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Dietary soy protein induces hepatic lipogenic enzyme gene expression while suppressing hepatosteatosis in obese female Zucker rats bearing DMBA-initiated mammary tumors.

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Abstract: Abstract Fatty liver is associated with obesity and breast cancer. We used an obese rat model of mammary cancer to examine whether hepatosteatosis is modifiable by diet and associated with altered expression of hepatic lipogenic enzyme genes, thyroid hormone system genes and cholesterol metabolism-related genes. Beginning at the age of 5 weeks, lean and obese female Zucker rats were fed high-isoflavone soy protein- or casein (control protein)-containing diets. Rats were euthanized at 200 days of age [corresponding to 147 days after administration of carcinogen to induce mammary tumors; (Hakkak et al. in, Oncol Lett 2:29-36, 2011)]. Obese rats had a greater degree of liver steatosis than lean rats. Obese casein-fed rats had marked steatosis with small foci of mononuclear infiltration, whereas obese soy protein-fed rats had a significantly lower steatosis index. Comparisons between lean and obese casein-fed rats showed that obesity was associated with significant reductions in hepatic mRNA abundance for Glucose 6-Phosphate Dehydrogenase (G6PD), 6-Phosphogluconate Dehydrogenase (6PGD), Thyroid Receptor Alpha 1 (TR?1), Thyroid Receptor Beta 1 (TR?1) and Iodothyronine Deiodinase 1 (DIO1). The soy protein diet was associated with increased expression of Fatty Acid Synthase (FASN), Malic Enzyme 1 (ME1), 6PGD, Sterol Regulatory Element Binding Protein-1c (SREBP-1c) and SREBP-2 genes in the livers of obese but not lean rats. Western blot analysis showed a significant induction of ME1 protein expression in the livers of obese, soy protein-fed rats, which paralleled the increased serum insulin level in this group. Long-term soy protein consumption can counter hepatic steatosis while coincidently promoting hepatic lipogenic gene expression, the latter likely a consequence of elevated serum insulin. We suggest that elevations in serum insulin, hepatic lipogenesis and cholesterol synthesis all contributed to the increased tumorigenesis previously observed for the obese, soy prot