The retinoic acid receptor-related orphan nuclear receptor α regulates adiposity and lipid homeostasis

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The nuclear hormone receptor (NR) superfamily encodes hormone-dependent DNA binding proteins that convert metabolic, nutritional and pathophysiological signals into gene regulation. The retinoic acid receptor-related orphan nuclear receptor α (ROR alpha) is a member of the NR superfamily, however, the endogenous native molecule(s) and/or synthetic compounds that regulate the activity/function of this orphan NR are unknown. *In vitro* and *in vivo* studies have implicated RORα in the regulation of lipid homeostasis. Insights into the function of this nuclear receptor have been gained from the analysis of staggerer mice (sg/sg) that have impaired RORα function and dyslipidemia. We utilized this mouse model to investigate the role of RORα in the control of adiposity, and the adaptation to changes in dietary status in the liver, adipose and skeletal muscle. Our initial studies indicate that RORα4 is the predominant isoform in wild-type mice, and that expression of RORα (1 and 4) transcripts are significantly attenuated in the liver, white adipose and skeletal muscle of staggerer mice. Moreover, we identify changes in gene expression that regulate several critical aspects of lipid metabolism in the major mass metabolic tissues. The dysfunctional RORα expression (and function) coupled to these changes in gene expression leads to changes in the physiological response to energy dense/high fat diets.