In vivo cerebrovascular characterization of CCM in a mouse model

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- **Collaborating labs:** Dr. Kevin Whitehead and Dr. KC Brennan
- **Objective:** To elucidate the vascular morphology and function of cavernous malformations and nearby cortical vessels in CCM mice in an in vivo setting.

**CCM:** Cerebrovascular malformation secondary to endothelial cell dysfunction.
- Spontaneous
- Familial (AD)
- 3 main genes responsible for CCM: **Krit1, CCM2, Pdcd10**

- **What we know?**
  - Krit1 and CCM2 are believed to act through similar molecular mechanisms: Prevent the activation of the GTPase Rho-A which is believed to be responsible for endothelial cell dysfunction and breakdown of cell-cell interaction.
  - Inhibition of RhoA and down stream Rho-Kinase with **simvastatin** and **Fausadil**, respectively, reversed many of the cell permeability and cytoskeletal aberrations observed with CCM KO mice: Improved cell resistance, improved endothelial cell alignment to laminar flow, and permeability.
  - Dr. Whitehead’s lab has early results showing that the structural and functional deficits observed with their CCM2 KO mice can be rescued with **Tempol**, a superoxide scavenger.

- **What we are trying to do?**
  - Expand our work to include in vivo characterization of the vascular defects of CCM mice using 2-photon microscopy and IOS/IOI.
    - SSER in arteries/arterioles
    - CSD induction threshold
    - Vasodilatory effects of Ach
    - Permeability studies
    - Neurovascular mapping
    - Attempt to rescue with tempol and simvastatin.