TRPC Channels in the Health and Disease of the Cardiomyocyte

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Major $\text{Ca}^{2+}$ entry pathways

ROC – receptor-operated channel; VOCC – voltage-operated calcium channel; SOC – store-operated channel; SERCA – SR/ER $\text{Ca}^{2+}$ ATPase; TG – thapsigargin; CPA – cyclopiazonic acid

Criteria for mechanically active channels

1. Localization to sites of increased stretch
2. Gated by stretch
3. Influence mechanical signal transduction
4. Pathophysiology of pressure overload and muscle dystrophy
TRPC signaling: local specialized membranes costamere

Millay et al. PNAS 2009
Vanderbrouk FASEB J. 2007 608-17
Mallouk PNAS 2000
Rosenberg, PNAS 2004

Ervasti JBC2007
Costameres, prestress and transverse forces
TRPC currents are induced by pressure overload
TRPC1 and the stretch response

![Bar graph showing fold change for GAPDH, ANF, and BNP in WT and Trpc1-/- mice under different conditions.](image)
TRPC1 deficiency protects the heart from pressure overload

TRPC1(+/+) sham  TRPC1(+/+) TAC  TRPC1(-/-) sham  TRPC1(-/-) TAC
Maladaptive hypertrophic signaling is blunted in the Trpc1 null mice
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