overweight/obesity. This is part of the focus of the chapter 'Ecological physiology of diet and digestive systems' by Karasov *et al*. The authors provide an overview of the evidence that suggests that diet and the characteristics of the microbiome appear to be correlated. For example, using the strategy of comparative physiology, it has been determined that bacterial diversity in the gut is lowest in carnivores, intermediate in omnivores and highest in herbivores. In most animals with well-developed microbiotas, diet changes are accompanied by changes in microbiome composition, diversity and function. Human obesity appears to be associated with lower phylum-level diversity in the microbiome.

Environmental impacts on respiratory function are dealt with in two separate chapters. Cigarette smoking is responsible for lung cancer and chronic obstructive pulmonary disease (COPD), among other problems. There are, however, no tools currently that predict the risk of developing these diseases at an individual level. The chapter 'Interaction of cigarette exposure and airway epithelial cell gene expression' by Brody and Steiling reviews data that measure global gene expression in epithelial cells in the airways to address this issue. The chapter 'The lung: the natural boundary between nature and nurture' by Seibold and Schwartz discusses the recent advances in knowledge and technology on the role of genetics, the environment and gene–environment interactions in the genesis of common lung diseases such as asthma, COPD and lung fibrosis.

The 'special topic' in the current volume focuses on thrombosis. 'The link between vascular features and thrombosis' by Charles and Naomi Esmon discusses the anticoagulant properties of the vascular endothelium, particularly in the microcirculation, which is characterized by a high ratio of endothelial cells to blood. The impact of inflammation and stasis on anticoagulation pathways in the endothelium is reviewed. Venous thromboembolic disease is a major cause of morbidity and mortality across the globe. In the other two chapters devoted to the discussion of thrombosis, Manly *et al*. discuss the 'Role of tissue factor in venous thrombosis', while Bovill and van der Vliet focus on the role of the venous valves in the genesis of a thrombus in the chapter entitled 'Venous valvular stasis – associated hypoxia and thrombosis: what is the link?' In both chapters, the authors discuss the molecular pathways involved in venous thrombosis and outline potential therapeutic targets that could lead to the prevention and treatment of venous thromboembolism.

This volume, like its predecessors, continues to have a wide appeal. The chapters cover a large part of the broad canvas of physiology. The approaches in the chapters are varied – some are more clinical and human, others more cellular in their content with comparisons across species. However, all provide readable material that would address the needs of a range of physiologists. For the student of physiology, the book is indispensable. For more focused researchers, the *Annual Review* provides a rapid overview of the advances in physiology across multiple systems. For me, the *Annual Review* has always been something to look forward to – this issue does not disappoint.

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Annual Review of Immunology, 2010. W. E. Paul, D. R. Littman and M. Yokoyama (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, California 94303-0139, USA. Vol. 28. vi + 694 pp. Price: US$ 89.

The topics covered in this volume can be broadly categorized into five areas: inflammatory responses, humoral or B cell responses, T cell biology, immune regulation and autoimmunity.

This volume starts off with an insightful observation by Max D. Cooper about the status of biomedical research these days: 'One of the most remarkable things about a career in biomedical research is that one can start almost anywhere and end up in the most unforeseen places, being constantly amazed by what you are learning along the way.' Cooper talks about his training as a doctor and his bewildering entry into immunology research. He recalls a talk by Linus Pauling on the structure of the antibody molecule, which is revealing of Pauling and times in those days: 'If I couldn't find out how monovalent Abs work, I figured God wouldn't either'. Cooper's use of diverse animals (chickens, frogs, rabbits, lampreys, etc.) to answer immunological questions is impressive. He has made several contributions, and the three main ones are: First, the identification of the bursa of fabricius as the site for B cell development and antibody production in chickens. Subsequently, efforts to find the bursa equivalent in mammals led to the identification of the mammalian hematopoietic tissue as sites where B cells are generated. Second, the demonstration that lymphocytes belong to at least two distinct categories: B cells (humoral response) and T cells (cellular response). These studies have implications for patients with immunodeficiencies. For example, patients suffering from Bruton's X-linked agammaglobulinemia are deficient in B cell differentiation and immunoglobulins, whereas those suffering from DiGeorge's syndrome have a deficient cellular immune response, but Ig amounts are not affected. Third, identification of mammalian equivalents of the adaptive immune system, i.e. B cell receptors (BCRs), T cell receptors (TCRs) and major histocompatibility complex-encoded molecules (MHC). Also several diverse leucine-rich repeat (LRR) sequences were identified in jawless vertebrates. Unlike the more evolved jawed vertebrates, jawless vertebrates use variable lymphocyte receptors (VLRs) comprising LRR sequences. In these cases, the VLR gene flanks hundreds of LRR coding sequences and VLRs are assembled by a gene-conversion process mediated by activation-induced cytidine deaminase (AID). Most interestingly, VLRA and VLRB are on distinct populations representing the counterparts of T and B cells.

Among the topics discussed is the inflammatory response, which results in redness, heat, swelling, pain and pus, and is well known to be involved in the immune response. However, it is a double-edged sword: defects in this pathway result in increased susceptibility to infections, whereas too much of a response leads to tissue/organ damage in the host. Microbial components, e.g. lipopolysaccharides are well known to activate this response; however, the role of endogenous activators of this pathway, e.g. urate crystals, dead cells, cholesterol crystals, etc. is emerging. In particular,

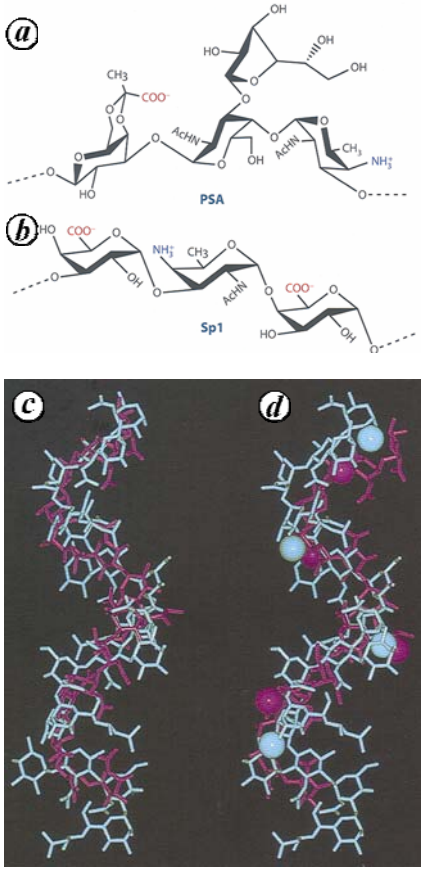
the role of the NLRP3/IL1 pathway in this process is extremely informative. Importantly, the use of inhibitors to this pathway in ameliorating some diseases, e.g. gout (inflammation of joints due to accumulation of urate crystals), is being explored. Another endogenous activator of this pathway is the high-mobility group box 1 (HMGB1), a DNA-binding nuclear protein. It binds to TLR2, TLR4 and receptor for advanced glycation end-products (RAGE), and an understanding of the HMGB1–RAGE pathway during inflammation, cancer and other diseases is useful. Also, the role of properdin, a plasma component and complement protein, in removing dangerous agents in the body has been covered in this volume. Interestingly, properdin is X chromosome-linked and deficiency of this protein is often observed in males who are highly prone to meningococcal diseases.

There are two reviews on B cell development and activation with an emphasis on the role of Ca^{2+}/NFAT, PI3K, NF-kappaB and the cytoskeletal pathways. In addition, the role of notch signalling during thymic education, T cell activation, B cell differentiation and myeloid development is reviewed. T cells differentiate and mature in the thymus to give rise to $CD4^+$ or $CD8^+$ T cells, which are required for cellular immunity. This process of thymic differentiation requires the appropriate selection of TCRs that are not self-reactive, but can recognize self-peptide-MHC (pMHC). The role of the strength of the TCR signal in this process is well known. Recent studies have shown the role of ThPOK, a transcription factor, that is required for the expression of CD4. Interestingly, there are no $CD4^+$ T cells found in mice harbouring mutant ThPOK, and some of the $CD8^+$ T cells are MHC class II restricted. The role of the different TCR domains in the selection of thymocytes has been particularly well explained in the chapter on the distinct preimmune T cell populations. Studies have shown that mouse preimmune T cells in secondary lymph nodes consist of ~70% naïve, ~10% recent thymic emigrants, ~10% memory T cells and ~10% natural regulatory T cells (nTregs). The role of two receptor–ligand interactions, namely OX40 (CD134)–OX40L (CD252) and B and T lymphocyte attenuator (BTLA)–Herpes entry mediator (HVEM), in different aspects of immune cell interactions is also reviewed. The lack of OX40–OX40L interactions leads to lowered accumulation of antigen-specific $CD4^+$ T cell responses and reduced cytokine production. Consequently, the efficacy of antibodies that signal via OX40 in boosting immune responses against pathogens and tumours is being explored. On the other hand, BTLA is an immunoglobulin family receptor with a cytoplasmic immunotyrosine-based inhibitor motif. However, mice lacking *Btla* do not show spontaneous autoimmunity, unlike those lacking *Ctla4* or *Pd1*, and the reasons for this are not clear.

Great strides have been made in our understanding of T cell motility and the synapse formation between the MHC and TCR and associated cell-surface receptors termed as the immunological synapse that play key roles in either enhancing or inhibiting T cell activation. Much of this progress has been due to two-photon laser scanning microscopic studies that have revolutionized our understanding of the distinct phases of T cell–APC interactions. T cells are in constant motion and rapidly scan for cognate TCR–pMHC interactions. The sensitivity is high enough such that ~10 pMHC can be detected by T cells, according to the authors. $CD4^+$ T cells are important in helping the differentiation of B cells, activation of macrophages and in resisting intracellular infections, tumours, etc. They differentiate into different subsets, e.g. TH1, TH2, TH17, iTreg, etc. Also, the role of different transcription factors, cytokine environments and signalling requirements has been discussed. Importantly, the discussion on human diseases, e.g. Omenn syndrome, Job syndrome, etc. that display a TH2 cytokine bias, probably because of the low signal strength due to restricted TCR usage, is illuminating.

Our gut is inhabited by microbes, including ~100 trillion bacteria. The role of these microbes in the host immune response has been reviewed in several chapters on intestinal bacteria, inflammatory bowel syndrome (IBD) and IgA in the gut. In fact, alterations in the quantity and diversity of the gut flora are associated with several diseases, including allergies, diabetes and autoimmune diseases such as IBD. The role of host responses, e.g. inflammation, autophagy, ER stress that modify the gut microflora is fascinating. For example, breast-fed infants possess higher numbers of *Bifidobacterium* and less numbers of *Escherichia coli*, *Clostridia*, etc. whereas the opposite is observed with formula-fed infants.

Our immune system is not perfect and in some cases there are situations that cause autoimmune diseases. The reasons for this are varied, and better understanding of this process is required. For example, mutations in *NOD2* are associated with Crohn's disease, a type of IBD. *NOD2* appears to inhibit the TLR activation of NF-kappaB, a transcription factor involved in the inflammatory response. The chapter on genomic analysis of immune cells during disease is most useful



Structural features of zwitterionic polysaccharides PSA and Sp1. Chemical structures of the tetrasaccharide repeating unit of PSA (*a*) and the trisaccharide repeating unit of Sp1 (*b*) are shown. Positively charged amino groups are labelled in red. Three-dimensional conformational structures of Sp1 (purple) and PSA2 (light blue) are shown superimposed on the basis of their glycosidic oxygen atoms (*c*) and their amino groups (*d*). Purple and light blue dots represent positive charges from Sp1 and PSA2 respectively. Sp1 and PSA2 display a similar zigzag positive-charge pattern with nearly equidistant charge separation of 15 Å. The images in parts (*c*) and (*d*) of this figure are reproduced, with permission, from *Biochemistry*.

for researchers interested in transcriptional changes. The authors point out that the mouse models of disease may not always reflect the human disease scenario; for example the role of Type 1 interferon as an important mediator during systemic lupus erythromatoses, an autoimmune disease. The authors surmise that transcriptional analysis together with flow cytometry and proteomic analysis will give a comprehensive profile of the immune status of individuals.

One of the major problems with vaccines against HIV is their failure to generate effective neutralizing antibodies that are effective against a broad variety of strains. There is an informative review on this aspect and it turns out that neutralizing antibodies are indeed generated by the host. However, these are produced later during infection and are effective against viruses that were present earlier, but are ineffective against current forms of the virus. The challenge will be to develop vaccines that generate high amounts of neutralizing antibodies that can prevent or lower viral entry and/or dissemination during the early infective phase. The major focus has been to map epitopes recognized by neutralizing antibodies on the surface Env protein encoded by HIV, which is composed of trimers of gp120 and gp41. Further optimization of immunogen design coupled with a better understanding of the structural basis of viral neutralizing antibodies will be required to enhance our understanding of this complex problem.

This volume contains a wealth of precious information on the fast and dynamic changes occurring in our understanding of the immune system. Perhaps, it is apt to end with two quotes from Cooper's autobiographical essay. He points out that 'it is humbling to realize that 150 years after Darwin published *Origin of the Species* we still have so much to learn about the how and why our complex immune system evolved'. The second quote is more endearing, 'I cannot imagine a field of research that is more exciting and one that offers better opportunity to explore the balance of life on our planet. Perhaps, this view explains why I am hooked for life with immunobiology.'

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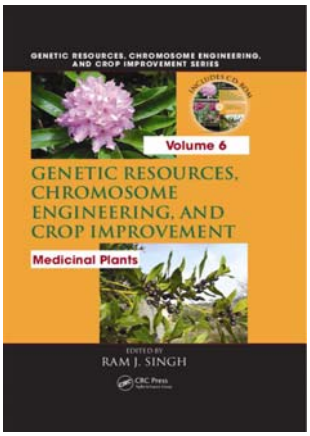

Genetic Resources, Chromosome Engineering, and Crop Improvement Series: Medicinal Plants. Ram J. Singh (ed.). CRC Press, Taylor & Francis Group, 6000 Broken Sound Parkway NW, Suite 300, Boca Raton, FL 33487-2742, USA. 2011. Vol. 6. 1066 pp. Price: US$ 133.11.

The book is an encyclopedia consolidating landmark research leads, with a description of medicinal plants of different countries. It contains 30 chapters by leading experts and panelists, presenting an exhaustive global update on medicinal plants, genetic resources and their increasing importance in pharmaceutical and cosmeceutical industries, medicine and nutrition around the world. Closer examination reveals a wealth of information on individual medicinal plants, including their history, genetic resources, cytogenetics and varietal improvement through conventional and modern methods. It also provides useful information on germplasm resources of medicinal plants, their history, taxonomy, biogeography, ecology and biodiversity.

The topic of medicine is of no small interest as the active ingredients from the medicinal plants described may be used as lead structures in modern medicinal chemistry. Molecular studies on many such plants used in Ayurveda and traditional Chinese medicine have been undertaken in recent years, and have already led to interesting lead structures. Those who are interested in specific plants will find a comprehensive compilation in this handbook, and can bank upon the useful literature and references provided.

The volume would be useful for students, teachers and academicians involved in human resource development and in research. It is especially recommended for the libraries of research institutions and research groups working on natural products, medicinal chemistry and traditional healing methods. It may also prove handy to scientific bodies, regulatory authorities, policy makers and the herbal industry, in addition to other institutions involved in the development, assessment and registration of such plants.

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