Functions of Pericytes in Ischemic Stroke

Half-time review of Michaela Roth

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Abstract

Background: Stroke is one of the leading causes of death worldwide, and beyond acute thrombolysis, there is currently no treatment available to reduce the damage or enhance the recovery after stroke. Therefore, there is an urgent need for new therapeutic approaches based on the full understanding of the underlying mechanisms after ischemic stroke. The acute phase after ischemic stroke, characterized by the breakdown of the blood-brain-barrier (BBB) and neuronal cell death, is followed by the chronic phase, where several repair mechanisms are induced. Pericytes, perivascular cells embedded within the basal lamina, are suggested to play an important role in the acute and chronic phase after stroke. Brain pericytes express Regulator of G-protein signaling 5 (RGS5), a protein that is upregulated after stroke when pericyte detach from the vessels. However, the exact role of RGS5 in the pericyte response and its impact on the different stages of stroke remains unknown. Further, the temporal sequence of events after stroke and how the BBB develops after stroke is still under debate.

Research question/Method: We investigate how the loss of RGS5 in pericytes impacts on (i) BBB integrity and neurovascular dysfunction, (ii) angiogenesis and (iii) scar formation after stroke as well as establish a timeline of vascular changes associated with BBB breakdown. We use a permanent middle cerebral occlusion model to mimic stroke in RGS5 knock-out and wildtype mice and analyze different time-points after stroke.

Preliminary results: In the acute phase, loss of RGS5 in pericytes resulted in higher number of pericytes, which was associated with a decrease in BBB breakdown and reduced neuronal death. In the chronic phase, loss of RGS5 lead to increased angiogenesis, higher pericyte coverage and less leakiness of the newly formed blood vessels and reduced the infiltration of peripheral monocytes. Further, preliminary data suggest that loss of RGS5 affects scar formation.

Significance: Our studies identify RGS5 as a modulator of pericyte-related BBB preservation, angiogenesis and scar formation in stroke. RGS5 in pericytes plays an important role in both the acute and chronic phase and therefore could be a potential target for modifying repair after ischemic stroke.