

## BOOK REVIEWS

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the present status on the development of immunotherapy and HPV vaccines.

Basic design of chimeric antigen receptor (CAR) on T cells, and advantages and disadvantages of their use compared to other immunotherapies for lymphomas are reviewed by Ramos *et al.* They also present the results of clinical trials using CARs and strategies to enhance their efficacy and safety.

Bisphosphonates are widely recommended to treat bone loss in patients with osteoporosis. They have been also tried for adjuvant therapy in women with hormone receptor-positive breast cancer to prevent bone-related complications secondary to cancer treatment, as well as to prevent recurrence and metastases. The first article in the volume summarizes the results of randomized clinical trials involving many thousands of patients as well as a recent meta analysis by Earl Breast Cancer Trialists' Collaborative Group (EBCTCG). Meta analysis by EBCTCG of data from about 19,000 patients reveals the beneficial effect of bisphosphonates on recurrence of bone metastases and overall survival in patients with breast cancer, who are post-menopausal at diagnosis or pre-menopausal women who received ovarian suppression treatment, i.e. in a low oestrogen environment at baseline of their treatment.

Risk profiling of acute myeloid leukaemia (AML) has evolved from traditional morphologic and cytogenetic analysis to next-generation sequencing studies which have provided significant novel insights into the molecular aspects of AML with normal karyotype. This new knowledge has implications for diagnosis, risk stratification and post-remission treatment of patients with AML. Komanduri and Levine demonstrate how molecular analysis and assessments of somatic mutations in leukaemic cells have helped guide selection of post-remission treatment strategies extending from chemotherapy to a combination of haematopoietic stem-cell transplants and immunotherapy.

Cystic neoplasms of pancreas, increasingly recognized now thanks to the wide use of abdominal cross-sectional imaging tools, are a diverse group of tumours classified according to their potential to turn malignant. Epidemiological and clinical features, classification, risk factors, pathogenesis, different means for diagnostic evaluation (including molecular diagnostics) and management strate-

gies of cystic pancreatic tumours form the theme of one of the reviews.

An article titled 'Molecular profiles of prostate cancer' examines commercially available as well as promising genomic tests in development. Their advantages and limitations in differentiating aggressive from non-aggressive prostate cancer are presented. New molecular profiling tests have better reproducibility compared to pathological or radiological grading. Hence they are promising for risk stratification to assist monitoring of patients and making therapeutic decisions.

Over the last two decades, advances in medical treatment for benign prostatic hyperplasia (BPH) and its related symptoms have led to decrease in surgical interventions. Another article catalogues various surgical and device treatments for BPH, treatment outcomes and associated complications. Pathogenesis of BPH is also discussed.

There are also reviews on other topics of considerable current interest. One of them presents the results of four major cardiovascular outcome trials on incretin-based therapies (with three DPP-4 inhibitors and a GLP antagonist) on cardiovascular outcomes or safety in patients with type-2 diabetes. Wong summarizes the understanding on the biological connection between vitamin D and the cardiovascular system and the results of ongoing prospective randomized trials on vitamin D supplementation in patients at risk for cardiovascular diseases. Surprisingly, accumulating evidence suggests that vitamin D supplementation has no influence on blood pressure.

Other interesting reviews in this volume deal with oral immunotherapy for peanut allergy, mechanisms for opioid analgesia, actions and side effects of opioid receptor agonists and antagonists, public health issues arising from marijuana legislation in USA, epidemiology of cognitive impairment in survivors of critical illnesses and approaches to the management of patients with critical illness brain injury, future of evidence-based therapy for nicotine addiction, mechanisms of action, and evidence for the use and adverse effects of pirfenidone, an antifibrotic agent which provides a new hope for patients with idiopathic pulmonary fibrosis.

In summary, the new edition of *Annual Review of Medicine* contains enlighten-

ing chronicles of advancing frontiers of a wide range of common clinical problems as well as simulating topics of contemporary interest. All the articles are lucidly composed. An appropriate background useful to readers unfamiliar to the review topic and a summary at the end are provided. Schematic illustrations of concepts, effective use of tables in presenting data and good quality photographs enhance the quality. All interesting and significant studies referred to in the reviews are brought to the reader's attention by providing their citations in bold font.

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This volume comprises reviews covering a wide range of topics. The editors have broadly classified them in different areas pertaining to cell and developmental biology. However, the reviews are highly focused.

The volume begins with a perspective by Lewis Wolpert. His transition from a civil engineer to a biologist makes fascinating reading. It is of interest to note how he began his research by applying the principles of mechanics to cell biology problems. The system in the UK would permit this transition with ease!

Wood and Nurse in their article entitled 'Sizing up to divide: mitotic cell-size control in fission yeast' discuss various aspects of cell size control which has been studied extensively but is yet to be resolved unequivocally. The quantitative aspect of this problem studied from 1900s has been summarized in the introduction. The review suggests that further investigations are necessary for better and clearer insights into the problem.

Translation of mRNA and translational machinery have been the subject of extensive investigations and the process is well established. Shi and Barna focus on tissue-specific regulation of mRNA translation. The authors essentially review regulation aspects of protein synthesis rates and translation of specific mRNAs in different cell types. They have addressed several future issues which would be of interest to researchers in the area.

Organelle inheritance is an important step in cell division. The molecular mechanisms are of considerable interest. Knoblich and Rachubinski review this aspect and focus on those of the transport and retention machineries. They discuss peroxisomes and lipid droplets which have attracted considerable attention in recent years. The references are annotated to highlight what in the authors' viewpoint are important findings.

Cianfrocco *et al.* focus on dyneins, a cytoskeletal motor perhaps less understood compared to others, according to them. Aspects such as structure and mechanochemical cycle along with a video (when the article is accessed online) are discussed extensively. In the future directions section, the authors comment on unanswered questions related to neurological diseases.

The secretory pathway of proteins, including vesicle traffic has been extensively studied in prokaryotes and eukaryotes and Nobel Prizes have been awarded in this area of research. Hence, one may wonder why a review in this area now. Malhotra and Erlmann specifically address secretion of collagen. This protein has been the subject of extensive structural and functional investigations. The review indicates various aspects of the transport pathway that is yet to be unravelled.

The hepatitis virus has been investigated extensively over the years, considering the number of infections worldwide. The serious consequences of the infection makes it a topic of discussion even today. The review by Li describes the recently identified functional receptor for hepatitis B virus (HBV). How this receptor was identified after years of research makes interesting reading. Mechanism of receptor-mediated HBV and hepatitis D virus (HDV) entry, role of the receptor in HBV infection and therapeutic approaches to fight HBV and HDV would be of interest to virologists, particularly those working on HBV.

The self-assembly of proteins to form aggregates like amyloids have been studied extensively, particularly their association with disease states. Prions have also been extensively investigated with respect to their self-assembly and associated diseases. The review by Si does not deal with these aspects, but on the role of prions other than in disease conditions, i.e. functional prions. The first figure shows folding behaviour of a protein forming amyloid fibrils due to misfolding versus formation of an ordered oligomer. Prions in immune response, epigenetic mechanisms, cellular memory and animal development are highlighted. The author also addresses whether functional prions can provide information about amyloid diseases.

The compact packing of genetic material has been recognized and appreciated for a long time. Badrinarayanan *et al.* deal with various aspects of chromosome organization in bacteria. They discuss extensively, how proteins play a role in this process. The authors also highlight important aspects to be addressed. They indicate how newly developed tools such as super-resolution fluorescence microscopy will play a role in delineating spatial organization of bacterial chromosomes.

The review by Le Fevre *et al.* addresses various aspects of plant-pathogen interactions, an area of intense research over several years. Specifically, they discuss aspects of microbe-induced cellular reprogramming and its impact. They also focus on pathogens that do not kill plant tissue immediately on infection. The table on plant diseases caused by pathogens that affect plant development would be of interest to researchers in the area and also those who went to initiate research in this area. A large number of host plants are related to agriculture. The authors discuss strategies that may be employed for crops.

The role of ion channels in modulating biochemical processes in neuronal and muscle cells has been investigated extensively. The review by Bates is focused on the role of ion channels in development and cancer. It provides insights into regulation of cellular proliferation in normal development and cancer cells by ion channels. The role of  $\text{Ca}^{2+}$  movement in the signalling pathway involving bone morphogenetic protein and vesicle secretion is also discussed. How ion channels could be targets for therapeutics

and other medical intervention is highlighted.

Fox *et al.* review the biology of a family of RNA-binding proteins with respect to stem cells and cancer. The family of proteins is named Musashi, a samurai. The prologue and epilogue about the life of Miyamoto Musashi is as interesting as the review. Musashi plays a crucial role in stem cell biology and this aspect is discussed in the review. The section on mechanism of action includes structure-function aspects of the protein, regulation of expression and downstream targets. The known Musashi targets are summarized in a table. Considering the role of Musashi in cancer, targeting this family of proteins for therapies is a prospect mentioned by the authors.

Date and Sato review the contributions of the mini-gut culture system in understanding stem cell niche. Various aspects of the self-renewal of intestinal stem cells are introduced. The authors then highlight the development of a mini-gut organoid culture system followed by translational application. Their application to other tissues is also discussed. The mini-gut organoids could in the future find application in clinical research, as suggested by the authors.

The review by Greenspan *et al.* deals with stem cells of the gonads. It is focused on *Drosophila* testes and ovarian niches as well as mammalian testis niches. These are discussed in detail along with illustrations that also show the signalling pathways. Various aspects such as stem cell self-renewal, stem cell competition and response to trauma are also reviewed. Like in several reviews related to stem cells, the authors also comment on how knowledge of such signalling may provide targets to future therapies.

Semrau and van Oudenaarden explore recent developments in the area of embryonic development. The model used is *in vitro* differentiation of embryonic stem cells. The review is extensive; covering aspects such as transcription factors involved, chromatin modification, gene regulation and signalling pathways. Emergence of quantitative breakthrough of regulatory processes such as gene regulatory networks is emphasized. There is extensive coverage of new tools employed in the area, particularly fluorescence imaging. Future directions include novel tools that would be employed in the coming years in the study of lineage decision making.

The review by Katta *et al.* deals with the response of organisms to force. In particular, this aspect in nematodes, fruit flies and laboratory mice is discussed. Specialized mechano-receptor cells, physical biology of mechanosensation and ionotropic receptors are discussed. Involvement of lipids and proteins in mechano-electrical transduction channel gating mechanism is highlighted. The authors have attempted to highlight the physics behind mechanosensation.

A review by Fernandez-Sanchez *et al.* also deals with mechanical aspects in animal development, evolution and tumorigenesis. Using *Drosophila* as a model, various aspects of translation of mechanical signals into biochemical signals are discussed. How proteins are involved in this process, as well as techniques employed are discussed with images from published work. The use of magnets and magnetic particles in imaging indicates the increasing application of physics in cell and development biology.

Regulation of gene expression has been extensively investigated over the years. A large amount of data has been generated with the help of rapid sequencing procedures. Thompson *et al.* review computational methods to study transcriptional gene regulatory networks. Major strategies used, and how regulatory genomics is analysed with regard to evolution are discussed in detail. The computational tools used have been summarized in a table that would be of interest to both experimental and computational biologists.

Transposable elements, referred to as TEs by Friedli and Trono, are abundant in the human genome. They have a long history beginning with their discovery by Barbara McClintock in 1950. Their importance in genetics is being increasingly evident. The review describes the developmental control of TEs and evolution of higher species. The authors discuss recent advances highlighting their influence on embryonic development.

Sommer and Mayer describe research on the nematode model, *Pristionchus pacificus*, more specifically an alternate larval stage in their review entitled 'Towards a synthesis of developmental biology of evolutionary theory and ecology'. They discuss various aspects of dauer stage, including the genetic basis of dauer development and pheromones that induce dauer formation. They discuss

how the *daf-12* gene regulates nematode and evolution.

Epigenetics and epigenetic mechanisms have been investigated extensively. Janke *et al.* review aspects of metabolism related to epigenetics. Aspects such as diet, and cell metabolism related to chromatin methylation are covered. Demethylation and the potential role of ascorbate and oncometabolites in regulating the action of specific dioxygenases are discussed. The fairly extensive review of various aspects of metabolism and epigenetics is highlighted in summary points.

Owusu-Ansah and Perrimon review aspects of stress signalling relayed between organs. They highlight these aspects in *Drosophila*, *Caenorhabditis elegans* and vertebrate systems. The review provides insights into how metabolic stress signals are transmitted from one tissue to other tissue and organs.

Various aspects of research on placenta have been the subject of intense research and interest to medical practitioners and researchers from time immemorial. Maltepe and Fisher review research in placental biology in relation to foetal and adult health. They review aspects of formation of placenta, what it does, including details of metabolism, the consequences of placenta failure and the future of placenta. They highlight the importance of paying attention to placental health.

Swarr and Morrisey discuss the developmental biology of lung endoderm. They present an overview of lung development, lung epithelial cell lineages, progenitor population, and transcriptional regulation of lung development and differentiation. Though medical and clinical aspects are not discussed extensively, the authors point out that basic research in this area would lead to better understanding of respiratory diseases that would aid in diagnostics and new therapies.

The review by Blasky *et al.* is in the area of epithelial tissue morphogenesis. Specifically, they discuss recent findings related to the mechanisms and regulation of *de novo* lumen, and formation *in vitro* and *in vivo*. They describe proteins involved in ensuring epithelial cell polarity. They also review *in vivo* lumen formation as described in *Drosophila*, *Caenorhabditis* and zebrafish.

Sauvanet *et al.* describe various aspects of microvilli on the apical domain

of epithelial cells. The review details structural and membrane components of microvilli. The structural biology of F-actin attachment to the plasma membrane and other proteins, and biochemistry of the process are discussed. The section on diseases should be of interest to cancer biologists and researchers working on clinical aspects of gastrointestinal diseases.

Yang and Mlodzik focus on aspects of planar cell polarity (PCP) in *Drosophila* and vertebrates. The genes involved in PCP are summarized in a table. Subsequent sections cover various aspects of how these genes operate. The authors show how *Drosophila* genetics has helped in understanding this process in vertebrates.

The review by Zollinger *et al.* details aspects of polarized membrane domains of axons and myelinating glia that establish these domains. The sections include the axon initial segment, the node of Ranvier and polarized membrane domains of myelinating glia.

The review by Catela *et al.* is related to neurobiology. Specifically, the authors discuss spinal circuits for motor control. The illustrations on patterning of neural tube, axon guidance of spinal cord, sensorimotor circuits, locomotor central pattern generators and circuits facilitating communication between the spinal cord and brain, give an excellent summary of the review. A sentence in the conclusion section on how genetics in *Drosophila* and zebra fish could provide important insights, highlights the usefulness of model systems in understanding the process in higher organism.

Lodato and Arlotta review aspects of structural and functional organization of the cerebral cortex. They cover broadly two areas – one related to tissue organization and neuronal composition of the neocortex, and the second on developmental generation of cortical neuronal subtypes. The illustrations give an excellent overview of the neocortex organization and neocortical interneurons. At the end, the authors indicate how the application of newer experiments has allowed better understanding of the area.

Monoallelic expression of olfactory receptors is the subject of review by Mohanan and Lomvardas. Apart from reviewing aspects of odorant detection, sorting of odorant information and olfactory receptors, they also discuss the role of chromatin and nuclear organization,

and questions that are yet to be answered in this area.

Lefebvre *et al.* review how cell type-specific dendrite patterns are formed during development. The section titles in the review summarize the aspects covered. The illustrations, starting with the diversity of dendrite morphology from Ramón Cajal's work in the late 1880s summarize various aspects of dendrite cell biology. The disease link to dendrites is highlighted in the concluding section, such as schizophrenia and autism.

Riccomagno and Kolodkin review restructuring of neural circuits by axon and dendrite pruning. Molecular mechanisms, role of glia, localized pruning and

pruning in human development and disease are discussed. The link between pruning and disease conditions is also discussed.

In summary, apart from detailing recent developments, perspectives and future directions, the reviews also highlight how newly emerging techniques can be applied to address important questions. This volume should be of particular interest to investigators who would like to venture into newer areas of cell and developmental biology, or are in search of newer methods and techniques to get better insights. In the Perspective article Wolpert mentions at the end, 'I find developmental journals rather disappoint-

ing as most of the articles are essentially just details with little general relevance'. In almost all the reviews related to developmental biology in this volume, the authors have attempted to bring out the relevance of extensive investigations and outlined unsolved problems, and have not documented just details.

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