

Satellite glial cells: more than just ‘rings around the neuron’

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When most neuroscientists discuss peripheral glia, it is usually about Schwann cells. However, the peripheral nervous system includes a large number of ganglia – sensory and autonomic – which contain specialized glial cells termed ‘satellite glial cells’ (SGCs). (The enteric nervous system has its own specialized glial cells.) SGCs surround the neurons and form a tight envelope around them. In tissue sections SGCs appear like a ring around the neuron, which is mostly very thin and occasionally can even be invisible under the light microscope. These cells could be regarded as a special type of Schwann cells, but their development, and especially their unique organization with respect to the neurons, make them a distinct cell type. The collection of articles in this issue is not meant to be the definitive word on SGCs. We are currently several years away from having a comprehensive understanding of these cells. Rather, these articles can serve as an introduction to this topic and for pointing to potentially important research directions.

In the first article Pannese (2010) describes the ultrastructure of SGCs. That this article will open this issue is appropriate at least for two reasons. First, Prof. Pannese has pioneered the research on SGCs, and his first article on this topic appeared over 50 years ago (Pannese, 1956). His 1981 monograph on SGCs is a must reading for anyone interested in this field, and is a classic of beauty, precision and clarity (Pannese, 1981). Second, structure is the best way to approach any study in biology because structure gives us important clues on function. Pannese’s article emphasizes the unique arrangement of SGC as a tight sheath around the neurons, which results in the formation of a discrete unit consisting of a neuronal cell body and the SGCs surrounding it. This organization distinguishes SGCs from Schwann cells and astrocytes, and has obvious functional implications, because even if the molecular and pharmacological properties of SGCs were similar to those of these other cell types, the functions of SGCs are very likely to be unique due to this special arrangement. Pannese also highlights the striking morphological changes that SGCs undergo after nerve injury, which include hypertrophy and the formation of bridges with other SGCs, which contain numerous newly formed gap junctions. Obviously, SGCs can sense injury-related changes in sensory neurons.

Garrett and Durham (2010) investigated the postnatal temporal and spatial morphological changes in trigeminal ganglia that lead to formation of neuron–SGC units described by Pannese. They found that the expression of the inwardly rectifying K^+ channel Kir4.1, the vesicle docking protein SNAP-25 and the neuropeptide CGRP correlate with the formation of these units.

Thippeswamy and his co-workers (e.g. Thippeswamy and Morris, 1997) were among the first to report the presence of two-way neuron–SGC chemical signaling, which involves the secretion nitric oxide (NO) from neurons. This NO stimulates SGCs to produce growth factors that have a

neuroprotective influence. In their article, Bradman *et al.* (2010) summarize their own work and that of others that demonstrate the NO-dependent bidirectional communications between neurons and SGCs.

Ng *et al.* (2010) report that SGC–neuron interactions include influence on neurite retraction in a subpopulation of dorsal root ganglia (DRG) neurons in culture. This work suggests that non-neuronal cells (presumably SGCs) can control neuronal characteristics in sensory ganglia.

The pharmacology of SGCs is just beginning to be unraveled. Currently, the only thoroughly characterized receptor type in these cells is the purinergic P₂, which responds to ATP and related nucleotides. Villa *et al.* (2010) review the available information of the response of SGCs to ATP, and conclude that these cells display a variety of P₂ receptors. It appears that SGCs can respond to ATP via both P₂Y (metabotropic) and P₂X (ionotropic) receptors, with the P₂Y being dominant. Interestingly, there is evidence for plasticity of P₂ receptors under injury.

Calcium waves have been proposed as an important means for information transmission in the astrocyte network, and are mediated by ATP release and subsequent activation of P₂ purinergic receptors, and also by gap junctions. Because SGCs have P₂ receptors and are also coupled by gap junctions, they have the potential to sustain calcium waves. This is now demonstrated by Suadicani *et al.* (2010) and serves as another evidence for the similarity between SGCs and astrocytes. This article also provides evidence that SGCs can release ATP, which is one of the main ‘gliotransmitters’.

Gu *et al.* (2010) summarize a series of studies done by L.Y. Huang and her co-workers. This series started with an innovative work showing that somata of sensory neurons can release substance P by Ca^{2+} -dependent exocytosis (Huang and Neher, 1996). Later work by Huang’s group showed that these neurons can also release ATP, to which SGCs respond by releasing ATP and the cytokine TNF α . These mediators, in turn, act on the neurons, causing profound functional changes in them. Thus, there is an elaborate bidirectional communication between these two cell types, which can have far-reaching implications for signaling in sensory ganglia.

The article by Ohara *et al.* (2010) describes how recent progress in the understanding of the properties of SGCs can help in developing pain therapies. It has been shown previously that nerve damage increases gap junction-mediated coupling between SGCs, which may contribute to chronic pain (Hanani *et al.*, 2002). Here, Ohara *et al.* (2010) demonstrate that knocking down the gap junction protein connexin 43 reduced pain in a rat model. They further report that SGCs can be exploited in other ways for pain therapeutic purposes.

Dubový *et al.* (2010) describe molecular changes that take place in SGCs in DRG following unilateral sciatic nerve injury, which induces neuropathic pain. They observed an increase in

the level of the proinflammatory cytokine IL-6 and its receptor (IL-6R) in SGCs in the ipsilateral DRG. Interestingly, SGCs in the contralateral DRG also displayed augmented IL-6 (but not IL-6R). These findings indicate that SGCs in ganglia affected by the injury and also in ganglia not affected by it become activated by the injury. This suggests that SGCs are sensitive to both local signals and to systemic ones.

As mentioned above, SGCs are present not only in sensory ganglia. In fact, there is a large population of these cells in all sympathetic and parasympathetic ganglia, which are part of the peripheral autonomic nervous system. However, research on SGCs in these ganglia has lagged behind that on SGCs in sensory ganglia. The article by Hanani *et al.* (2010) highlights some similarities between SGCs in sympathetic ganglia and those in sensory ganglia. Because neurons in autonomic ganglia (unlike neurons in sensory ganglia) receive synapses, SGCs in these ganglia are likely to possess some special characteristics. The potential influence of SGCs on synaptic transmission in autonomic ganglia is a promising avenue for future research.

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