MitoEAGLE Conference and MC/WG Meeting – jointly organized by MiP*society* and MitoEAGLE
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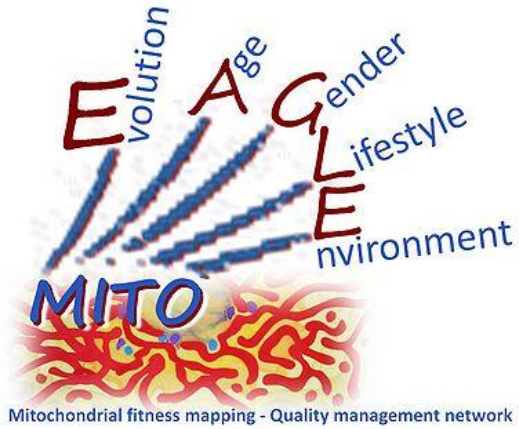

Mitochondria-Targeted Antioxidants in Aging related functional changes in the heart and aorta: MitoTEMPO improves aged-cardiovascular performance

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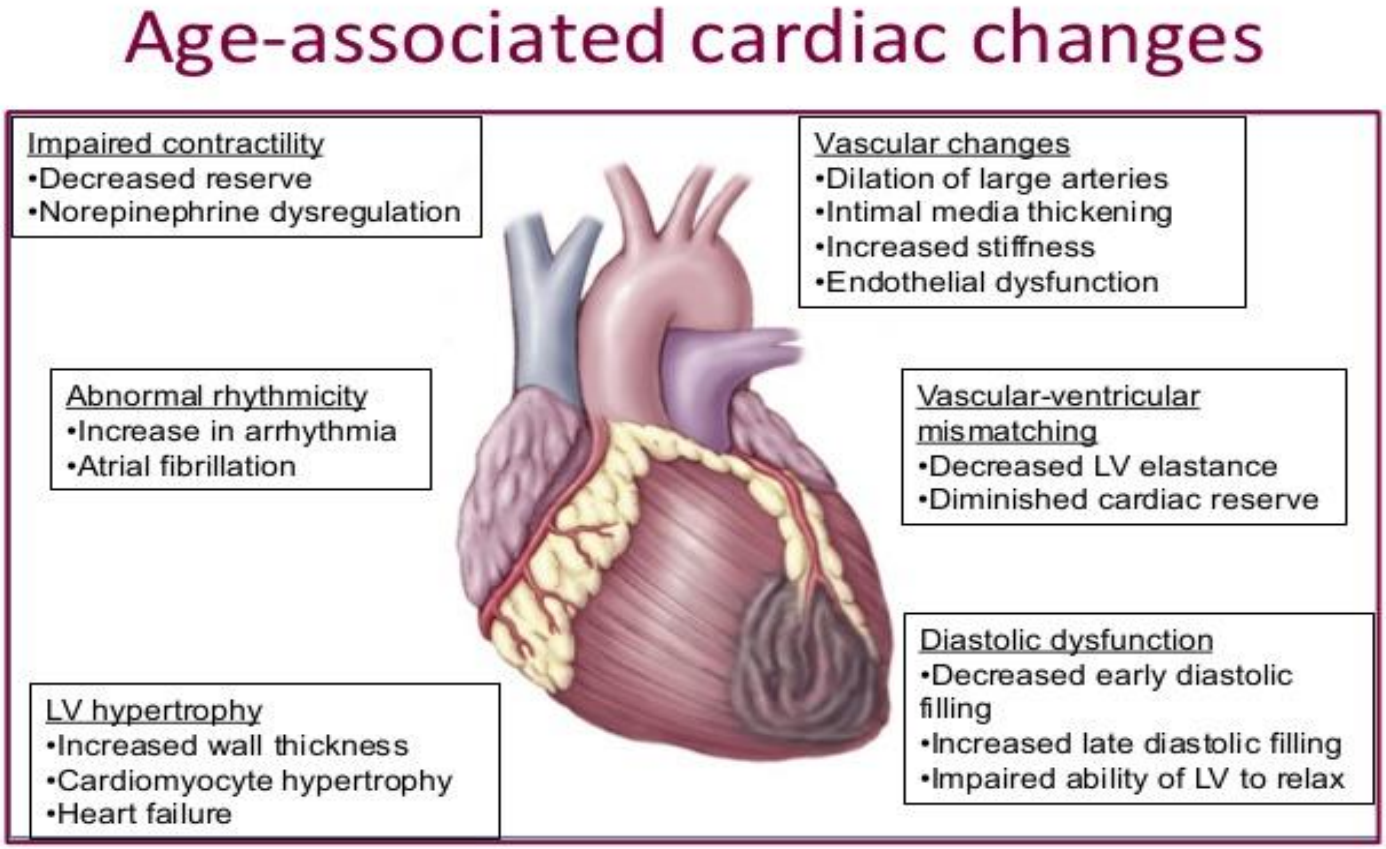
Aging related Cardiac Alterations

Aging **is accumulation of numerous modifications at different levels of the cardiovascular system, resulting in adverse remodelling of the heart and blood vessels**



Aging and Oxidative Stress

- In 1972 Denham Darman suggested that free radicals cause damage of mitochondria a key determinant of aging processes.

- Unbalanced ROS leading to cellular disfunction

- Mitochondria the main source of ROS production

Therefore maintain mitochondrial function is good strategy to protect heart during aging.

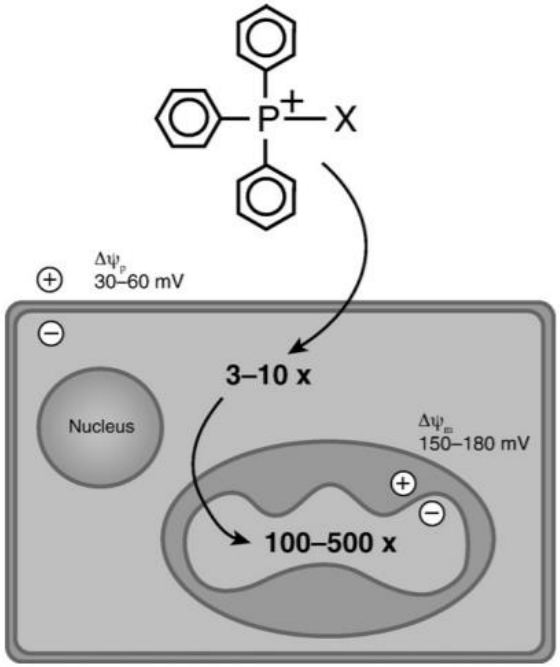
Mitochondrial Targeted Antioxidants

- Decreasing mitochondrial ROS prevents myocardial dysfunction

- Low molecular weight antioxidants (α-Tocopherol, N-acetylcysteine) decreased mitochondrial damage *in vitro*, but their effects *in vivo* is limited

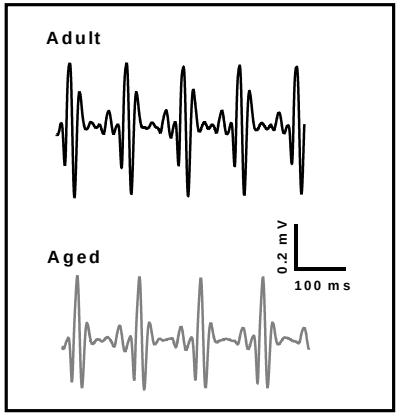
- Antioxidants can be targeted to mitochondria by several methods
  - Hydrophobicity and positive charge
  - Binding with high affinity to intramitochondrial structure
  - Metabolic conversions by specific mitochondrial enzymes

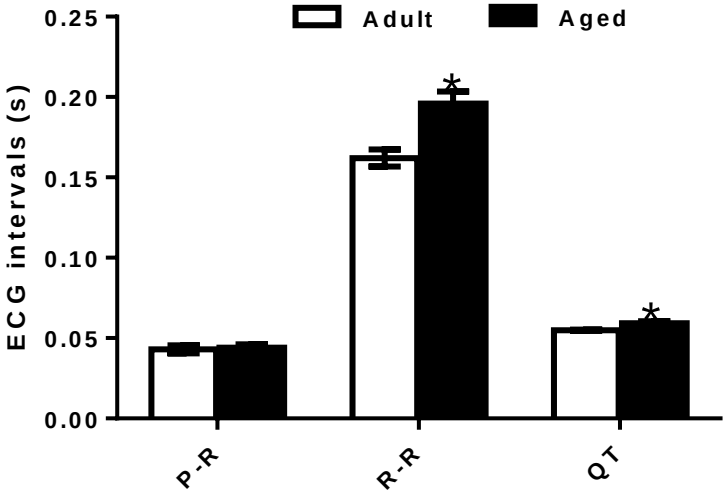
MitoTEMPO conjugated with lipophylic cation TPMP and accumulates 100-500 fold in mitochondria

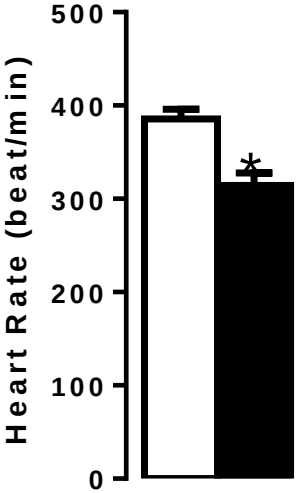


General findings of experimental animals (6- vs. 24- month)

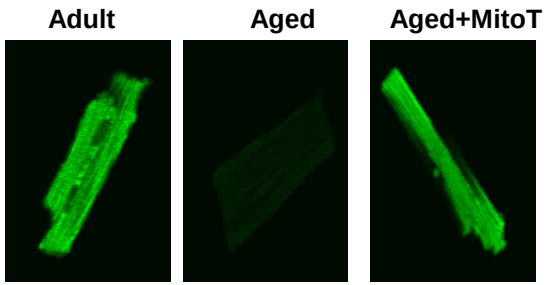
Groups	Body Weight (g)	Heart Weight/Body Weight	Systolic pressure (mmHg)	Diastolic pressure (mmHg)	TAS (mM Trolox)	TOS (µM H_2O_2)
Adult-rats (n=30)	330±11	0.43±0.02	119±2	75±0.6	1.05±0.11	0.25±0.06
Aged-rats (n=35)	380±8.3*	0.52±0.02*	143±4*	83±1.1*	0.37±0.09*	0.77±0.22*

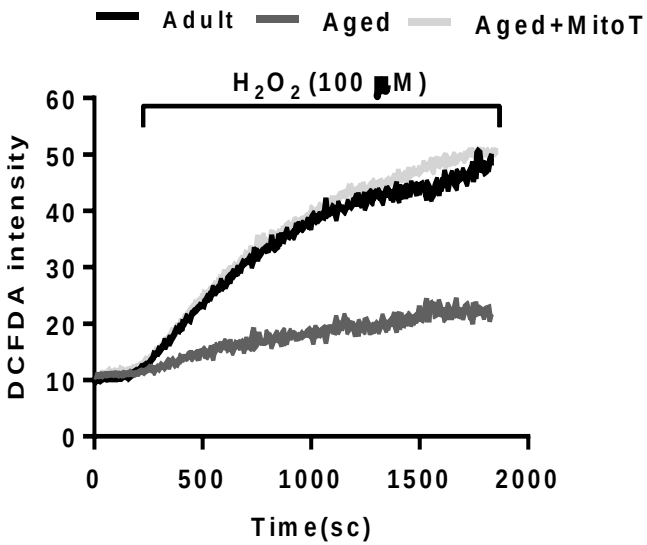


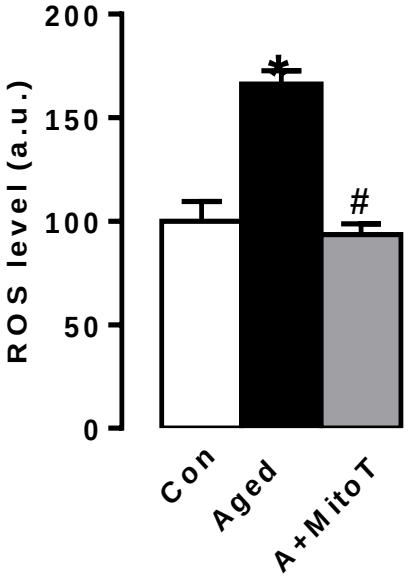




Mitotempo treatment reduces ROS level in senescent cardiomyocytes

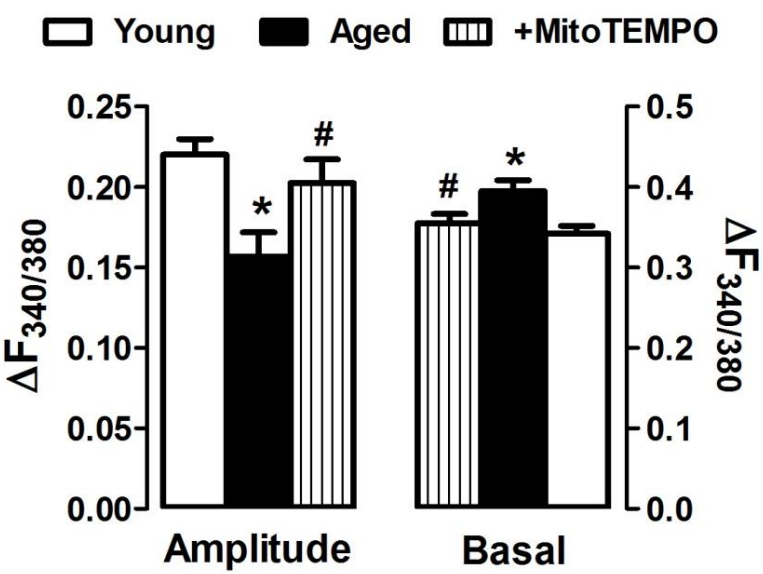


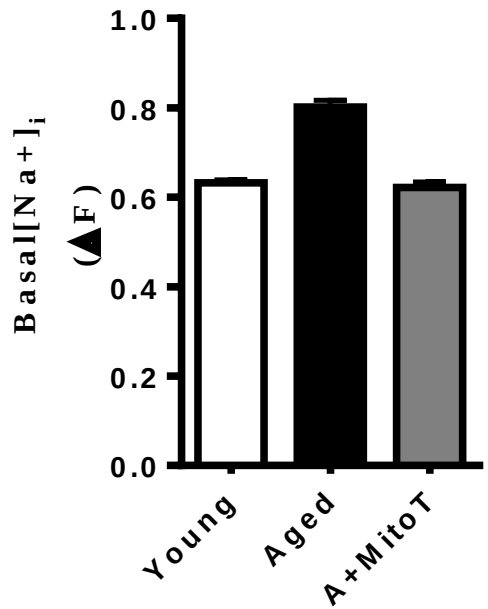


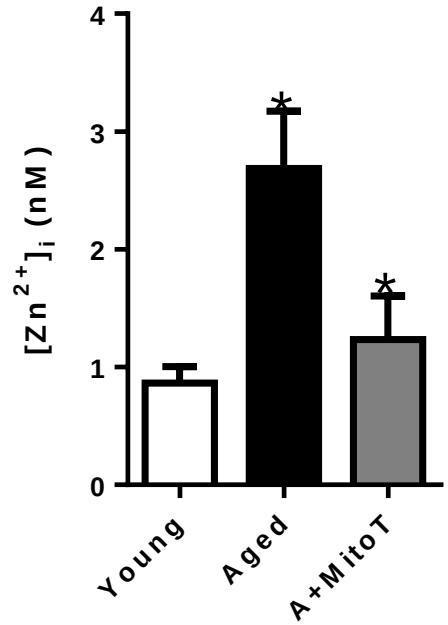


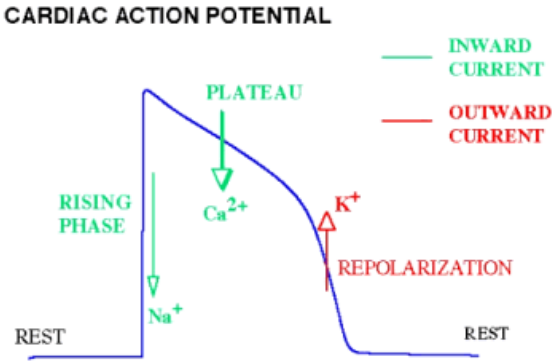
mitoTempo: 1 μM- 1-Hour

Mitotempo restores cytosolic Na^+, Ca^{2+} and Zn^{2+} levels in senescent cardiomyocytes

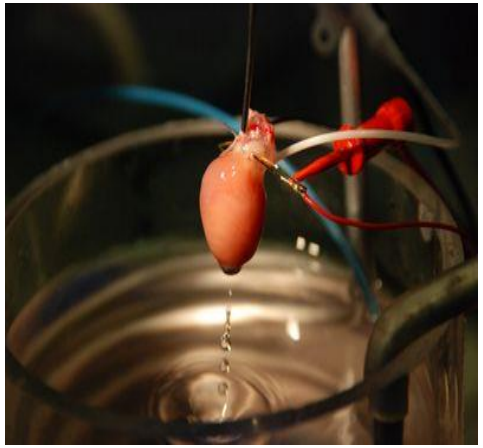




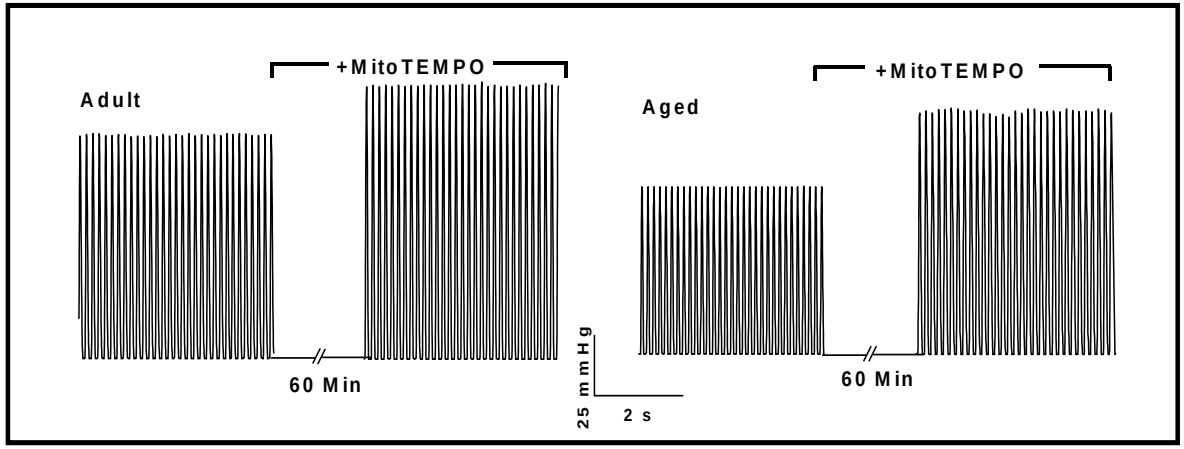


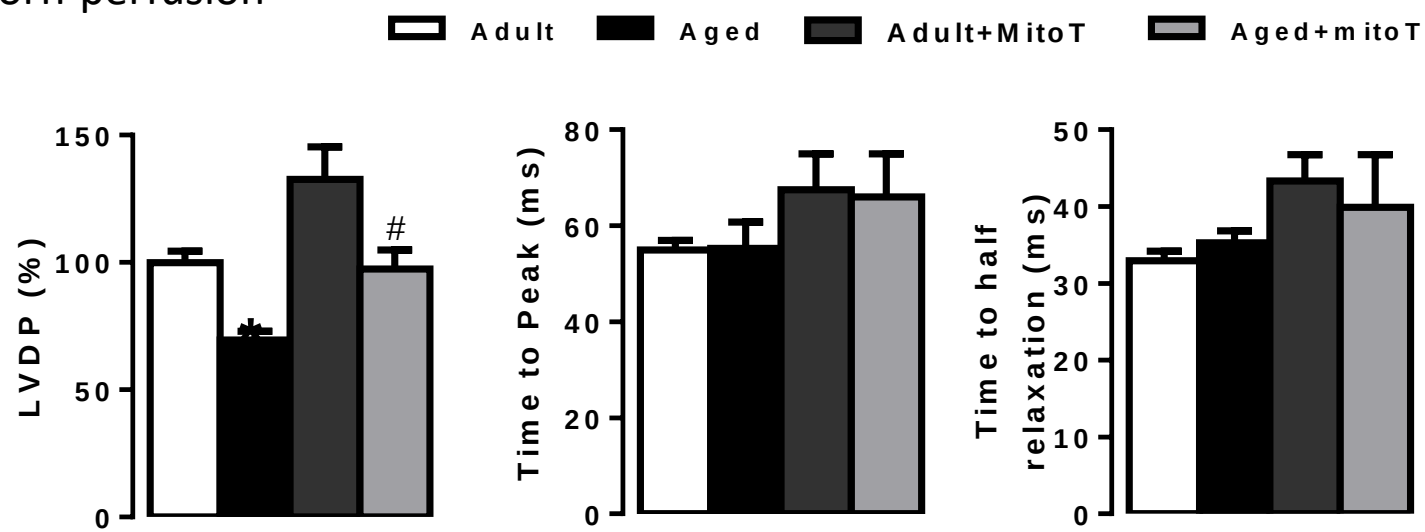


Mitotempo improves Left Ventricular function in senescent cardiomyocytes

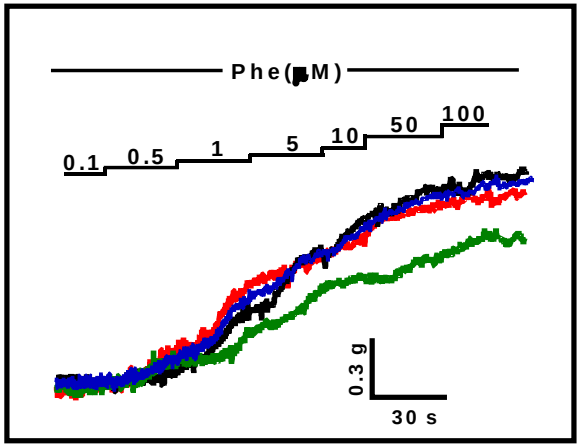


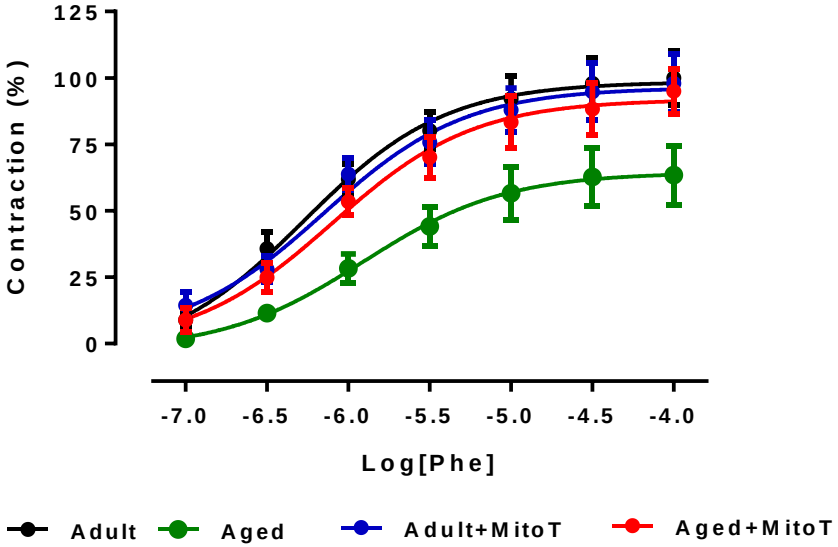
Langendorff perfusion

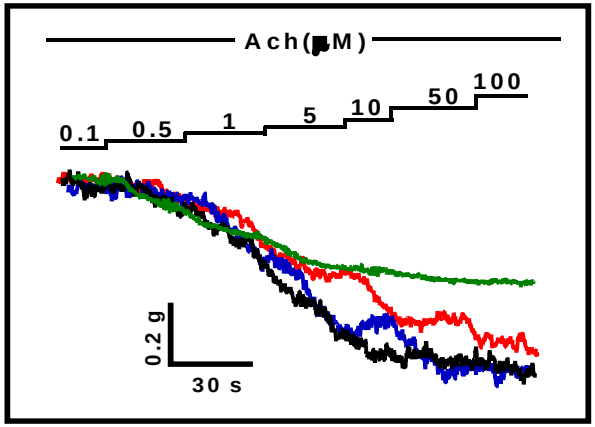


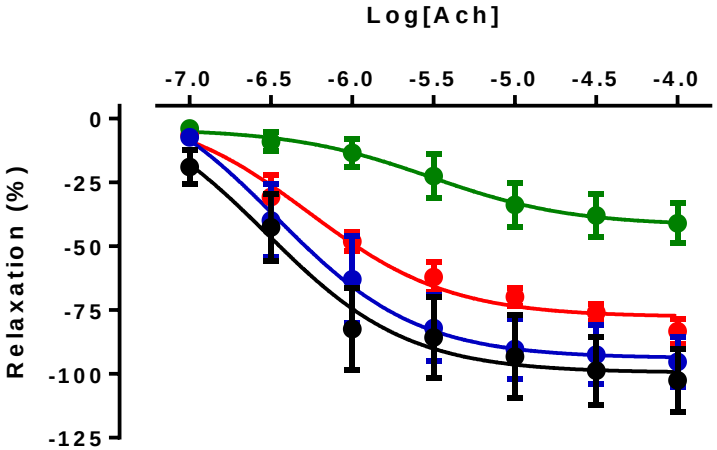


Mitotempo improves contraction-relaxation function of aortic rings in senescent cardiomyocytes









TURAN's Lab