

ImmunoVision – issue 4 of our new newsletter

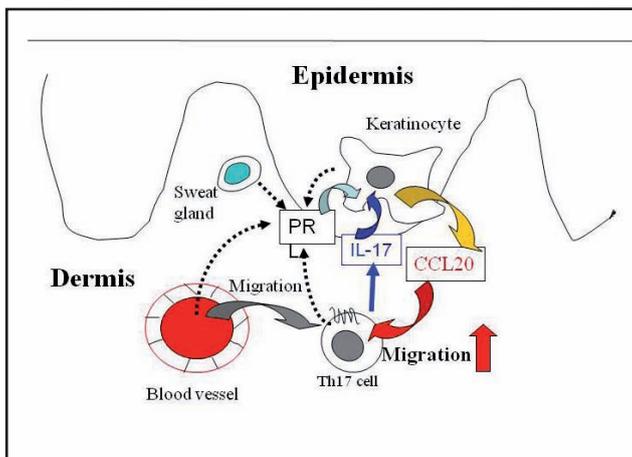
ImmunoVision is a new quarterly newsletter brought to you by Wiley-Blackwell highlighting the best immunological research, the latest books published, news on the key players in the field and other such items of interest to the immunological community. As immunology impacts on so many areas of research, this newsletter serves to distil the findings from across a range of disciplines into one highly valuable resource.

ImmunoVision is brought to you by the editorial team of the *European Journal of Immunology (EJI)* and can be found online in the “News” section of EJI. We welcome items for inclusion in the news section and all suggestions should be emailed to the contact email given below.

URL: www3.interscience.wiley.com/journal/25061/home/news/index.html
 e-mail: ejied@wiley-vch.de

ImmunoDigest

Prolactin promotes Th17-mediated skin inflammation



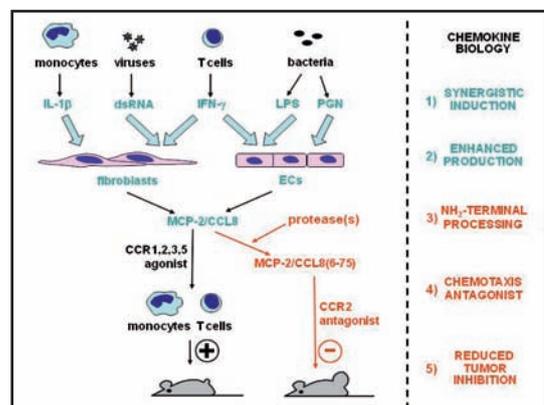
Psoriasis vulgaris is an autoimmune dermatosis characterized by alterations in several immune-parameters. Some changes include an abundance of Th17 cell infiltration, as well as prolactin and CCL20 dysregulation. Kanda *et al.* demonstrate that these are not independent events but are in fact intimately linked. The authors show that prolactin increases epidermal keratinocyte CCL20 production both alone and in synergy with IL-17. CCL20 production induced by prolactin was mediated *via* the activation of AP-1 and NF- κ B through the MEK/ERK and JNK pathways; CCL20 in turn recruits Th17 cells *via* CCR6. Understanding the various components of this inflammatory loop may provide novel therapeutic targets for the treatment of psoriasis.

Kanda, N. *et al.*, *Eur. J. Immunol.* 2009. 39: 996-1006
<http://doi.wiley.com/10.1002/eji.200838852>

MCP-2/CCL8 chemokine activity in inflammation and cancer

Chemokines activate leukocytes *via* G protein-coupled receptors (GPCR) to regulate inflammation and tumor development. MCP-2/CCL8 is a pluripotent CC chemokine binding several GPCR allowing recruitment of most leukocyte subtypes. MCP-2/CCL8 upregulation requires combined TLR and cytokine stimulation, *e.g.* LPS and IFN- γ , or dsRNA and IFN- γ . Struyf *et al.* demonstrate that this pro-inflammatory phenomenon is counteracted by NH₂-terminal processing of MCP-2/CCL8, which results in a double negative feedback, *i.e.* loss of GPCR signaling and antagonism of intact chemokines *via* receptor blockade by MCP-2/CCL8(6-75). In contrast to the potent anti-tumoral capacity of the related MCP-3/CCL7, MCP-2/CCL8 failed to inhibit melanoma growth *in vivo* due to proteolytic processing. This study shows that such limited chemokine cleavage not only dampens inflammation, but also limits the anti-tumoral capacity of chemokines. Therefore, it is crucial to determine (*via* proteomics, rather than ELISA) whether a chemokine remains intact or is processed *in vivo* in order to predict its role in pathology.

Struyf, S. *et al.*, *Eur. J. Immunol.* 2009. 39: 843-857
<http://doi.wiley.com/eji.200838660>



More on Calcineurin's Role

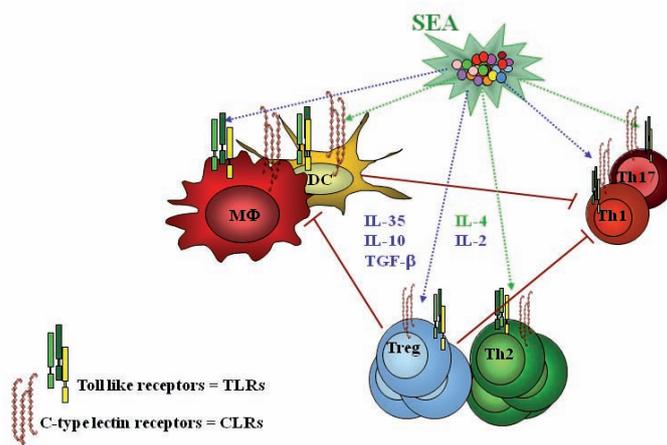
Protein phosphorylation/dephosphorylation plays a dominant role in controlling many cellular processes. In endothelial cells (EC), cytoskeletal rearrangement evoked by thrombin results in stress fiber formation which correlates with the elevated phosphorylation state of EC myosin light chain. Attenuated thrombin-induced stress fiber formation can be detected in EC transfected by a constitutively active form of the calcineurin (Cn) catalytic subunit, while inhibition of calcineurin by cyclosporin A or FK506 caused prolonged contraction of the cells. Calcineurin is involved in the recovery of EC from thrombin-induced dysfunction. Immunofluorescent detection of EC transfection with Cn catalytic subunit isoforms and Texas red-phalloidin staining was visualized on paraformaldehyde-fixed bovine pulmonary artery EC. The role of calcineurin in EC contraction induced by inflammatory mediators has special significance since Cn inhibitors are used as immunosuppressive drugs and their side effect is reported to induce endothelial dysfunction.

Bakó *et al.* *Cytometry A* 2009. 75A:405-411
<http://doi.wiley.com/10.1002/cyto.a.20707>

Synergy between innate and adaptive immunity drives Schistosoma-mediated prevention of autoimmune diabetes

Although it is known that the soluble extract of *Schistosoma mansoni* eggs (SEA) prevents autoimmune diabetes in NOD mice, the mechanism of action remains unclear. Zaccane *et al.* show that Foxp3+ Treg numbers increase in the pancreas following SEA treatment of NOD mice. Furthermore, SEA has direct effects on both DC and T cells. On DC, SEA upregulates IL-2 and IL-10 secretion, and also upregulates C-type lectin receptors. In the absence of APC, SEA upregulates TGF- β and galectins on CD4+ T cells, and induces Foxp3+CD4+ T cells in a TGF- β -dependent fashion. In the context of type 1 diabetes inhibition by SEA, it appears that early expansion of Treg is an important event for immunomodulation and diabetes prevention.

Zaccane, P. *et al.*, *Eur. J. Immunol.* 2009. 39: 1098-1107
<http://doi.wiley.com/10.1002/eji.200838871>



Analysis of islet inflammation in human type 1 diabetes

Welcome advances in type-1 diabetes (T1D) disease management have nevertheless meant that data regarding advanced disease progression in humans is now largely absent. This retrospective study from Morgan *et al.* analysing tissue samples, painstakingly gathered post-mortem over a 25-year period, originating with individuals with T1D disease onset, therefore represents an important window into the disease process – importantly the immune cell types present. As such, this is an important contribution to the current debate regarding the nature of disease progression, and further provides important impetus for further research.

Willcox, A. *et al.* *Clin. Exp. Immunol.* 2009. 156: 173-181.
<http://doi.wiley.com/10.1111/j.1365-2249.2008.03860.x>

New Members Elected to the National Academy of Sciences

On 28 April 2009, the National Academy of Sciences (www.nasonline.org/) announced the election of 72 new members and 18 foreign associates from 15 countries in recognition of their distinguished and continuing achievements in original research. Many of these eminent scientists have published articles and books with Wiley-Blackwell. Notably, in relation to immunology, two of the newly elected members (Prof Rafi Ahmed and Dr Douglas Lowy) contributed articles to the European Journal of Immunology's Supplement on Breakthroughs in Immunology. Rafi Ahmed and colleagues chronicled the discovery of CD8 T cells; Doug Lowy wrote, together with John Schiller and Ian Frazer, about the development of a vaccine for human papillomavirus.

Prevention of cancer through immunization: Prospects and challenges for the 21st century
 Frazer, IH, Lowy, DR and Schiller, JT

Eur J Immunol 2007. 37:S148-S155
<http://doi.wiley.com/10.1002/eji.200737820>

A brief history of CD8 T cells Masopust, D, Vezys, V, Wherry, EJ and Ahmed, R
Eur J Immunol 2007. 37:S103-S110
<http://doi.wiley.com/10.1002/eji.200737820>

Biomarkers Found For Rheumatoid Arthritis

Rheumatoid arthritis (RA), the most common autoimmune inflammatory arthritis, is thought to have both genetic and environmental components to its origins. Evidence suggests that it develops in three phases: a period of genetic risk but with no symptoms; a preclinical phase in which RA-related autoantibodies can be detected; and a clinical phase with signs and symptoms of the disease. A new study in *Arthritis & Rheumatism* examined whether women who developed RA would have evidence of immune activation prior to developing symptoms, compared with women who did not develop the disease.

Led by Elizabeth Karlson of Brigham and Women's Hospital and Harvard Medical School, the study involved samples from two large studies involving women: the Women's Health Study and the Nurses' Health Study. Researchers analyzed 170 blood samples obtained prior to symptom onset in women who later developed RA and compared them with three controls per case that were randomly chosen and matched for age, menopausal status, hormone use, and day, time and fasting status at the time of collection. They tested for interleukin-6 (IL-6) and tumor necrosis factor α (TNF α), two cytokines (proteins released by the immune system) that are elevated in the serum and joints during active RA. Since TNF α degrades rapidly in stored samples, they used soluble TNF receptor II (sTNFR II) as a surrogate marker for TNF α . They also tested for high-sensitivity C-reactive protein (hsCRP), a biomarker of inflammation.

The results showed that levels of sTNFR II were elevated up to 12 years prior to the development of RA symptoms and were associated with a 2-fold elevation in risk of RA. The authors note that the levels measured during the preclinical period were much lower than those typically seen

in patients with active RA, which suggests that few of the women had active joint inflammation at the time the samples were taken. "However, even modest elevations in these biomarkers were predictive in time intervals up to 8 years before the onset of RA symptoms," they state. Elevated IL-6 levels were also associated with RA, but only less than four years before symptom onset.

Previous studies have detected the presence of preclinical autoantibodies in RA, a finding that has revolutionized thinking about the origins of autoimmune disease. Studies suggest that when a genetically susceptible host is exposed to environmental factors, autoantibody production is triggered; a second event or exposure might trigger the onset of clinical symptoms. The complex interaction between genes and environmental factors is not yet fully understood, however. "Our findings suggest that during the preclinical phase of autoantibody production, there is immune reactivity, with production of proinflammatory cytokines that are typically seen in symptomatic RA, namely IL-6 and TNF," the authors state. The authors suggest that the results of the current study could have implications regarding screening for biomarkers that could be used for RA risk counseling or for targeted interventions to prevent the disease. They note that targeted therapies are being developed to prevent type 1 diabetes, another autoimmune disease that is thought to share some genetic risk factors to RA. They conclude that further studies with repeated blood collections along with assessments of environmental factors prior to RA symptoms may shed light on the pathway by which immune activation progresses to symptomatic RA. *Karlson, EW et al. Arthritis Rheum. 2009. 60:641-652. <http://doi.wiley.com/10.1002/art.24350>*



Sept 13-16, 2009, Berlin, Germany

KEY DATE

Standard Registration Fee Deadline: August 31, 2009

For full details, visit <http://www.eci-berlin2009.com/>

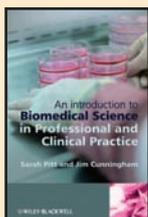
2nd European Congress of Immunology, Immunity for Life — Immunology for Health

The 2nd European Congress of Immunology ECI 2009 will take place in September in Berlin. Under the auspices of the European Federation of Immunological Societies (EFIS), to which 27 national societies belong with a total of 13,000 members, European immunologists will present and discuss newly acquired knowledge in Immunology.

"The overall importance of a functional immune system for our well being and health is not known to most people", says the President of the Congress Professor Reinhold E. Schmidt, Klinik für Immunologie und Rheumatologie der Medizinischen Hochschule Hannover. "Disturbances in the defence system can result in various forms of disease, such as allergy, rheumatic disease, infection or cancer." The most frequent causes of immunodeficiencies world wide include malnutrition, poor hygienic conditions or an infection with HIV. In addition, other factors such as ageing, treatment with certain drugs, radiation, surgical stress and malignant tumours of the bone marrow and lymph nodes can lead to strengthening or long term damage of the immune system. In comparison, primary immunodeficiencies, with a frequency of 1 in 500, are rather rare, and yet they provide important insights into the structure and function of the immune system. Innate and acquired immunodeficiencies, as well as the treatment of the respective diseases, will be a focus of this congress. High expectations result from reports on various new instruments, such as the European register for primary immunodeficiencies, a register containing enormous amounts of information on more than 9,000 patients. Moreover, the first experiences with integrated research and treatment centres for chronic immunodeficiencies are presented. Such centres are currently founded at various German universities with the support of BMBF (German Ministry of Science). This interaction between basic research and patient care is thought to speed up the transfer of newly acquired knowledge from the laboratory to the bedside. The idea behind these centres is that the results of immunological research could promote urgently needed progress in various areas of medicine. In order to draw the attention of the public to the important role of immunology, EFIS recently conducted an international short-film competition. The Italian contribution titled "The Immunology Knight" presents immunological knowledge in an easy to understand language in the context of a short humorous story. The winning film will be shown at the ECI 2009.

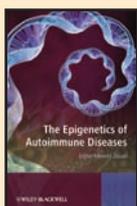
"Immunity for Life - Immunology for Health": The motto of the Congress clearly states that without a functional immune system there can be neither health nor life.

ImmunoBooks



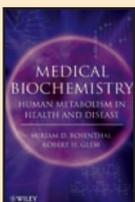
An Introduction to Biomedical Science in Professional and Clinical Practice

S. J. Pitt, J. Cunningham
ISBN: 978-0-470-05714-8,
March 2009



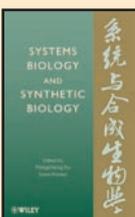
The Epigenetics of Autoimmune Diseases

M. Zouali (Editor)
ISBN: 978-0-470-75861-8,
April 2009



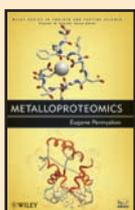
Medical Biochemistry: Human Metabolism in Health and Disease

M. D. Rosenthal, R. H. Glew
ISBN: 978-0-470-12237-2,
April 2009



Systems Biology and Synthetic Biology

P. Fu, S. Panke (Editors)
ISBN: 978-0-471-76778-7,
April 2009



Metalloproteomics

E. Permyakov
ISBN: 978-0-470-39248-5,
May 2009

ImmunoProtocols

Current Protocols: The Fine Art of Experimentation

Discover the new Current Protocols website (www.currentprotocols.com/) where you can

- browse, rate, and comment on our entire collection of protocols
- sign up for new protocol alerts
- access useful scientific tools and calculators
- post or answer questions in our forums
- view video protocols
- read and comment on our blog, Beyond the Bench
- register and upload your own protocols

What's new and updated in Current Protocols in Immunology

Unit 2.9 Isolation of Murine and Human Immunoglobulin M and Murine Immunoglobulin D

This unit describes two classical protocols for the purification of IgM—dialysis of ascites fluid, tissue culture medium, or bioreactor supernatants against distilled water to precipitate pure IgM, and ammonium sulfate precipitation. Both protocols can be followed by size-exclusion chromatography to obtain a highly purified product. Recently, an affinity method for purification of IgM has been developed using mannan-binding protein, and is described here. The third approach presented is a one-step IgD purification method, designed specifically for murine derived samples, that uses Sepharose coupled to lectin derived from the seeds of *Griffonia simplicifolia*-1. This represents a simple, rapid, and gentle, approach to isolating this highly labile immunoglobulin from IgD-containing ascites or hybridoma sources.

Curr. Protoc. Immunol. 85:2.9.1-2.9.8.
<http://doi.wiley.com/10.1002/0471142735.im0209s85>

Unit 2.9B Measurement of Human Serum IgD Levels

This unit describes an ELISA for the quantitative measurement of IgD levels in human serum. The ELISA is highly specific and sensitive, with a minimum detectable concentration of 30 pg/ml and more than 10,000-fold specificity for IgD over all other human immunoglobulins. Linear dilution characteristics enable measurement of IgD concentrations ranging over 5 orders of magnitude. These factors are vital for the IgD assay, since IgD makes up only a small proportion of the total immunoglobulins present in normal sera, and IgD serum concentrations are known to vary widely between individuals.

Curr. Protoc. Immunol. 85:2.9B.1-2.9B.7.
<http://doi.wiley.com/10.1002/0471142735.im0209bs85>

Unit 2.15 Vaccination of Mice with Baculovirus-Infected Insect Cells Expressing Antigenic Proteins

Methods to induce antigen-specific immune responses in mice using insect cells infected with recombinant baculoviruses are described in this unit. Although this vaccine strategy has been used to generate both antibody and T cell responses, it has been more thoroughly characterized for the peptide-specific cytotoxic T cell responses. Nonspecific responses to the vaccine vehicle are controlled for by vaccinating with insect cells infected with baculoviruses encoding irrelevant antigens or no antigen. The baculovirus-infected insect cells alone are an effective immune adjuvant to elicit antigen-specific T cells. Overall, immune responses generated using this approach are similar to those generated by more conventional vaccine strategies.

Curr. Protoc. Immunol. 85:2.15.1-2.15.23.
<http://doi.wiley.com/10.1002/0471142735.im0215s85>

ImmunoProtocols

Unit 7.1 Isolation of Whole Mononuclear Cells from Peripheral Blood and Cord Blood

Peripheral blood is the primary source of lymphoid cells for investigation of the human immune system. Its use is facilitated by Ficoll-Hypaque density gradient centrifugation—a simple and rapid method of purifying peripheral blood mononuclear cells (PBMC) that takes advantage of the density differences between mononuclear cells and other elements found in the blood sample. Thus, cells are distributed in the solution in layers based on the differences in their density/size. Additional purification methods can be employed as the mononuclear cell sample can be purified from monocytes by adherence or by exposure to l-leucine methyl ester; these methods are described for both procedures. Cord blood and peripheral blood from infants contain immature cells, including nucleated red cells, which can result in significant contamination of the mononuclear cell layer, and removal of these cells requires additional steps that are described. The isolation procedures presented here can also be applied to cell populations derived from tissues.

Curr. Protoc. Immunol. 85:7.1.1-7.1.8.

<http://doi.wiley.com/10.1002/0471142735.im0701s85>

Unit 7.4 Immunomagnetic Purification of T Cell Subpopulations

There are two types of magnetic cell isolation technologies, one column-based and the other tube-based. The column-based technology utilizes nano-sized particles that need to pass through a ferromagnetic spheres column to increase cell-capture capacity. The tube-based system utilizes micron-sized beads that can be selected using a magnet applied to the tube. The beads are used for direct or indirect labeling of cells. Direct labeling is achieved with antibodies coupled to magnetic particles directly added to the cell suspension. For indirect labeling the cells are first labeled with the antibody of interest; the antibody can be simple, biotinylated, or fluorochrome-conjugated. Subsequently, beads coated with streptavidin or anti-immunoglobulin, anti-biotin, anti-fluorochrome antibodies are used to specifically mark the subpopulation of interest. Separation of target cells can be achieved using positive or negative selection or a combination of the two. Quality of the sample preparation is critical to obtain good purification and yield.

Curr. Protoc. Immunol. 85:7.4.1-7.4.9.

<http://doi.wiley.com/10.1002/0471142735.im0704s85>

Unit 15.2 Experimental Autoimmune Encephalomyelitis in the Rat

There are several diverse rat models of experimental autoimmune encephalomyelitis (EAE) that can be used to investigate the pathogenesis and regulation of autoimmunity against CNS myelin. The disease course of these models ranges from an acute monophasic disease with limited demyelination to a chronic relapsing or chronic progressive course marked by severe demyelination. These models enable the study of encephalitogenic T cells and demyelinating antibody specific for major neuroantigens such as myelin basic protein (MBP), myelin oligodendrocyte glycoprotein (MOG), or proteolipid protein (PLP), among other important CNS autoantigens. Overall, this unit provides an overview of common methods for induction of active and passive EAE, assessment and analysis of clinical disease, preparation and purification of myelin basic protein, and derivation of neuroantigen-specific rat T cell lines. This unit also provides a brief discussion of the basic characteristics of these models.

Curr. Protoc. Immunol. 85:15.2.1-15.2.15.

<http://doi.wiley.com/10.1002/0471142735.im1502s85>

Unit 20.11 The Immune Response to Tumors

The immune response to tumors is complex. Cells of the immune system can inhibit tumor growth and progression through the recognition and rejection of malignant cells, a process referred to as immunoeediting. Yet, immune responses can also promote tumor cell growth, survival, and angiogenesis through the induction of oncogenic inflammation. Immunodeficiency can predispose to the development of spontaneous and virally induced cancer, and established tumors often generate immunosuppressive microenvironments that can block productive antitumor immunity, serving as a substantial barrier to effective immune therapy. Through a deeper understanding of the complicated relationship between tumors and the immune system, tumor immunology strives to harness the immune system to generate protective antitumor responses in patients.

Curr. Protoc. Immunol. 85:20.11.1-20.11.4.

<http://doi.wiley.com/10.1002/0471142735.im2011s85>

ImmunoBooks

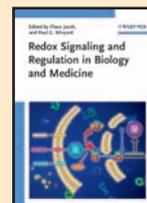


Bioinformatics and Functional Genomics, 2nd Edition

J. Pevsner

ISBN: 978-0-470-08585-1,

May 2009

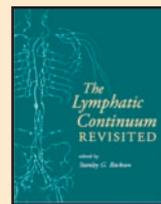


Redox Signaling and Regulation in Biology and Medicine

C. Jacob, P. G. Winyard (Editors)

ISBN: 978-3-527-31925-1,

April 2009

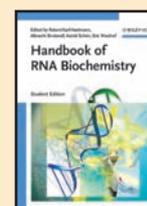


Lymphatic Continuum Revisited

S. G. Rockson (Editor)

ISBN: 978-1-57331-699-6,

August 2008



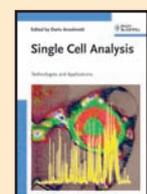
Handbook of RNA Biochemistry: Student Edition

R. K. Hartmann, A. Bindereif,

A. Schön, E. Westhof (Editors)

ISBN: 978-3-527-32534-4,

December 2008



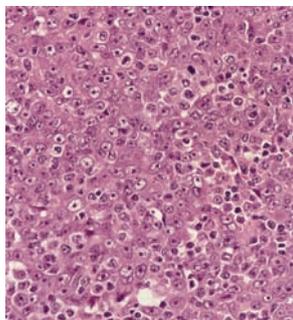
Single Cell Analysis: Technologies and Applications

Dario Anselmetti (Editor)

ISBN: 978-3-527-31864-3,

March 2009

O-acetylated sialic acids: Multifaceted role in childhood acute lymphoblastic leukaemia



Changes in protein glycosylation are a hallmark of many diseases. In this review, scientists from Kolkata give an overview of their research about increased 9-O-acetylated sialic acid (9,5-NeuAc) occurrence in childhood acute lymphoblastic leukemia (ALL). Mandal & Chowdhury report the isolation and purification of the Achatinin-H lectin which specifically binds to 9,5-NeuAc and agglutinates leukemic lymphoblasts stronger than normal cells. Cell cytometry analyses with fluorescent Achatinin-H show that 9,5-NeuAc is strongly expressed on ALL leukocytes whereas it is absent on normal and other leukemic cells. Also, the amount of lymphoblastic glycoproteins carrying 9,5-NeuAc is increased on ALL compared to normal cells. Thus, 9,5-NeuAc is a promising ALL biomarker candidate, and acetyltransferase inhibitors may even be applied to block generation of 9,5-NeuAc-carrying glycoproteins and ALL development.

Chowdhury, S. and Mandal, C *Biotechnol. J.* 2009. 4: 361-374
<http://doi.wiley.com/10.1002/biot.200800253>

Can genomics stop TB?

While anti-tuberculosis drugs and a vaccine have been available for many years, neither are completely effective in the fight against TB, and *Mycobacterium tuberculosis*, the bacterial pathogen responsible for tuberculosis, remains one of the most significant agents of human and animal disease. Worldwide, there are 8 million new cases of tuberculosis with 2 million deaths each year, the majority being in developing countries where the situation is exacerbated by co-incidence with the HIV epidemic. The publication of the genome sequence of *M. tuberculosis* H37Rv in 1998 has been followed by a decade long growth of genomic data utilized in the hunt for factors responsible for pathogenicity and for possible vulnerabilities which could be targeted by drug treatment. Gordon *et al.* discuss how genomics has transformed research in this field and is being utilized for drug discovery, improved vaccines and diagnostics.

Gordon, SV *et al. Bioessays* 2009. 31: 378-388.
<http://doi.wiley.com/10.1002/bies.200800191>

NEW to Immunological Reviews! Audio Podcasts

Each volume of *Immunological Reviews* is devoted to a single topic of immunological research and is guest edited by a leading expert in that area. Each volume therefore fills a unique niche by bringing together investigators who have made major contributions to their fields, encouraging them not only to review their area of expertise but also to emphasize their own perspective on the relationship of their work to that of others in the field.

To further explore these unique volumes we are pleased to publish audio podcasts of interviews with the guest editors. Each podcast is free and available for you to download and listen.

Now available: Interview with Dr Arthur Weiss on Kinases and Phosphatases of the Immune System

To listen to the podcast visit: www.immunologicalreviews.com

Read the APMIS special issue on Host-Microbe Relations online now!

"This special issue of *APMIS* includes papers concerned with relational aspects between hosts and their infectious world, focused on selected important intracellularly located microbes belonging to all three major groups of infectious pathogens, including bacteria, viruses and parasites. It gives the reader a comprehensive overview of the diverse world of host-microbe relations."

Elling Ulvestad and Allan Randrup Thomsen

The special issue includes articles such as 'Innate recognition of intracellular pathogens: detection and activation of the first line of defense' by Paludan and colleagues; 'Virus-specific CD8 T cells: activation, differentiation and memory formation' by Oxenius, A and colleagues; and 'Interaction of *Mycobacterium tuberculosis* with the host: consequences for vaccine development' by Dietrich, J and Doherty, M

To access the issue, go to www3.interscience.wiley.com/journal/117978595/home

Th17 viewpoints in the March issue of EJI

EJI's third Viewpoints series focuses on one of the most exciting areas in current immunological research, namely Th17/IL-17. Experts including Sergio Romagnani, Chen Dong and Brigitta Stockinger debate topics such as the regulation of development/function, role in infection/disease and therapeutic potential of Th17/IL-17 in mice and humans; Casey Weaver introduces the series. The listing of all the Th17/IL-17 articles can be found in the March issue (www3.interscience.wiley.com/journal/122254993/issue).

Th17: The Ascent of a New Effector T-cell Subset Weaver, C. *Eur. J. Immunol.* 39: 634-636.
<http://doi.wiley.com/10.1002/eji.200939260>

Rethinking Typhoid Fever Vaccines

In this review the authors conclude "There is a large global burden of disease associated with enteric fever; the proportion of disease due to *S* paratyphi, for which we have no licensed vaccines, is rising, and the antimicrobial resistance of *S* typhi and *S* paratyphi has greatly increased. As huge investments and infrastructures are needed for the development of sanitation and safe water systems in endemic countries and these infrastructures may take years to develop, vaccination programs of nursery school- and school-aged children in endemic areas are currently the best means to control disease in conjunction with sanitation and poverty alleviation programs. More effective vaccines in the form of conjugate vaccines or improved live oral vaccines that also protect young children against *S* typhi and *S* paratyphi are vital. These vaccines would benefit both travelers and inhabitants of endemic areas." *Whitaker, JA et al. J Travel Med* 2009 16: 46-52. <http://doi.wiley.com/10.1111/j.1708-8305.2008.00273.x>

Vaccines for preventing anthrax

Background: Anthrax is a bacterial zoonosis that occasionally causes human disease and is potentially fatal. Anthrax vaccines include a live-attenuated vaccine, an alum-precipitated cell-free filtrate vaccine, and a recombinant protein vaccine. Extract from Implications for Practice: Based on data from five randomized controlled trials, there is evidence of protection against clinical anthrax for STI vaccine, although safety concerns with live vaccines mean specialists are more likely to recommend the AVA or rPA102. *Donegan S, Bellamy R, Gamble CL. Cochrane Database of Systematic Reviews* 2009, Issue 2. Art. No.: CD006403. <http://doi.wiley.com/10.1002/14651858.CD006403.pub2>

Removing Obstacles for the Clinical Application of Tregs

CD4+CD25+ T regulatory cells are powerful suppressive cells which hold promise as an alternative to standard immunosuppressive drugs. Currently, there are several ongoing trials in Europe and the US testing the possibility to introduce adoptive therapy with those cells to the clinical routine. Such a treatment could only be possible thanks to the recent achievements in multicolor flow cytometry and cell sorting as well as cellular immunology. *Trzonkowski* and co-workers focus on the current progress in the application of T regulatory cells in medicine. Their review not only summarizes the knowledge on the characterization, isolation and expansion of those cells but also illustrates, with examples, laboratory approaches to the sorting, expansion and safety control of expanded T regulatory cells for the clinic. Finally, initial results in healthy human volunteers are described in which the application of expanded T regulatory cells was assessed to be safe. *Trzonkowski et al. Cytometry A* 2009. 75A: 175-188. <http://doi.wiley.com/10.1002/cyto.a.20659>

Genetic and epigenetic networks controlling T helper 1 cell differentiation

Significant progress has been made during the past years in our understanding of the mechanisms that control the differentiation of naïve CD4+ T cells into effector T-cell subsets with distinct functional properties. In this review *Rogge et al.* highlight advances that have been made in unravelling the genetic and epigenetic networks controlling differentiation of naïve CD4+ T cells into interferon- γ (IFN- γ)-secreting T helper type 1 (Th1) cells. *Placek, K et al. Immunology* 127: 155-162 <http://doi.wiley.com/10.1111/j.1365-2567.2009.03059.x>

Following TRAIL's path in the immune system

The TNF-related apoptosis-inducing ligand (TRAIL/Apo2L) belongs to the subfamily of ligands that is responsible for extrinsic induction of cell death. Depending on their status of stimulation, TRAIL can be expressed by various cells of the immune system. TRAIL has been implicated in immunosuppressive, immunoregulatory and immune-effector functions. With respect to pathological challenges, TRAIL and its receptors have been shown to play important roles in the immune response to viral infections and in immune surveillance of tumours and metastases. In this review *Walczak et al.* summarise the current knowledge on the role of TRAIL and its receptors in the immune system and, based on this, discuss future directions of research into the diverse functions of this fascinating receptor-ligand system. *Falschlehner, C et al. Immunology* 127: 145-154 <http://doi.wiley.com/10.1111/j.1365-2567.2009.03058.x>

Clinical Immunology Review Series: An approach to the patient with angio-oedema

The sinopulmonary tract is the major site of infection in patients with primary antibody deficiency syndromes, and structural lung damage arising from repeated sepsis is a major determinant of morbidity and mortality. Patients with common variable immunodeficiency may, in addition, develop inflammatory lung disease, often associated with multi-system granulomatous disease. This review from *Longhurst et al.* discusses the presentation and management of lung disease in patients with primary antibody deficiency. *Grigoriadou, S and Longhurst, H. J. Clin. Exp. Immunol.* 2009. 155: 367-377 <http://doi.wiley.com/10.1111/j.1365-2249.2008.03845.x>

Immune and Nervous Systems Share Molecular and Functional Similarities: Memory Storage Mechanism *Habibi, L et al. Scand. J. Immunol.* 2009. 69: 291-301 <http://doi.wiley.com/10.1111/j.1365-3083.2008.02215.x>

Interleukin-17 in host defence against bacterial, mycobacterial and fungal pathogens *Curtis, MM and Way, SS. Immunology.* 2009. 126: 177-185. <http://doi.wiley.com/10.1111/10.1111/j.1365-2567.2008.03017.x>

Biology and clinical relevance of granulysin *Krensky, AM and Clayberger, C. Tissue Antigens* 2009. 73: 193-198. <http://doi.wiley.com/10.1111/j.1399-0039.2008.01218.x>

Enhancing immune responses by targeting antigen to DC *Caminschi, I et al. Eur J Immunol* 2009. 39: 931-938. <http://doi.wiley.com/10.1111/10.1002/eji.200839035>

Regulatory T cells overturned: the effectors fight back *Walker, LSK. Immunology.* 2009. 126: 466-474 <http://doi.wiley.com/10.1111/j.1365-2567.2009.03053.x>

The Tec kinases Itk and Rlk regulate conventional versus innate T-cell development *Prince, AL et al. Immunol Rev* 2009. 228: 115-131 <http://doi.wiley.com/10.1111/j.1600-065X.2008.00746.x>

Immunity against helminths and immunological phenomena in modern human populations: coevolutionary legacies? *Jackson, JA et al. Immunology.* 2009. 126: 18-27. <http://doi.wiley.com/10.1111/j.1365-2567.2008.03010.x>

Autoimmune thyroid diseases: genetic susceptibility of thyroid-specific genes and thyroid autoantigens contributions *Hadj-Kacem, H et al. Int J Immunogenet* 36: 85-96. <http://doi.wiley.com/10.1111/j.1744-313X.2009.00830.x>

Thymic emigration: Sphingosine-1-phosphatase receptor-1-dependent models and beyond *Drennan, M. B. et al., Eur. J. Immunol.* 2009. 39: 925-930 <http://doi.wiley.com/10.1002/eji.200838912>

ImmunoDigest

Early targets in human systemic lupus erythematosus

In this study, the authors aim was “to use a unique collection of serial samples obtained from patients before and after the development of nuclear RNP (nRNP) antibodies to investigate early humoral events in the development of anti-nRNP autoimmunity.” The results obtained led the authors to conclude that “Autoantibodies to nRNP A and nRNP C initially targeted restricted, proline-rich motifs. Antibody binding subsequently spread to other epitopes. The similarity and cross-reactivity between the initial targets of nRNP and Sm autoantibodies identifies a likely commonality in cause and a focal point for inter-molecular epitope spreading.”

Poole, BD *et al. Arthritis & Rheum.* 2009. 60: 848-859.
<http://doi.wiley.com/10.1002/art.24306>

Humoral immunity in natural infection by tick-borne encephalitis virus

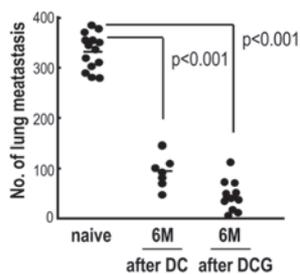
As detailed by the authors “tick-borne encephalitis (TBE) virus is one of the most important flaviviruses associated with neurological disease in Europe. Cross-reactive antibodies elicited by different flaviviruses can make difficult the interpretation of ELISA and hemagglutination-inhibition (HI) tests for the diagnosis of TBE. Neutralization tests, which are more specific, are not in common use because they are difficult to perform and standardize.” In this study, the authors compared results from a plaque reduction neutralization test (PRNT) with those of ELISA and HI tests. The authors concluded that “neutralization assays can be useful for the diagnosis and serosurveys of TBE.”

Venturi, G *et al. J. Med. Virol.* 2009. 81: 665-671
<http://doi.wiley.com/10.1002/jmv.21431>

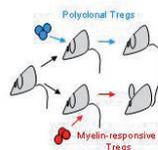
Bonus benefits of DC therapy: Long-lasting NK activation

Dendritic cell immunotherapy against cancer may have added benefits that we are not previously aware of. Shimizu *et al.* show, as expected, that natural killer (NK) cells respond to DC administered intravenously to mice. What is not expected is that NK cells remain activated for many months, even a year after DC injection. This activation prevents metastasis of the B16 melanoma, a known target for activated NK cells. Shimizu *et al.* reveal several underlying mechanisms. Surprisingly, long-lasting NK cell activation requires both the presence of DC and CD4+ T cells in the recipient. Interestingly, this long-lived NK reactivity is not due to “NK memory” but rather, continued generation of activated NK cells. Perhaps there is more to DC immunotherapy than meets the eye?

Shimizu, K. *et al. Eur. J. Immunol.* 2009. 39: 457-468
<http://doi.wiley.com/10.1002/eji.200838794>



Two key requirements for therapeutic Treg



Harnessing the powerful immunoregulatory properties of Foxp3+ Treg is the Holy Grail for many immunologists. Stephens *et al.* have tested the requirements for Treg-mediated immunosuppression using the commonly used mouse model of multiple sclerosis, EAE. Transfer of Treg prior to immunization could completely prevent EAE development. Moreover, transfer of Treg in low numbers after disease onset could reverse progression of the chronic phase of disease, *i.e.* cure the disease. In both settings, the Treg's effects were conditional upon recognition of myelin autoantigen; polyclonal Treg were completely ineffective, indicating that translation to the clinic will require knowledge of the disease-relevant autoantigens recognized by Treg. Furthermore, CD4+CD25+ Treg could be divided into CD62L^{lo} and CD62L^{hi} subsets, with the latter giving the best protection against EAE. This was attributed to a loss of Foxp3 expression by the CD62L^{lo} subset after transfer. The CD62L^{hi} population maintained Foxp3 expression, but lost CD25 upon *in vivo* activation. The study suggests two key requirements for successful use of Treg in the clinic: identification of the autoantigen and the development of a new method of Treg purification that is independent of CD25.

Stephens, L. A. *et al., Eur. J. Immunol.* 2009. 39: 1108-1117
<http://doi.wiley.com/10.1002/eji.200839073>

ImmunoRead

Widely read articles

How B cells shape the immune response against *Mycobacterium tuberculosis*

Maglione, PJ and Chan, J. *Eur J Immunol* 39: 676-686
<http://doi.wiley.com/10.1002/eji.200839148>

A ceramide-1-phosphate analogue, PCERA-1, simultaneously suppresses tumour necrosis factor- and induces interleukin-10 production in activated macrophages

Goldsmith, J *et al. Immunology* 2009. 127:103-115
<http://doi.wiley.com/10.1111/j.1365-2567.2008.02928.x>

Loss of FOXP3 expression in natural human CD4+CD25+ regulatory T cells upon repetitive *in vitro* stimulation

Hoffman, P *et al Eur J Immunol* 39: 1088-1097
<http://doi.wiley.com/10.1002/eji.200838904>

Flow and image cytometry side by side for the new frontiers in quantitative single-cell analysis

Tárnok, A *Cytometry A* 2009. 75A:169-171.
<http://doi.wiley.com/10.1002/cyto.a.20709>

Comparison of stable human Treg and Th clones by transcriptional profiling

Stockis, J *et al Eur J Immunol* 39: 869-882
<http://doi.wiley.com/10.1002/eji.200838807>

ImmunoRead

Toward standardization of Foxp3+ regulatory T-cell measurement in clinical settings
 Lanza, F *Cytometry B* 2009. 76B:67-68.
<http://doi.wiley.com/10.1002/cyto.b.20471>

Contribution of Intestinal Epithelial Cells to Innate Immunity of the Human Gut – Studies on Polarized Monolayers of Colon Carcinoma Cells
 Ou, G *et al. Scand J Immunol* 2009 69:150-161
<http://doi.wiley.com/10.1111/j.1365-3083.2008.02208.x>

Immunomagnetic isolation of CD4+CD25+FoxP3+ natural T regulatory lymphocytes for clinical applications
 Di Ianni, M *et al. Clin Exp Immunol* 2009. 156: 246-253
<http://doi.wiley.com/10.1111/j.1365-2249.2009.03901.x>

TNFR signaling: ubiquitin-conjugated TRAF6 signals control stop-and-go for MAPK signaling complexes
 Karin, M and Gallagher, E *Immunol Rev* 228: 225-240
<http://doi.wiley.com/10.1111/j.1600-065X.2008.00755.x>

Differences in clinical manifestations of influenza-associated encephalopathy by age
 Wada T *et al Microbiol Immunol* 2009 53 :83-88
<http://doi.wiley.com/10.1111/10.1111/j.1348-0421.2008.00100.x>

ImmunoDigest

Cost–Benefit Analysis of WC/rBS Oral Cholera Vaccine

Enterotoxigenic *Escherichia coli* (ETEC) has the potential to disrupt an otherwise productive business trip or relaxing vacation as this bacterium is the most common cause of travelers' diarrhea (TD). The costs in relation to vaccination against ETEC using whole-cell/recombinant-B-subunit oral cholera vaccine were assessed in this interesting study and the authors also provide an updated ETEC map illustrating the proportion of ETEC-caused TD was created. The authors concluded that "vaccination would be considered cost-effective at incidence rates of ETEC-caused TD above about 13 and 9% for leisure and business travelers, respectively" but noted that it is "important to keep in mind that it is the value of the travel for the individual traveler that will decide if the vaccination provides good value for money"
 Lundkvist, J *et al. J. Travel Med.* 2009. 16: 28-34.
<http://doi.wiley.com/10.1111/j.1708-8305.2008.00270.x>

Human monoclonal IgG selection of *Plasmodium falciparum* for the expression of placental malaria-specific variant surface antigens

Pregnancy-associated *Plasmodium falciparum* malaria (PAM) is a major cause of morbidity and mortality in African women and their offspring. PAM is characterized by accumulation of infected erythrocytes (IE) that adhere to chondroitin sulphate A (CSA) in the placental intervillous space. We show here that human monoclonal IgG antibodies with specificity for variant

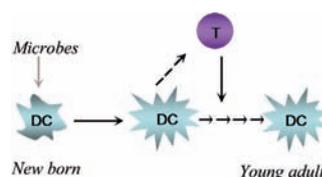
surface antigens (VSA) specifically expressed by CSA-adhering IE (VSAPAM) can be used *in vitro* to select parasites from nonpregnant donors to express VSAPAM and that this selection for VSAPAM expression results in preferential transcription of var2csa. The results corroborate current efforts to develop PAM-specific vaccines based on VAR2CSA.

Soerli, J *et al. Parasite Immunol.* 2009 31:341-346
<http://doi.wiley.com/10.1111/j.1365-3024.2009.01097.x>

Educating the immune system: Start early

Dendritic cells (DC) are key in determining immune responses. Environmental factors such as infections in early life are influential to the development of the immune system. Jiao *et al.* show that microbial exposure in newborn mice changes the function of DC in the development of allergy/asthma in adulthood. DC from adult mice with early-life exposure to microbes are inhibitory for allergic asthmatic reactions. Moreover T cells are important in maintaining these functional changes of DC. The study suggests that early-life-exposure to microbes can imprint the immune system and thus influence future responses of effector immune cells. The finding provides an additional mechanism in support of the hygiene hypothesis.

Jiao, L. *et al. Eur. J. Immunol.* 2009. 39: 469-480
<http://doi.wiley.com/10.1002/eji.200838367>



ADHD as a (non) allergic hypersensitivity disorder: A hypothesis

Research data concerning the causal association between attention deficit hyperactivity disorder (ADHD) and allergies are conflicting. Allergic disorders, like asthma and eczema are clinical syndromes in which both genetic predisposition and environmental factors (pets, pollen and foods) contribute to its development. The hypothesis of ADHD, in some children also being an allergic disorder, is postulated based on comparison of the mechanisms underlying the development of ADHD and allergic disorders. According to the accepted terminology, ADHD may comply with the criteria of hypersensitivity, allergy and atopy. This hypothesis has to be thoroughly tested by randomized controlled trials using environmental triggers and immunologic research. As genes related to the immune system may be associated with ADHD, further genetic research is compulsory. Immunotherapeutic approaches, using immunotherapy and probiotics, can subsequently be implicated in the treatment of ADHD. If hypersensitivity to environmental stimuli like foods contributes to the development of ADHD, the assessment and treatment of ADHD will have to be reconsidered, thereby improving the quality of care for these patients.

Pelsser, LM *et al Pediatr Allergy Immunol* 2009 20:07-112
<http://doi.wiley.com/10.1111/j.1399-3038.2008.00749.x>