The Effects of Hyperglycemia on the Regression of Atherosclerosis

Goldberg/Fisher Project
Edward A. Fisher, MD, PhD
Leon H. Charney Professor of Cardiovascular Medicine, NYU

Non-surgical Model of Regression

Basic goal: significant lowering of LDL-C *after plaques form* to simulate aggressive lipid management

Two approaches:

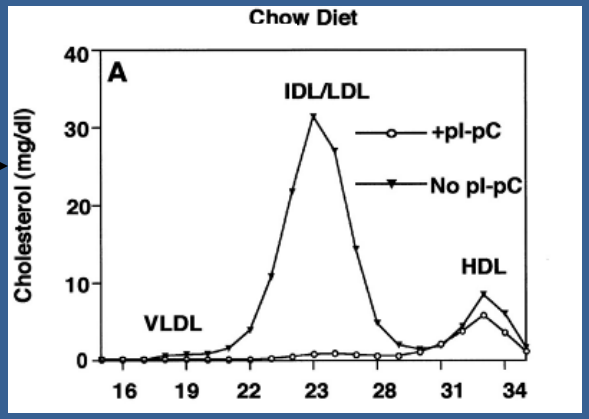
Reversa mouse: a genetic switch that shuts off VLDL/LDL production conditionally

LDLR-/- mice treated with adenoviral LDLR

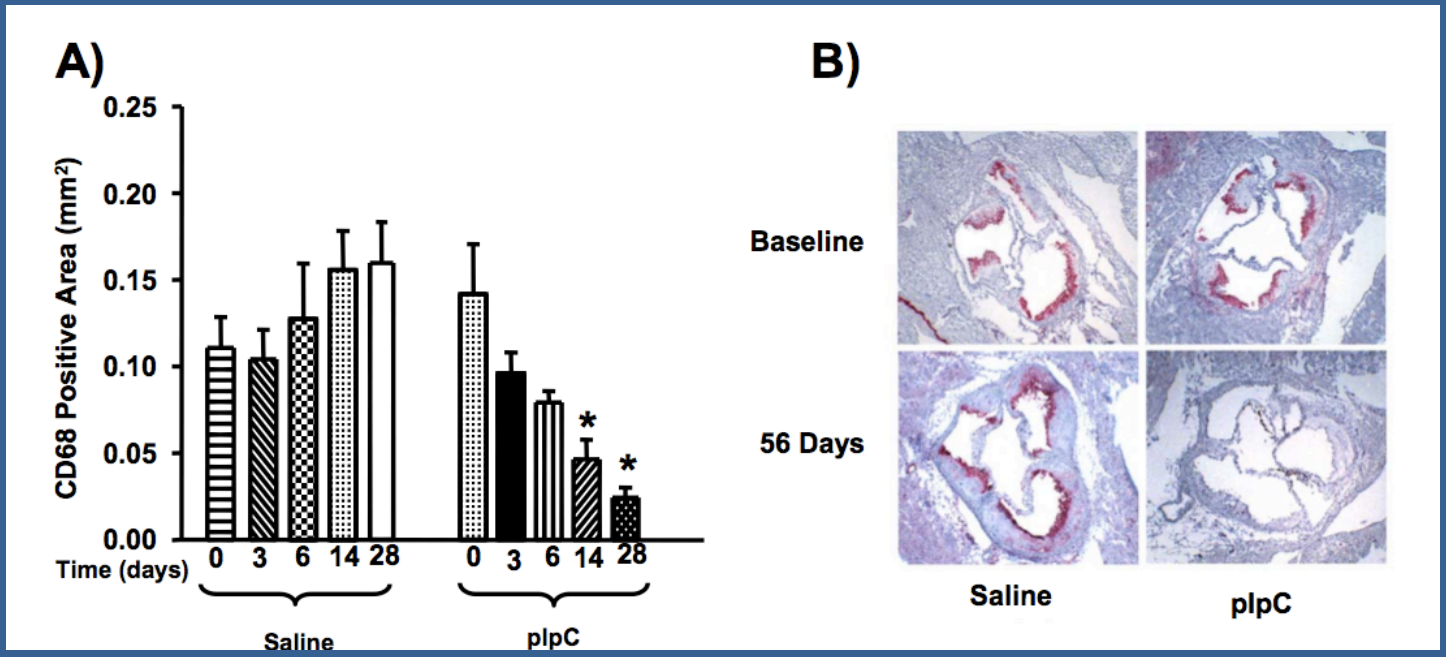
Regression model - Reversa mouse

Inactivation of *Mttp*

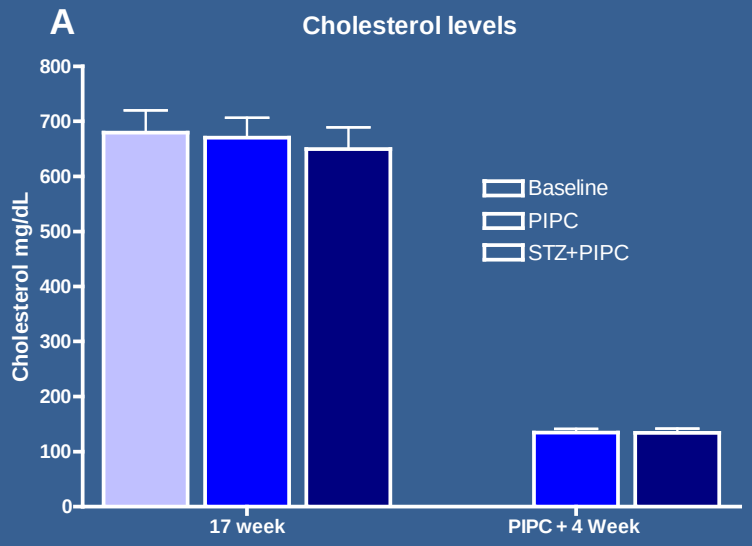
apoB is degraded

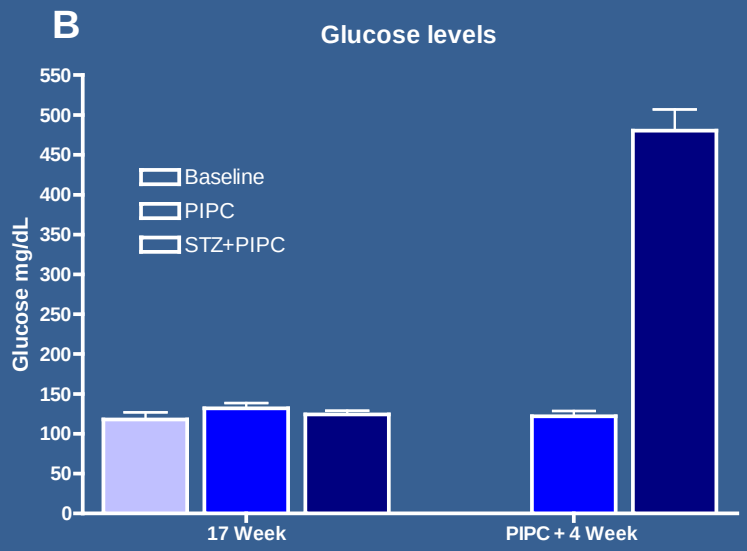


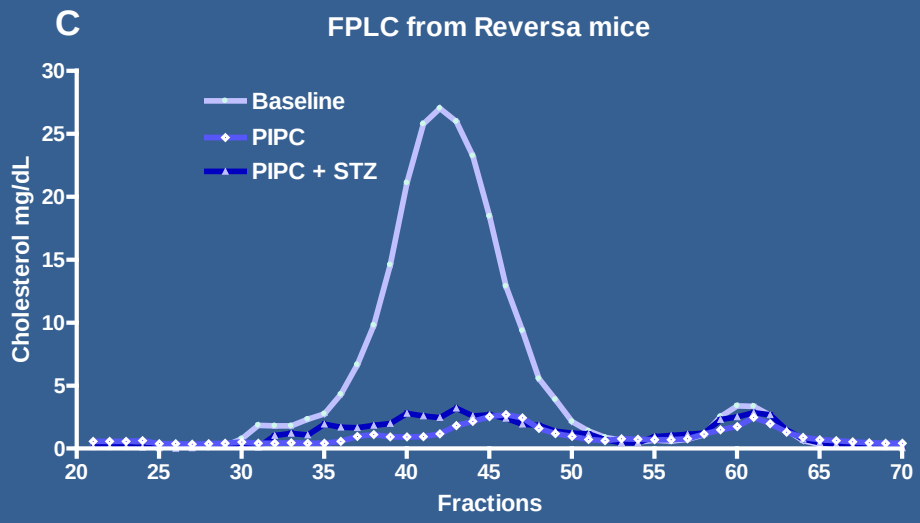
Lieu *et al*. Circulation 2003



Experimental Design

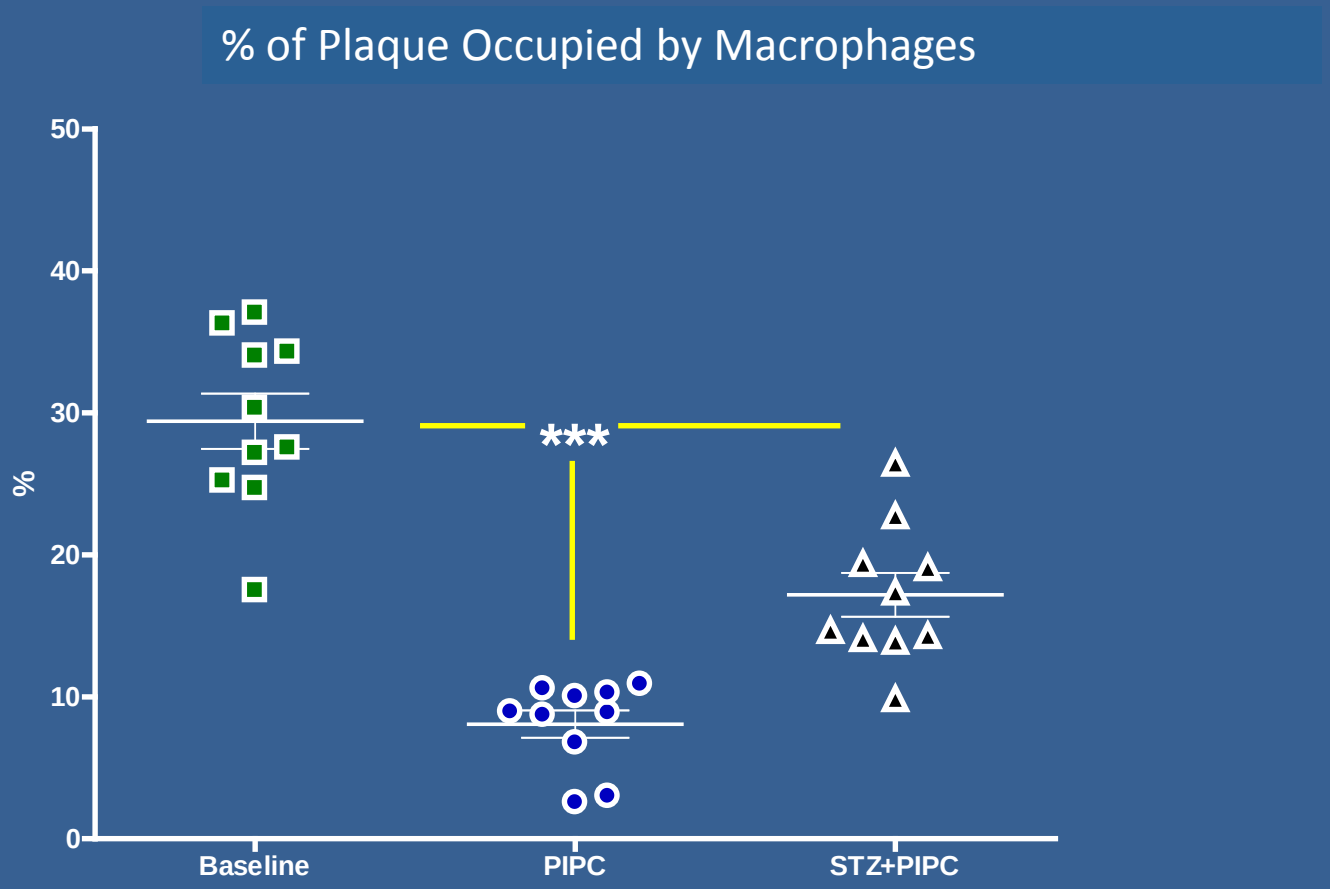




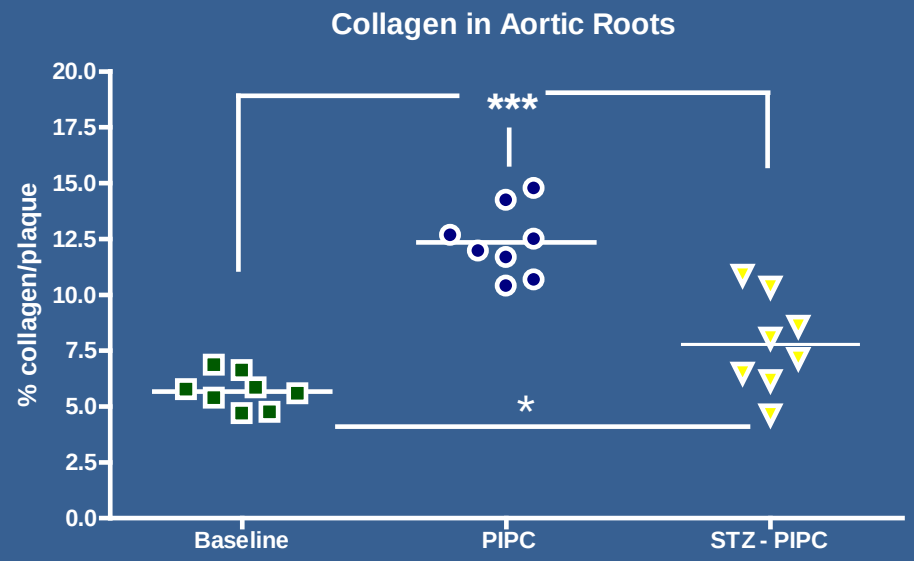


Lipid levels are similar between control and STZ mice

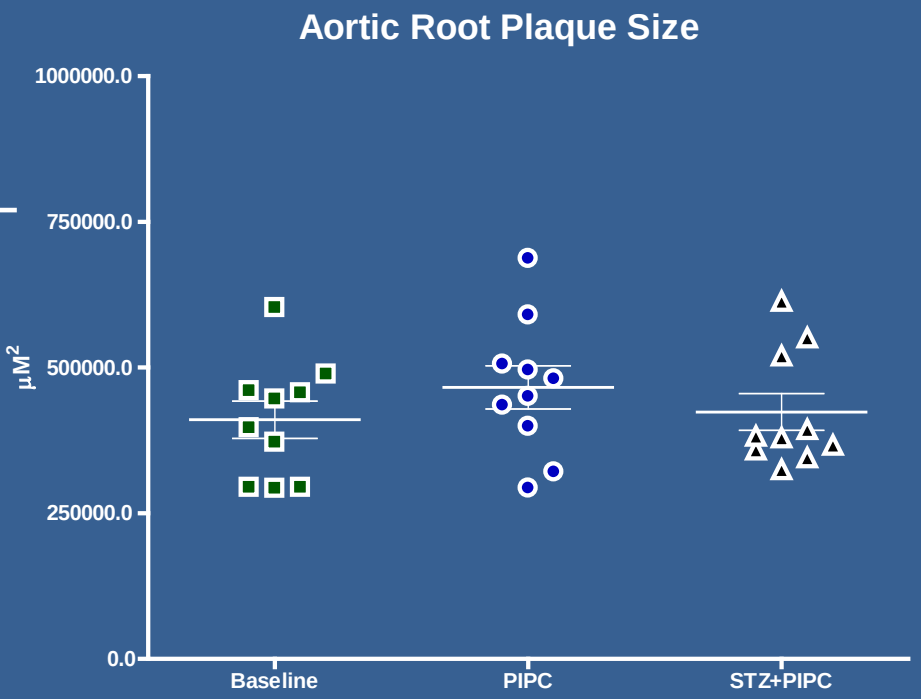
Morphometric Results



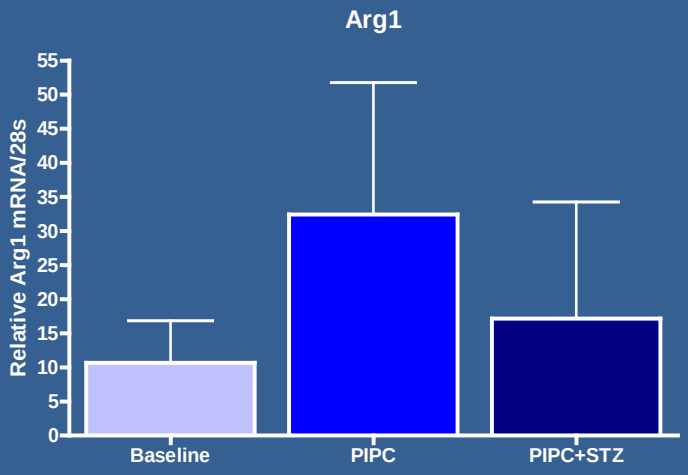
Morphometric Results

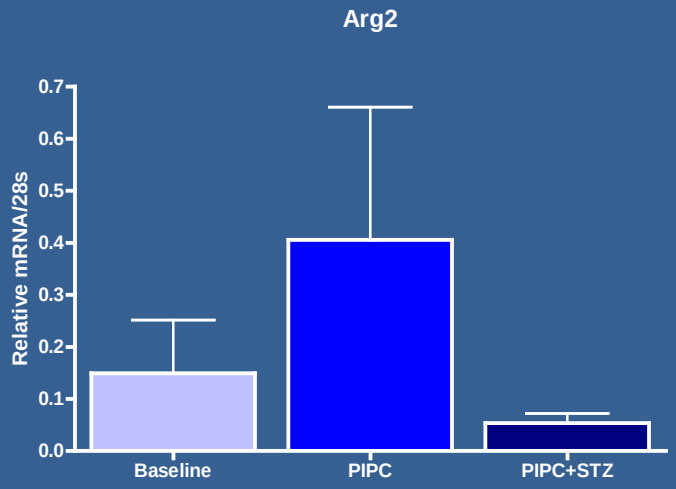


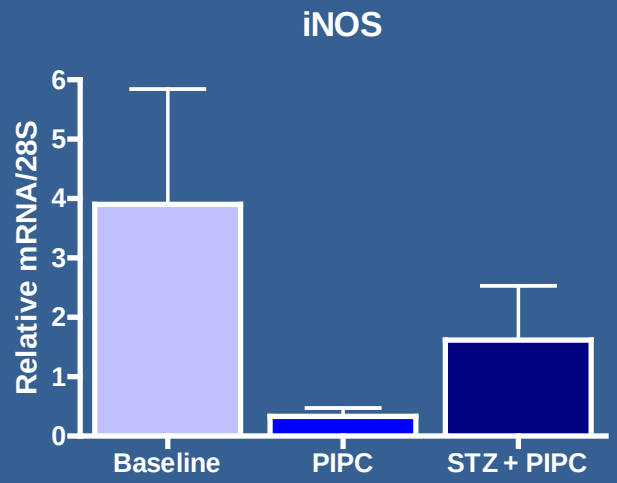
Polarized microscopy, sirius red

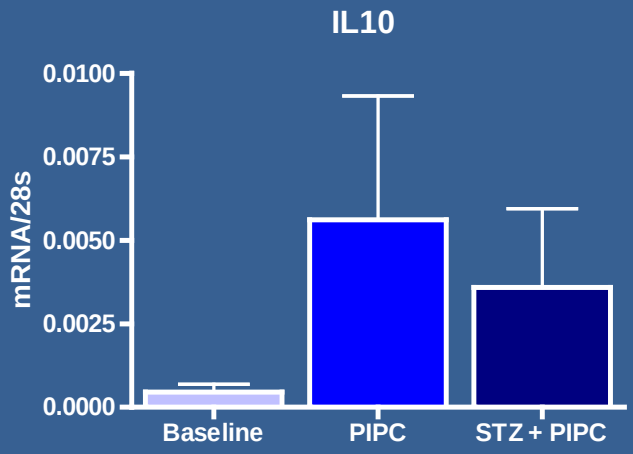


Hyperglycemia impairs the polarization of macrophages during regression to the anti-inflammatory M2 state



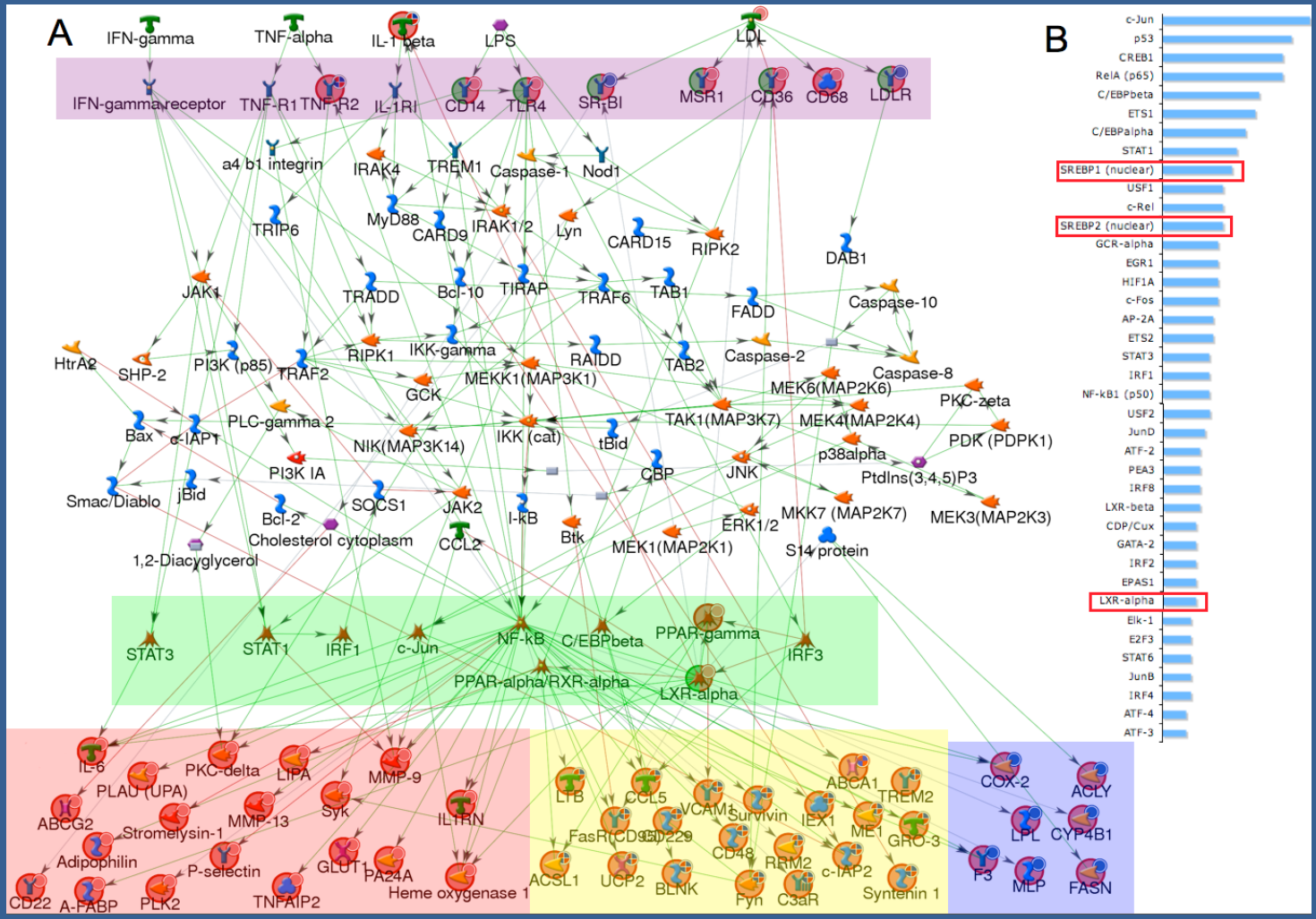






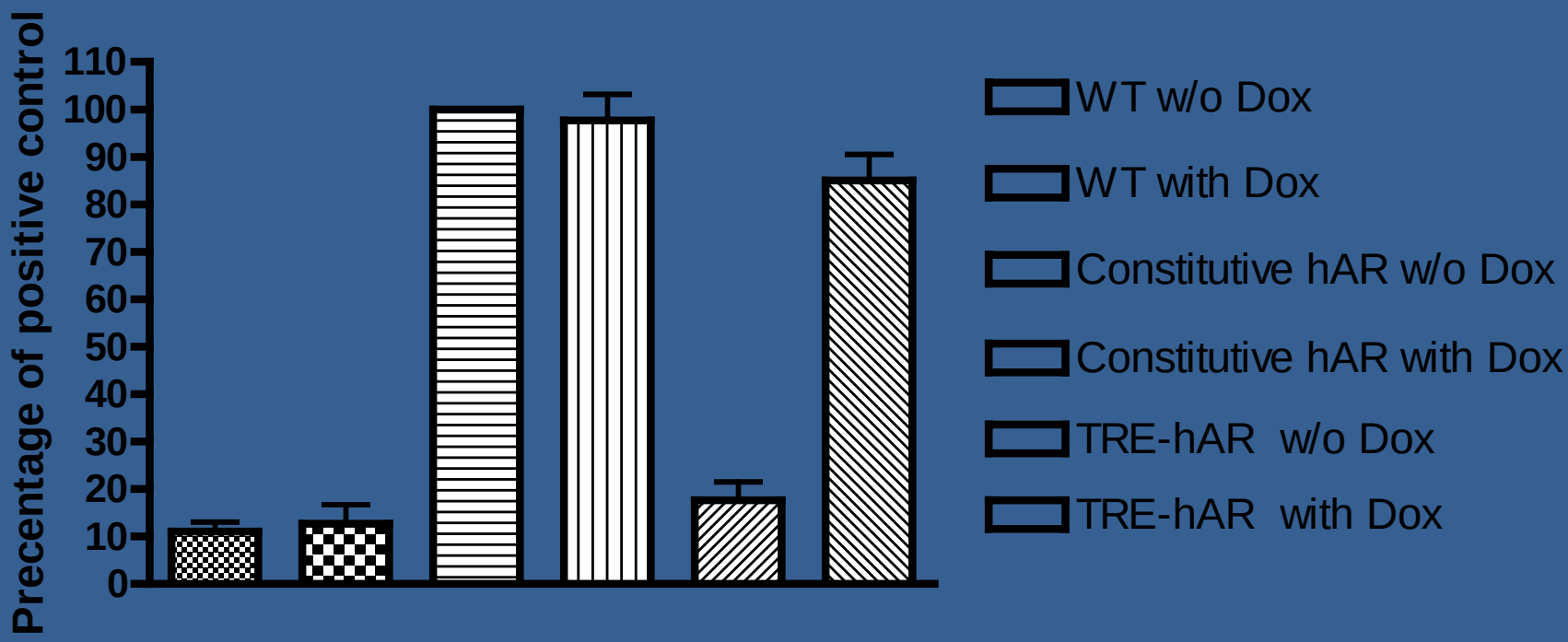
Similar results (to date) with LDLR-adenoviral and surgical approaches

A Systems Biological Approach to Regression and its Dysregulation by Hyperglycemia



w/Liz Gold, Steve Ramsey, Alan Aderem, Institute for Systems Biology, Seattle

Other goal: an inducible hAR mouse



w/JAX crew; Tet on system driven by the generally expressing promoter H-2K^{d}; being bred to LDLR-/-

Acknowledgements

- Saj Parathath
- Chujun Yuan

- Ira Goldberg
- Li-shin Huang

- NIH- for $$ and the advisory board who encouraged new models of regression