

## Local regulation of lipid metabolism in peripheral nerves

Chrast R, Burrola P, Smit AB\*, Lemke G, Verheijen MHG\*

Molecular Neurobiology Laboratory, The Salk Institute, La Jolla, USA, \*Dept of Molecular and Cellular Neurobiology, Vrije Universiteit, Amsterdam

We have comprehensively analyzed gene expression during peripheral nerve development by performing microarray analyses of premyelinating, myelinating, and post-myelinating mouse sciatic nerves, and have generated a database of candidate genes to be tested in mapped peripheral neuropathies. Unexpectedly, we identified a large cluster of genes that are (a) maximally expressed only in the mature nerve, after myelination is complete, and (b) tied to the metabolism of storage (energy) lipids. Many of these late-onset genes are expressed by adipocytes, which we find constitute the bulk of the epineurial compartment of the adult nerve. However, several such genes, including *SREBP-1*, *SREBP-2* and *Lpin1*, are also expressed in the endoneurium. We find that *Lpin1* null mutations lead to lipoatrophy of the epineurium, and to the dysregulation of a battery of genes required for the regulation of storage lipid metabolism in both the endoneurium and peri/epineurium. Together with the observation that these mutations also result in peripheral neuropathy, our findings demonstrate a crucial role for local storage lipid metabolism in mature peripheral nerve function, and have important implications for the understanding and treatment of peripheral neuropathies that are commonly associated with metabolic diseases such as lipodystrophy and diabetes.

Mark H.G. Verheijen, Department of Molecular and Cellular Neurobiology, Research Institute Neurosciences, Faculty of Earth and Life Sciences, Vrije Universiteit, De Boelelaan 1085, 1081 HV Amsterdam, The Netherlands. t 020 444 7120, e-mail [mverhe@bio.vu.nl](mailto:mverhe@bio.vu.nl)

Neuroscience poster session 1