# Review of: "Imbalance of Neuregulin1-ErbB2/3 signaling underlies altered myelin homeostasis in models of Charcot-Marie-Tooth disease type 4H"

Bogdan Beirowski[1]

1 State University of New York at Buffalo

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This is an interesting manuscript describing the discovery of dysregulated Nrg1/ErbB2/3 signaling in peripheral nerves of mutants lacking FGD4/FRABIN in Schwann cells (SCs). This mouse mutant recapitulates important features of the peripheral neuropathy observed in patients with CMT4H. The authors generate a mouse model with deletion of FGD4 in SCs which they use for biochemical and transcriptional analyses as well as for production of neuron/SC co-cultures. The co-cultures from these animals display focal hypermyelination in vitro characteristic of the CMT4H phenotype. To gain insight in the molecular mechanisms underlying this phenotype they carry out a screening experiment to identity interactors of FGD4, and find SNX3 as a potential binding partner. This molecule appears to be involved in the regulation of endocytic trafficking, and the authors implicate this finding in aberrant endocytic trafficking of ErbB2/3 in this neuropathy model. Accordingly, the authors demonstrate dysregulated downstream mTOR signaling, which appears to be counteracted by Niacin (Vitamin B3) treatment (Niacin is a NAD precursor). Overall, this study provides a conceptual advance for our understanding of CMT4H neuropathy. The figures appear to support the conclusion of the study. However, this reviewer had no access to the supplementary figures.