What activates TCR Vc9-Vδ2 cells during bacterial infection?

Human TCR Vγ9-Vδ2 cells recognize non-peptidic ligands in the absence of MHC and CD1 restriction. Kistowska et al. investigated the mechanisms of TCR Vγ9-Vδ2 cell activation during bacterial infections. By infecting DC and monocytes with different bacteria, the authors show that TCR Vγ9-Vδ2 cells are activated by mevalonate metabolites of host-origin. Bacterial infection induces rapid activation of the mevalonate pathway by modifying a key enzyme and promoting the synthesis of a stimulatory endogenous metabolite. Thus TCR Vγ9-Vδ2 cells, by sensing the host mevalonate pathway altered during infection, immediately provide effector functions, when bacteria-specific T cells are not yet available.

http://www3.interscience.wiley.com/journal/120775995/abstract
DOI: 10.1002/eji.200838366

MTP regulates lipid antigen presentation beyond CD1d molecules

While the majority of CD1 family members present lipid antigen to T cells with diverse TCR-α and -β chains, CD1d lipid antigen presentation is restricted to the natural killer T (NKT) cells. It is well established that lipid antigen presentation by CD1d is regulated by the microsomal triglyceride transfer protein (MTP). What is not known, however, is whether MTP is also involved in regulating lipid antigen presentation by other CD1 molecules, namely CD1a, CD1b and CD1c. Kaser et al. reported that MTP regulates both endogenous and – surprisingly – exogenous (microbial) lipid antigen presentation by CD1a, CD1b, and CD1c. As MTP is resident in the endoplasmic reticulum, the authors conclude that MTP can ultimately function distally, regulating the presentation of exogenous, endosomally-loaded, microbial lipid antigens.

http://www3.interscience.wiley.com/journal/120775914/abstract
DOI: 10.1002/eji.200838366
Wiley Authors Once Again Receive Nobel Prize in Chemistry

Hoboken, N.J., October 8, 2008—John Wiley & Sons, Inc. (NYSE: JWA & JWB) is pleased to announce that all three 2008 Chemistry Nobel laureates are part of our publishing community. We congratulate Dr. Osamu Shimomura, Dr. Martin Chalfie, and Dr. Roger Y. Tsien on their award for having discovered green fluorescent protein and related marine photoproteins, and for having developed them into highly useful tools for chemical, biological, and medical analysis. The original discovery of green fluorescent protein was reported by Osamu Shimomura in 1962 in Wiley’s Journal of Cellular and Comparative Physiology.

Wiley Authors Win Nobel Prize in Physiology or Medicine for 2008

Hoboken, N.J., October 7, 2008 — John Wiley & Sons, Inc. is pleased to announce that the Nobel Assembly at Karolinska Institutet has awarded the Nobel Prize in Physiology or Medicine for 2008 to Prof. Harald zur Hausen and jointly to Prof. Françoise Barré-Sinoussi and Prof. Luc Montagnier.

“We are honored that all three Nobel laureates are part of our publishing community. We congratulate Prof. Harald zur Hausen, Prof. Françoise Barré-Sinoussi and Prof. Luc Montagnier for their recognition of their lifetime achievements which have changed the course of science and medicine, as well as the lives of human beings,” said Mike Davis, Vice President and Managing Director, Life Sciences.

Prof. Harald zur Hausen, of Germany, receives the Nobel Prize in Physiology or Medicine for his studies of human papilloma viruses causing cervical cancer. He is Editor-in-Chief of the International Journal of Cancer, has contributed several articles to Wiley–Blackwell journals, and is the book author of Infections Causing Human Cancer, published by Wiley-VCH in 2006.

Prof. Françoise Barré-Sinoussi and Prof. Luc Montagnier, of France, were awarded the Nobel Prize in Physiology or Medicine for discovering the human immunodeficiency virus. Both contributed various articles to Wiley–Blackwell journals and were involved in numerous book projects.

Stem Cells: How Do They Behave When Cultured Under Physiological Conditions?

Embryonic stem (ES) cells hold promise for providing unlimited quantities of specialized cells to treat a wide range of diseases. Little is known about their proliferation and differentiation at low partial pressures of oxygen (pO₂), even though the early embryo is normally exposed to such conditions. Powers and co-workers investigate the effects of oxygen on undifferentiated mouse ES cell growth, phenotype retention, and cellular energetics. Growth rate is maximal at intermediate pO₂ and declines modestly at the extremes over the range of 285–0 mmHg. When cultured at low pO₂ under conditions that normally maintain the stem cell state, expression of self-renewal genes decreases, but pluripotency is maintained. Following a decrease to low pO₂, aerobic metabolism decreases and anaerobic metabolism increases so that the total ATP generation rate remains constant. This work helps us understand the behavior of ES cells at physiological oxygen levels.


http://www3.interscience.wiley.com/journal/119815678/abstract

Is it Possible to Completely Camouflage the Surface of Red Blood Cells?

The ever increasing shortage of donated human blood has prompted the development of hemoglobin-based oxygen carriers (HBOCs) for use in transfusion medicine. HBOCs are in development range from polymerized hemoglobins to particle encapsulated hemoglobins. However, by taking hemoglobin outside of its native environment—the red blood cell (RBC)—HBOCs exhibit increased NO scavenging compared to RBCs. Previous work addressed this problem by PEGylating bovine RBCs (bRBCs) in order to camouflage potential antigens while maintaining hemoglobin in its native environment (Gundersen and Palmer, 2007. Biotechnol Bioeng 96:1199–1210). PEGylated bRBCs should be physically capable of oxygen transport within the human vasculature but can we really fool the immune system by camouflaging xenogenic cells with methoxypolyethylene glycol? In this B&B issue, Gundersen, Kennedy and Palmer demonstrate that we unfortunately cannot fool nature yet. The primary xenot antigen, Gala(1,3)Gal, still remains exposed on the surface of the RBC and is still immunoreactive at all tested levels of PEGylation. The authors recommend a completely fresh approach using siRNA to knock out Gala(1,3)Gal synthesis, creating a immunologically silent, natural, hemoglobin carrier.


DOI: 10.1002/bit.21908

5-aminolaevulinic acid and photodynamic therapy reduce HSV-1 replication in HaCat cells through an apoptosis-independent mechanism

In this study, the photo-inactivati on of herpes simplex virus type 1 (HSV-1) in human keratinocytes using 5-aminolaevulinic acid (5-ala) was investigated. We have demonstrated that ALA-PDT treatment acts on HSV-1 replication only in post-absorption condition, reducing HSV-1 replication by about 70%. We did not detect any evidence of apoptosis in the viral reduction observed after ALA-PDT treatment in keratinocytes. So our data suggest that the target of photo-inactivation appears to be viral replication and not a cellular response.

http://www3.interscience.wiley.com/journal/121405721/abstract


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http://www3.interscience.wiley.com/journal/121405721/abstract

**ImmunoFeature**

**Viewpoints on NK cells**

Following on from EJI’s successful first Viewpoints on Treg cells (http://www3.interscience.wiley.com/journal/117954013/issue), the latest discoveries and advances in the field of NK cells are presented in the November issue of EJI. Experts such as James Di Santo, Hans-Gustaf Ljunggren and Mark Smyth discuss aspects ranging from NK cell education and adaptive immunity crosstalk through to immunoevasion and potential therapeutic targets. Find out more about the latest Viewpoint series at www.eji-journal.eu

In addition, published articles on NK cells in recent years in EJI include:

Allelic expression patterns of KIR3DS1 and 3DL1 using the Z27 and DX9 antibodies

John Trowsdale and colleagues

http://www3.interscience.wiley.com/journal/114122280/abstract

DOI 10.1002/eji.200636773

Germ-line and rearranged Tcrd transcription distinguish bona fide NK cells and NK-like T cells

Immo Prinz and colleagues

http://www3.interscience.wiley.com/journal/114261942/abstract

DOI 10.1002/eji.200737354

**ImmunoDigest**

**Blocking Chemokine Receptors May Help Arthritis**

Coelho et al. have shown, in murine models of monarticular antigen-induced arthritis, that blockage of the chemokine receptors known as CXCR1/CXCR2 prevents tissue inflammation, local cytokine production, joint damage, and inflammatory pain. The mechanism by which the drugs (reparixin or DF2162, allosteric inhibitors of CXCR1/CXCR2) act in the system is by preventing the ability of neutrophils to adhere to the vascular endothelium in the joint, thus preventing their extravasation and consequent joint damage. In addition to preventing neutrophil influx and consequent joint damage, the compounds prevented the local production of tumor necrosis factor (TNF), suggesting that neutrophils and their CXCR1/CXCR2 receptors contribute to the local production of TNF. The authors believe their research suggests that compounds, such as agonists of CXCR1/CXCR2 which prevent the interaction between endothelial cells and neutrophils, may be useful for the treatment of human arthritis. As well as preventing tissue inflammation and joint damage, these compounds appear to have the added benefit of ameliorating the pain associated with arthritis, as measured by diminished hypernociception.


http://www3.interscience.wiley.com/journal/121358012/abstract

DOI 10.1002/art.23622

**Balancing tolerance and immunity by B cells**

B cells are not only precursors for antibody-producing plasma cells but are also APC. Shah and Qiao demonstrate another role for B cells in the maintenance of a population of Treg. Resting B cells are shown to support the survival and expansion of CD41CD251Foxp31 Treg via the production of TGF-b3. Production of TGFb3 by B cells is in turn down-regulated by TLR signaling or via BCR cross-linking. Reduced TGF-b3 secretion by activated B cells results in decreased survival and expansion of Treg but increased expansion of effector CD41 T cells. Thus, in addition to humoral immune responses, B cells play an important role in balancing T-cell tolerance and immunity, and in preventing autoimmune diseases.


http://www3.interscience.wiley.com/journal/121407419/abstract

DOI: 10.1002/eji.200838413

**Proteasomal activation in the CNS: A link between inflammation and neurodegeneration**

Multiple sclerosis (MS) is an inflammatory and autoimmune disease of the CNS leading to axonal and neuronal loss. Using the standard experimental model of MS, namely EAE, Fissolo et al. demonstrated increased and altered proteasomal activity in macro- and microglia in the CNS, as well as in lymphoid tissues, in comparison with activity in non-EAE controls. Inhibition of the proteasome with or without inhibition of lysosomal proteases led to amelioration of EAE. This protective effect is most likely due to a reversal of the effects of proteasomal activation, such as increased availability of antigenic peptides, up-regulation of proinflammatory molecules and changes in histone de-ubiquitination. These novel findings indicate that understanding proteasomal activity in the CNS may be a key to a better understanding of neurodegenerative diseases.


http://www3.interscience.wiley.com/journal/121407419/abstract

DOI: 10.1002/eji.200838413
Performing aseptic survival surgery in rodents can be challenging. This unit describes some basic principles to assist clinicians, researchers, and technicians in becoming proficient in performing aseptic rodent surgery.

**Unit 2.4 Production of Polyclonal Antisera**

Much of modern biology and biochemistry relies on the availability of highly specific antibodies for use in such ubiquitous techniques as immunohistochemistry, ELISAs, immunoprecipitation, and immunoblotting. Thus, the generation of large quantities of specific antibodies directed to proteins or peptides of interest is essential to the success of both basic and applied research programs. In addition, with the advent of antibody-based proteomic strategies for profiling protein expression and post-translational modification, a requirement for timely production of specific antibodies has emerged. Polyclonal antibodies derived from animals immunized with purified proteins or peptides are particularly valuable for use in the laboratory. This unit provides protocols for the production of polyclonal antisera specific for protein antigens in rabbits, rats, mice, and hamsters.

**Unit 7.10 Measurement of Proliferative Responses of Cultured Lymphocytes**

Measurement of proliferative responses of human lymphocytes is a fundamental technique for the assessment of their biological responses to various stimuli. Most simply, this involves measurement of the number of cells present in a culture before and after the addition of a stimulating agent. This unit contains several different prototype protocols to measure the proliferative response of lymphocytes following exposure to mitogens, antigens, allogeneic or autologous cells, or soluble factors. Each of these protocols can be used in conjunction with an accompanying support protocol which contains methods for pulsing cultures with [3H]thymidine and determining incorporation of [3H]thymidine into DNA or assessing cell proliferation by nonradioactive methods, e.g., reduction of tetrazolium salts (MTT). The protocols described here provide an estimate of DNA synthesis and cell proliferation in an entire cell population, but do not provide information on the proliferation of individual cells. A protocol for CFSE labeling allows specific subpopulations of cells to be separated viably for further analysis.

**Unit 20.9 ErbB2 Transgenic Mice: A Tool for Investigation of the Immune Prevention and Treatment of Mammary Carcinomas**

The epidermal growth factor receptor belongs to a superfamily of receptor tyrosine kinases (RTK) that includes ErbB2. ErbB2 is involved in normal physiological processes, such as embryogenesis, cell proliferation, differentiation, adhesion motility, and apoptosis, while its malfunction or overexpression is responsible for development defects, diabetes, and cancer. The human ortholog of ErbB2 is referred as Her-2 (human ErbB2) while the rat ortholog is referred as neu (rat ErbB2). As ErbB2 is directly involved in carcinogenesis, mice transgenic for the rat neu oncogene allow straightforward assessment of the ability of drugs and vaccines to inhibit the progression of neu-driven cancer. Information from this model may provide indications on the efficacy of similar treatments in patients. This commentary provides key information regarding the use of these transgenic mouse models for evaluation of the efficacy of anti-tumor strategies.
Malaria parasites impair the host immune system

Malaria is famous amongst immunologists for its chameleon-like camouflage ability and evasion of the immune system. Jangpatarapongsa et al. explored the various mechanisms exploited by malaria parasites to elude the immune system. Acute Plasmodium vivax infection leads to activation of two Treg subpopulations, FOXP3+ Treg and Tr1 cells. The authors report an association between the level of Treg, IL-10, plasmacytoid DC during acute P. vivax malaria. While the overall levels of DC were reduced, the balance between the two DC types was found to be altered. These findings indicate immunosuppression of both cell- and antibody-mediated immunity resulting in hindered parasite clearance.

http://www3.interscience.wiley.com/journal/121426028/abstract
DOI: 10.1002/eji.200838186

Disrupted Joint–Immune System–Brain Communication in Arthritis

Investigating experimental arthritis in rats, del Rey et al. (p. 3090) have provided the first evidence that changes in cytokine expression in the hypothalamus are observed during a specific peripheral immune response. In their study, this response resulted later in the development of type II collagen (CII)–induced arthritis, a model that has many features in common with human arthritis. Additionally, the researchers found that the cytokine-mediated brain–joint communication is disrupted during the development of the disease. This disruption results in an interruption of two main anti-inflammatory pathways controlled at the central nervous system (CNS) level—the hypothalamic–pituitary–adrenal (HPA) axis and the sympathetic nervous system (SNS)—which may contribute to aggravated disease. The authors noted that although defects in these pathways have been previously described in patients with rheumatoid arthritis (RA), it was not known that central mechanisms might be involved in these alterations. While it was already known that proinflammatory cytokines are expressed in parallel in the CNS and in the periphery following acute immune challenge, the researchers observed that immunization with CII antigens induces increased hypothalamic expression of interleukin-1 (IL-1) and IL-6 prior to the enhanced production of these cytokines in the periphery. Paradoxically, such increase in the brain disappears when arthritis is manifested and there is maximal production of proinflammatory cytokines in the periphery.

http://www3.interscience.wiley.com/journal/121425882/abstract
DOI: 10.1002/art.23869

You are what you eat: Disrupted cells interfere with TLR-mediated DC activation

Effective anti-tumour adaptive immunity requires efficient delivery of tumor-associated antigens in the context of appropriate innate immune activation. Both freeze-and-thaw-disrupted tumor cells and DC activation by TLR ligands have been studied extensively for antigen delivery and innate immune activation, respectively. Nevertheless, little is known about DC activation in response to TLR ligands in the presence of freeze-and-thaw-disrupted tumour cells. Tirapu et al. reported that disruption of membrane integrity does not affect the uptake of tumourcell material by DC, but suppresses the responsiveness of DC to TLR-mediated activation. The inhibitory activity associated with disrupted cells is neither cell type- nor species-specific, is instantly accessible upon freeze-and-thaw-disruption, and appears to be independent of phosphatidylyserine-mediated inhibition of DC activation.

http://www3.interscience.wiley.com/journal/121416311/abstract
DOI: 10.1002/eji.200838284
Summarising the findings of the important recent 25th Anniversary HIV meeting held at the Institut Pasteur in Paris, this review by Scherer, Douek & McMichael provides an important overview of current research endeavours to find the elusive cure for this devastating condition. We are grateful to the authors for their special attention to this important commission that complements the excellent historical perspective provided earlier this year by Robin Weiss. Both papers are of especial interest in the light of the recent Nobel announcements regarding Françoise Barré-Sinoussi & Luc Montagnier. Scherer, E., et al., Clin. Exp. Immunol. 154; 6-14. http://www3.interscience.wiley.com/journal/121392066/abstract DOI: 10.1111/j.1365-2249.2008.03750.x

Induction, function and regulation of IL-17-producing T cells

Regulatory B cells as inhibitors of immune responses and inflammation

Early T-cell responses in tuberculosis immunity

Cytokine Gene Polymorphisms in Recurrent Spontaneous Abortions: A Comprehensive Review

Lessons learnt from many years of experience using anti-D in humans for prevention of RhD immunization and haemolytic disease of the fetus and newborn
Translation of novel immunotherapies into the human setting represents an ongoing challenge for researchers. Pooling of knowledge from relevant arenas – such as trials involving monoclonal/recombinant antibodies – may be key to developing the means to both predict desired responses, and anticipate deleterious ones. Anti-D therapy for haemolytic disease of the newborn represents an established therapy where alternatives to plasma-derived polyclonal IgG, in the form of monoclonal/recombinant antibodies, have been sought. As it involves a well-established intervention, this transition may represent an ideal means by which to observe the particular response characteristics engendered by antibodies produced by, for instance, different expression systems. This review by Kumpels et al. summarises trial data hitherto and speculates on what might be learned – with particular reference to the TGN1412 trial in which unintended consequences played such a drastic role. B. M. Kumpel Clin Exp Immunol 154: 1-5 http://www3.interscience.wiley.com/journal/121385811/abstract DOI: 10.1111/j.1365-2249.2008.03735.x

A chromatic explosion: the development and future of multiparameter flow cytometry
Multiparameter flow cytometry has matured tremendously since the 1990s, giving rise to a technology that allows us to study the immune system in unprecedented detail. In this article, Chattopadhyay, Hogerkorp & Roederer review the development of hardware, reagents, and data analysis tools for multiparameter flow cytometry and discuss future advances in the field. Finally, we highlight new applications that use this technology to reveal previously unappreciated aspects of cell biology and immunity. Pratip K. Chattopadhyay, Carl-Magnus Hogerkorp and Mario Roederer Immunology 125: 441-449 http://www3.interscience.wiley.com/journal/121493771/abstract doi: 10.1111/j.1365-2567.2008.02989.x

The T-cell receptor repertoire of regulatory T cells
The CD4+ CD25+ regulatory population of T cells (Treg cells) is the key component of the peripheral tolerance mechanism that protects us from a variety of autoimmune diseases. Experimental evidence shows that Treg cells recognize a wide range of antigenic specificities with increased reactivity to self antigens, although the affinity of these interactions remains to be further defined. In this review, Pacholczyk & Kern discuss how different features of the Treg repertoire influence our understanding of Treg specificities and the role of self reactivity in the generation of this population. Rafał Pacholczyk and Joanna Kern Immunology 125: 450-458 http://www3.interscience.wiley.com/journal/121502258/abstract doi: 10.1111/j.1365-2567.2008.02992.x

Insights into Langerhans cell function from Langerhans cell ablation models

25 years of HIV research on virology, virus restriction, immunopathogenesis, genes and vaccines

A comprehensive review

Regulatory B cells as inhibitors of immune responses and inflammation

Early T-cell responses in tuberculosis immunity

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Monoclonal antibodies (mAbs) are increasingly used to treat human diseases, but as they are predominantly generated from mouse hybridomas their application has been hampered by their immunogenicity. To minimize antigenic reactions, researchers from Genmab in The Netherlands established a transgenic mouse platform for the routine production of fully humanized mAbs. In an overview of recent clinical research, the authors describe efficacy and mechanism of action of three novel humanized mAbs derived from this platform. Zanolimumab, Ofatumumab and Zalutumumab are designed to target CD4, CD20 and the epidermal growth factor receptor overexpressed on cancer cells and to attract cytotoxic reactions against them. All three humanized mAbs show improved efficacy in treatment trials of T-cell lymphomas, B-cell leukemias and head and neck cancer.


http://www3.interscience.wiley.com/journal/121377802/abstract
DOI: 10.1002/biot.200800110

The ability of IL-4 to antagonize antitumour immunity is well recognized. What is less known, however, is the role of IL-4 in effector CD8 T-cell trafficking. Sasaki et al. showed that IL-4 suppresses the migration of protective CD8 T cells into tumor lesions. IL-4 is expressed by various immune cells as well as cancer cells. In tumor-bearing animals, IL-4 suppresses expression of the integrin VLA-4. Suppression of VLA-4 renders antitumor CD8 effector T cells incapable of binding to their molecular counterpart, vascular cell adhesion molecule-1 (VCAM-1) which is expressed on the tumor-associated vasculature. As a consequence, these anti-tumor effector T cells fail to infiltrate tumor and prevent disease progression. Interestingly, the inhibitory effect of IL-4 on VLA-4 expression is reversed by IL-12 but not IFN-g. The current results suggest that there may be yet another level to the intricacies of IL-4, IL-12 and IFN-g interactions.


http://www3.interscience.wiley.com/journal/121407413/abstract
DOI: 10.1002/eji.200838318

How antirheumatic drugs protect joints from damage in rheumatoid arthritis


http://www3.interscience.wiley.com/cgi-bin/abstract/121425883/ABSTRACT
DOI: 10.1002/art.23952

Enhanced B-cell activation mediated by TLR4 and BCR crosstalk


http://www3.interscience.wiley.com/journal/121408228/abstract
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Flowcytometric phenotyping of common variable immunodeficiency

Warnatz, K and Schlesier, M Cytometry B 2008. 74B: 261-271

A novel CD11c.DTR transgenic mouse for depletion of dendritic cells reveals their requirement for homeostatic proliferation of natural killer cells


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The NrL3 inflammasome is critical for aluminium hydroxide-mediated IL-1 secretion but dispensable for adjuvant activity


http://www3.interscience.wiley.com/journal/120775943/abstract
DOI: 10.1002/eji.200838549

Phenotype and function of human T lymphocyte subsets: Consensus and issues


http://www3.interscience.wiley.com/journal/121404281/abstract
DOI: 10.1002/cyto.a.20643

The effect of glucosamine and/or chondroitin sulfate on the progression of knee osteoarthritis: A report from the glucosamine/ chondroitin arthritis intervention trial


http://www3.interscience.wiley.com/journal/121425887/abstract
DOI: 10.1002/art.23973

Alum adjuvanticity: Unraveling a century old mystery


http://www3.interscience.wiley.com/journal/120846849/abstract
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Hypoxia controls CD4+CD25+ regulatory T-cell homeostasis via hypoxia-inducible factor-1


http://www3.interscience.wiley.com/journal/121407413/abstract
DOI: 10.1002/eji.200838334

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DOI: 10.1002/eji.200838541
**Hype or Hope After Genome-wide SNP Studies in Rheumatology?**

An editorial by van der Helm-van Mil et al. takes a critical look at new genome-wide association studies of single-nucleotide polymorphisms in rheumatology. The authors ask whether these studies are raising hopes for future understanding of diseases and the development of personalized medicine, or if they are mainly hype, built on our fascination with impressive technologies. Using specific examples, the authors noted that single genes, in particular those with small odds ratios, play a limited role in predicting risk of disease onset. Additionally, they stated that very few studies have been performed on the effect of genetics on the progression of disease or response to therapy. When several genetic variations with moderate risk are combined, the risk for disease may increase, but the portion of the population affected will diminish, they continued. Their examples brought the authors to the conclusion that combinations of several genetic variants can provide important pathogetic insights, but they are uncertain if this is a basis for meaningful clinical predictions. Regarding the combination of genetic context with environmental factors, they said the impact of a gene variant increases considerably with this combination. A direct correlate of findings from genomewide association studies is that criterion-based syndromes can now be subdivided, or sometimes merged into new categories that are more meaningful from pathogenetic perspectives. The most important drawback of testing many variants without any prior hypothesis is the chance of obtaining false-positive findings, they noted, recommending replication in independent case-control studies. Noting that the ultimate goal of a genetic association study is to identify biologic pathways that may help to create new therapies, the researchers offered a 3-step process. However, they noted that, “thus far, the findings have not resulted in novel diagnostic tools that significantly refine the currently available measures for risk stratification and fit easily into daily clinical practice.”

http://www3.interscience.wiley.com/journal/121391305/abstract
DOI: 10.1002/art.23751

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**Making regulatory T cells ex vivo: IFN-γ is a good cytokine after all**

Transplantation saves lives and improves the quality of life for thousands of organ failure patients. Transplantation is, however, not without cost to the patient; non-specific immunosuppression results in complications such as increased risk of infection and cancer. The induction of immunological tolerance for long-term graft survival in the absence of long-term non-specific immunosuppression remains elusive. A promising new development lies in immunotherapy with ex vivo generated or expanded regulatory T cells (Treg). Feng et al. described a novel protocol for selection of donor-reactive Foxp3+ Treg ex vivo by activating CD4+ T cells with GM-CSF/TGF-b-conditioned DC in the presence of IFN-γ. Interestingly, this results in the preferential death of effector cells, suppression of Th17 responses, expansion of naturally occurring Treg and direct conversion of non-Treg precursors. More importantly, these cells prevent transplant rejection without additional manipulation, supporting their further development for the clinical transplantation setting and treatment of autoimmune diseases.

http://www3.interscience.wiley.com/journal/121408240/abstract
DOI: 10.1002/eji.200838411

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**Automated Analysis of Flow Cytometry Data**

Advances in the optics and electronics of flow cytometers have led to their widespread introduction in many areas of biology and clinical research. However, tools used in the analysis of the data generated have been slower to advance. The automated processing tool developed by Jeffries and co-workers uses a number of different algorithms and processing techniques to define and describe subpopulations of cells. They demonstrate the usefulness of this software when applied to the immunophenotyping of T-cells in a typical clinical research study. Their effort highlights the different features of the APT which is used to objectively define populations of FOXP3+ cells in HIV-infected individuals as well as different CD8 T cell populations in CMV infected children in The Gambia.

http://www3.interscience.wiley.com/journal/120735832/abstract
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**A novel regulator at the DC–T cell interface: gp49B**

DC express several cell-surface, ITIM harbouring immune inhibitory receptors that maintain adequate DC development and/or function; however, little is known about these receptors’ immunoregulatory functions in the context of T-cell activation. In this issue, Kasai et al. demonstrated that gp49B, an ITIM-harboring receptor for αvβ3 integrin, is expressed on DC, and that gp49B-deficient DC induce enhanced proliferation of, and IL-2 secretion by, antigen-specific CD4+ and CD8+ T cells in a cell–cell contact manner. The inhibitory role of gp49B at the DC–T cell interface is further demonstrated by the accelerated, lethal acute GVH disease in gp49B-deficient recipients, indicating that gp49B negatively regulates DC function in vitro and in vivo. Previous studies have revealed that gp49B attenuates cytokine and chemokine production by mast cells or macrophages. The present findings highlight the versatility of the inhibitory role of gp49B at the DC–T cell interface in a physiological setting.

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