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Sex Hormone-Binding Globulin a New Therapeutic Target against Obesity: Regulation by Nutritional Factors and Role in Obesity Development and Progression

Abstract:

Human sex hormone-binding globulin (SHBG) is produced by the liver and secreted into the circulation where it binds androgens and estrogens with high affinity. Low plasma SHBG levels are associated with obesity, fatty liver disease, abdominal adiposity and metabolic syndrome, and predict the development of type 2 diabetes and cardiovascular disease. The SHBG gene has changed its tissue expression and therefore its function during the evolution. Rodents do not express the SHBG in the liver. The generation of different transgenic mice expressing the human SHBG gene has allowed us to study the SHBG expression and regulation in vivo. We have used these mice, HepG2 cells and human samples to describe the molecular mechanisms by which thyroid hormone, proinflammatory cytokines (TNF α and IL1 β), adiponectin, monosaccharides, olive oil, resveratrol (red wine), caffeine and TGF β 1 regulate hepatic SHBG expression. These findings explain why diseases such as obesity, type 2 diabetes, hyperthyroidism, fatty liver disease and inflammatory disease (rheumatoid arthritis) have altered plasma SHBG levels. Moreover, the generation of these mouse models has allowed us to demonstrate that SHBG overexpression can protect against obesity development point-out SHBG modulation as a novel therapeutic strategy for the treatment of these prevalent diseases. Finally, we have recently demonstrated for the first time that increase in plasma SHBG levels within the first month after bariatric surgery is a good predictor of total weight loss and weight regain response after 2 years.

Biography

David M. Selva got Bachelor's Degree in Biology in 1996 at the UB, Spain. I obtained my PhD in Biochemistry and Molecular Biology at the UAB in 2001, Spain. After my PhD I accepted a postdoctoral position for 7 years in Prof. Hammond laboratory first at the LRCC in the UWO (Canada) and later on at the CFRI in the UBC (Canada) where I worked on the molecular mechanisms regulating hepatic SHBG production in several human SHBG transgenic mice. In 2009 I obtained a principal investigator position at the Diabetes and Metabolism Department at the Vall d'Hebron Research Institute in Barcelona, Spain. For the last ten years I have developed several projects of the Spanish Research Council and published the results in more than 20 papers as a corresponding author, filed several patents and created a spin-off company.