

## Introduction and Experiment Design

- IMG-1 is a novel biologic therapeutic for the treatment of diabetes and its associated complications
- IMG-1 has been shown to successfully treat both Type I and Type II in animal models by decreasing insulin resistance and lowering glucagon (see poster 1215-P and poster 1115-P)
- To assess how IMG-1 decreases insulin resistance in both type I and type II diet-Induced Obese (DIO) C57BL/6J mice were used in a hyperinsulinemic-euglycemic clamp assay



- IMG-1 treated animals (n=8) and control (n=8), diet-Induced Obese (DIO) C57BL/6J mice underwent a 2-h hyperinsulinemic-euglycemic clamping procedure
- A constant plasma insulin level above fasting was maintained, while glucose was fixed at a basal level, (between 100-150 mg/dl)
- 2µg IMG-1 was administered intravenously via tail veins at 48 hours and 24 hours prior to the clamp test
- Basal and insulin-stimulated whole-body glucose turnover was estimated with a continuous infusion of [3-3H] glucose for 2 h before (0.05 $\mu$ Ci/ min) and throughout the clamp (0.1µCi/min)
- The glucose infusion rate (GIR), hepatic glucose production (HGP) and insulin-stimulated whole-body glucose turnover were determined

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Figure. Diet-Induced Obese (DIO) C57BL/6J mice underwent a 2-h hyperinsulinemiceuglycemic clamping to assess insulin action and glucose metabolism in IMG-1 treated (2µg IMG-1 administered IV via tail vein 48 and 24hrs prior to the clamp test, n=8) or PBS treated

animals (n=8). IMG-1 treated animals had a significantly higher steady-state glucose infusion rates during clamping than PBS treated animals (A). Glucose metabolism in skeletal muscle and adipose tissue was measured post clamp analysis (B), and showed no significant different in

### IMG-1 Lowers Insulin Resistance by Decreasing Hepatic Glucose Production in a DIO Mouse Clamp Test

# IMG-1 Decreases Insulin Resistance and Inhibits Hepatic Glucose Production







either IMG-1 or PBS treated animals, while hepatic Glucose Production (HGP) was dramatically suppressed in all animals treated with IMG-1 (C), but IMG-1 did not affect whole-body glucose turnover, glycolysis or glycogen synthesis in any of the treated animals (D).



#### Summary

- IMG-1 represents a novel therapeutic for Diabetes
- IMG-1 has been shown to successfully treat Type I mice and rats (STZ models, see poster 1215-P)
- IMG-1 has been show to effectively treat Type II Diabetic ZDF rats and its associated cardiovascular complications (see poster 1115-P).
- IMG-1 Decreases Insulin Resistance
- IMG-1 Inhibits Hepatic Glucose Production in Diet-Induced Obese Mice
- IMG-1 Does not Affect Skeletal Muscle or Adipose Tissue Glucose Uptake
- IMG-1 Does not Affect whole-body glucose turnover, glycolysis or glycogen synthesis

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