Cellular and Molecular Mechanisms of Brain Arteriovenous Malformations

February 20

Tuesday, 12:30 pm

Billings Building—Rosedale Room

SPEAKER:

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Host: Host: Sunghee Cho, Ph.D.

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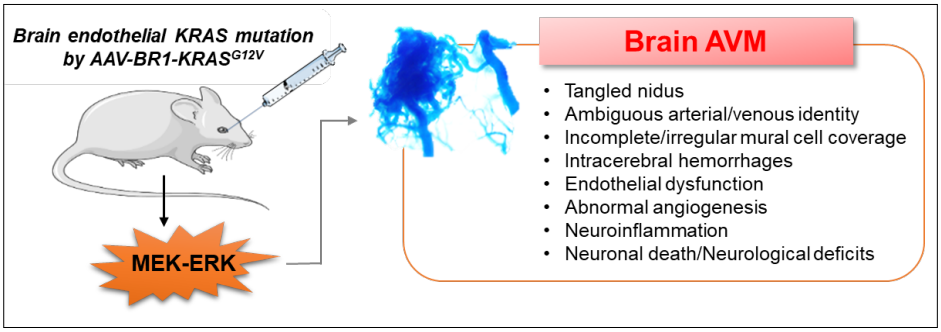
Abstract

Brain arteriovenous malformation (bAVM) is a tangle of blood vessels with aberrant connections between arteries and veins without an intervening capillary bed. Although bAVM is rare, bAVM patients are at high risk of life-threatening intracerebral hemorrhages (ICHs). However, the treatment options for patients are limited, primarily relying on surgical methods, which can lead to neurological deficits or death. No pharmacologic drug is available, primarily because of the poor understanding of pathophysiologic mechanisms in bAVM. Clinical studies have recently found endothelial cell (EC)-specific somatic activating KRAS mutations in up to 76% of sporadic bAVMs, which account for over 95% of bAVM cases. By KRASG12V overexpression in mouse brain ECs using AAV-BR1, we confirmed that KRAS mutation is sufficient for bAVM development and established a novel animal model of bAVM that displayed salient features of human bAVM. Using the novel clinically relevant mouse model of bAVMs, our current research focuses on identifying cellular and molecular mechanisms underlying bAVM pathophysiology.



Publications

1. Park ES, Kim S, Huang S, Yoo JY, Korbelin J, Lee TJ, Kaur B, Dash PK, Chen PR*, and Kim E* (2021) Selective endothelial hyperactivation of oncogenic KRAS induces bAVMs in mice. Annals of Neurology, 2021 May; 89(5)926-941. Doi: 10.1002/ana.26059. Epub 2021 Mar 22. PMCID: PMC8835690 (Featured in Cover*)

2. Park, ES*, Kim S, Yao DC, Savarraj JPJ, Choi HA, Chen PR, and Kim E* (2022) Soluble endoglin stimulates inflammatory and angiogenic responses in microglia that are associated with endothelial dysfunction. Int J Mol Sci. 2022. 23(3), 1225. Doi: 10.3390/ijms23031225 PMCID: PMC8835690

3. Kim S, Park ES, Chen PR, and Kim E* (2022) Dysregulated hypothalamic-pituitary-adrenal axis is associated with increased inflammation and worse outcomes after ischemic stroke in diabetic mice. Frontiers in Immunology. doi.org/10.3389/fimmu.2022.864858

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