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Molecular & cellular biology of platelet formation: Implications in health & disease, Harald Schulze, Joseph Italiano, editors (Springer International Publishing, Switzerland) 2016. 460 pages. Price: Not mentioned

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This book provides a comprehensive overview of the current knowledge and research potential in the field of platelet biogenesis, and the topics covered range from the basic cellular biology of megakaryocytes and platelets to the elucidation of genetic and molecular mechanisms of clinical disorders characterized by thrombocytopenia and the potential of gene engineering and platelet generation *in vitro* from stem cells. The contents of the book have been organized into four parts.

The first part, 'Megakaryocytes and Thrombopoiesis' has five chapters and begins with an overview of the process by which megakaryocytes form and release platelets into the circulation. It describes the commitment of haematopoietic stem cells to megakaryocytic lineage, morphological development of megakaryocytes, polyploidization through endomitosis, cytoplasmic maturation and the role of microtubules and actin in proplatelet formation and platelet release. It is followed by two closely related chapters where a detailed review of transcription factors and signalling pathways involved in the process in normal and disease situations is presented. The core transcription factors function in a networked and complex manner to generate a megakaryocyte transcription factor 'enhanceosome' complex and some of these factors have an overlap with haematopoietic stem cell transcriptional regulators. The association between mutations in genes encoding megakaryocytic transcription factors and human thrombopoiesis and predisposition to leukaemia is also reviewed. Chapter 4 gives a good description of the haematopoietic niches – osteoblastic niche and vascular niche and the role of matrix proteins which form a three-dimensional network that supports the directed migration towards the endothelial barrier. The bone marrow vascular niche has served as a model for creating bioreactors for *in vitro* megakaryopoiesis and platelet production. In addition to the bone marrow niche, evidence is emerging that megakaryocytes are retained in the pulmonary microvasculature and may contribute to platelet release into the circulation. Another intriguing phenomenon discussed is the circulating preplatelet which is discoid in shape, larger than the

normal platelet, but retains the capacity to elongate and form proplatelets in the circulation.

The second part of the book, 'Platelet Biology: Signals and Functions' has six chapters (chapter 6-11). Chapter 6 addresses the current knowledge as well as unanswered questions on the functional platelet contents – alpha and dense granules and the platelet membrane systems and how they participate in a broad array of functions including haemostasis, inflammation, angiogenesis, wound repair and innate immunity. The next two chapters focus on signalling pathways regulating platelet production and functions. Role of thrombopoietin, its receptor Mpl, a tyrosine kinase-linked protein and the intracellular signalling pathways for optimum megakaryopoiesis are discussed in chapter 7. It is recognized that a different set of signalling events directs platelet production from megakaryocytes and subsequent release of platelets into the circulation, this developmental – functional switching is also highlighted. The role of RAP (receptor-associated protein) proteins (small GTPases)-based signalling in important platelet functions such as integrin activation, thromboxane A_2 generation, granule release and clot retraction is given in detail in chapter 8. RAP proteins affect signalling pathways in megakaryocytes also, but its exact role needs to be established. Chapter 9 addresses the role of apoptotic mechanisms in ensuring a dynamic balance between platelet production and consumption.

The haemostatic functions of platelets are well known. Chapter 10 deals with the non-haemostatic functions under two broad categories: (*i*) 'platelets versus pathogens', and (*ii*) 'platelet-target cell communication'. In the former category, the role of platelets in pathogen reduction, retainment and elimination as well as platelet clearance by cross-reacting antibodies is discussed. The latter category includes platelet proinflammatory soluble mediators, microparticles and immune modulators. Basic and pre-clinical research is heavily dependent on appropriate animal models. Chapter 11 elaborates on various mouse models to study platelet production and function.

Part III of the book addresses the broad areas of 'Platelets in Health and Disease' and contains six chapters (chapter 12–17). It begins with a chapter which brings out major differences between foetal/neonatal megakaryopoiesis as compared to adults in terms of megakaryocyte ploidy and proliferative potential and the probable molecular mechanisms which give rise to these differences. Platelet hypofunctionality and its implications in term and preterm neonates is also discussed. The prothrombotic function of platelets in the initiation and progression of ischaemic stroke has been recognized since long. Less well known is the emerging role of platelets in reperfusion injury and the potential for the novel therapeutic approach. Chapter 13 describes the importance of mechanisms involved in early platelet adhesion and activation in the pathophysiology of acute ischaemic stroke. The next two chapters focus on inherited and acquired thrombocytopenias, respectively. Chapter 14 gives insight into genetic defects in megakaryopoiesis and platelet biogenesis in the inherited thrombocytopenias and the potential of genome-wide and whole-exome sequencing for screening and discovery of further genetic defects. Chapter 15 outlines various causes of acquired thrombocytopenias with focus on immune mechanisms of destruction. The next chapter focuses on how certain viruses modulate megakaryopoiesis and platelet production and may give rise to life-threatening thrombocytopenias as seen in the viral haemorrhagic fevers. In the last chapter of Part III, an overview of diagnostic tests for inherited and acquired platelet disorders is provided along with the challenges involved in testing and interpretation.

Part IV addresses 'Future Perspectives for Platelet Biogenesis' and contains three chapters (18–20). Chapter 18 reviews the genetic and functional defects in Wiskott Aldrich syndrome. It also describes the supportive therapies, haematopoietic stem cell transplantation and gene therapy in this syndrome. It also weighs the option of gene engineering – the true mutational correction instead of retro/lentiviral gene insertion and the consequent risk of genotoxicity. Chapter 19 gives information on the current status and challenges in generating red blood cells and platelets from induced pluripotent stem cells (iPSCs). The generation of iPSCs has intensified interest and research in the field of stem cell therapies as they allow the conversion of any cell in the body to another type and thus make autologous red cell and platelet production possible. The last chapter of the book describes strategies for gene modification of megakaryopoiesis and platelets. Some of the established systems are knock out mouse models, transgenic models and knock-in mouse models, which are largely used to study gene defects. For functional studies on megakaryopoiesis and platelet production, insight is given on novel viral vectors

for lineage-specific expression to reflect biological situations.

Platelet biogenesis and biology is a rapidly advancing field. Understanding of the haemostatic and non-haemostatic functions of platelets has important clinical implications and research questions in a wide variety of clinical disorders for the insights into pathophysiology, diagnosis and interventions. The chapters provide in-depth and updated information and have been contributed by renowned international experts. This book will be useful to all experts engaged in or planning basic and pre-clinical research in the areas of platelet biology, stem cell therapies and gene manipulations. Chapters with clinical, diagnostic and therapeutic applications would be of interest to the neonatologists, haematologists, transfusion medicine specialists and pathologists. Overall, the book contains valuable information on all the important aspects of platelet biology in one place and provides direction for future research in this field.

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