

TRPV1 Activation Counters Vascular Dysfunction by Increasing PPARs, SiRT-1, PGC1 α , and UCP-1 Expression in the Thoracic Aorta

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Background

Obesity occurs due to imbalance between energy intake and expenditure

- Leads to increased visceral fat accumulation

Foreshadows metabolic diseases and causes complications such as:

- Impaired glucose metabolism
- Non alcoholic fatty liver disease
- Cardiovascular diseases

Vascular dysfunction associated obesity causes:

- Hypertension
- Heart disease
- Myocardial Infarction

Hypothesis

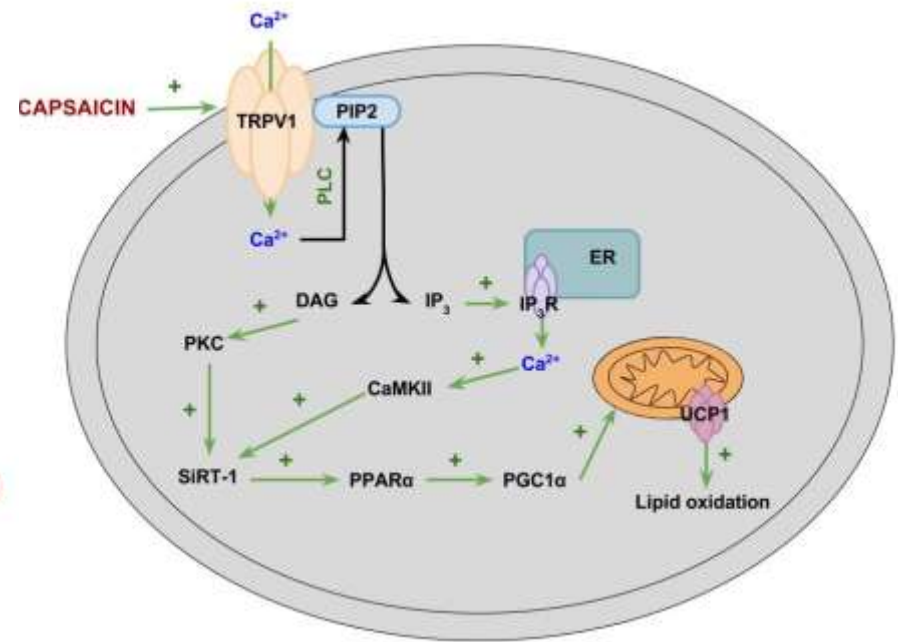
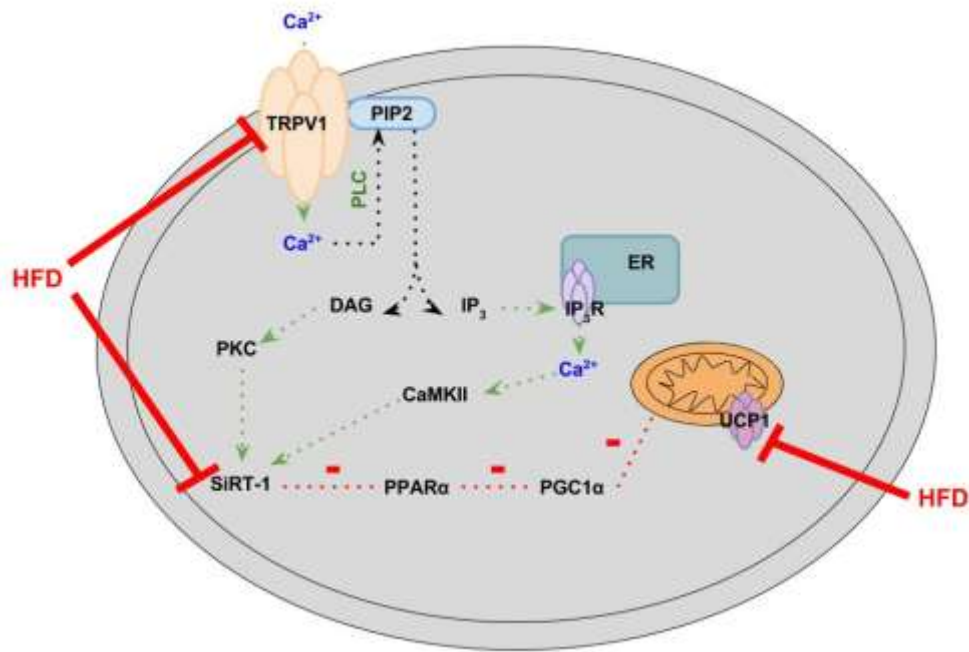
Activation of TRPV1 enhances expression in the thoracic aorta vasculature suppresses the development of hypertension and vascular damage

Enhances the expression of metabolically important:

- Peroxisome proliferator activated receptor alpha (PPAR α)
- Sirtuin-1 (SiRT-1; central cellular metabolic sensor)
- PPAR γ coactivator 1 α (PGC-1 α)
- Uncoupling protein 1 (UCP-1).

TRPV1 Pathway

Recent research suggests that activating transient receptor potential vanilloid subfamily 1 (TRPV1) pathway with capsaicin is a good strategy to counter obesity and metabolic complications.



Methods

Wild type and TRPV 1^{-/-} mice were fed diets consisting of:

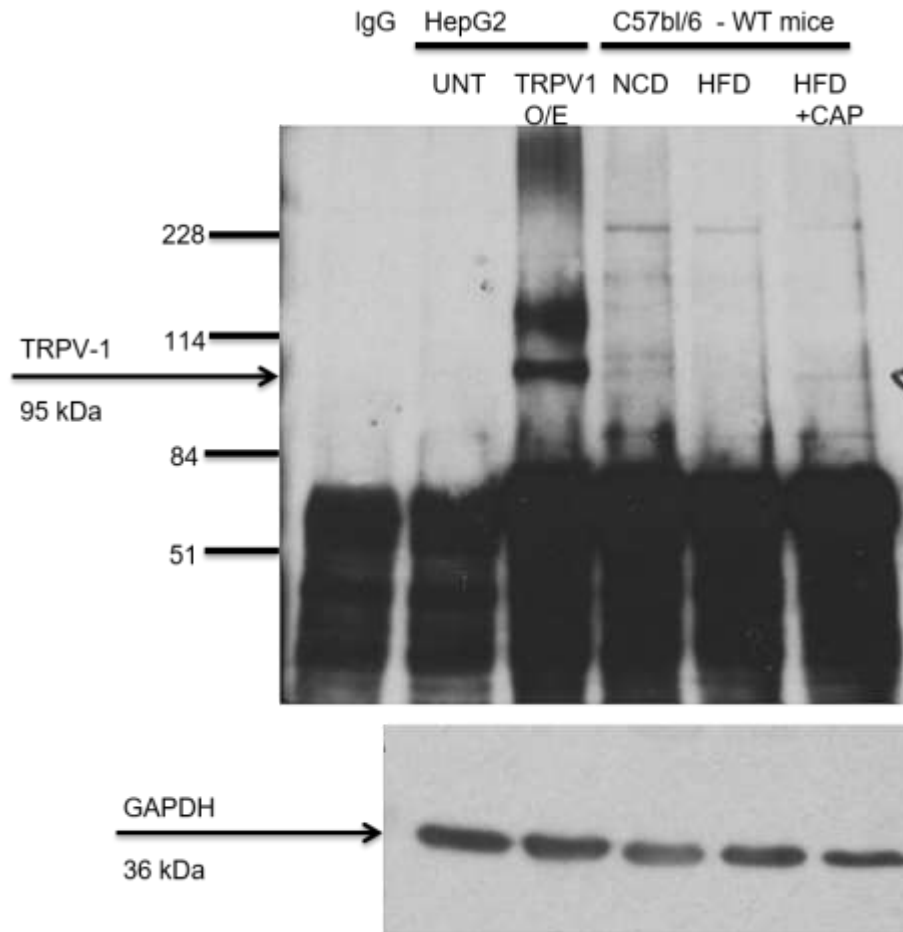
- Normal chow diet
- High fat diet (60% calories from fat)
- High fat diet with capsaicin (0.01% w/w; 1.33 mg/kg)

Diets began at 6 weeks of age and continued for 32 weeks

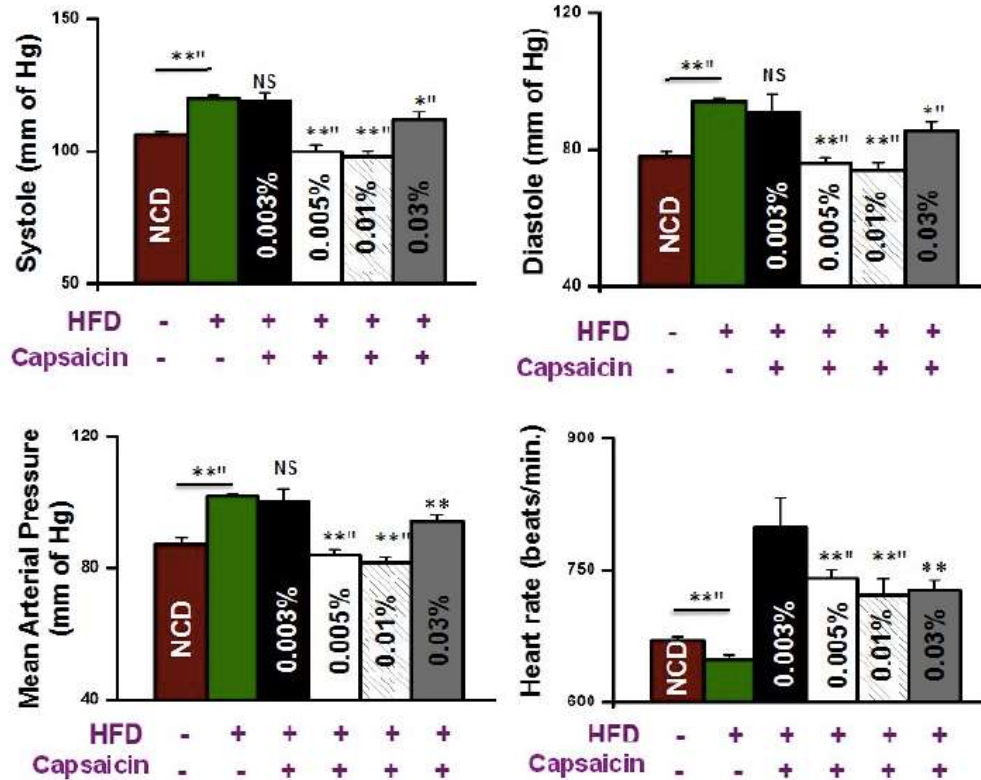
At 38 weeks of age:

- Non-invasive tail cuff blood pressure
- Echocardiogram
- Thoracic aorta harvested
- Western blot analysis

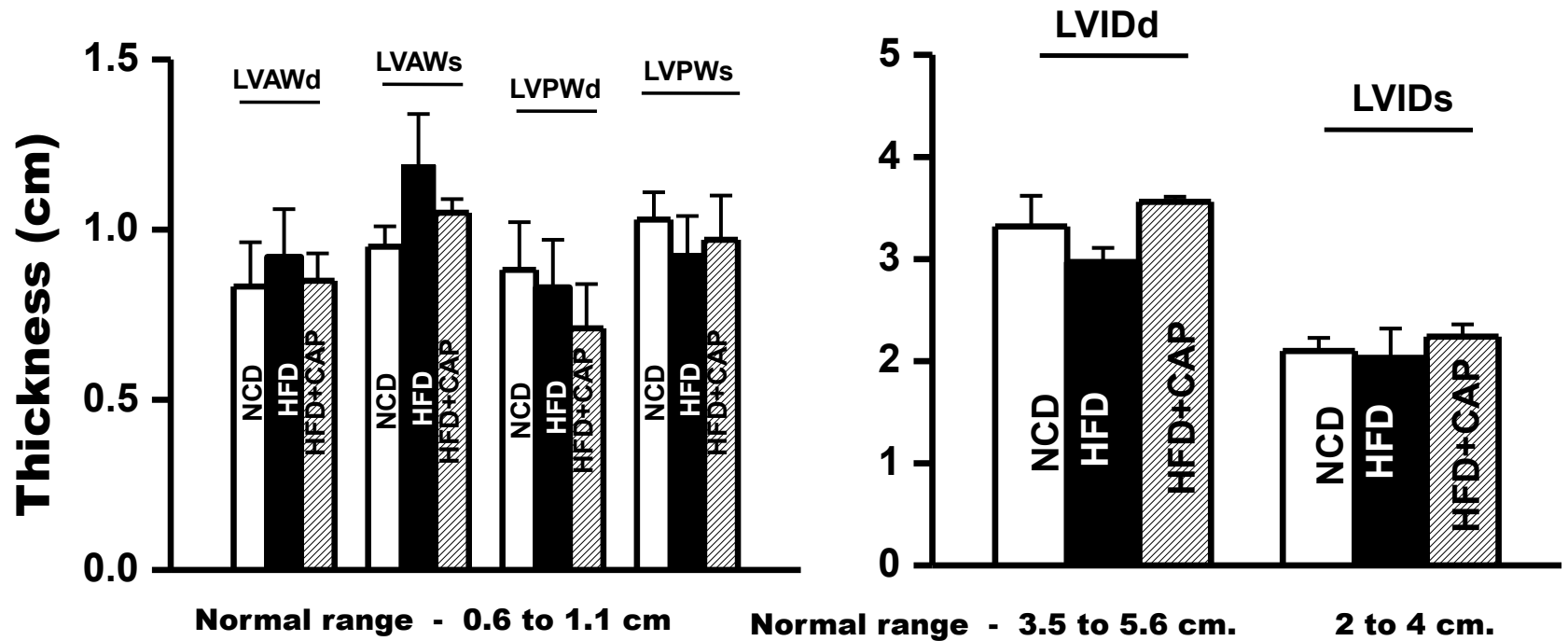
TRPV1 Expressed in Mammalian Thoracic Aorta



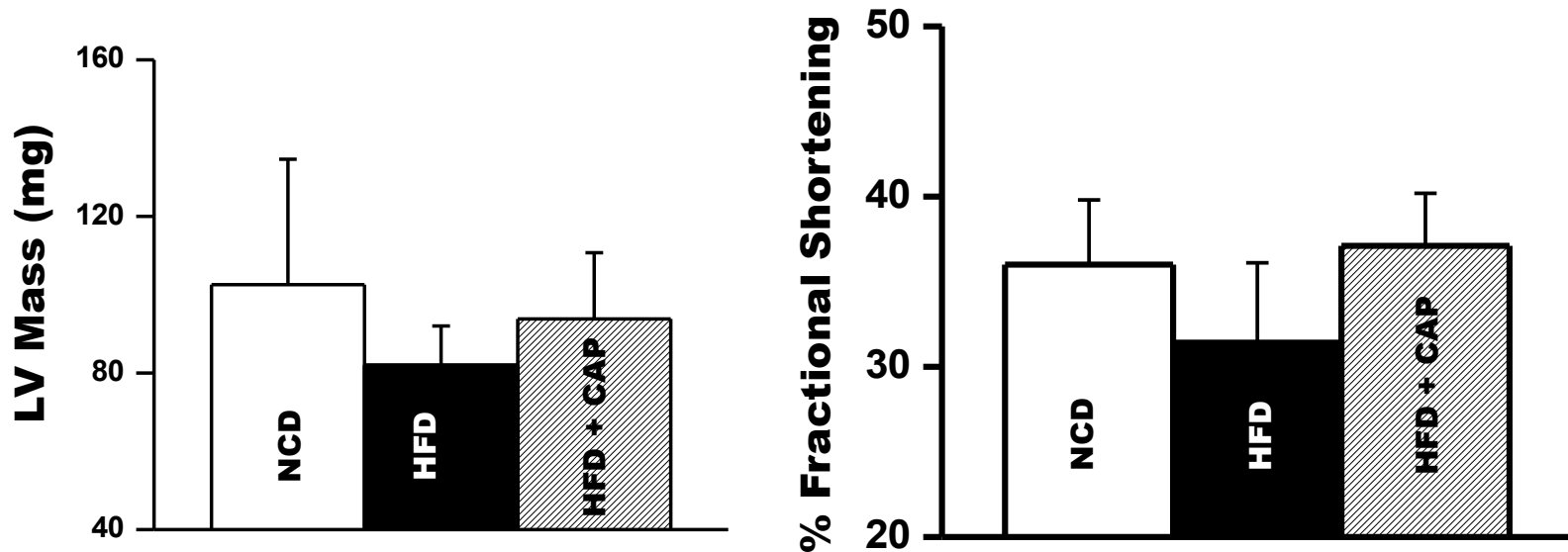
Blood pressure of Mice receiving HFD ± Capsaicin



Echocardiograph data of C57BL6 mice fed with HFD \pm 0.01% CAP

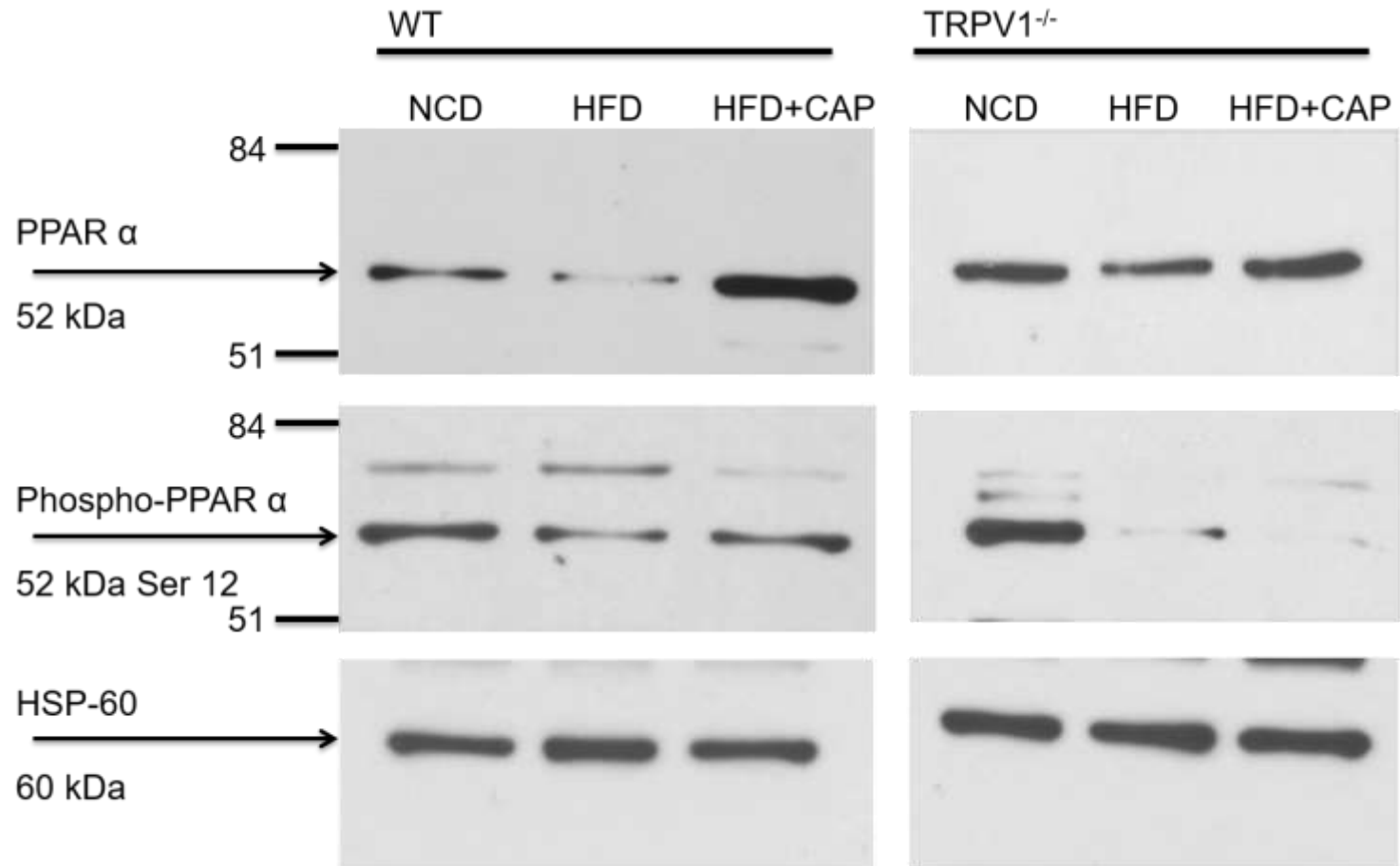


Echocardiograph data of C57BL6 mice fed with HFD \pm 0.01% CAP

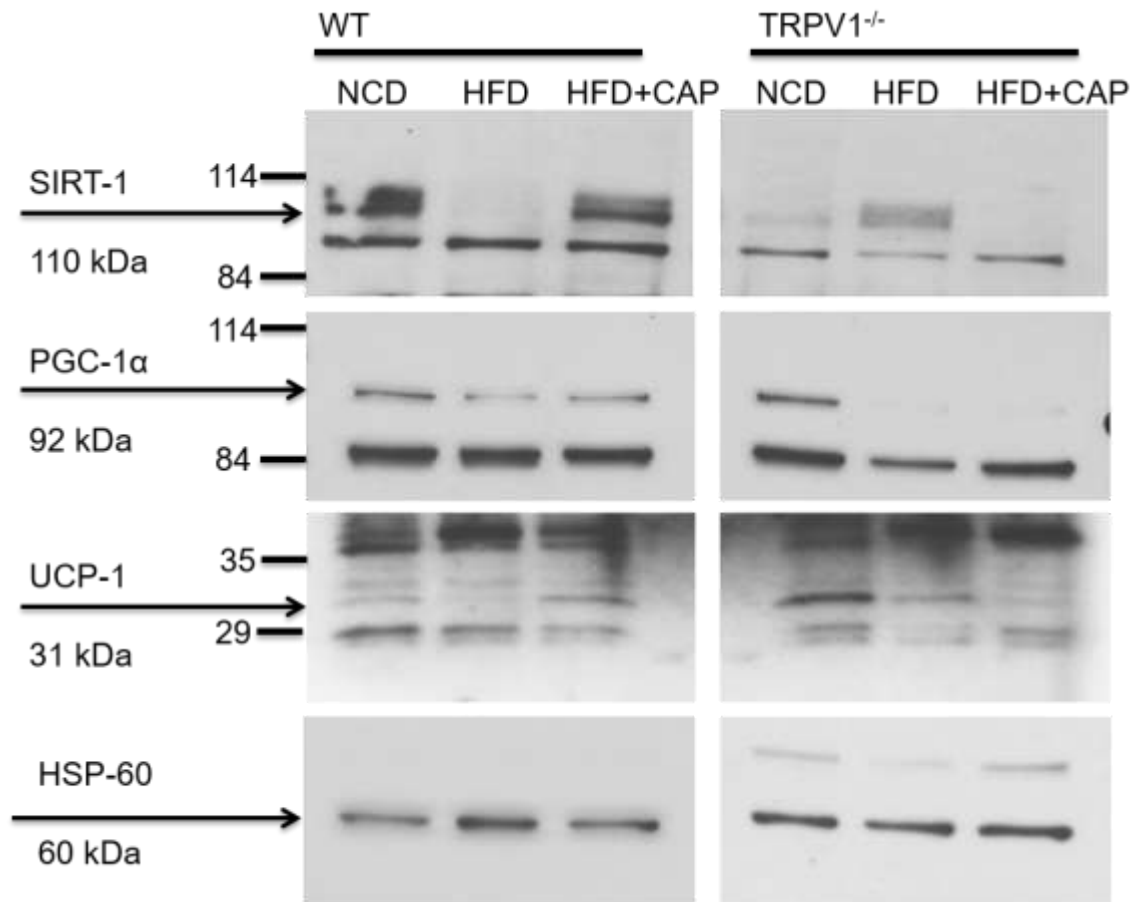


Normal range - 62 to 210 mg

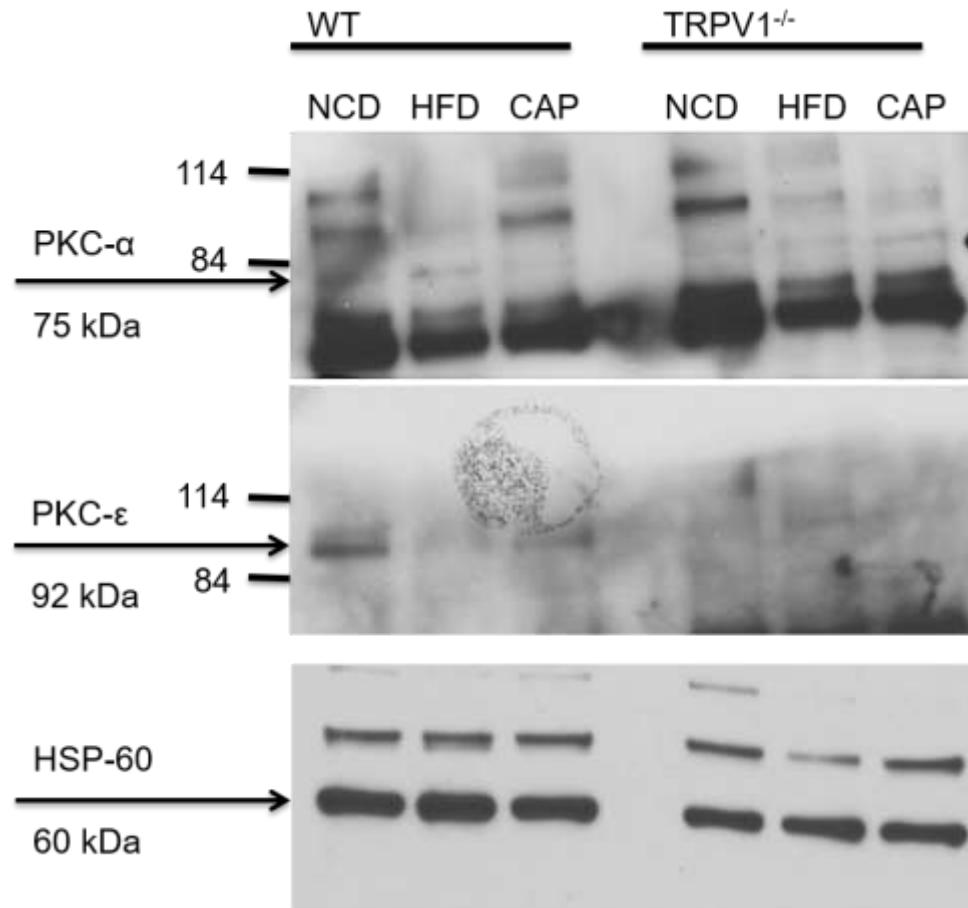
Western Blot Analysis of Thoracic Aorta



Western Blot Analysis of Thoracic Aorta



Western Blot Analysis of Thoracic Aorta



Summary

- Our diet induced obese mice were hypertensive and also had poor left ventricular function
- Capsaicin increased PPAR α , PGC1 α , SIRT1 and UCP1 – thereby preventing lipid accumulation and increasing insulin sensitivity and energy homeostasis.
- Capsaicin decreased PKC α - a vasoconstrictor, but increased PKC ϵ which is known to inhibit hypertension.
- Thus, capsaicin improved vascular functions by preserving TRPV1 expression and activity in thoracic aorta.

Acknowledgments

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