Part VIII
Conduction System and Arrhythmia

Perspective

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One of the fascinating and essential characteristics of the cardiovascular system is that it functions automatically without requiring conscious input. In other words, the normal heart beats regularly and spontaneously regardless of whether or not the individual is thinking about it. Electrical impulses arise in the sinoatrial node, pass through the atria, pause at the atrioventricular node, and then are distributed in a tightly orchestrated spatial and temporal manner to the ventricles for coordinated and effective pumping activity. This elegantly synchronized process repeats itself over and over approximately three billion times during the average human life. Even minor disruptions in this normal process can have devastating consequences. Considerable morbidity and mortality result from abnormalities in intrinsic cardiac pacemaker activity and conduction of impulses. Congenital and acquired arrhythmias remain a significant health problem. Consequently, a clear understanding of the molecular and cellular processes involved in the formation and maintenance of normal electrical signaling in the heart has profound implications for human cardiovascular health and disease. Furthermore, it is likely that insights into the developmental processes involved in building a cardiac conduction system will likely have implications for understanding fundamental biology applicable to other organ systems.

This part reviews and summarizes the current state of understanding of the development of spontaneous pacemaker activity and the cardiac conduction system. Christoffels’ group reviews the signaling pathways and molecules involved in the

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development of the cardiac conduction system. The authors emphasize the importance of understanding the three-dimensional architecture of genomic loci to provide insight into the regulation (normal and abnormal) of gene expression. Mikawa and colleagues identify and characterize a previously unrecognized source of cells that are destined to become pacemaker cells, even before cardiac morphogenesis begins. These results will likely lead to better understanding of the mechanisms involved in pacemaker cell differentiation, which in turn may ultimately have therapeutic implications. Additional information on the mechanisms, molecular signals, and pathways involved in specification of cell fate are provided by Asai et al. and by Morikawa et al. Taken together, the papers presented in Part VIII provide an interesting, informative, and elegant overview of the current understanding of pacemaker and conduction system development. Moreover, they provide a road map for future investigations into this essential and fundamental biological process.