

Novel Whole-Mount Model of Vascular Remodelling in Ischemic Mouse Spinotrapezius Muscle

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Cardiovascular disease and many other pathologies are associated with ischemia, making it critical to understand microvascular remodeling during this injury in order to develop treatments to either augment or recover a tissue's native response. This however requires a level of detailed analysis that current animal models, such as the hindlimb ischemia models, cannot provide—they require tissue sectioning which produces only correlative evidence and precludes the study of spatial and anatomical relationships, such as vessel type and vascular and perivascular cell interactions. We have developed a novel whole-mount model of microvascular remodeling in the mouse spinotrapezius muscle following ischemic injury which enables *en face* visualization and analysis of vessel network adaptations with single-cell resolution. Using surgical ligations on feeding arterioles, localized muscle ischemia in the mouse spinotrapezius was induced, and the vasculature's response was compared to the contralateral side using immunofluorescence and intravital microscopy. Five days post-intervention, mice undergoing surgery (n=6) showed a 37.7% +/- 8.6% increase in functional vascular density, as well as a significant increase in spinal vessel branching (68.9%) and the preferential development of bridging collaterals (57.5%). Both angio- and arteriogenesis as well as increased vessel tortuosity is evident. This model of skeletal muscle ischemia generates reproducible microvascular adaptations that allow the study of remodeling at a greater level of detail than previously possible.