Matrix metalloproteinase 9

Matrix metalloproteinase 9 (MMP-9), also known as 92 kDa type IV collagenase, 92 kDa gelatinase or gelatinase B (GELB), is a matrixin.

In humans the MMP9 gene encodes for a signal peptide, a propeptide, a catalytic domain with inserted three repeats of fibronectin type II domain followed by a C-terminal hemopexin-like domain.

Histological investigations have shown that disruption of the blood brain barrier (BBB) is well correlated with the degradation of collagen IV, a major component of the BBB [1]. Among other basal lamina proteins, collagen IV is often degraded by metalloproteinase-9 (MMP-9).

Animal and clinical studies have identified MMP-9 overexpression as a key factor responsible for the development of vasogenic edema, and deletion of Matrix metalloproteinase 9 (MMP-9) is correlated with significantly less brain edema and better neurological recovery in SAH mice models [2].

SAH was induced by endovascular perforation in adult male mice. The following 3 experiments were devised: (1) mice underwent magnetic resonance imaging at 24 h after SAH and were euthanized to determine BBB disruption and MMP-9 activation in white matter; (2) to investigate the role of MMP-9 in BBB disruption, lesion volumes on magnetic resonance imaging were compared between wild-type (WT) and MMP-9 knockout (MMP-9-/-) mice at 24 h after SAH; (3) WT and MMP-9-/- mice underwent magnetic resonance imaging at 1 and 8 days after SAH to detect time-dependent changes in brain injury. Brains were used to investigate myelin integrity in white matter.

In WT mice with SAH, white matter showed BBB disruption (albumin leakage) and T2 hyperintensity on magnetic resonance imaging. MMP-9 activity was elevated at 24 h after SAH. MMP-9-/- mice had less white matter T2 hyperintensity after SAH than WT mice. At 8 days after SAH, WT mice had decreased myelin integrity and MMP-9-/- mice developed less white matter injury.

SAH causes BBB disruption and consequent injury in white matter. MMP-9 plays an important role in those pathologies and could be a therapeutic target for SAH-induced white matter injury [3].

1)
Egashira Y, Zhao H, Hua Y, Keep RF, Xi G. White matter injury after subarachnoid hemorrhage: role of blood-brain barrier disruption and matrix metalloproteinase-9. Stroke. 2015;46(10):2909–2915.
2), 3)
Egashira Y, Zhao H, Hua Y, Keep RF, Xi G. White Matter Injury After Subarachnoid Hemorrhage: Role of Blood-Brain Barrier Disruption and Matrix Metalloproteinase-9. Stroke. 2015 Oct;46(10):2909-15. doi: 10.1161/STROKEAHA.115.010351. Epub 2015 Sep 15. PubMed PMID: 26374478; PubMed Central PMCID: PMC4589516.