Role of connexin-based gap junction channels in communication of myelin sheath in schwann cells

Cisterna B.A.

Arroyo P.

Puebla C.

Peripheral nerves have the capacity to conduct action potentials along great distances and quickly recover following damage which is mainly due to Schwann cells (SCs), the most abundant glial cells of the peripheral nervous system (PNS). SCs wrap around an axonal segment multiple times, forming a myelin sheath, allowing for a significant increase in action potential conduction by insulating the axons. Mature myelin consists of compact and non-compact (or cytoplasmic) myelin zones. Non-compact myelin is found in paranodal loops bordering the nodes of Ranvier, and in the inner and outermost cytoplasmic tongues and is the region in which Schmidt-Lanterman incisures (SLI; continuous spirals of overlapping cytoplasmic expansions within areas of compact myelin) are located. Using different technologies, it was shown that the layers of non-compact myelin could be connected to each other by gap junction channels (GJCs), formed by connexin 32 (Cx32), and their relative abundance allows for the transfer of ions and different small molecules. Likewise, Cx29 is expressed in the innermost layer of the myelin sheath. Here it does not form GJCs but colocalizes with Kv1, which implies that the SCs play an active role in the electrical condition in mammals. The critical role of GJCs in the functioning of myelinating SCs is evident in Charcot-Marie-Tooth disease (CMT), X-linked form 1 (CMTX1), which is caused by mutations in the gap junction protein beta 1 (GJB1) gene that codes for Cx32. Although the management of CMT symptoms is currently supportive, there is a recent method for targeted gene delivery to myelinating cells, which rescues the phenotype in KO-Cx32 mice, a model of CMTX1. In this mini-review article, we discuss the current knowledge on the role of Cxs in myelin-forming SCs and summarize recent discoveries that may become a real treatment possibility for patients with disorders such as CMT.

Charcot-Marie-Tooth disease

CMTX1

Connexins

Gap junction channels

Myelin sheath

Schmidt-Lanterman incisure

connexin 29

connexin 32

connexin 43

connexin 46

gap junction protein

gap junction protein beta 1

maltose binding protein

myelin

peripheral myelin protein 22

potassium channel Kv1.1

unclassified drug

action potential

central nervous system

chromosome Xq

demyelinating neuropathy

demyelination

electrostimulation

foot malformation

gap junction

gene mutation

gene targeting

gene therapy

hereditary motor sensory neuropathy

human

immunocytochemistry

immunofluorescence test

immunogold labeling

motor performance

muscle atrophy

muscular dystrophy

myelin sheath

nerve conduction

nerve conduction velocity

nerve degeneration

nonhuman

perception deafness

peripheral neuropathy

protein expression

Schwann cell

sensory nerve cell

Short Survey

X chromosome linked disorder