

STEAROYL-COA DESATURASE GENE TRANSCRIPTION, mRNA, AND ACTIVITY IN RESPONSE TO *TRANS*-VACCENIC ACID AND CONJUGATED LINOLEIC ACID ISOMERS

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(ABSTRACT)

Studies were conducted to investigate: 1) desaturation of dietary *trans*-vaccenic acid (TVA, *trans*11-18:1) to the *cis*9,*trans*11-18:2 isomer of conjugated linoleic acid (9/11CLA), 2) effects of two conjugated linoleic acid isomers [9/11CLA or *trans*10,*cis*12-18:2 (10/12CLA)] and TVA on enzyme activities and mRNA abundance for lipogenic enzymes, and 3) regulation of stearoyl-CoA desaturase (SCD) gene transcription. In the first study, lactating mice were fed 3% linoleic acid (LA), or 2% LA plus 1% stearic acid (SA), 1% TVA, or 1% CLA mixture. Dietary TVA enriched the 9/11CLA content of carcass, liver, and mammary tissue of lactating mice. A similar enhancement of 9/11CLA also was observed in liver, but not carcass, of suckling pups nursing TVA-fed dams. The CLA mixture decreased mammary acetyl-CoA carboxylase (ACC) activity compared with other treatments. However, total fatty acid content of mammary tissue was reduced only when compared with TVA. In the second experiment, lactating mice were fed 3% canola oil (OA), or 2% OA plus 1% SA, 1% TVA, 1% 9/11CLA, or 1% 10/12CLA. Dietary TVA, 9/11CLA, and 10/12CLA decreased mRNA abundance for ACC and fatty acid synthase (FAS) in mammary tissue, suggesting each had the potential to reduce *de novo* fatty acid synthesis. However, only the CLA isomers decreased ACC activity in mammary tissue and concentration of medium-chain fatty acids (MCFA = 12:0+14:0+16:0) in milk fat. The 10/12CLA isomer caused greater reductions in MCFA and milk fat percentage than the 9/11CLA, indicating that 10/12CLA is the primary CLA isomer affecting lipid metabolism in the mammary gland. Dietary TVA, 9/11CLA, or 10/12CLA decreased SCD enzyme activity and mRNA abundance in mammary tissue. In study 3, mouse (COMMA-D/MME) and bovine (Mac-T) mammary epithelial cells were transfected with the putative promoter (600 bp) of SCD gene. The 9/11CLA reduced SCD gene transcription in mouse cells, but not bovine cells. Transcription, however, was reduced in both cell lines by 10/12CLA, linoleic acid, and linolenic acid. Thus, reduced SCD transcription in response to the CLA isomers in mouse mammary cells *in vitro* may provide an explanation for reduced SCD enzyme activity and mRNA abundance in mammary tissue when lactating mice were fed either of the CLA isomers. In contrast, stearic acid, oleic acid, and TVA did not affect SCD transcription. Although TVA did not reduce SCD

transcription in mouse mammary cells in vitro, it did reduce SCD enzyme activity and mRNA abundance in mammary tissue when fed to lactating mice. The results suggested TVA may influence SCD mRNA processing or stability in the nucleus after transcription. Despite the reduction in SCD mRNA and enzyme activity, however, substantial quantities of TVA were desaturated to the 9/11CLA isomer when TVA was fed to lactating mice in the first two studies. Thus, dietary TVA provides an alternate supply of the anticarcinogenic 9/11CLA isomer in tissues.