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MicroRNA based therapy in disease models of heart failure and stroke

Statement of the Problem: Cardiovascular diseases are the main cause of death worldwide. Aging populations show higher incidences of myocardial infarction, heart failure and stroke. MicroRNAs (miRs), a group of non-coding RNAs involved in mRNA regulation, have been demonstrated to play a role in many cardiovascular disorders. Blood-brain barrier (BBB) integrity is one of the important elements of central nervous system (CNS) homeostasis. Studies on regulators of BBB-physiology in health and disease may lead to new therapeutic strategies in cardiovascular system.

Methodology & Theoretical: An overview of the newest literature considering the miRs and their role in cardiovascular system will be given. *In vitro* and *in vivo* models for studying these regulations will be presented with methodological details. An example of experimental work on brain microvascular endothelial cells and an experimental stroke model will be presented.

Orientation Findings: MiR-132/212 has been identified to be increased in hypoxic brain micro-vascular endothelial cells from mouse and humans. Specific targets of these miRs have been identified and studied for their miR-132/212-mediated regulation *in vitro*. In addition, *in vivo* inhibition of miRs has been examined in experimental stroke model. Cerebral capillaries were isolated from the control and hypoxic group. The selected target genes were also regulated by miRs in vivo. Inhibition of miRs in experimental stroke led to a decreased apoptosis of hippocampal neurons, as shown by TUNEL staining. However, there was no effect on lesion size and functional outcome.

Conclusion & Significance: Elucidating the role of miRs in cardiovascular system may open new avenues for therapies and drug delivery.

Biography

Carola Y Förster has a convincing track record in Neurophysiology with a strong focus on the dysfunctions of the blood-brain barrier (BBB). A significant aspect of her research is related to regulation of gene expression at the BBB, specifically by non-coding RNA, particular microRNA, to offer pharmacological solutions to the observed BBB alterations. For this, CF systematically studies the mechanisms from gene regulation, through transcription, to protein degradation and cellular morphology, linking basic science with clinical aspects. After years of experience in research, evaluation, teaching and administration both in hospital and education institutions, CF developed different *in vitro* and *in vivo* models of cerebrovascular disease and established recently a division of computational model to further strengthen this area of research.

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