Smooth muscle cell dysfunction reduces functional vasodilation in pre-existing and newly-formed arterial collaterals

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Clinical Motivation (Why Study Collateral Vasodilation?)

• Ischemic Disease
  – Impaired vasodilation
  – Timing of symptoms
  – Efficacy of vasodilating therapies
Collateral Vasodilation

• Preexisting collaterals
  – Profunda-gracilis circuit + femoral artery ligation

• Newly-formed collaterals
  – Arterialized capillaries + spinotrapezius feed artery ligation
PSS, heated to ~35°C and bubbled w/ 5% CO₂-95% N₂ + pharmacological agent

Field stimulation near NMJ (1mA, 500 μs, 2-8Hz, 2min)
Preexisting Collaterals – Vasodilation at day-7

- Functional vasodilation

(A) Preexisting collaterals
(B) Functional vasodilation

(C) Diameter comparison:
- **A**: Day 7
- **B**: Sham

(D) Percent change in diameter (%):
- **Day 7**
- **Sham**

* indicates statistical significance.
Preexisting Collaterals – Vasodilation at day-7

- Particle-image velocimetry

[Images of particle-tracking velocimetry]

[Graph showing percent change in flow, with Day 7 and Sham groups compared]

Al-Khazraji BK, 2012
Preexisting Collaterals – Vasodilation at day-7

Endothelial & Smooth Muscle Pathways

Acetylcholine

Na-nitroprusside
Preexisting Collaterals – Vasodilation at day-7

• Summary & Interpretations
  – Reduced functional vasodilation & hyperemia
  – Impaired smooth muscle-dependent vasodilation
  – Smooth muscle phenotype
    • No increase in synthetic SMCs
    • Mechanoadaptation?
Collateral Vasodilation

• Preexisting collaterals
  – Profunda-gracilis circuit + femoral artery ligation

• Newly-formed collaterals
  – Arterialized capillaries + spinotrapezius feed artery ligation
Newly-Formed Collaterals – Spinotrapezius

• Superficial & thin tissue
  – Intravital microscopy
  – Whole-mount staining

• Capillary arterialization
  – Balb/C

Bailey et al, 2008
Guendel et al, 2013
Arterialized Capillaries – Spinotrapezius

• Enlargement & Smooth Muscle Investment

Mac Gabhann et al, 2010
Arterialized Capillaries – Vasodilation at day-7

• Functional vasodilation

Cutts, unpublished
Arterialized Capillaries – Vasodilation at day-7

• Endothelial & Smooth Muscle Pathways

![Graphs showing vasodilation at day-7](image-url)
Arterialized Capillaries – Vasodilation at day-7

• Summary & Interpretation
  – Absent functional vasodilation
  – Impaired smooth muscle-dependent vasodilation
  – Impaired ascending vasodilation?
  – Absent adrenergic constriction
  – Lack of sympathetic innervation?
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Ligated
Sham
Saphenous
Profunda femoris

Danzeiser, unpublished

Chacon, unpublished
Newly-Formed Collaterals – Spinotrapezius

C57Bl/6

Balb/C

Mac Gabhann et al, 2010