

Effect of CARD9 on adipocyte lipolysis

Samantha E. Haller, Kayla A. Wilson, Matthew R. Peterson,
Guanglong He

Relevance

- More than one third of adults in America are obese [1]
- Obesity is associated with an excess of white adipose tissue, due to increased triglyceride storage [2]
- Excess white adipose tissue leads to chronic inflammation [3]
 - Adipokines
 - Free fatty acids

Background-Basal lipolysis

- Basal lipolysis is the breakdown of triglycerides into fatty acids and glycerol in the absence of stimulatory factors [4]
- Obesity leads to increased rate of basal lipolysis [2]
- Basal lipolysis leads to an excess of free fatty acids [4]
 - Excessive free fatty acids lead to insulin resistance

Background- Basal Lipolysis

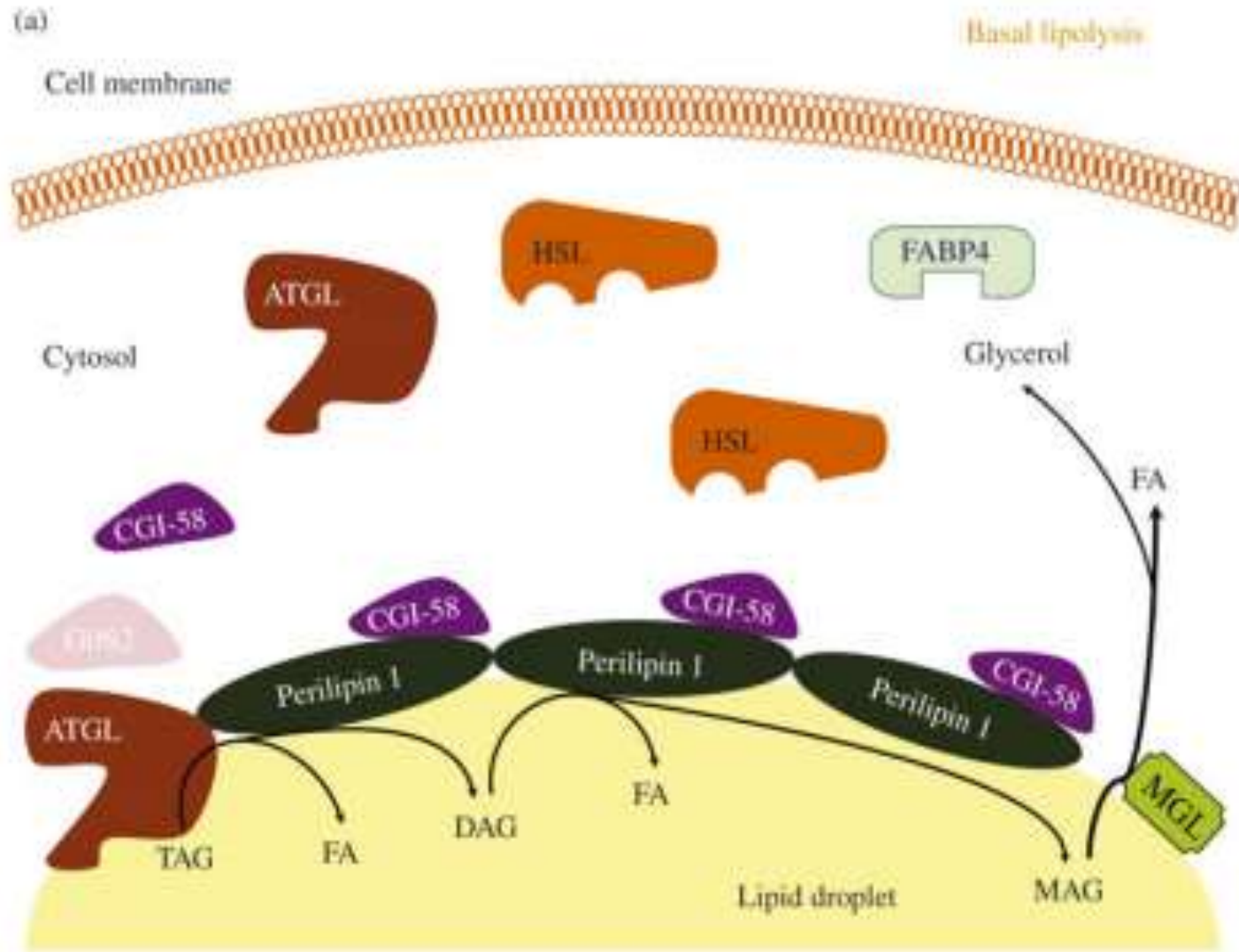
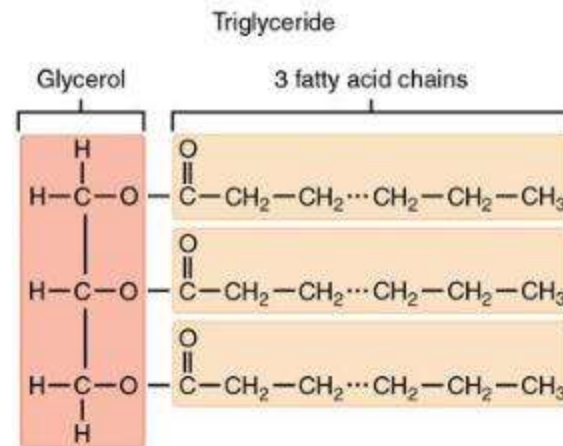


Figure adapted for use from Frühbeck, 2014

Background-Stimulated Lipolysis

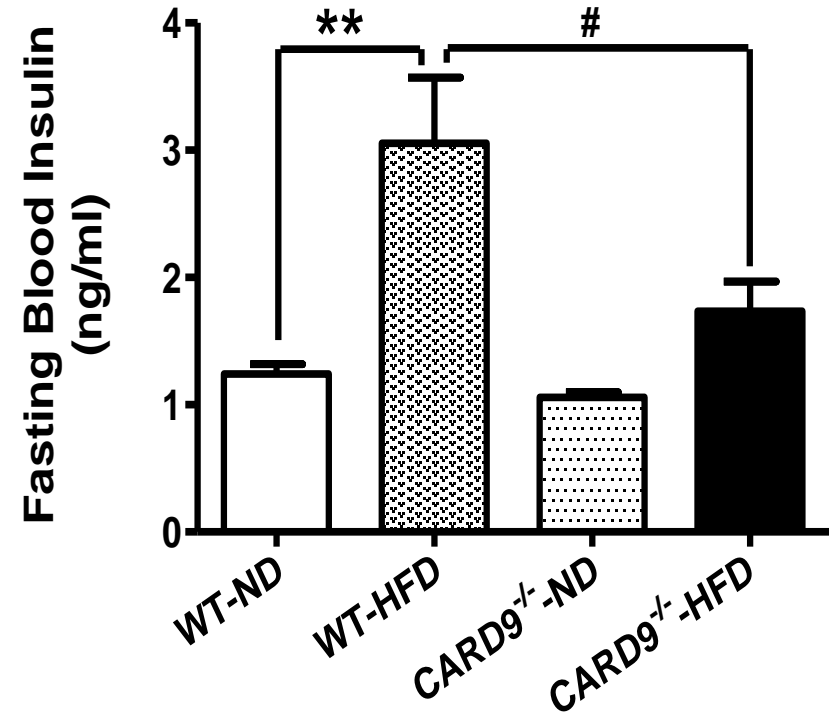
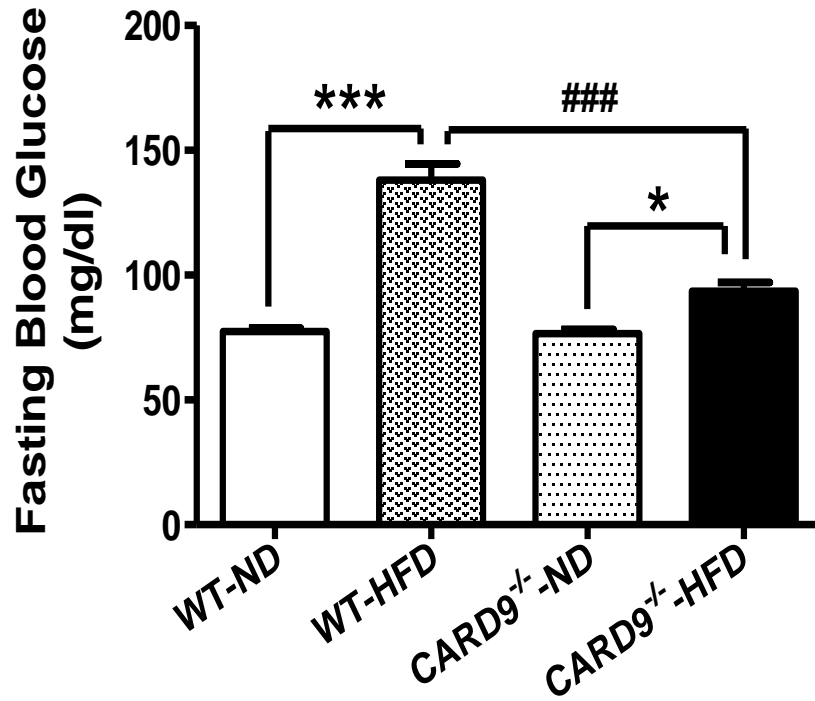
- Activated by catecholamines such as adrenaline and noradrenaline [4]
- Activation leads to the breakdown of triglycerides into free fatty acids and glycerol
- Obesity leads to a decreased rate of stimulated lipolysis [2]



Background-CARD9

- Caspase recruitment domain-containing protein 9
- Regulatory protein in the immune response
 - Activates pro-inflammatory cytokines
- CARD9^{-/-} improves insulin sensitivity [6]

Background-CARD9



WT: Wild Type ND: Normal Diet HFD: High Diet

Figure adapted for use from Cao, 2016

Hypothesis

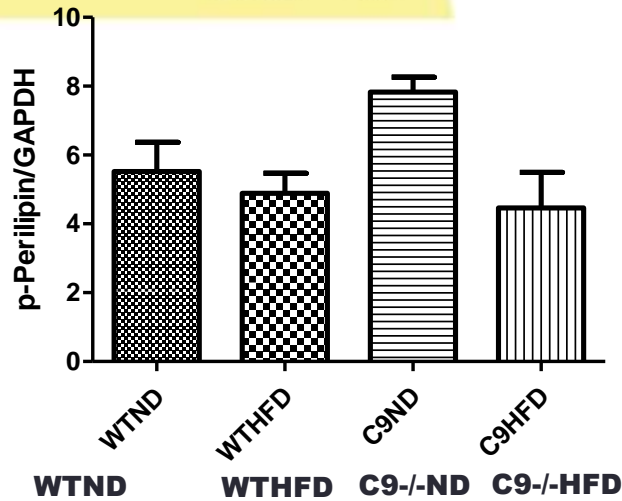
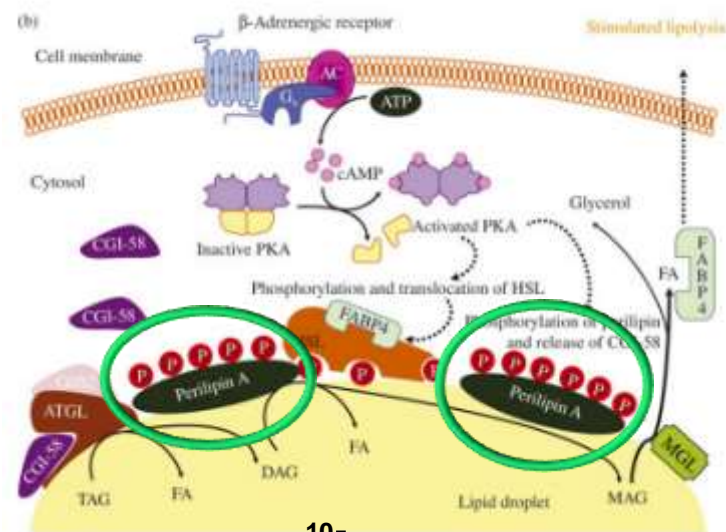
- CARD9 induced inflammation and adipose tissue lipolysis independently contribute to insulin resistance

Experimental Design

- C57BL/6 wild-type and $CARD9^{-/-}$ mice were fed on a normal diet (ND) or a high fat diet (HFD) for five months.
- Visceral abdominal adipose tissue was collected
- Western immunoblotting analyses performed
- Sample size = 3

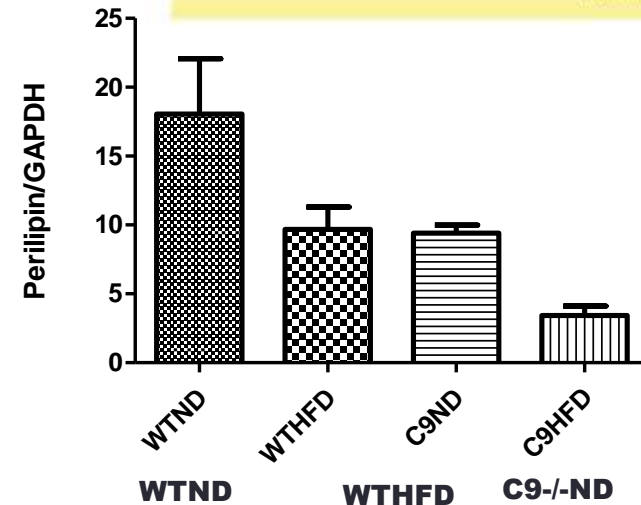
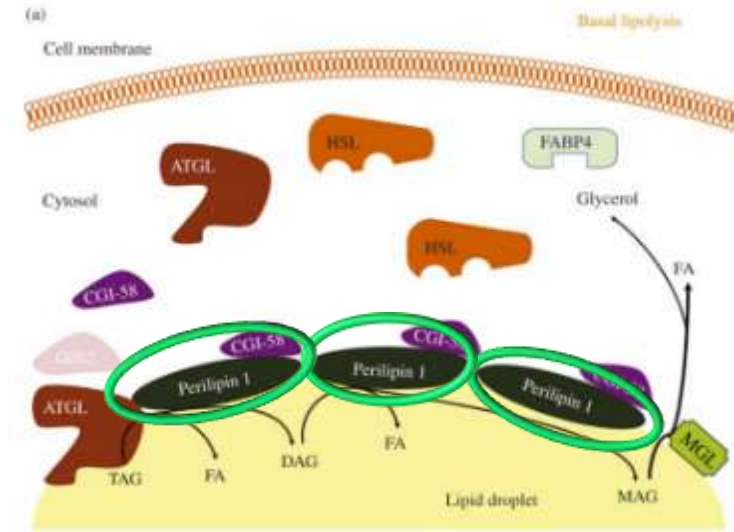
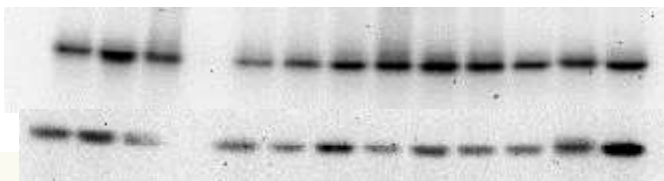


Results- Stimulated and Basal Lipolysis



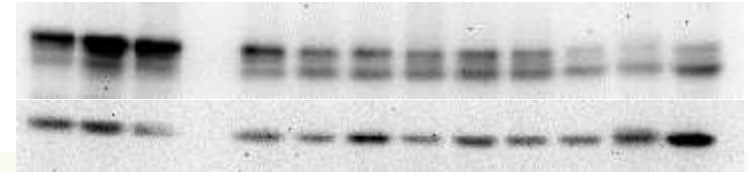
p-Perilipin

GAPDH

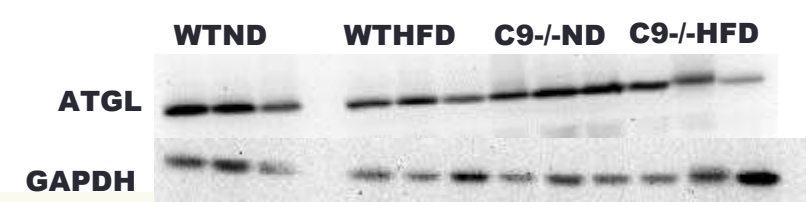
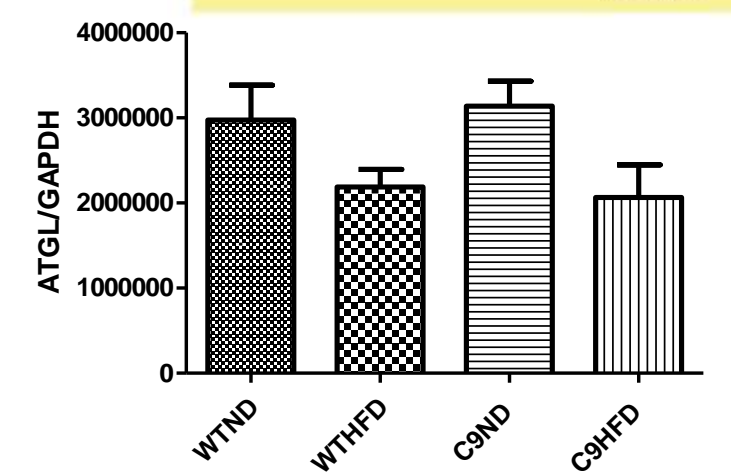
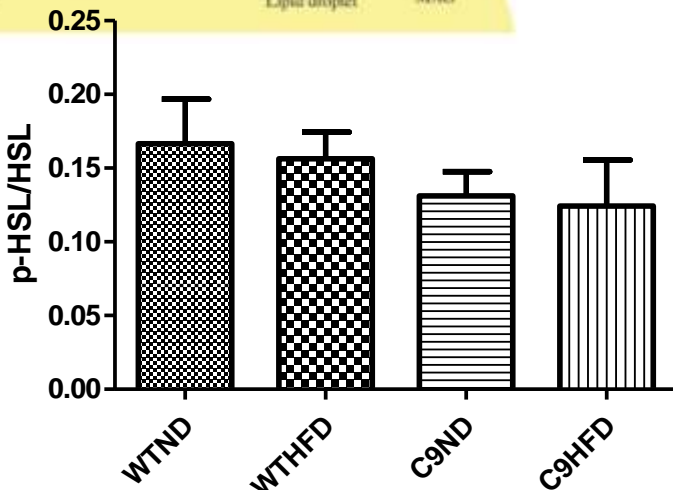
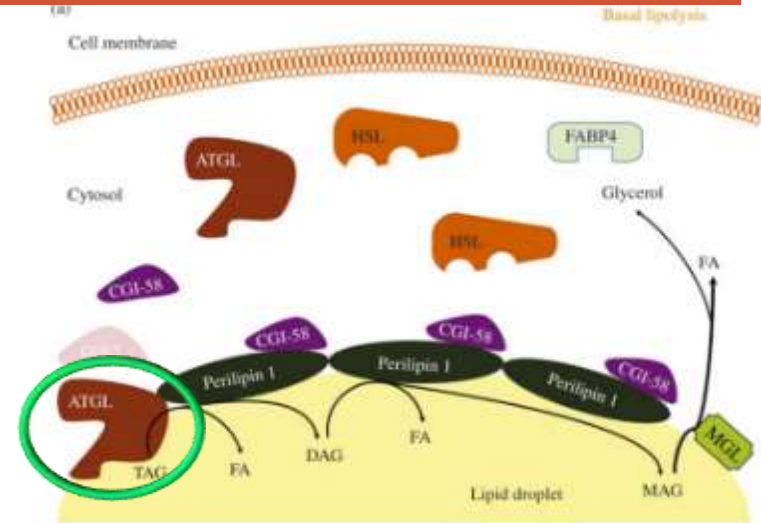
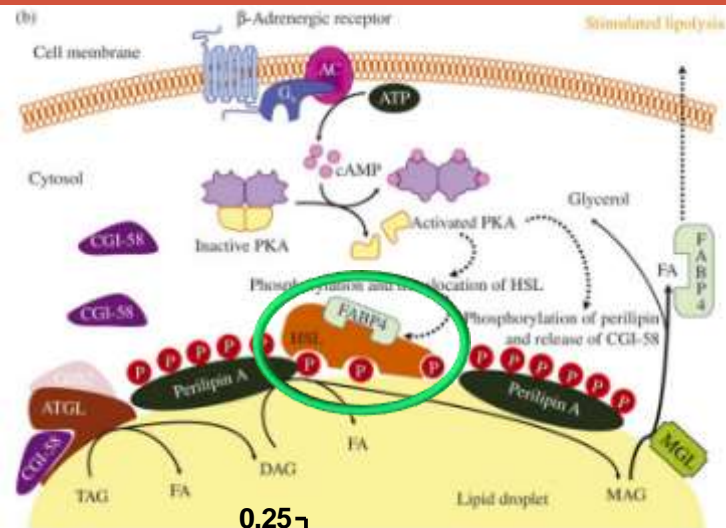


Perilipin

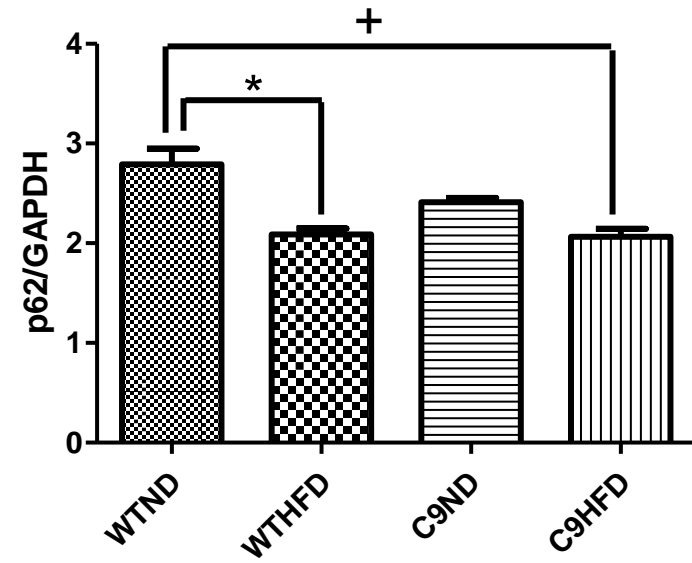
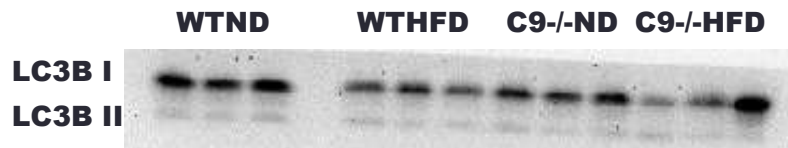
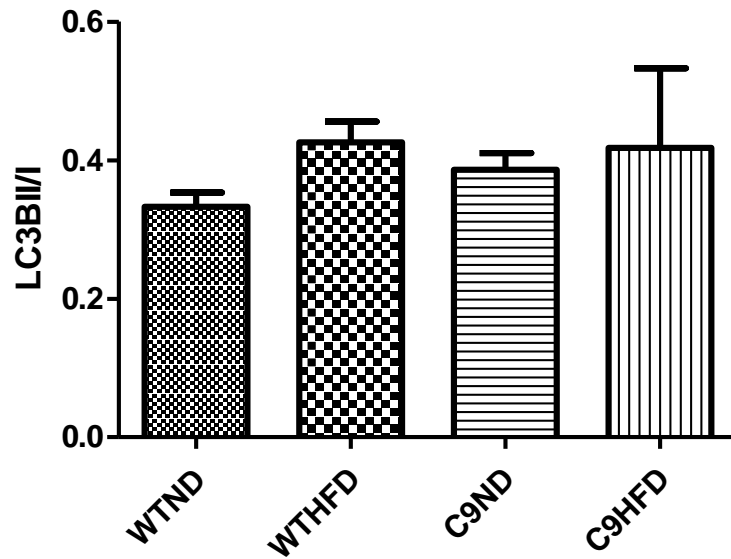
GAPDH



Results- Stimulated Adipose Tissue Lipolysis



Results- Autophagy



Additional Data

- ▣ AMPK and AKT
 - ▣ No trend
- ▣ TNF alpha
 - ▣ Higher trend in both HFD groups
- ▣ JNK
 - ▣ Lower trend in both HFD groups
- ▣ ERK
 - ▣ No trend

Conclusion-*Interim

- ▣ Obesity increases basal lipolysis but decreases stimulated lipolysis
- ▣ CARD9 induced inflammation and adipose tissue lipolysis appear to have independent effects on insulin resistance

Future Directions

- ▣ Increase sample size
- ▣ Confirm findings
- ▣ Additional proteins
- ▣ Other sources of adipose tissue

Literature Cited

- [1] Ogden CL, Carroll MD, Kit BK, Flegal KM, Prevalence of childhood and adult obesity in the united states, 2011-2012, JAMA. 311 (2014) 806–814. doi:10.1001/jama.2014.732.
- [2] R.E. Duncan, M. Ahmadian, K. Jaworski, E. Sarkadi-Nagy, H.S. Sul, Regulation of Lipolysis in Adipocytes, Annu. Rev. Nutr. 27 (2007) 79–101. doi:10.1146/annurev.nutr.27.061406.093734.
- [3] K. Eguchi, I. Manabe, Toll-like receptor, lipotoxicity and chronic inflammation: the pathological link between obesity and cardiometabolic disease, J. Atheroscler. Thromb. 21 (2014) 629–639.
- [4] P. Morigny, M. Houssier, E. Mouisel, D. Langin, Adipocyte lipolysis and insulin resistance, Biochimie. (n.d.). doi:10.1016/j.biochi.2015.10.024.
- [5] G. Frühbeck, L. Méndez-Giménez, J.-A. Fernández-Formoso, S. Fernández, A. Rodríguez, Regulation of adipocyte lipolysis, Nutr. Res. Rev. 27 (2014) 63–93. doi:10.1017/S095442241400002X.
- [6] L. Cao, X. Qin, M.R. Peterson, S.E. Haller, K.A. Wilson, N. Hu, et al., CARD9 knockout ameliorates myocardial dysfunction associated with high fat diet-induced obesity, J. Mol. Cell. Cardiol. 92 (2016) 185–195. doi:10.1016/j.yjmcc.2016.02.014.

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