Coronary microvascular dysfunction is linked to altered TRPV1 channels function in metabolic syndrome

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Background
- TRPV1 are non-selective cation channels first characterized in primary sensory neurons and sensory C- and Aδ-fibers.
- Recently, they have been identified in cardiac myocytes, vascular smooth muscle and endothelial cells and have been implicated in cardiac protection after I/R injury, however the role TRPV1 plays in the vascular reactivity is still unknown.

Hypothesis
1. TRPV1 channels are involved in the regulation of vascular tone.
2. Microvascular dysfunction, myocardial perfusion abnormalities and cardiac failure in diabetic cardiomyopathy are related to impaired contribution of vascular TRPV1.

Materials and Methods
In Vivo study:
- db/db with a spontaneous Leprdr mutation, their heterozygous littermate and TRPV1/-/- mice were administered the TRPV1 agonist Capsaicin (Cap 1-10-20 µg/kg/min), under anesthesia, after hexamethonium injection.
- Mean Arterial Pressure (MAP) and heart rate (HR) were recorded using a Millar probe located in abdominal aorta, for Double Product (MAP * HR) measurement as a surrogate of Cardiac Work.
- Quantification of MBF (ml/min/g) was performed with Real-Time-MCE, ACUSON SEQUOIA 512 Ultrasound System (Siemens) and contrast (50 µl/min, Vevo ® Visual Sonic) were used.

Molecular Studies:
Western Immunoblotting was performed to determine cardiac TRPV1 channel expression

Summary
- TRPV1 protein expression was decreased in whole hearts from db/db mice.
- Myocardial blood flow and mean arterial pressure changes in response to capsaicin were attenuated in db/db mice.
- TRPV1 channels contribute to the metabolic regulation of myocardial blood flow and systemic arterial pressure.

Conclusions
- TRPV1 channels may be an ionic mechanism involved in the coupling of myocardial blood flow to cardiac metabolism and this coupling appears to be corrupted in db/db mice.
- We conclude that TRPV1 diminished functional expression and/or dysfunction may underlie the diabetic coronary microvascular and vascular complications typically seen in patients and animal models of diabetic cardiomyopathy.