Functional role for Wnt/β–Catenin for remyelination (failure) in MS

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Research question and background

Multiple sclerosis (MS) is the most frequent demyelinating disease of the human CNS and one of the leading causes for permanent disability in young adults. So far, no treatment strategies exist to prevent the progressive disease phase. Underlying cause for permanent neurological disability is axonal loss and damage. Demyelination, a key characteristic of MS, increases axonal vulnerability to immune mediated damage and leads to lack of trophic support. Differentiation of oligodendroglial progenitors and remyelination, an endogenous repair process, is limited in chronic MS lesions. Activation of the wnt/ß-catenin pathway blocks the differentiation of oligodendrocytes in vitro and remyelination in animal models suggesting that this pathway might contribute to oligodendroglial differentiation block observed in MS. The aims of the study are to analyze and correlate the presence and absence of different members of the Wnt/ß-catenin pathway with presence of remyelination in MS lesions.

Methods and tissues used

We received 8 tissue samples from 8 different patients containing 14 lesions with different inflammatory and demyelinating activity. We performed conventional (HE) and immunohistological staings (CD68, CD45, MBP) as well as Western blots.

Results and conclusion

We stained tissue sections from all tissue blocks to locate the lesions and extracted proteins from 7 lesions (3 shadow plaques, 3 (chronic) active lesions, 1 inactive lesion) as well as from NAWM of all patients. We performed Western blots for β-catenin and observed a marked upregulation of β-catenin in all shadow plaques compared to NAWM. In contrast, in active and inactive lesions total β-catenin levels were comparable to levels in NAWM. Active β-catenin was upregulated in shadow plaques whereas phosphorylated β-catenin was mostly found in the NAWM. To further study the expression and nuclear localization of β-catenin in oligodendrocytes we established proximity ligation assays (PLA). Using PLA we could demonstrate a decrease of nuclear β-catenin during the differentiation of primary murine oligodendrocytes. Our results demonstrate the presence of β-catenin in MS lesions with different demyelinating and inflammatory activity and in differentiating oligodendrocytes. Further studies are required to determine the cellular source and location of β-catenin in MS lesions.