

NG2 modulates tight junction integrity in brain microvessels

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In this work we addressed the putative role of NG2 in the control of endothelial tight junction (TJ) dismantling, blood-brain barrier (BBB) breakdown, and leukocyte transendothelial migration in inflammatory/degenerative neurological disorders. During CNS development two cell types are known to express the transmembrane proteoglycan NG2, namely oligodendrocyte precursors (OPCs) and microvessel-associated pericytes. In both cell types expression of NG2 is a hallmark of cell activation in response to signalling molecules, mainly growth factors, and via interaction with ECM components. According to our previous results in a chronic model of experimental autoimmune encephalomyelitis (EAE) induced in C57BL/6 mice, NG2-expressing OPCs react to demyelination by an increasing proliferation and this phenomenon seems to be promoted by the interactions of NG2 with naked axons. In this condition, a dismantled TJ-induced microvessel leakage is associated with an increased number of NG2-bearing pericytes and perivascular OPCs. By comparing these data with observations made in naïve and EAE NG2 null mice, which show a constitutive alteration of the TJ staining pattern apparently restored during EAE, a key role is disclosed for NG2 in the regulation of the dynamics of TJ components and how these are remodelled during pathological conditions. Our evidence is that loss of NG2 causes a reduced deposition of collagen type IV of the vascular basement membrane and a parallel reduction in collagen type VI microfilaments associated with this membrane. This in turn causes a disruption of the pericyte-endothelial cell interactions that indirectly modulate TJ integrity.

Keywords: Experimental autoimmune encephalomyelitis, NG2 null mice, blood-brain barrier, collagens IV/VI, confocal microscopy