FEEDING POLYUNSATURATED FATTY ACIDS INHIBITS EXPRESSION OF THE LIPID SYNTHESIS TRANSCRIPTION FACTOR LXR IN PORCINE LIVER

Meadus W. Jon; Dugan, Mike; Rolland, Dave; MacInnis, Robin.
Lacombe Research Center, Agriculture Canada, Lacombe, Alberta, Canada. T4L 1W1.
E-mail: meadusj@agr.gc.ca.

Background

Lipid synthesis verses oxidation in the liver are under the control of transcription factors which respond to specific types of fatty acids. In human and rat liver culture studies, Liver orphan receptor (LxR) and Peroxisome proliferator activated receptor-alpha (PPAR) are key transcription factors which respond to oxysterols and polyunsaturated fatty acids (PUFAs), respectfully (Jump et al., 1999). Activation of PPARa with fenofibrate drugs or PUFAs will induce it to bind with the retinoic acid receptor (RxR) and activate predominantly, lipid oxidation genes such as Acyl CoA oxidase (ACO) in the liver. PPAR combining with RxR competitively inhibits LxR from forming a LxR/RxR dimer and effectively blocks activation of the fat synthesis genes including the transcription factor SREBP-1c and fatty acid synthase (FAS) gene. This pathway was examined in the live pigs, fed diets high in either saturated fats (tallow) or polyunsaturated fats (flax or conjugated linoleic acid).

Objective

Examine if liver transcription factors can be used to indicate the dietary status of the pigs prior to slaughter. Investigate if LxR-alpha expression can be correlated with carcasss backfat depth. The LxR gene is located in a major pig quality trait loci (QTL) for backfat on chromosome 2.

Methods

The pig livers were collected from 3 separate feeding trials. Group one animals were fed for ~ 40 days on barley based diets supplemented with either 5% tallow (n = 6) or 5% canola oil (n = 6). Group 2 animals were supplemented with 5% flax oil (n = 10) or 5% tallow oil (n = 10) and group 3 were supplement with 2% CLA (n = 5). Liver samples were collected at the point of slaughter from the pigs which weighed approximately 110kg and stored at -80C. RNA was extracted from the livers and used to prepare cDNA using oligo-dT and random hexamer primers, as outlined in Meadus 2003. The porcine version of nuclear oxysterol receptor LxR-alpha mRNA was amplified using degenerate primers based on human and murine LxR mrRNA sequences and cloned into pCR2.1 plasmid for DNA sequencing (Meadus et al., 2003) The LxR cDNA sequence had 92% homology with the equivalent mouse LxR cDNA region, 100% homology with the mouse amino acid sequence region, and 97% homology with the equivalent human LxR amino acid sequence region (GenBank # AY170462: Meadus et al., 2003). LxR, PPARa, FAS and ACO gene expression was estimated using semi-quantitative RT-PCR methods multiplexing LxR with PPARa and FAS with ACO. The cDNA samples were also standardized using b-actin mRNA expression as an internal control.

Results and Discussion

Previous studies by Dugan and co-workers have shown that supplementing pig finisher diets with various types of lipids can have a profound effect on carcass composition contradicting basic assumptions that dietary energy simply increases carcass fat (Dugan et al., 1997). The ability of dietary fatty acids to act as endocrine factors becomes more apparent when viewed from a molecular angle. PPAR and LxR represent a relatively new class of hormone receptors that require fatty acids for activation. The pigs fed the saturated fat diets (tallow) consistently had >2-fold higher levels of LxR gene expression than the PUFA diets (flax, canola, CLA) (**Fig. 1**). LxR gene expression is increased by it own product by positive feedback regulation (Laffitte et al., 2001). PPARa gene activity is primarily under circadian rhythm but its protein and mRNA are stabilized by ligand activation (Yaacob et al., 2001). Increasing the level of saturated fats in the diet increased LxR expression, reduced PPARa mRNA levels and subsequently increased through the SREBP-1c transcription factor, expression of FAS relative to ACO (**Fig. 2**).

Conclusions

- Tallow at 5% increased liver LxR and fatty acid synthase gene activity relative to the 2% PUFA supplemented diets.
- Pig LxR gene expression can be used to indicate the pigs dietary status prior to slaughter.

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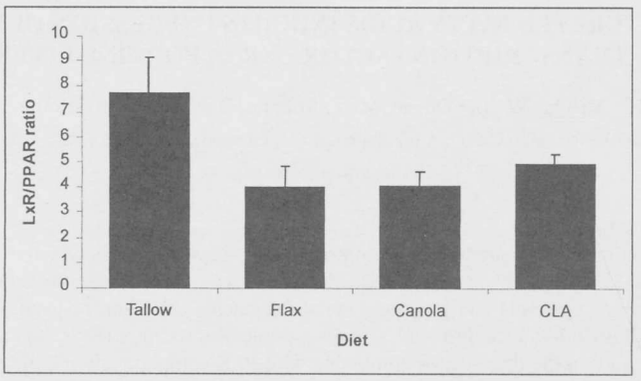

Figure 1. The effect of 5% tallow, 5% canola, 2% CLA, or 2% flax oil diet supplements on porcine liver LxR gene expression. Error bars represent SEM. Tallow fed animals had approximately 2.5-times higher LxR liver gene expression relative to flax, canola or CLA supplemented animals ($P < 0.05$).

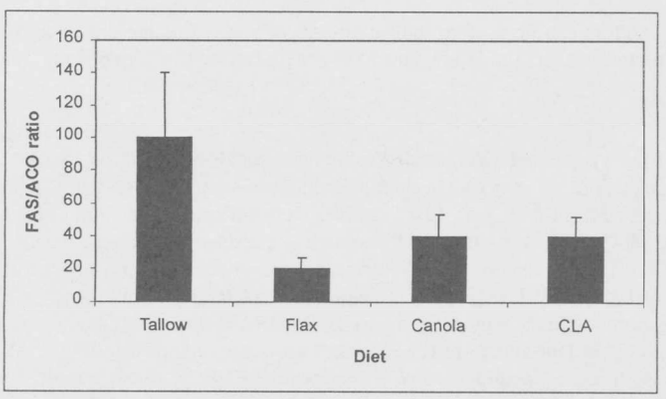

Figure 2. The response of FAS relative to ACO in the liver of the animals fed the oil supplemented diets. Bar values adjusted relative to the tallow liver group's gene expression set at 100%. Error bars represent SEM.