The protective role of Sestrin 2 in high fat diet-induced nephropathy

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Background

- Due to the high prevalence of obesity, the number of cases of diabetes are rising Qatar.
- Diabetes is a major public health problem that affects about 17% of the Qatari population.
- Diabetes is associated with several metabolic risk factors that contribute to a high rate of micro- and macrovascular events.
- Diabetic nephropathy (DN), is a major complication of diabetes and the leading cause of end stage renal disease and cardiovascular morbidity and mortality.
- Multiple redox-sensitive pathways orchestrate the key pathological events of DN.
- Sestrin 2 (Sesn2), is a novel stress-inducible protein, that suppresses reactive oxygen species and protects from oxidative stress; however, its role in diabetes and its complications is yet to be fully delineated.

Aim of the Study

- Genetic studies showed that Sesn2 contributes to the maintenance of metabolic homeostasis such as normalization of metabolic derangements during obesity and protects cells and organisms from age-related physiological abnormalities.
- However, the role of Sesn2 in renal physiopathology and in the pathogenesis of diabetic kidney disease and glomerular cell injury associated with diabetes is currently still lacking.
- Therefore, the aim of this study was to assess the impact of Sesn2 deletion on the onset of nephropathy associated with high fat diet (HFD)-induced obesity in mice.

Methods

- HFD-induced obesity caused upregulation of CD36, an indicator of lipid uptake, and promoted lipogenic enzymes ACLY and FASN, an indicator of de novo lipid synthesis, as well as lipid accumulation in kidney.
- Sesn2 deletion exacerbated HFD-induced renal fibrotic injury
- Taken together, this study provides, for the first time, evidence that Sesn2 is renoprotective in obesity by diminishing lipid accumulation and blocking excessive lipid uptake and de novo lipid synthesis.

Conclusions

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