

# The Effect of Saturated Fatty Acids on Lipogenic Gene Expression in Rat Primary Hepatocytes

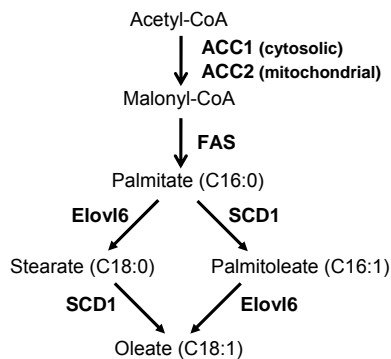


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## Saturated Fats are Linked to Several Health Conditions

- Increased intake of saturated fat has been linked to the onset of obesity, diabetes, hepatic steatosis and related diseases<sup>1</sup>
- Mice fed a diet high in saturated fat have increased expression of lipogenic enzymes in the liver, which may lead to fatty liver and dyslipidemia<sup>2</sup>
- Lipogenic enzymes are involved in de novo fatty acid synthesis – See Figure 1

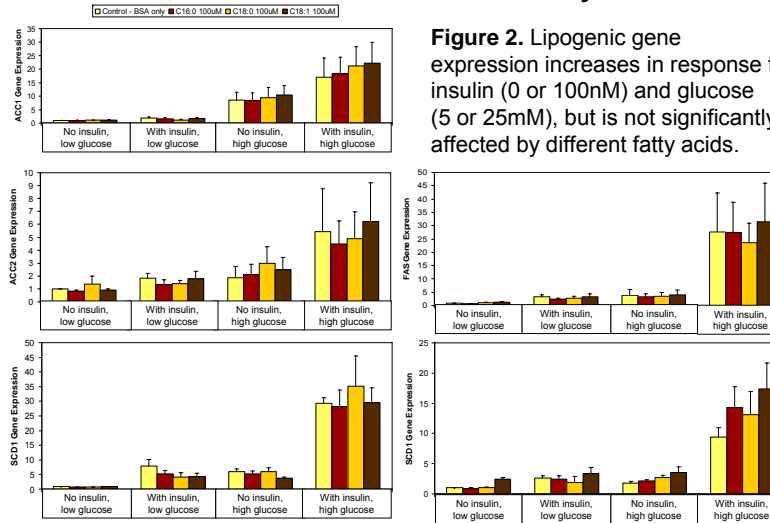


**Figure 1.** A simplified version of *de novo* lipogenesis. ACC: acetyl-coA carboxylase, FAS: fatty acid synthase, SCD1: stearoyl-coA desaturase 1, Elov6: fatty acid elongase 6

## Experimental Design

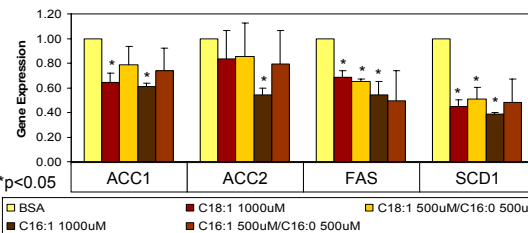
- To determine the direct effects of fatty acids, cultured rat primary hepatocytes were treated with fatty acids along with BSA or BSA alone
- After a 24 hr incubation period, RNA was harvested from the cells and subsequently used to make cDNA
- Quantitative real-time PCR was used to determine the expression of several lipogenic genes indicated in Figure 1

## Lipogenic Gene Expression is Not Increased Due to Direct Effects of Saturated Fatty Acids



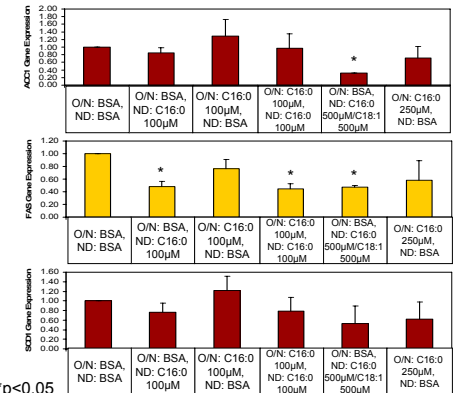
**Figure 2.** Lipogenic gene expression increases in response to insulin (0 or 100nM) and glucose (5 or 25mM), but is not significantly affected by different fatty acids.

**Figure 3.** Lipogenic gene expression is slightly decreased in response to high concentrations of fatty acids.



- Enzymes of lipogenesis are upregulated in response to both glucose and insulin signals
- Although in vivo studies have shown increased expression of lipogenic genes in response to increased saturated fat intake, this response does not appear to occur as a direct effect of saturated fatty acids
- Another possible mechanism by which saturated fats elicit effects may be due to signals from adipose tissue
- A co-culture of hepatocytes and adipocytes treated with fatty acids can determine whether a signal from adipose tissue is needed for saturated fats to increase expression of lipogenic genes

## Co-culture with Adipocytes Did Not Increase the Expression of Hepatic Lipogenic Genes



\*p<0.05

**Figure 4.** Lipogenic gene expression was not increased in response to co-culture with adipocytes. O/N: Treatment applied to adipocytes 18 hrs before hepatocytes were added in co-culture. ND: Next day treatment applied to hepatocytes and adipocytes in co-culture.

## Conclusion

- Saturated fats do not directly increase enzymes of lipogenesis in the liver
- Co-culture results indicate that adipocytes are not involved in upregulating lipogenesis in response to fatty acid treatment
- Further experiments will attempt to elucidate the mechanisms responsible for increased hepatic lipogenic gene expression following consumption of high saturated fat diets

## References

- Frank M Sacks and Martijn Katan. Randomized clinical trials on the effects of dietary fat and carbohydrate on plasma lipoproteins and cardiovascular disease. *Amer Jour of Medicine.* 2002; 113: 13-24.
- Harini Sampath, Makoto Miyazaki, Agnieszka Dobrzyn, and James M Ntambi. Stearoyl-CoA Desaturase-1 Mediates the Pro-lipogenic Effects of Dietary Saturated Fat. *J. Biol. Chem.* 2007; 282: 2483-2493.