Published on *Eli and Edythe Broad Center of Regeneration Medicine and Stem Cell Research* (http://stemcell.ucsf.edu)

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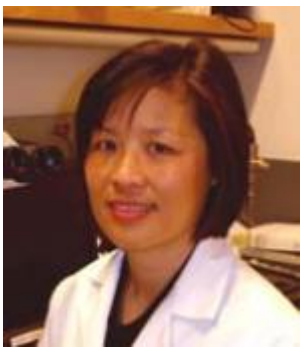

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Program Member Type
Affiliated
Research Interest

Our research focuses on angiogenic gene and cell therapies for cerebrovascular disorders, include brain arteriovenous malformation and stroke.

Brain arteriovenous malformation (BAVM) can cause life-threatening hemorrhage and stroke. The risk of developing BAVM increases significantly in Hereditary Hemorrhagic Telangectasia patients with haploinsufficiency of endoglin (ENG) or activin receptor-like kinase 1 (ALK1). The underlying mechanisms are unknown. There is no medical therapy available to directly treat AVM or decrease spontaneous rupture risk. To study potential mechanisms for AVM pathogenesis and to develop new therapies, surrogate models for the lesion phenotype are needed. We have successfully created a BAVM model in adult mouse brain using several strategies, including conditional gene knockout and viral vector mediated gene overexpression. We are using this model to analyze the underlying mechanism and to test new therapies for the treatment of BAVM.

Brain ischemia occurs in many brain injuries and diseases. The innate angiogenesis in response to brain injury is not sufficient to prevent ischemia induced tissue damage. However, to induce angiogenesis in the brain by delivery exogenous angiogenesis apposes a number of particular challenges. We are trying to develop an innovative approach to express angiogenic factors in a specific window at the surrounding area of ischemia tissue and induce neovasculatures that have intact brain blood barrier (BBB) by: 1) conditionally inducing new blood vessel formation in injured areas using hypoxia-inducible system; and 2) promoting neovasculature maturation to minimizing BBB leakage by co-expression of VEGF with other transcription factors such as homeobox D3 (HOXD3) and angiopoietin-1. We are also testing a clinical applicable method by targeted delivery of angiogenic gene through intravenous injection.

By collaborating with several investigators in UCSF and other campus of University of California, we are testing therapeutic efficacy of different stem cells include neural progenitor

cells derived from embryonic stem cells, embryo/fetal tissues, bone marrow derive mesenchymal stem cells, and endothelial progenitor cells using rat and mouse ischemic stroke models.

Complete Publications [3]

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