# Effects of short-term adiponectin receptor agonism on cardiac function and energetics in diabetic *db/db* mice

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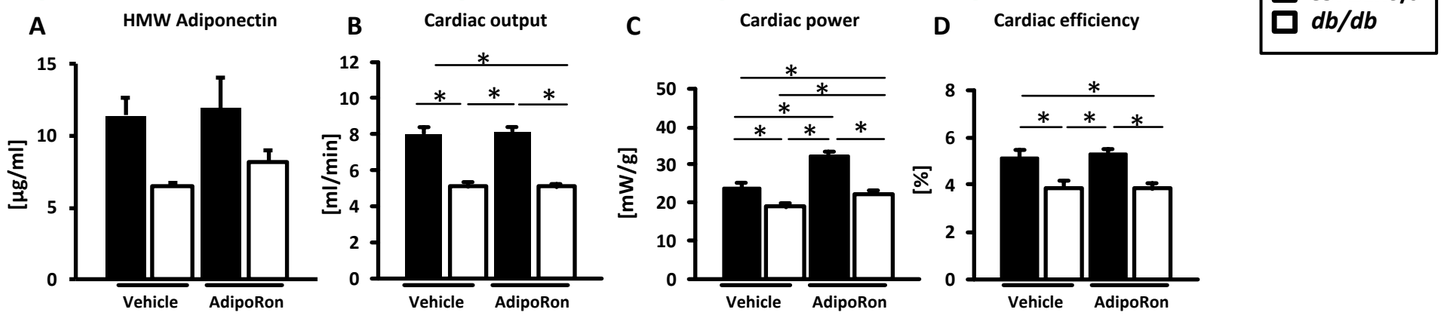
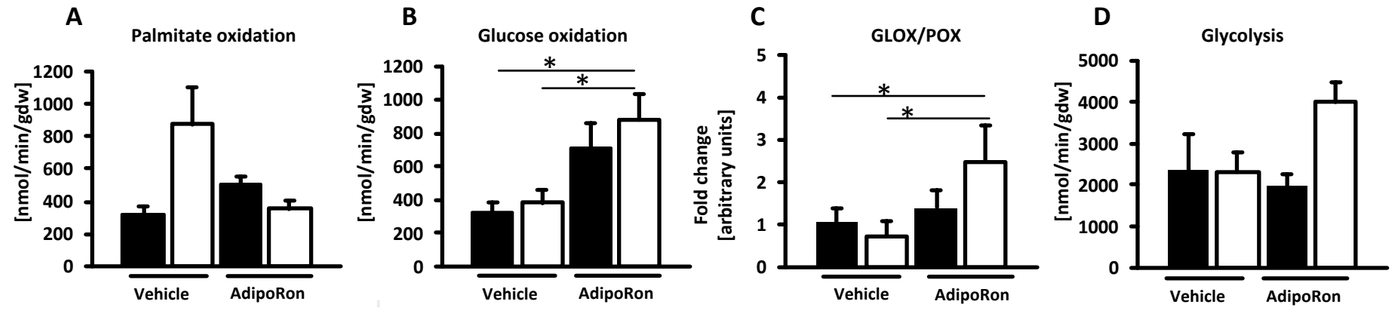
**Introduction**: Adiponectin is an adipose-derived cytokine which coregulates body glucose and fatty acid metabolism. It also exerts cardio-protective effects in the heart, including a decrease in cardiac infarct size following LAD ligation and attenuation of TAC-induced cardiac hypertrophy. We previously reported that lack of Adiponectin Receptor 1 (AdipoR1) impairs cardiac efficiency in non-diabetic animals, caused by ROS-induced mitochondrial uncoupling. A typical trait of diabetic cardiomyopathy observed in models of type 2 diabetes is impaired cardiac efficiency, related to increased myocardial FA utilization. Underlying mechanisms of impaired cardiac efficiency may include FA-induced ROS-mediated activation of mitochondrial uncoupling proteins, and/or oxygen waste for non-contractile processes. Since serum adiponectin levels are decreased in animal models of type 2 diabetes, we hypothesized that impaired cardiac energetics and reduced cardiac efficiency may be related to impaired cardiac adiponectin action.

**Hypothesis**: Adiponectin receptor agonism may improve cardiac function and energetics, and attenuate diabetic cardiomyopathy in Type 2 diabetic mice.

## AdipoRon treatment did not improve cardiac output and efficiency in *db/db* mice




## AdipoRon treatment shifts myocardial substrate preference towards increased glucose utilization




**Methods**:

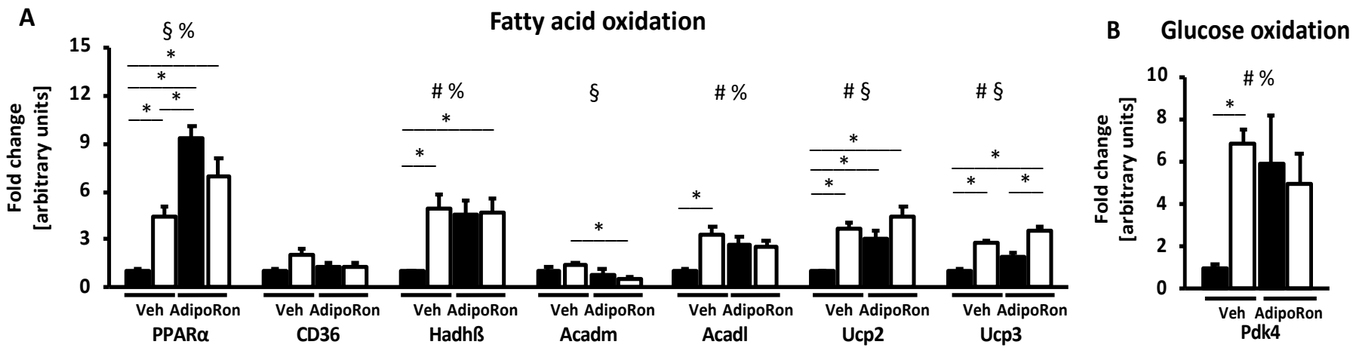
AdipoRon treatment: Mice were treated with 10mg/kg (i.p.) AdipoRon or vehicle for 10 days.

Myocardial ex vivo contractile function: Hearts of 10 weeks old male wild type and *db/db* mice were perfused in working mode using Krebs-Henseleit buffer containing 0.8 mM palmitate and 11 mM glucose. MVO2 was measured using a fiberoptic probe, and rates of energy metabolism using radiolabeled substrates (glucose, palmitate).

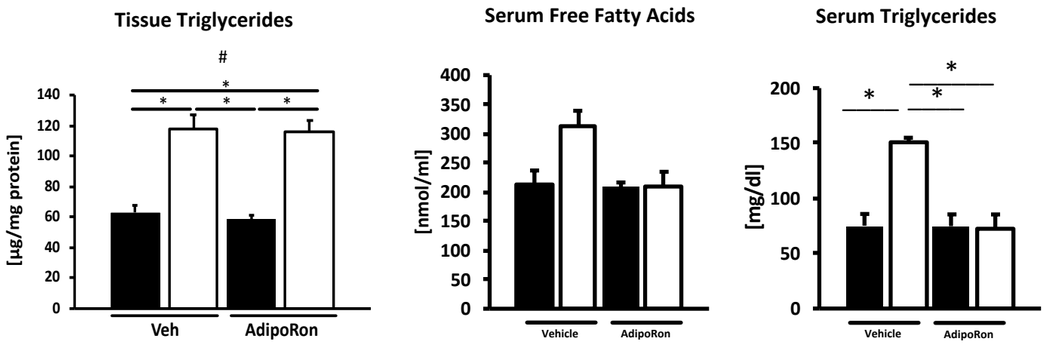
Gene expression was measured using real-time RT-PCR.

Serum metabolites were measured using commercially available kits.

## Gene expression pattern does not match shift in substrate oxidation in *db/db* mice




## AdipoRon treatment reduced serum FFA and TG level




**Conclusions:** AdipoRon treatment shifts myocardial substrate preference towards increased glucose utilization, likely by decreasing fatty acid delivery to the heart, but was not sufficient to improve cardiac output and efficiency in *db/db* mice.