

Insights: Publications

NF1-dependent disruption of the blood-nerve-barrier is improved by blockade of P2RY14

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The blood-nerve-barrier (BNB) that regulates peripheral nerve homeostasis is formed by endoneurial capillaries and perineurial cells surrounding the Schwann cell (SC)-rich endoneurium. Barrier dysfunction is common in human tumorigenesis, including in some nerve tumors. We identify barrier disruption in human NF1 deficient neurofibromas, which were characterized by reduced perineurial cell glucose transporter 1 (GLUT1) expression and increased endoneurial fibrin(ogen) deposition. Conditional Nf1 loss in murine SCs recapitulated these alterations and revealed decreased tight junctions and decreased caveolin-1 (Cav1) expression in mutant nerves and in tumors, implicating reduced Cav1-mediated transcytosis in barrier disruption and tumorigenesis. Additionally, elevated receptor tyrosine kinase activity and genetic deletion of Cav1 increased endoneurial fibrin(ogen), and promoted SC tumor formation. Finally, when SC lacked Nf1, genetic loss or pharmacological inhibition of P2RY14 rescued Cav1 expression and barrier function. Thus, loss of Nf1 in SC causes dysfunction of the BNB via P2RY14-mediated G-protein coupled receptor (GPCR) signaling.

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