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The role of Purkinje cell-derived VEGF in cerebellar astrogliosis in Niemann-Pick type C mice

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ABSTRACT

Niemann-Pick type C disease (NP-C) is a fatal neurodegenerative disorder caused by a deficiency of *NPC1* gene function, which leads to severe neuroinflammation such as astrogliosis. While reports demonstrating neuroinflammation are prevalent in NP-C, information about the onset and progression of cerebellar astrogliosis in this disorder is lacking. Using gene targeting, we generated vascular endothelial growth factor (VEGF) conditional null mutant mice. Deletion of VEGF in cerebellar Purkinje neurons (PNs) led to a significant increase of astrogliosis in the brain of NP-C mice in addition to the loss of PNs, suggesting PN-derived VEGF as an important factor in NP-C pathology. Moreover, replenishment of VEGF in neurons improved brain pathology in NP-C mice. Overall, our data provide a new pathological perspective on cerebellar astrogliosis in NP-C and suggest the importance of VEGF as a therapeutic target for this disease.