GLIA 56:1479–1480 (2008)

INTRODUCTION

Recent years have seen a major expansion in our understanding of Schwann cell biology. A particular thrust has been in pinpointing the molecular mechanisms and pathways that control Schwann cell development, myelination and myelin maintenance, and in defining the molecules that mediate the interactions between Schwann cells and their environment, be it axons, extracellular matrix, connective tissue cells or macrophages. This Special Issue of Glia brings together articles that analyse major areas of recent progress and current significance, written by many of the foremost researchers in this field.

Important advances have been made in our understanding of the development of both Schwann and satellite glial cells from the neural crest, defining the key developmental steps, revealing the developmental potential of cells at different stages of the lineage, and determining the differences between Schwann and satellite cells. Progress has also been made in understanding some of the signals that underlie either lineage progression or lineage choice and these issues are discussed in the article by Woodhoo and Sommer. An emerging theme from these and other studies is the realisation that the same signals may be used at different cellular stages of the lineage to achieve different outcomes, emphasising the importance of the cellular context in controlling the interpretation of the signal(s). This is particularly well illustrated in the case of the axonal signal neuregulin. The multiple actions of this factor at different stages of the lineage are discussed in several articles, and treated in depth by Birchmeier and Nave. Schwann cell development is also critically controlled by the extracellular matrix. Recent work has revealed the importance of specific matrix components and matrix receptors, i.e. integrins and dystroglycans, in Schwann cell biology as reviewed by Chernousov and colleagues. In particular, matrix signals combine with signals from axons to control the complex process of ensheathment and radial sorting of axons by myelinating and non-myelinating Schwann cells via small intracellular GTPases. This rapidly moving field is critically reviewed in the article by Feltri, Suter and Relvas.

Small diameter axons are not myelinated but rather are ensheathed by non-myelinating (Remak) Schwann cells. Other important categories of Schwann cells that do not make myelin are found in association with motor and sensory nerve terminals and with neuronal cell bodies. Thus it is too often ignored that myelinating cells are in fact a Schwann cell sub-population, albeit an important and prominent one. The role of Schwann cells that do not make myelin is highlighted by Griffin and Thompson. Salzer, Brophy and Peles discuss myelinated fibers and describe our current understanding of the axonal and Schwann cell molecules that contribute to setting up and maintaining their amazingly compartmentalised and regionally specialised structure. Although we know little about transcriptional control of differentiation of non-myelinating Schwann cells, progress in analysing transcriptional mechanisms that drive myelination has been impressive as discussed in the article by Svaren and Meijer.

The idea that myelination is controlled not only by forward drivers of the myelination program but by active negative regulators of the process, that potentially push cells towards demyelination, is discussed by Jessen and Mirsky. Such negative regulators of myelination are likely to be important for controlling the remarkable dedifferentiation of Schwann cells in injured nerves, a process required for nerve repair. It is also possible that they are relevant for the demyelination seen in inherited peripheral neuropathies. Scherer and Wrabetz describe these conditions and the enormous advances in understanding the molecular mutations that underlie them, while the importance of interac-

DOI 10.1002/glia.20779
Published online 19 September 2008 in Wiley InterScience (www.interscience.wiley.com).

tions between Schwann cells and macrophages both in these neuropathies and in nerve injury is emphasised by Martini and colleagues. Another aspect of nerve pathology and aberrant differentiation is seen in the malignant nerve sheath tumours of neurofibromatosis type 1. This topic is analysed by Carroll and Ratner who discuss evidence that these tumours arise from an early cell in the lineage, rather than Schwann cells themselves, and argue that another cell type, the mast cell, interacts with these cells to generate the nerve pathology seen in neurofibromatosis type 1.

The selection of topics presented here span a broad range, although there will inevitably be some issues that might have been more fully explored had space permitted. We hope that this collection will provide a progressive, accessible and exciting update on Schwann cell biology that will be useful to experts and amateurs alike. We would like to thank all those who have contributed their scholarship, time and expertise to this endeavour.

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