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Innervation of developing and adult organs

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I am delighted to have the opportunity to edit this Special Issue on the peripheral nervous system, which focuses on the nerves that innervate internal organs, i.e., the "autonomic nervous system," rather than the voluntary motor system (striated muscle). The autonomic nervous system is fundamentally responsible for regulation of all other tissues outside of the central nervous system (brain and spinal cord). However, despite its complexity and sophistication, the autonomic nervous system is too frequently described in over-simplified catchphrases such as "fight-or-flight" (sympathetic) and "rest-and-digest" (parasympathetic). Therefore a priority for this Special Issue is to introduce the topic in a way that does justice to this intriguing area of neuroscience. The outline provided by Gibbins (p. 169) does just this and I urge readers to peruse this Review first, irrespective of your specific area of interest. As you will see as you progress through each of the elegant reviews in this issue, there are numerous reasons to develop a thorough understanding of the autonomic nerve supply of a given organ or tissue of interest, whether it be from the perspective of development, regeneration or disease.

Most obviously, we think of nerves as being necessary for an organ to function—in some cases being essential for the organ to function at all and, in others, for the organ to function appropriately to a changing circumstance. On this basis alone, a priority of organ regeneration or transplantation research should be to simultaneously optimize reconnection of the nerve supply. This means not only promoting reinnervation but also promoting appropriate reinnervation. Peripheral nerves have rather a nice habit of growing along blood vessels, so there is a very good chance that a new piece of tissue will be found by nerves—but ensuring that the correct number and type of connections are made may provide the bigger challenge. Although great advances have been made in understanding how tissue-derived neurotrophic and neural guidance factors drive axon growth and determine its directionality during development, there are still many gaps to fill. In this issue, intriguing insights are provided into the developing innervation of the heart (Hasan, p. 176) and airways (Aven and Ai, p. 194). Probing the activities and mechanisms of the developing nervous system is of course a worthy endeavor in its own right, but an obvious extension is to consider how developmental cues and signals may potentially be adopted to drive growth in the adult system, either after nerve damage or in the case of reconnecting with a regenerated or transplanted tissue. In yet another context, and as outlined for various aspects of cardiac pathologies by Hasan, some of these cues, and potential imbalance between them, may also be involved in driving disease states.

Beyond the classical concept of neural transmission to alter tissue function, there are other ways in which the nervous system and the organs interact and communicate. The review by Ferreira and Hoffman (p. 199) on autonomic innervation of salivary gland illustrates the impact that autonomic nerves have on tissue growth during initial organogenesis and regeneration. Taken further, this raises the question of how autonomic nerves may impact on tissue growth and organ responses during aging, or under conditions of abnormal tissue growth, such as in cancer. These aspects are discussed by White et al. (p. 206) in the context of the prostate gland. A further aspect of autonomic innervation that is insufficiently understood but critical for homeostasis is its interactions with the immune system. The review by Costes et al. (p. 216) summarizes neural-immune interactions in the digestive tract. This includes discussion of how the gut immune system impacts on the local enteric nervous system as well as on the extrinsic neurons of sympathetic and parasympathetic systems—and ultimately to impact on brain function. Finally, it is frequently forgotten that for organs to be controlled properly they not only need an intact and appropriately behaving autonomic (i.e., motor) system, but also require healthy, functional sensory nerves. Typically these travel to the organs with the motor nerves but can have quite different growth and targeting mechanisms. The review by Eastham and Gillespie (p. 224) adds an intriguing dimension to this story, by considering how motor and sensory activity are interlinked and, specifically, how motor activity may impact on sensory function, establishing powerful peripheral feedback mechanisms.

Together these timely reviews provide a snapshot of organ innervation in its many contexts and in various life stages—development, healthy adult function, aging and disease. I hope that this issue will lead to further appreciation of the importance of organ innervation in the developing and adult system, and drive new collaborations to solve the puzzles embedded within it.

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