Sex Hormone-Binding Globulin: Regulation by Nutritional Factors and Role in Obesity Development and Progression

David M. Selva
Universitat Autònoma de Barcelona and CIBERDEM (ISCIII), Barcelona, Spain

Human sex hormone-binding globulin (SHBG) is produced by the liver and secreted it into the circulation where it binds androgens and estrogens with high affinity. Therefore, SHBG acts as a carrier of these sex steroids and regulates their bioavailability. Low plasma SHBG levels are associated with obesity, fatty liver disease, abdominal adiposity and metabolic syndrome, and predict the development of type 2 diabetes. In addition, an inverse relationship between plasma SHBG levels and risk of cardiovascular disease has been reported. The SHBG gene has changed its tissue expression and therefore its function during the evolution. Rodents express the SHBG gene in the Sertoli cells of the testis. While in humans, the SHBG gene is expressed in the liver and in the germ cells of the testis. This change of function and tissue expression can be explained by the appearance during evolution of new footprinted regions in the human promoter and an alternative promoter. 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 provide evidences that SHBG expression is regulated by different nutritional factors such as monosaccharides, olive oil, red wine (resveratrol) or caffeine. We have described the underlying molecular mechanisms by which all these factors regulate SHBG gene expression that involve the regulation of several transcription factors, such as HNF4α, PPARγ and CAR. Finally, the generation of new mouse models has allowed us to demonstrate that SHBG overexpression can protect against obesity point-out SHBG modulation as a novel therapeutic strategy for the treatment of these prevalent diseases.

david.martinez.selva@vhir.org