Vasculome

Stroke remains a major unmet clinical need that warrants novel therapies. Following an ischemic insult, the cerebral vasculature secretes inflammatory molecules, creating the stroke vasculome profile. The present study evaluated the therapeutic effects of endothelial cells on the inflammation-associated stroke vasculome. qRT-PCR analysis revealed that specific inflammation-related vasculome genes BRM, IκB, Foxf1, and ITIH-5 significantly upregulated by oxygen glucose deprivation (OGD. Interestingly, co-culture of human endothelial cells (HEN6) with human endothelial cells (EPCs) during OGD significantly blocked the elevations of BRM, IκB, and Foxf1, but not ITIH-5. Next, employing the knockdown/antisense technology, silencing the inflammation-associated stroke vasculome gene, IκB, as opposed to scrambled knockdown, blocked the EPC-mediated protection of HEN6 against OGD. In vivo, stroke animals transplanted with intracerebral human EPCs (300,000 cells) into the striatum and cortex 4 h post ischemic stroke displayed significant behavioral recovery up to 30 days post-transplantation compared to vehicle-treated stroke animals. At 7 days post-transplantation, quantification of the fluorescent staining intensity in the cortex and striatum revealed significant upregulation of the endothelial marker RECA1 and a downregulation of the stroke-associated vasculome BRM, IKB, Foxf1, ITIH-5 and PMCA2 in the ipsilateral side of cortex and striatum of EPC-transplanted stroke animals relative to vehicle-treated stroke animals. Altogether, these results demonstrate that EPCs exert therapeutic effects in experimental stroke possibly by modulating the inflammation-plagued vasculome [1)].

1)
Acosta SA, Lee JY, Nguyen H, Kaneko Y, Borlongan CV. Endothelial Progenitor Cells Modulate Inflammation-Associated Stroke Vasculome. Stem Cell Rev. 2019 Feb 9. doi: 10.1007/s12015-019-9873-x. [Epub ahead of print] PubMed PMID: 30739275.