of encephalitogenic CD4 positive T cells, which are essential for the disease induction and progression. It was previously shown that these encephalitogenic T cells express pro-inflammatory cytokines such as IL17, Interferon gamma and TNF alpha, but the exact necessity of these cytokines is not determined. Using mouse models that allow the deletion of cytokines and their receptors, or the overexpression of IL17, we show that what determines susceptibility to EAE is the balance between proinflammatory T cells and regulatory T cells, rather than the exact combination of cytokines produced by encephalitogenic T cells.

11.01.2011
Sebastian Amigorena
Paris, France
Antigen presentation and T cell activation by dendritic cells

18.01.2011
Erik Glocker
London, UK

Title & synopsis
Monogenic causes for early-onset inflammatory bowel disease

Inflammatory bowel disease (IBD) is caused by dysregulation of the immune system and is characterized by a chronic and relapsing course with abdominal pain, diarrhea, bleeding and malabsorption. It comprises the major forms of Crohn's disease (CD) and ulcerative colitis (UC) as well as indeterminate colitis with overlapping features of CD and UC. The disease affects about 2.2 millions in Europe and 1.4 million people in the USA. The incidence of IBD in the United Kingdom amounts to 5-10/100,000 individuals with Crohn's disease and 10-20/100,000 for ulcerative colitis.

IBD usually manifests in the second or third decade of life, but it may also be present in infancy with a severe and therapy resistant course of the disease.

Comprehensive research work on the pathogenesis suggests that IBD results from disturbed interactions between the innate and adaptive immune system and commensal bacteria of the gut. Genetic studies identified a variety of genes that may render individuals more susceptible to IBD, thereby indicating the complexity and multifactorial genesis of IBD.

We recently demonstrated that early-onset IBD may be monogenic: homozygous point mutations in the IL10 receptor genes IL10RA and IL10RB cause severe difficult-to-treat colitis in small children. This discovery enabled us to carry out a successful curative hematopoietic stem cell transplantation (HSCT) in one of the affected patients. A similar phenotype is observed in infants with homozygous point mutations, who present with a massive therapy-refractory colitis and severe perianal disease.

These findings not only highlight the vital role of IL10 in keeping the immune system in balance, they also suggest that in a subgroup of patients IBD is distinct from classical forms such as CD or UC.

25.01.2011
Kasper Hoebe
Cincinnati, USA
Understanding the genetic basis of immune deficiencies: a small scale ENU mutagenesis approach

01.02.2011
Caetano Reis e Sousa
London, UK

Title & synopsis
Innate regulation of adaptive immunity by dendritic cells

Direct sensing of pathogen components is a major trigger of dendritic cell (DC) activation, leading to adaptive immunity. We have been studying multiple pattern-recognition pathways that mediate DC activation. One pathway for sensing infection by RNA viruses involves recognition of viral genomes or virally-infected cells in endosomal compartments and utilises members of the toll-like receptor (TLRs) family, including TLR9, 7, or 3. Viral genomes can additionally be recognised in the cytosol by DExD/H-box helicases such as RIG-I, which are activated by RNAs bearing 5' triphosphates. Finally, a distinct pathway involves cell surface and phagosomal recognition of fungi by C-type lectins, which signal via Syk kinase. Notably, some of these pathways are involved not only in direct sensing of pathogens but also in the recognition of self alterations that might accompany infection, such as induction of cell death. These studies help build a global picture of the receptors and signaling pathways that regulate DC activation and have applications in immunotherapy of cancer and infectious diseases.

08.02.2011
To be announced

Conferences organized by MICE members

Oct. 8 – 10, 2010
SFB 423 3rd International Symposium
Moleclar Targets in Renal Disease
Bamberg

This symposium organized by the SFB 423, a collaborative research center on kidney injury funded by the German Research Foundation (DFG) at the Friedrich-Alexander University Erlangen-Nuremberg, focuses on molecular targets in renal disease. The objective is to review important pathomechanisms of renal disease and to discuss the molecular basis for potential strategies for intervention in different compartments of the kidney.

www.sfb423.uk-erlangen.de

March 24 – 25, 2011
Cellular Therapy 2011
Erlangen

The 6th International Cellular Therapy Symposium organized by Andreas Mackensen, Erlangen, Gerold Schuler, Erlangen, and Reinhard Andreesen, Regensburg, provides scientific sessions on Antigen-specific T cells, Regulatory T cells, B cells, NK-cells, Antigen presenting cells, Adoptive transfer, vaccination, and Allogeneic stem cell transplantation.

www.cellular-therapy.de

May 14 – 17, 2011
13th International CMV/BetaHerpesvirus Workshop
Nuremberg

This interdisciplinary workshop (chair: Thomas Stamminger, Erlangen) adresses clinical and molecular aspects of cytomegaloviruses and related betaherpesviruses.

www.cmvworkshop.org

Further conferences of interest

Oct. 06 – 07, 2010
Symposium of the SFB 455 junior faculty
Catch me if you can: viral offense and immune defense
Munich

www.sfb455-symposium.org

Oct. 29 – 30, 2010
Fraunhofer Life Science Symposium
Immunotherapy – the cutting edge of stem cell applications
Leipzig

www.fs-leipzig.com

Dec. 4 – 7, 2010
American Society of Hematology – Annual Meeting
Orlando, USA

www.hematology.org/Meetings/Annual-Meeting/

Dec. 9 – 10, 2010
International Mast Cell and Basophil Meeting
Berlin

www.mcbm2010.net

Jan. 7 – 12, 2011
TGF-beta in Immune Responses: From Bench to Bedside (A2)
Snowbird, USA

www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=1104

Jan. 9 – 14, 2011
NK and NKT Cell Biology: Specificity and Redundancy of Innate Responses (A4)
Breckenridge, USA

www.keystonesymposia.org/Meetings/ViewMeetings.cfm?MeetingID=1072

Jan. 13 – 15, 2011
European Society for Clinical Virology Winter Meeting
London, UK

www.escv.org

Jan. 24 – 25, 2011
T lymphocyte dynamics in acute and chronic viral infection
London, UK

http://idrn.org/events/upcoming/lymphocyte-dynamics.php

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We are looking forward to suggestions for the next MICE letter.

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