MicroRNAs regulate human brain endothelial cell barrier function in inflammation: implications for multiple sclerosis

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Background

The blood-brain barrier (BBB) tightly controls the homeostasis of the central nervous system (CNS) and actively limits entry of blood-borne molecules and circulating leukocytes. In essence the BBB is formed by specialized endothelial cells that are sealed together by intercellular tight junction protein complexes. Disruption and immune activation of the BBB is a central and early feature of multiple sclerosis (MS), a chronic inflammatory disorder of the central nervous system (CNS). Grasping of the underlying mechanisms of barrier disruption in MS may lead to the development of novel and selective routes of intervention to prevent the influx of inflammatory cells into the CNS. MicroRNAs, endogenous non-coding small RNAs, are now recognized to play a critical role in key cellular functions by specifically repressing gene expression. There are several microRNAs that have been identified in endothelial cells and they have been implicated in primary endothelial cell function and angiogenesis, but to date no microRNAs that regulate barrier function have been identified.

Material and Methods

The tissues were obtained from The Netherlands Brain Bank (NBB), Netherlands Institute for Neuroscience, Amsterdam. Brain capillaries were isolated from periventricular non-neurological patient tissue, periventricular normal appearing white matter (NAWM) and periventricular MS lesions from post-mortem MS patients. Using a genomics approach, we defined a microRNA signature which is altered at the BBB of MS patients.

Results and conclusion

Our novel data show that a set of microRNAs modulates BBB function under normal and inflammatory conditions. Most importantly, levels of BBB-associated microRNAs were diminished in isolated MS patient capillaries. Together, our findings uncover an unprecedented and exciting regulatory mechanism of brain endothelial cell barrier function in health and disease and provide novel opportunities to treat neurovascular-dependent brain diseases through microRNAs.

Reference: Reijerkerk et al., J Neuroscience 2013