



Title: Exosomes in combination with thrombolytic and mechanical thrombectomy for treatment of stroke

Author / Authors: Michael Chopp / Vice Chair Neurology and Distinguished Prof Zheng Gang Zhang / Senior Scientist

Li Zhang, Chunyang Wang, Chao Li, Zheng Gang Zhang, Michael Chopp#

Department of Neurology, Henry Ford Hospital, Detroit Michigan USA, and # Department of Physics, Oakland University, Rochester Michigan , USA

Abstract

Therapeutic benefit for ischemic stroke, as a cerebrovascular disease, would benefit by direct treatment of the cerebrovasculature. Here, we describe our experimental stroke studies demonstrating critical roles of distinctive small extracellular vesicles , primarily exosomes, both in promoting neurovascular dysfunction, e.g., exosomes released by platelets post stroke, and as a therapeutic using cerebral endothelial cell exosomes to treat stroke. Studies described will demonstrate that platelets mediate vascular permeability and inflammation, which is exacerbated by thrombolytic treatment with tPA. We show that exosomes released from platelets post stroke promote thrombin deposition in the microvasculature post stroke which mediate vascular dysfunction. Importantly, this platelet exosomal mediated damage may be ameliorated by using exosomes derived from non-stroke cerebral endothelial cells. We also demonstrate that exosomes derived from healthy cerebral endothelial cells when used in combination with thrombolytic and mechanical thrombectomy treatments of experimental stroke greatly enhance therapeutic outcome. The critical take-home message is, we show that exosomes harvested from intact cerebral endothelial cells may be used to efficaciously treat ischemic stroke and augment the therapeutic benefits of thrombolytic and mechanical thrombectomy treatment of stroke.