



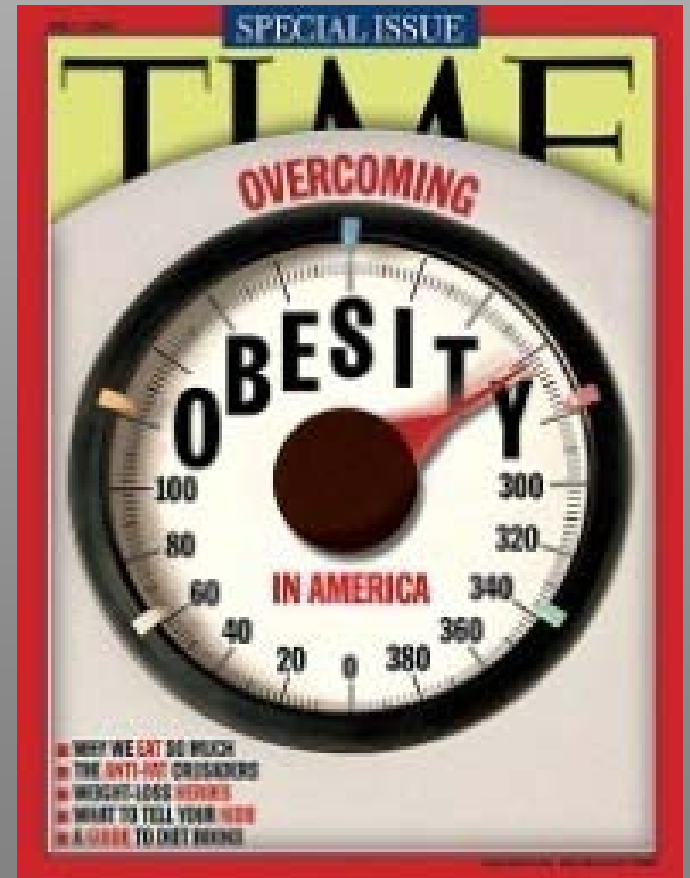
Aldose Reductase-Dependent Effects on Endothelial Dysfunction and Endothelial Progenitor Cells in Diet- Induced Obesity

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Background

- Diabetes and obesity are reaching epidemic levels in the United States.
 - Currently ~ 16 million diabetics and greater than 30 million obese and prediabetic individuals.
- Diabetes and obesity enhance cardiovascular disease risk by 2-9 times.



**One common environmental factor is
high fat diet**



High Fat Diet

Obesity

Metabolic Syndrome

Hypercholesterolemia

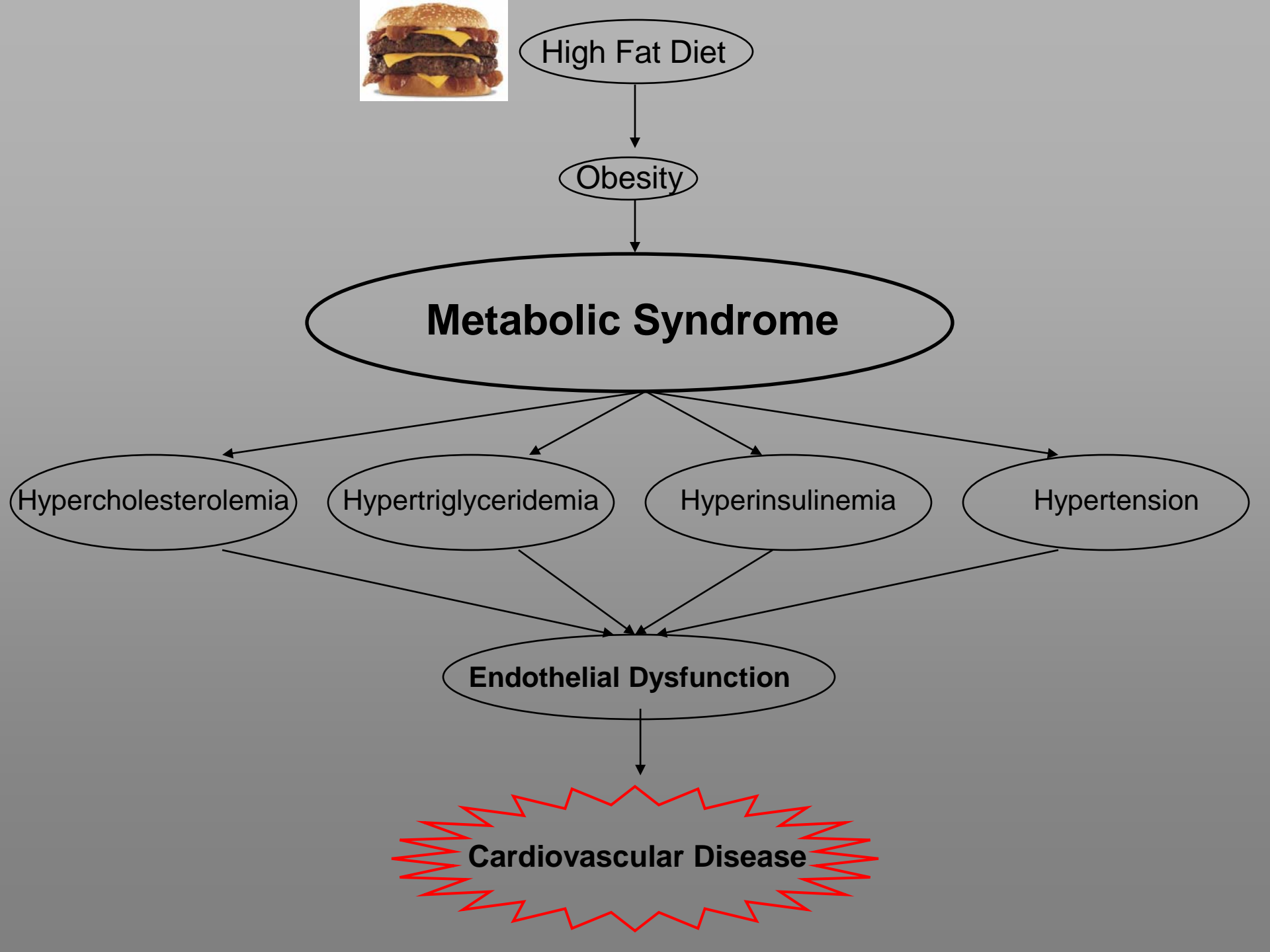
Hypertriglyceridemia

Hyperinsulinemia

Hypertension

Endothelial Dysfunction

Cardiovascular Disease



Aldose Reductase is Important in Detoxification Metabolism

High Fat Diet



Oxidative Stress

Lipid Peroxidation

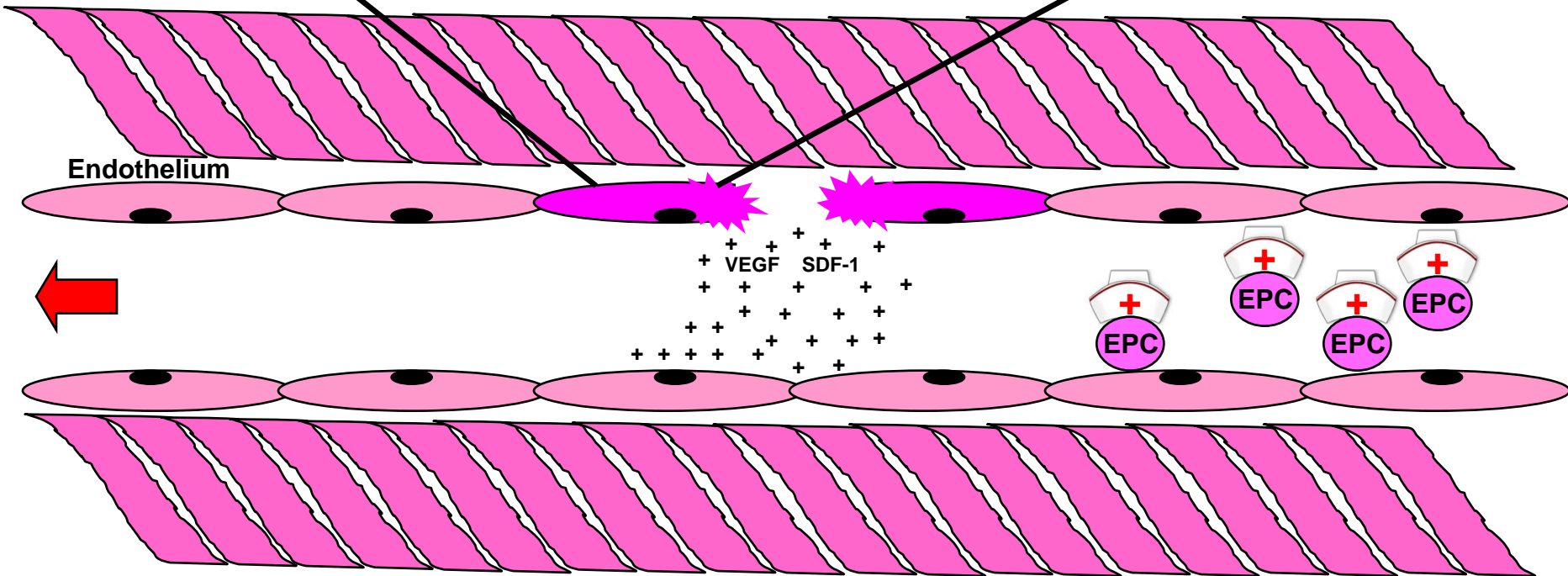
Unsaturated Aldehydes

Toxic (Dysfunction)

Aldose Reductase

Alcohol

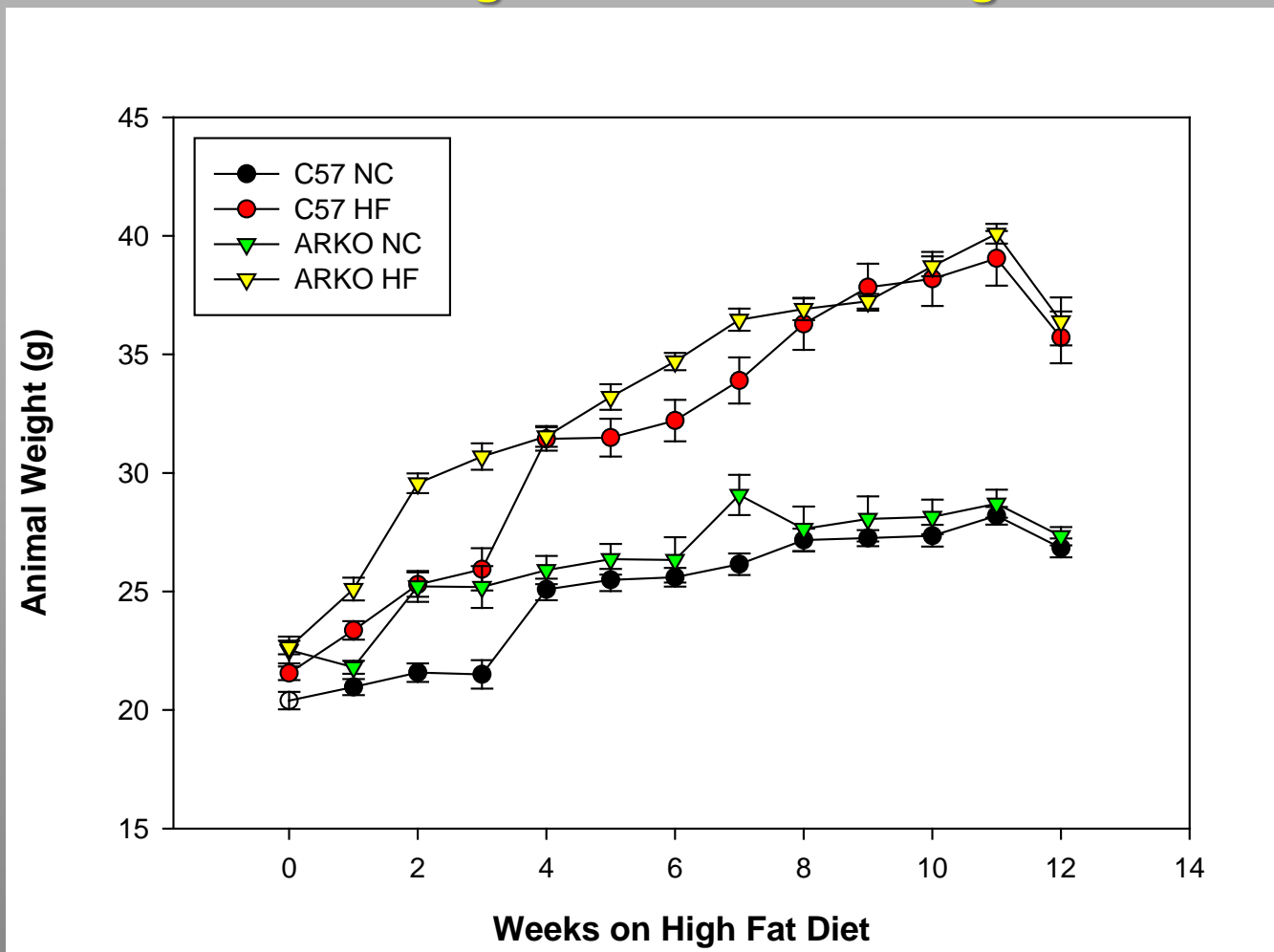
Less Toxic
(maintain function)



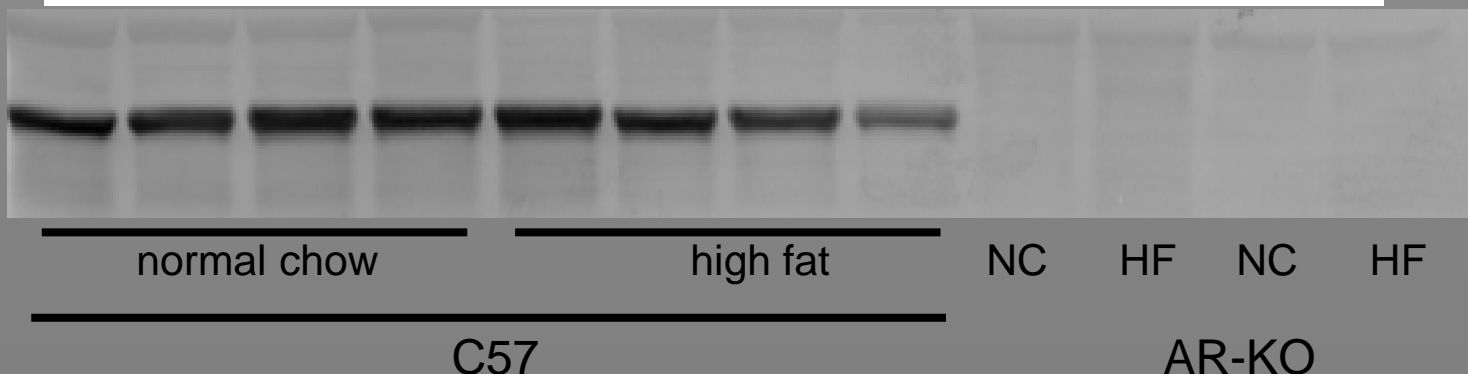
Methods

- C57B/6 (C57) and aldose reductase null (ARKO) male mice were placed onto either a 13.5% kcal from fat normal chow (NC) diet or a 42% kcal from fat high fat (HF) diet for 12 weeks
 - Plasma Levels
 - Cholesterol
 - Triglycerides
 - Insulin
 - Endothelial Function
 - Endothelial Progenitor Cells

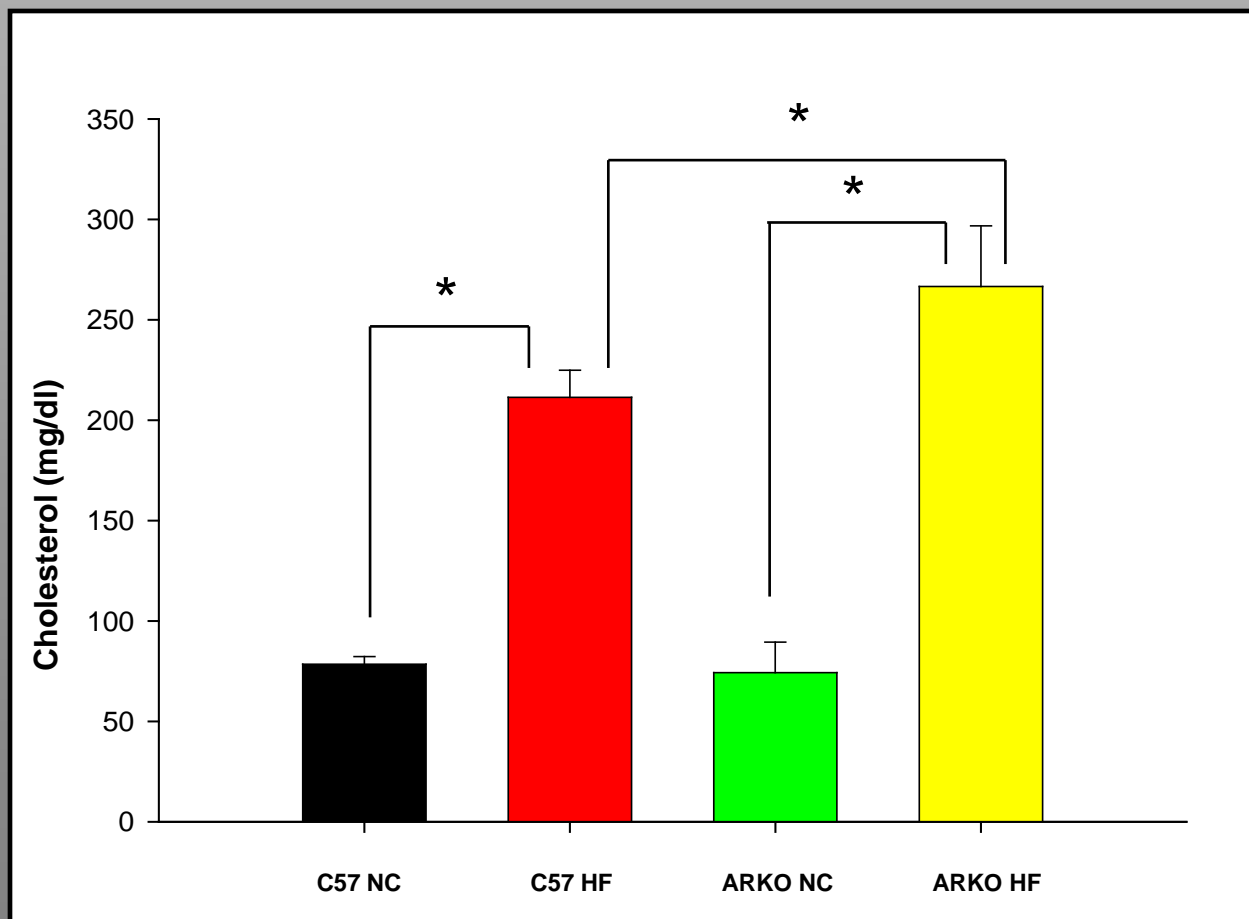
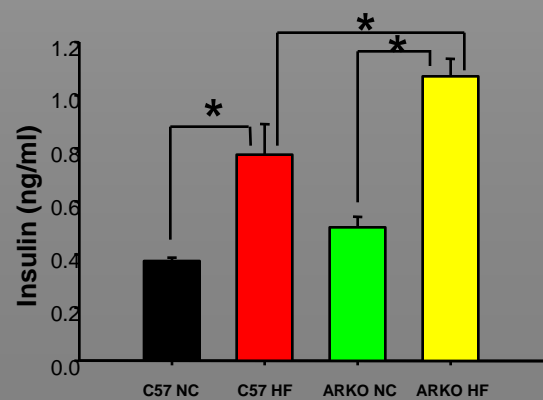
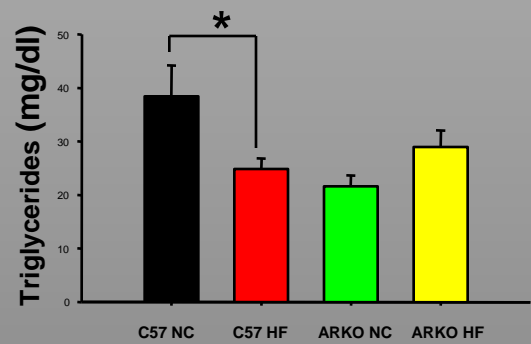
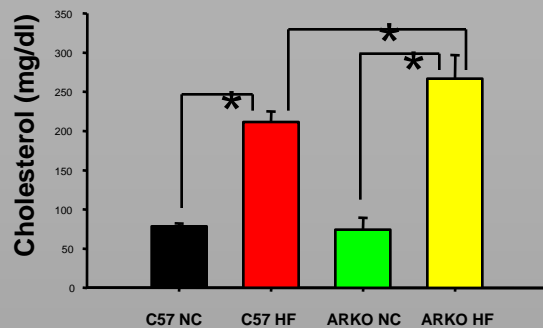
C57 and ARKO Animals on High Fat Diet Gain Weight at the Same Rate



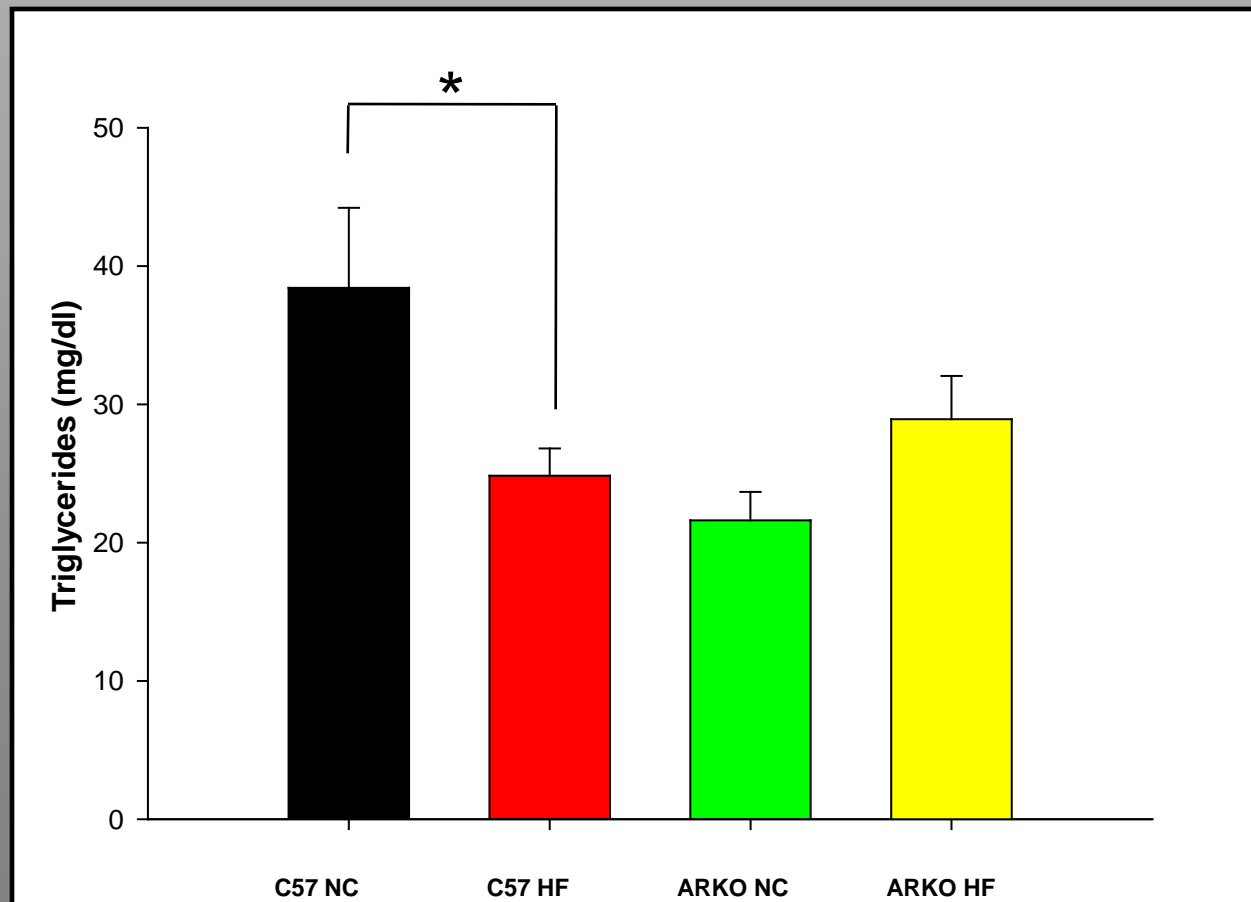
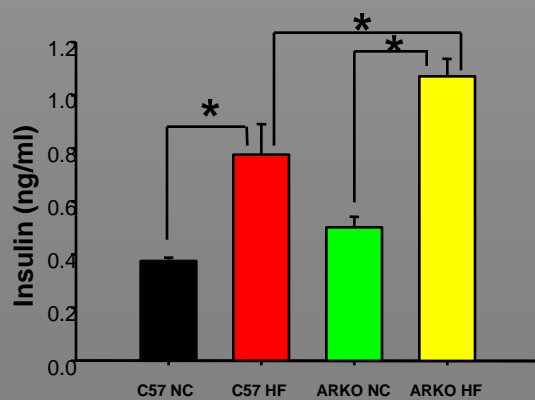
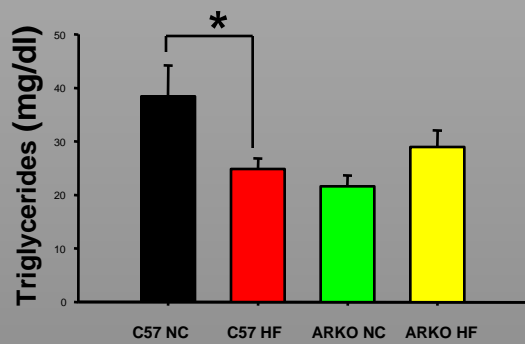
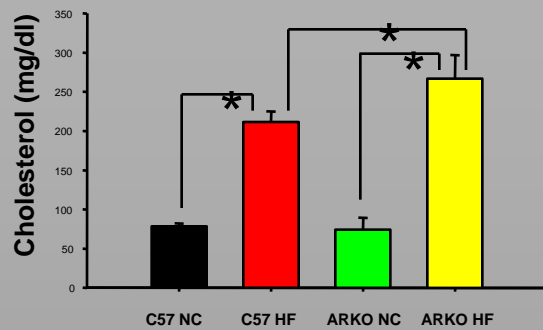
Aldose
Reductase



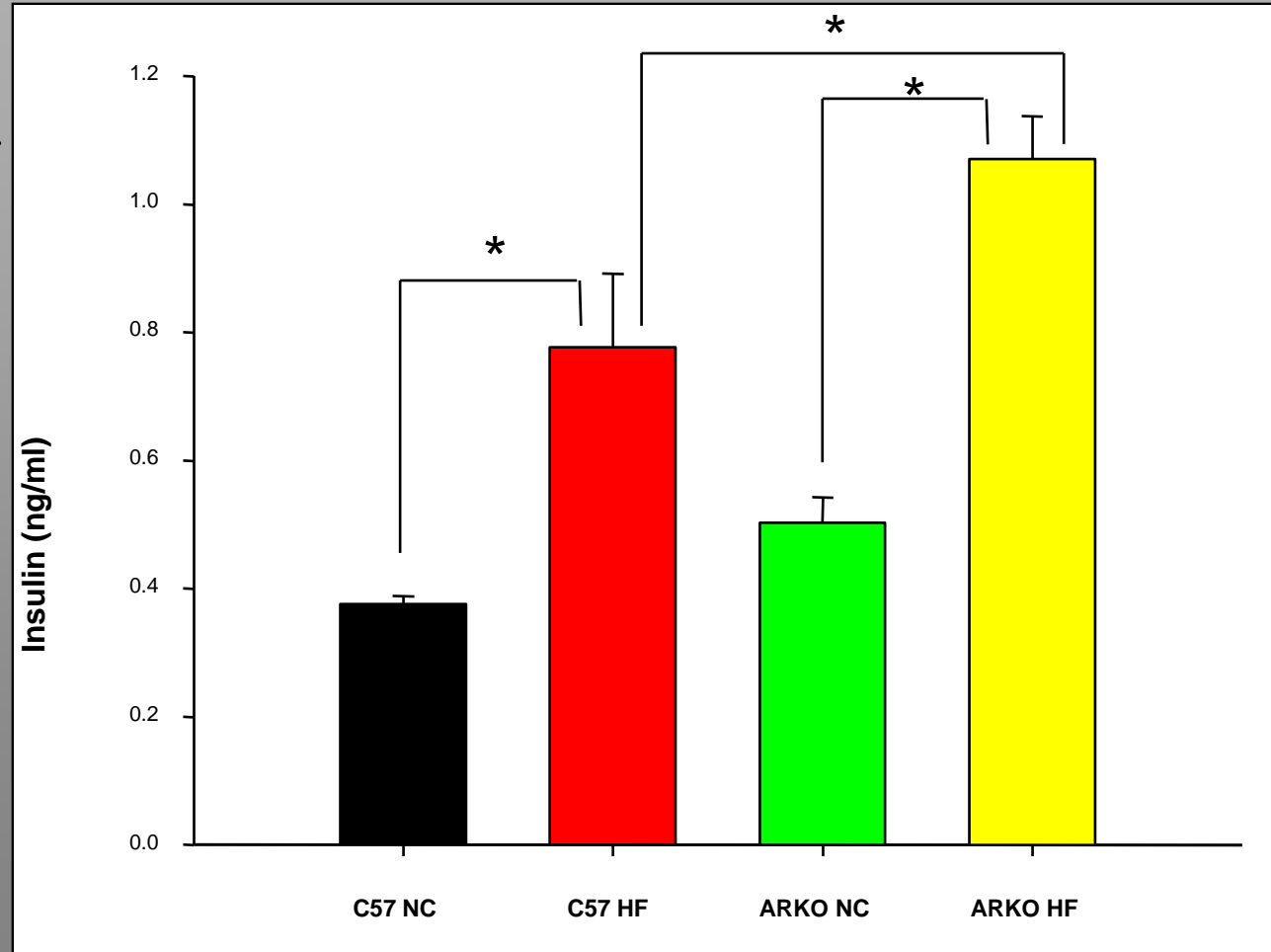
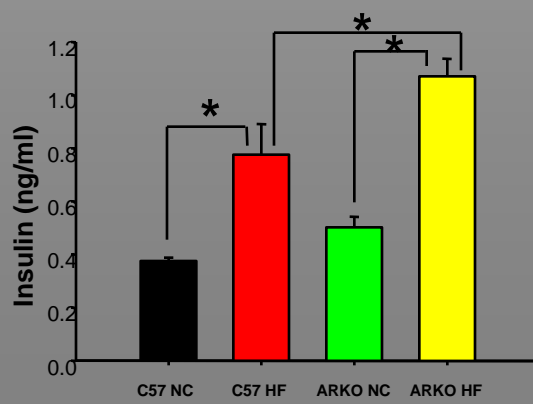
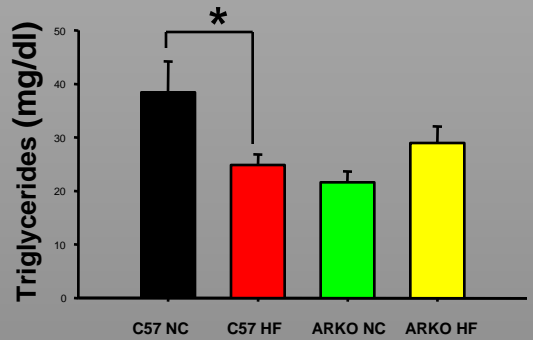
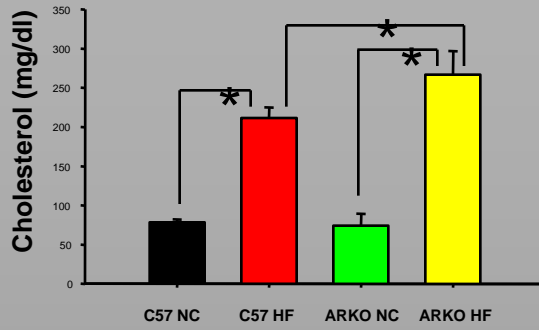
C57 and ARKO Animals on High Fat Diet Display Hypercholesterolemia



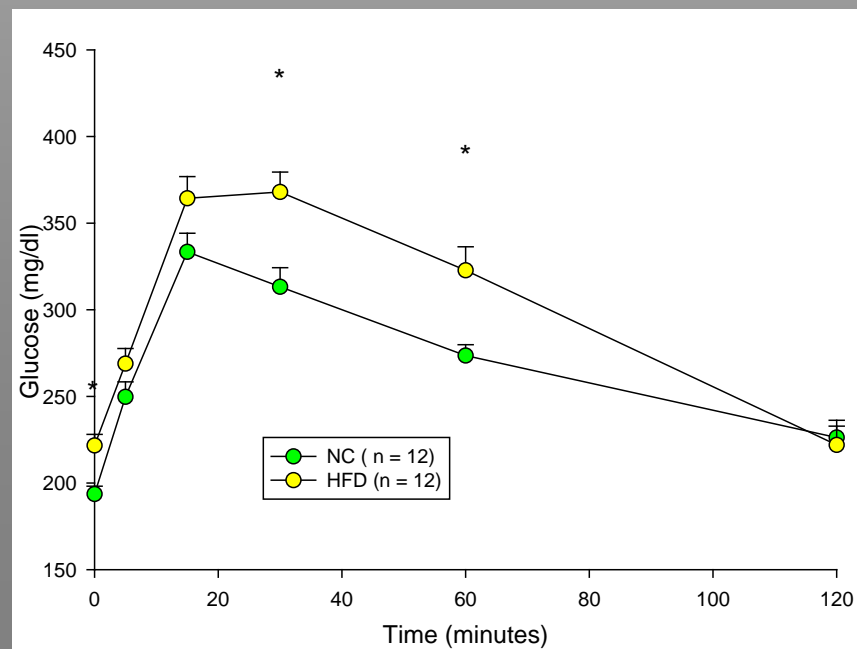
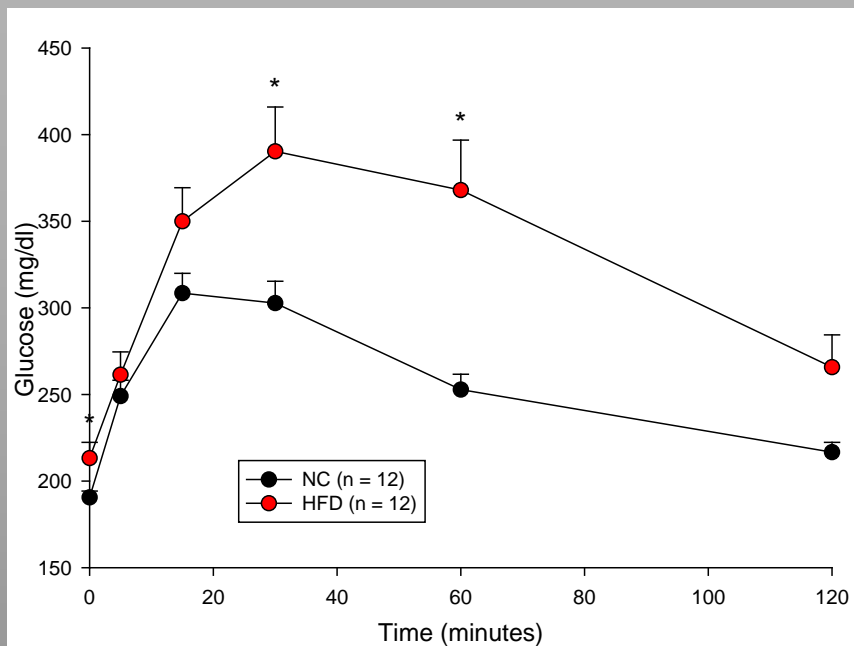
C57 and ARKO Animals on High Fat Diet Do Not Display Hypertriglyceridemia



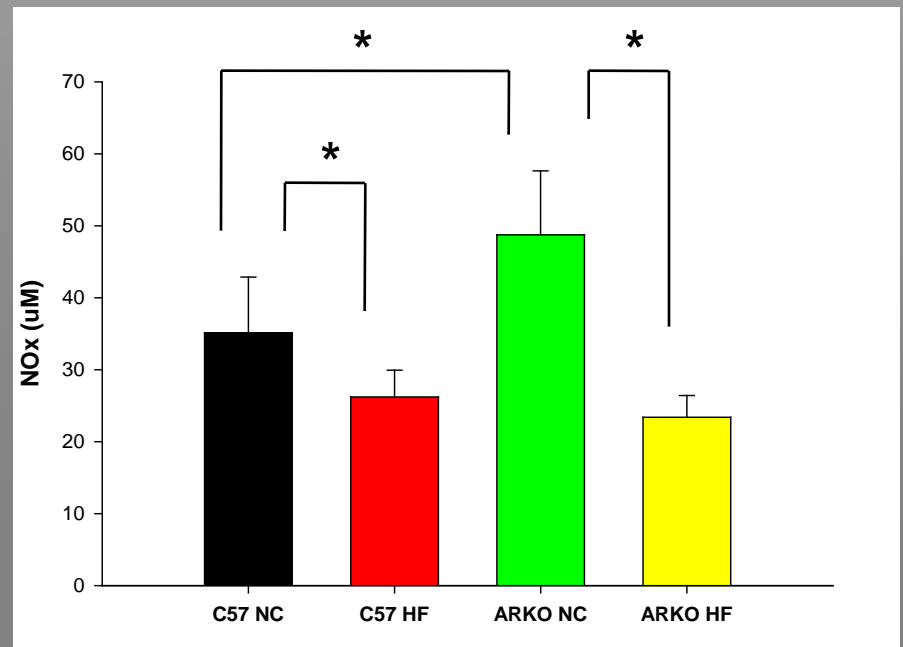
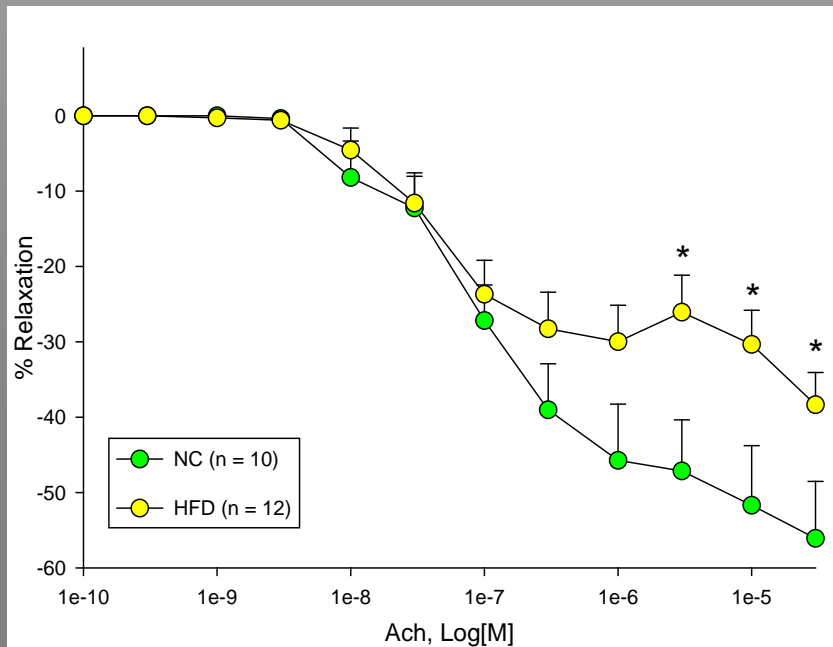
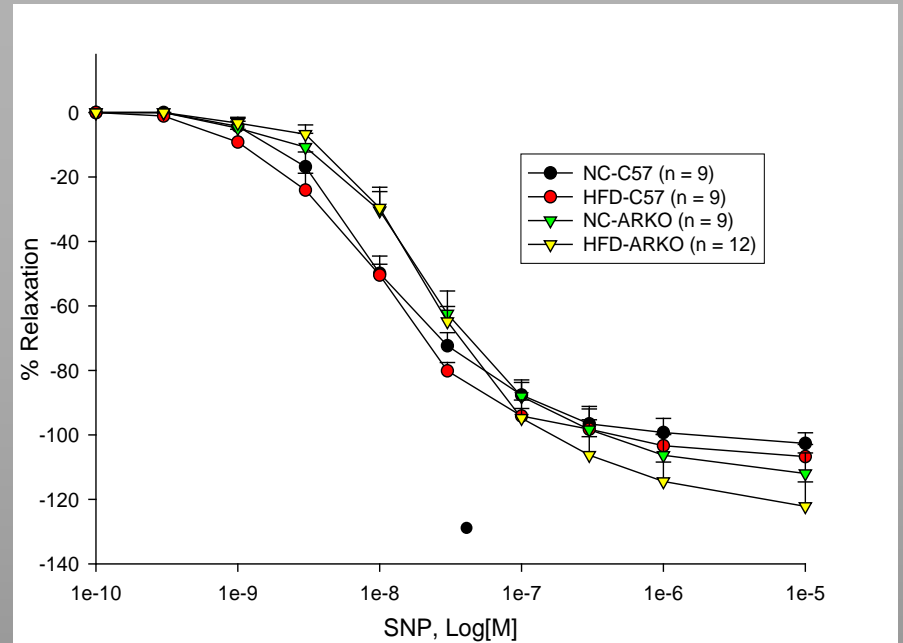
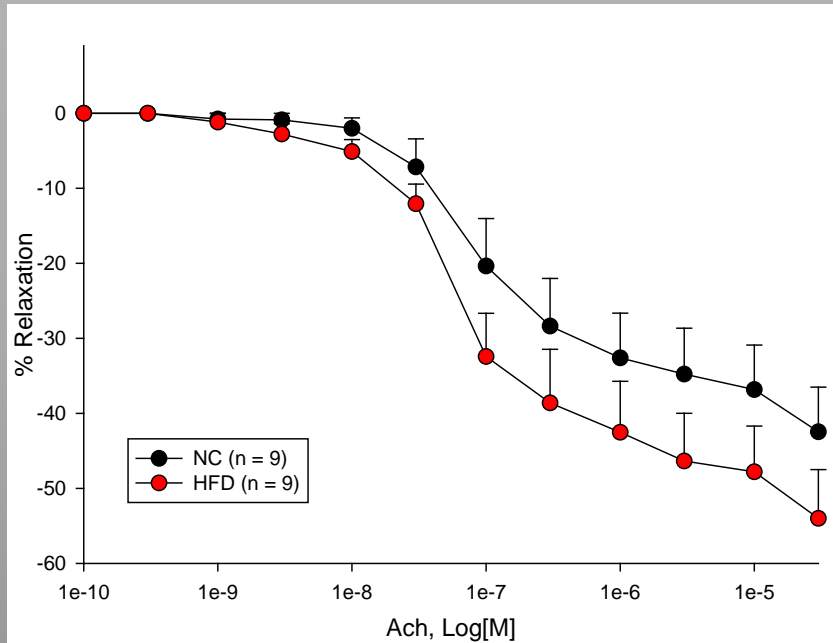
C57 and ARKO Animals on High Fat Diet Display Hyperinsulinemia



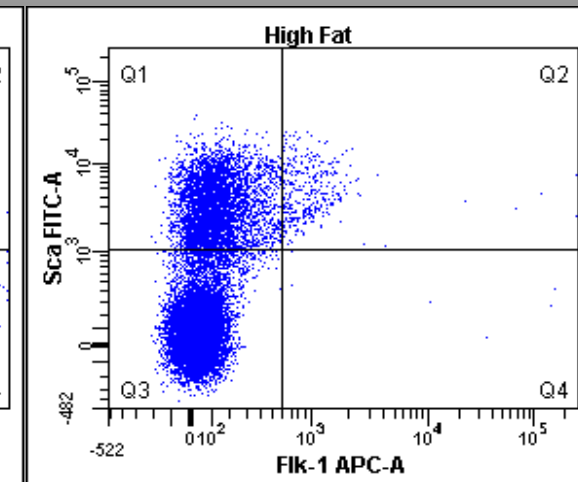
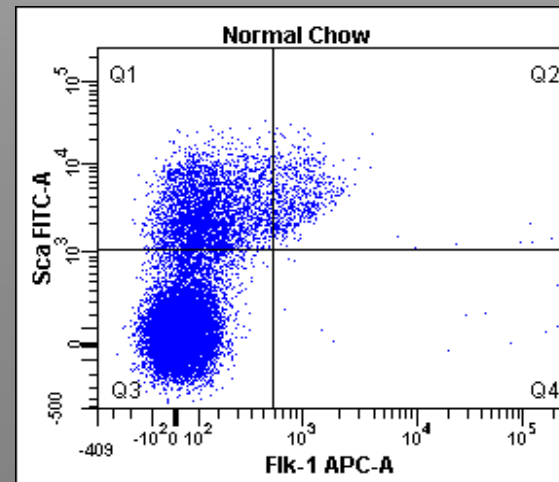
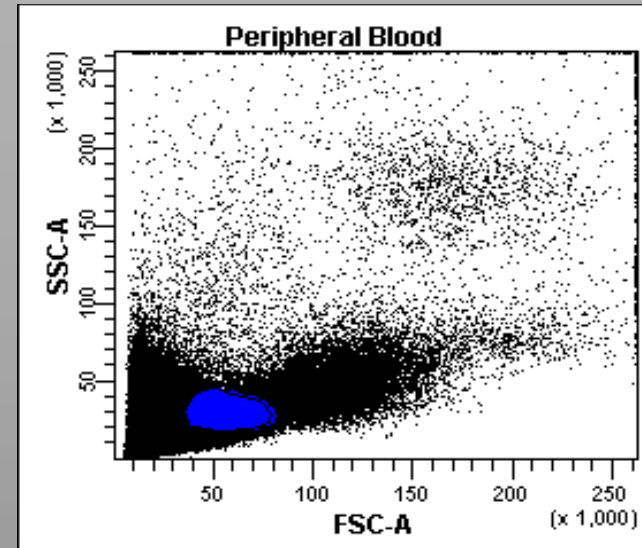
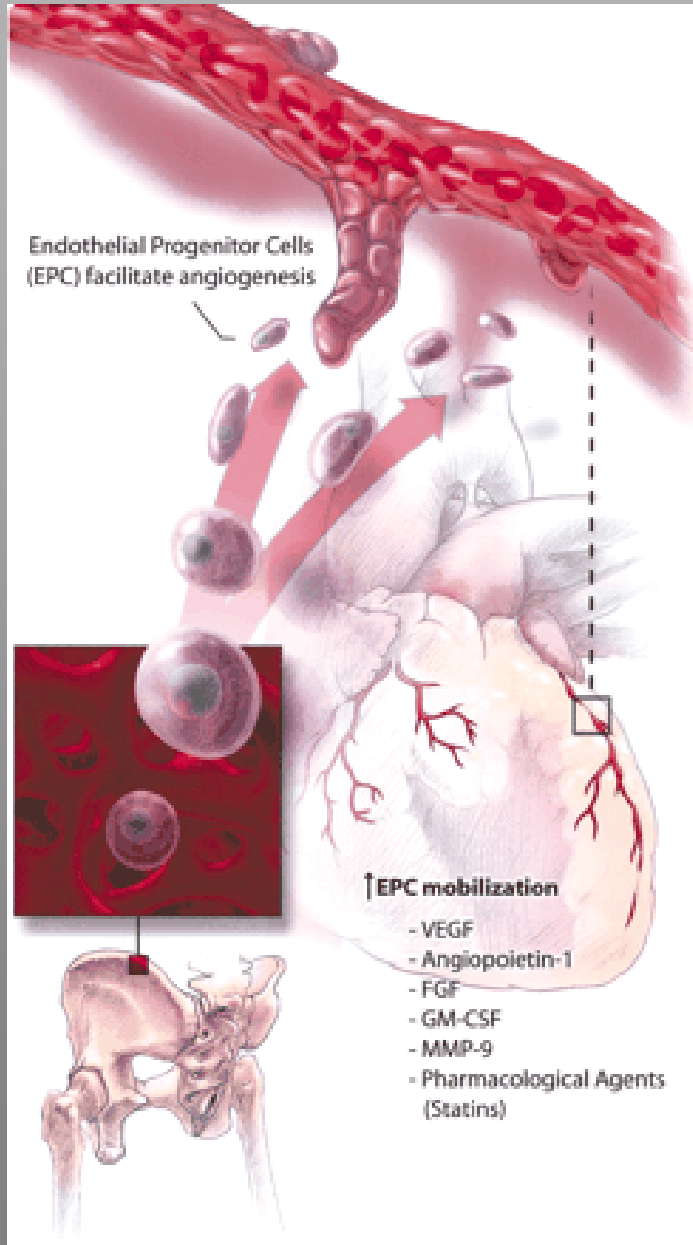
C57 and ARKO Animals on High Fat Diet Display Delayed Glucose Disposal Rate



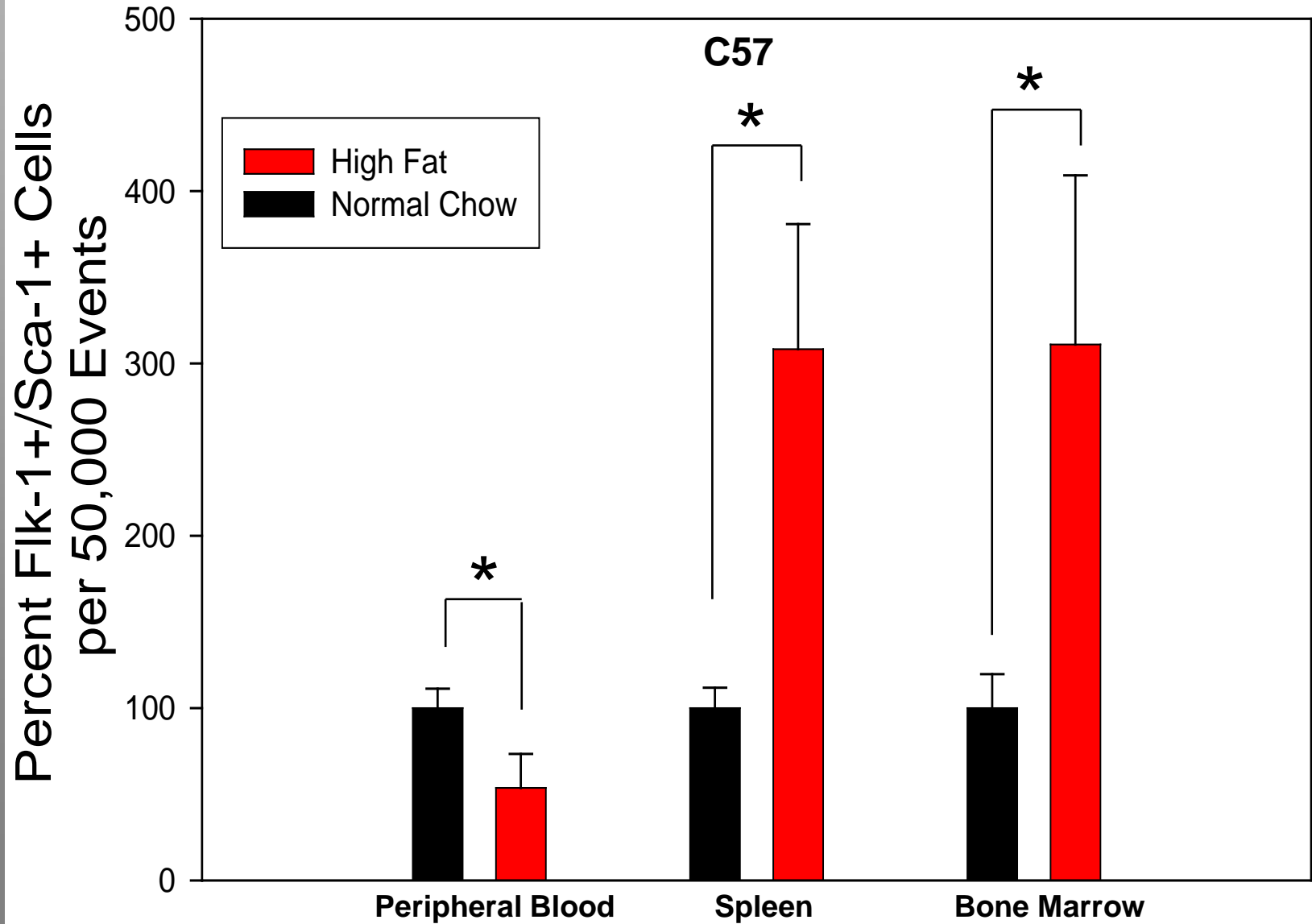
ARKO Animals on High Fat Diet Display Endothelial Dysfunction



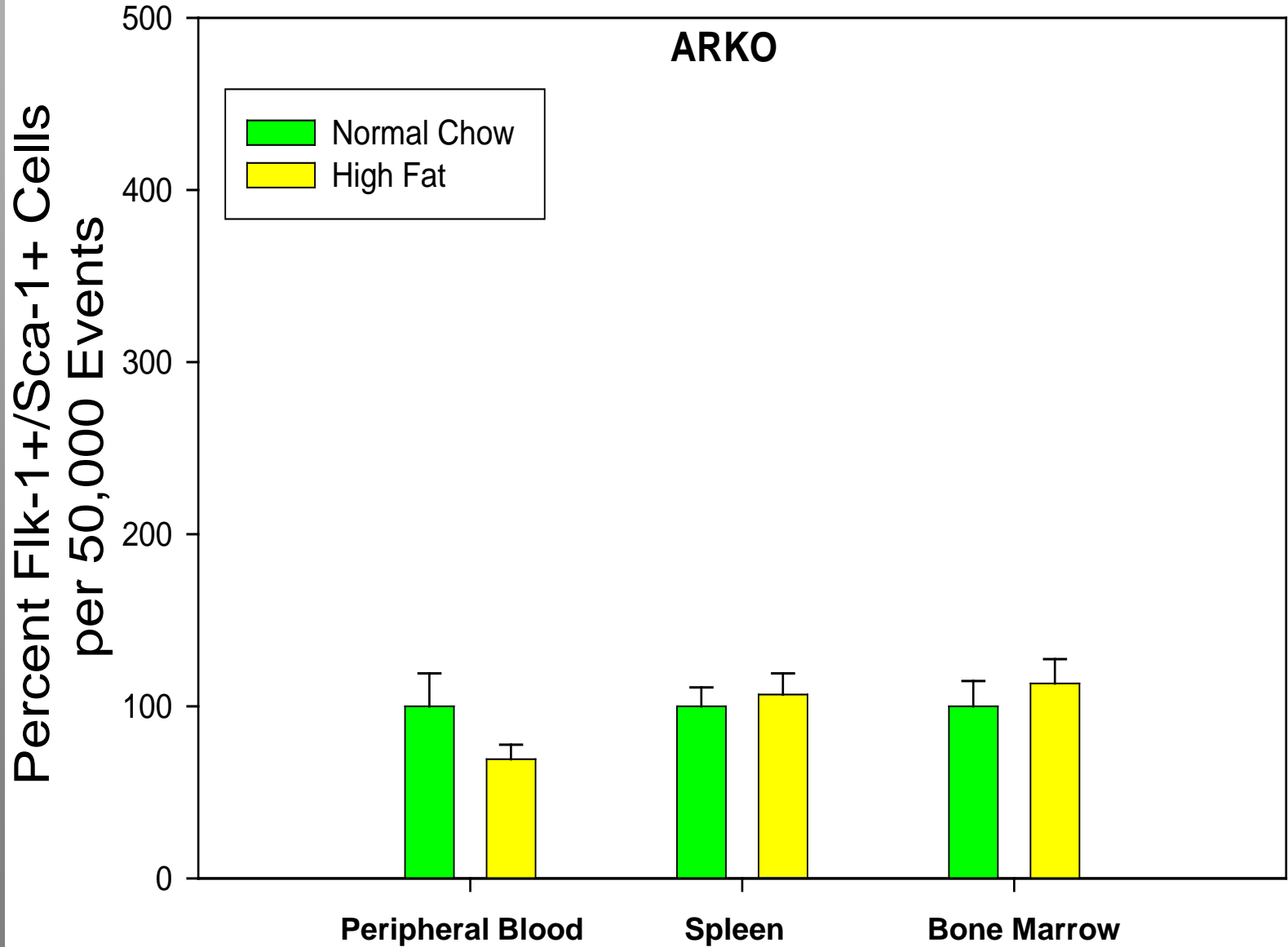
High Fat Diet Results in Decreased Endothelial Progenitor Cells in Peripheral Blood



C57 Animals on High Fat Diet Show EPC Mobilization



ARKO Animals on High Fat Diet Do Not Show EPC Mobilization



Conclusion

- Aldose reductase deficiency enhances the sensitivity of the endothelium to oxidative stress induced by high fat diet, perhaps through the accrual of lipid peroxidation products and could result in endothelial dysfunction.

Acknowledgments

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