Annual Review of Immunology, 2008. William E. Paul and Dan R. Littman (eds). Annual Reviews, 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0139, USA. Vol. 26. 794 pp. Price not mentioned.

This volume contains articles on different aspects of the immune response, ranging from cellular immune processes, autoimmunity, cytokines, genes important for the immune response, etc.

The roles of the components of the host defense system during infections are covered by several chapters on monocyte subsets, cytidine deaminase during retroviral infections, IRF family members, etc. One of my favourite chapters was the one on identification (gene mapping and cloning) and roles of single host genes during infection. The sheer variety of different host proteins playing varied roles during the host immune response is remarkable: membrane proteins, GTPases, NK receptors, enzymes (e.g. oligoadenylate synthetase), complement components and signalling molecules. For example, the natural resistance-associated macrophage protein 1 (NRAMP1) is an iron transporter located in the membranes of lysosomes and granules of neutrophils. Mutations in NRAMP1 that affect function lead to increased pathogen load and greater susceptibility to infection by intracellular bacteria. Another example is the deficiency in the complement component C5 which leads to severe susceptibility to *C. albicans* infection. C5 is processed and binds microbes with bound antibodies (i.e. opsonized) leading to the formation of pores and microbial lysis. Genetic studies have also revealed the critical role of IFNγ-induced GTPases during a wide variety of infections (e.g. Salmonella, Mycobacterium, *T. gondi*, *L. major*, Coxsackie and vesicular stomatitis virus). The chapter reinforces the enormous role of the laboratory mouse in the discovery of host genes (including the MHC) during infection. The authors suggest that role of gene diversity during different immune responses needs to be assessed. In these days of large screens, it is not too surprising that the goal of assessing the role of every single gene in the genome during infection is underway.

There are several chapters devoted to aspects of T cell biology. T cells are activated upon binding of the T cell receptor to its cognate MHC containing the antigenic peptide on antigen presenting cells. The site of interaction between the TCR and the MHC and the roles of conserved amino acids in the MHC are reviewed in depth. Extensive studies on different TCR-MHC structures led the authors to suggest that the exposed areas on the MHC that lie diagonally opposite one another are the binding sites for the TCR. Another chapter is on the role of actin cytoskeleton after T cell activation. This branched network is formed after T cell activation and allows for recruitment of cellular mediators in microclusters at the site of TCR–MHC interaction known as the immunological synapse. Upon activation, T cells differentiate into effectors and a newly discovered subset are T follicular helper cells (T_{FH}) which are distinct from other $CD4^+$ T cell effectors: T_{H1}, T_{H2}, T_{REG} and T_{H17}. These are present, primarily, in germinal centers and are important for the initiation of the immune response. Apart from the location, T_{FH} cells express the chemokine receptor CXCR5 which binds to the ligand CXCL13 (produced by follicular dendritic cells). CXCR5 expression is absent in $CD8^+$ T cells and naïve $CD4^+$ T cells and is transiently induced upon antigen stimulation. Notably, T_{FH} cells produce large amounts of IL-21 which are required for the differentiation of B cells into plasma cells in germinal centres in immune organs.

The critical role of Blimp-1, a transcriptional repressor, which inhibits transcription by recruiting corepressors, leading to a more repressed chromatin structure, is also reviewed. Immune molecules can play several roles in different cells and this point is illustrated well in case of Blimp-1: it is required for plasma cell formation and immunoglobulin secretion in B cells. In T cells, Blimp-1 is activated via the IL-2 receptor to lower IL-2 production. Also, Blimp-1 enhances Th2 responses and increases cell death of effector T cells.

Cytokines are molecules that are secreted by immune cells and modulate responses. Two cytokines, IL-2 and IL-21, are discussed in detail in this volume. Interestingly, a common receptor subunit known as γ_c is shared by receptors that bind to several cytokines, including IL-2, IL-21, IL-4, IL-7, IL-9 and IL-15. IL-2 is a well known *in vitro* growth factor of T cells; however, mice lacking Il-2 or its receptor subunits demonstrate, unexpectedly, hyperactive T cells leading to autoimmunity. Further studies revealed that IL-2 is required for the development and homeostasis of regulator T cells (T_{REG}), which suppress the basal activation of T cells. Consequently, lower numbers of T_{REG} lead to autoimmunity. This finding may be clinically relevant as polymorphisms in *Il-2* (*Idd3*) leads to lower amounts of IL-2 and increased autoimmunity in non-obsese diabetic (nod) mice. IL-2 is also required for the development of memory $CD8^+$ T cells. IL-21 is produced by activated $CD4^+$ T cells and NK T cells and the primary targets appear to be B cells, NK cells and T_{H17} cells. Similar to other immune molecules, IL-21 modulates several responses. IL-21 may have therapeutic applications as it reduces tumours but increases autoimmunity. Possible therapeutic interventions with IL-21 need to be tempered by the fact that IL-21 can increase or decrease responses. Therefore, a better understanding on how IL-21 signalling is integrated with other molecules in the environments is desirable.

Paul Ehlrich is well known for several discoveries: dyes that stain bacteria, toxin–antitoxin reaction, side chain theory for antibody formation, chemicals to treat trypanosomiasis and syphilis, etc. He also came up with the term known as 'horror autotoxicus' which predicts that the immune system is disinclined to generate a response against the host. However, we are now aware that autoimmunity does occur and the host is capable of generating an excessive inflammatory response that is harmful. Autoimmunity involves several molecular players: genes encoded in the MHC (HLA variants) play a major role, and other molecules, e.g. CTLA4 and protein tyrosine phosphatases (PTP), also contribute to disease. Humans possess about 107 genes encoding protein tyrosine phosphatases or like proteins. Mutations in several of these genes result in autoimmunity, e.g. PTPN22, PTPRC (CD45), PTPN6 (Shp1). The different mutations and biochemical pathways involved are described in great detail. It is possible that the MHC haplotype and PTPN22 genotype may offer a better predictive value. Also, the use of inhibitors to selectively target defined phosphatases is discussed.

Intravenous Immunoglobulin G (IVIG) consists of pooled sera from several donors and is used to treat patients with low

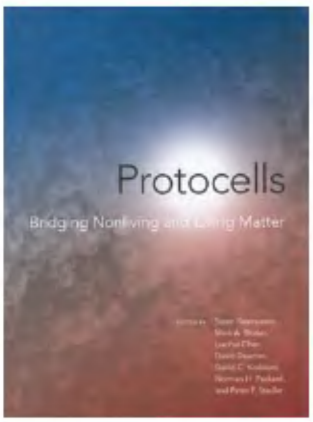
amounts of circulating Ig (replacement therapy) and several inflammatory diseases. The mechanisms involved in its use as an anti-inflammatory agent are discussed and involves competing with auto-antibodies to bind IgG receptors on cells. Antibodies to citrullinated proteins as a diagnostic tool in rheumatoid arthritis, the roles of programmed death (PD-1) and its ligands and mast cells are also reviewed.

Finally, the autobiographical piece by K. Frank Austen entitled, 'Doing what I like' looks back at the twists and turns of his distinguished research career. He recounts his contributions in the field of inflammation, namely cysteinyl leukotrienes, mast cells and complement components. Two notable findings are highlighted – his group identified slow reacting substance of anaphylaxis (SRS-A) from lung, which is distinct from histamines, and mediates bronchial constriction during asthma (an inflammatory condition). Subsequent studies demonstrated that SRS-A is composed of three cysteinyl leukotrienes: intracellular leukotriene C4 and its extracellular metabolites, LTD4 and LTE4. His collaborations with E. J. Corey led to proper characterization of the biological functions of these defined molecules. In addition, his laboratory characterized the role of the leukocyte immunoglobulin (Ig)-like receptor (gp49B1) containing an immunoreceptor tyrosine-based inhibition motif (ITIM) in reducing mast cell function. Overall, he tried to understand how immunological reactions contribute to biochemical changes that lead to different functional outcomes. He suggests that 'experience with focus provides insights and inclination for measured risks that is productive for research in a setting with talented trainees and wise colleagues' – an useful thought for the turbulent times that we live in!

Overall, this volume offers fascinating information on different aspects of the immune response and is a must read for naive, differentiating and mature immunologists!

DIPANKAR NANDI

Department of Biochemistry,
Indian Institute of Science,
Bangalore 560 012, India
e-mail: nandi@biochem.iisc.ernet.in



Protocells: Bridging Nonliving and Living Matter. Rasmussen *et al.* (eds). MIT Press, 55, Hayward Street, Cambridge, MA 02142. 2009. 684 pp. Price: $ 75.

What is life? Several historically important texts begin with this question and somehow end up towards the same question following a spiritualistic approach. Scientifically, the challenge lies in actually defining (measurable) parameters through which a system called 'life' can be constructed. The book edited by Rasmussen *et al.* attempts exactly to do that in the form of a cohesive text that attempts to integrate the evolution of parameterization of a system known as 'life'. While doing so, it uniquely (and boldly) introduces a variety of experimental and theoretical approaches that have been developed in different forms to mimic 'operational functionalities' that define 'life'. From my point of view, the book essentially exemplifies the inter- and multi-disciplinary nature of modern biology. An important feature of the book is that it makes the reader appreciate the requirement of the so-called reductionist approach in experimental (both wet and dry) biology. It does so elegantly without compromising on the need to be constantly reminded of the complexity resulting in nature through biological evolution. Before delving into brief specifics about the contents of the book, I would like to emphasize that this is certainly a book that should become a part of every library that caters to undergraduate students, postgraduate students and 'independent' researchers at all levels (from entry level scientists/faculty to seniormost level) and not necessarily specializing in only biological research.

The book is divided into four major parts. The first part lays the foundation of scientific thought that went into description and acceptance of 'protocells' as a term that would experimentally define a living form within the definition of life. This definition of life essentially comprises of three components (referred to as 'operational functionalities'): (a) extraction and use of energy from the environment, (b) chemical realization of informational control that can be replicated or passed on and (c) a closed system or a 'container' that can keep the first two together and segregated from the surroundings. Through the various chapters in the first part, especially the one written by Deamer (chapter 2), the book provides a good summary of different experimental attempts, with due attention to the historical thought process that went into the design of those experiments, at creation, measurement and objective assessment of the 'operational functionalities'. The best aspect of this part of the book for me as a reader was its fresh presentation unlike so many aspects of modern biology in which hypothesis-driven work often tries to force the reader into a certain direction of thought. The authors in this section are careful in presenting a body of experimental work that is open to interpretation, with clear mention of the limitations of the systems. The only major drawback was lack of sufficient information on the failed experiments or experiments with negative results. As an example, elegant experiments with DMPC vesicles encapsulating RNA polymerase or 'self-reproduction' of caprylate micelles do seem fascinating; however, the specific choices leading to these experimental systems were surely driven by several attempts with different combinations of amphipathic and enzymatic molecules. A brief outlook towards why one system works in a certain way compared to another would have definitely added a more thought provoking value. Nevertheless the quality of writing and description of the results do allow the reader to build an independent perspective rather than get entangled into the limitations of the experimental systems or interpretations of the results as mentioned by the authors.

The second and third parts of the book are quite interrelated, with the aims of 'Integration' and 'Components' and are not exactly independent of each other. Both these parts oscillate frequently between the chemistry of wet experimen-