كلية الصيدلة
College of Pharmacy
QATAR UNIVERSITY جامعة قطر

Faculty and PostDoc, Medical, Biomedical and Health Sciences

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

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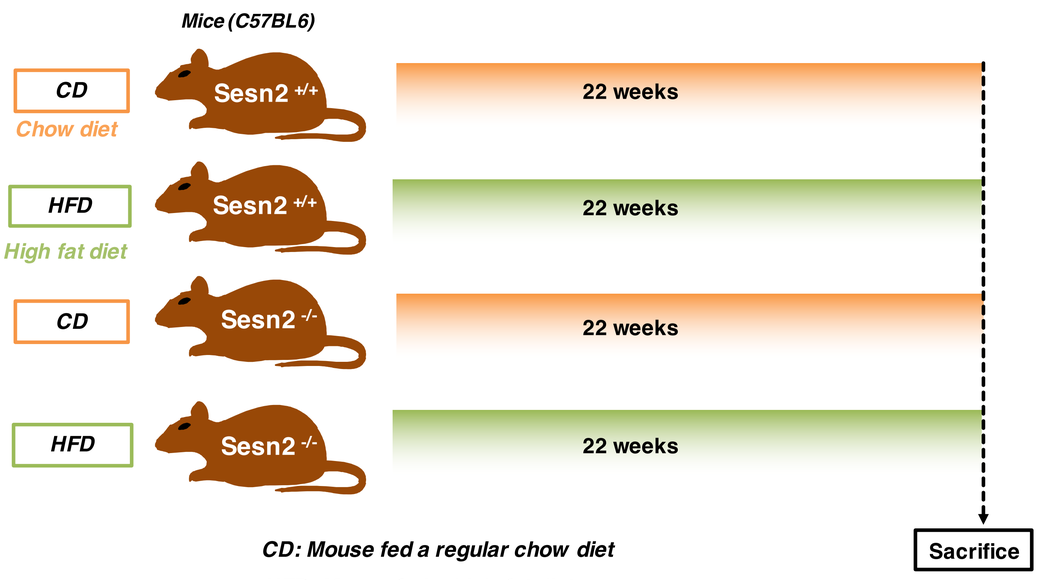
Background

- 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



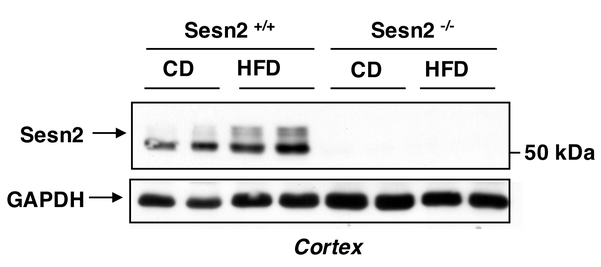
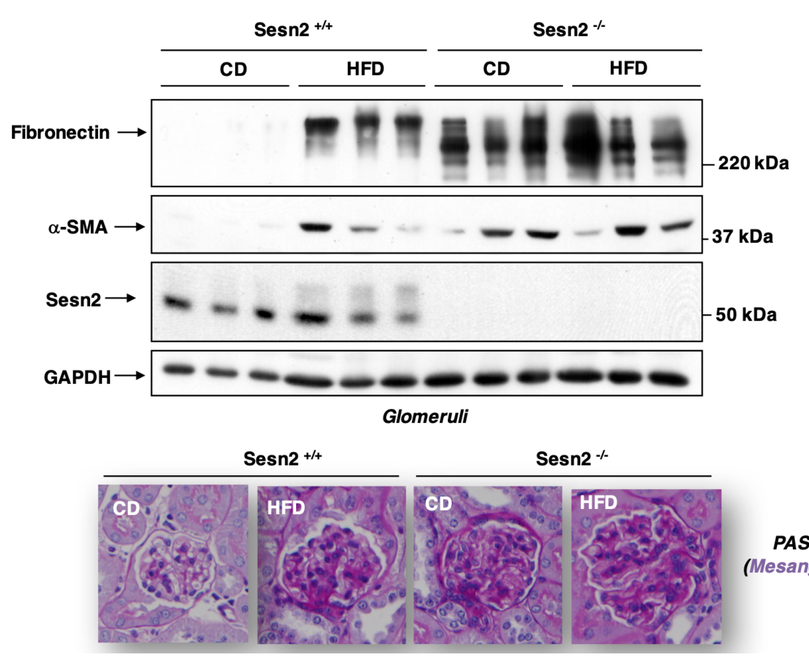


FIGURE 1 | Wild type (Sesn2$^{+/+}$) and Sesn2-deficient (Sesn2$^{-/-}$) mice were fed either a chow (CD) or high fat diet (HFD) for 22 weeks, then the structure and function of kidneys from mice were assessed.

Conclusions

- 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.

Results



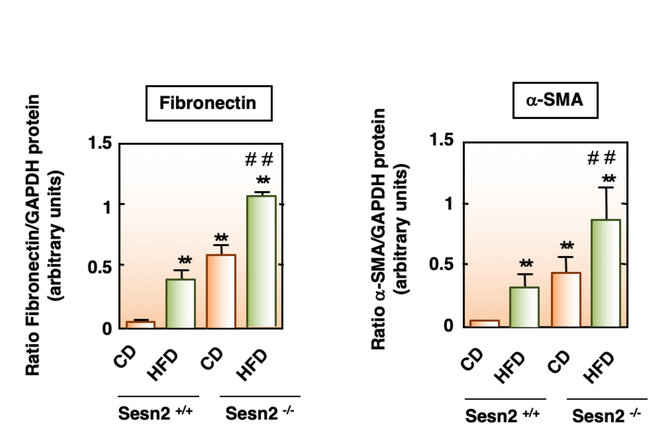
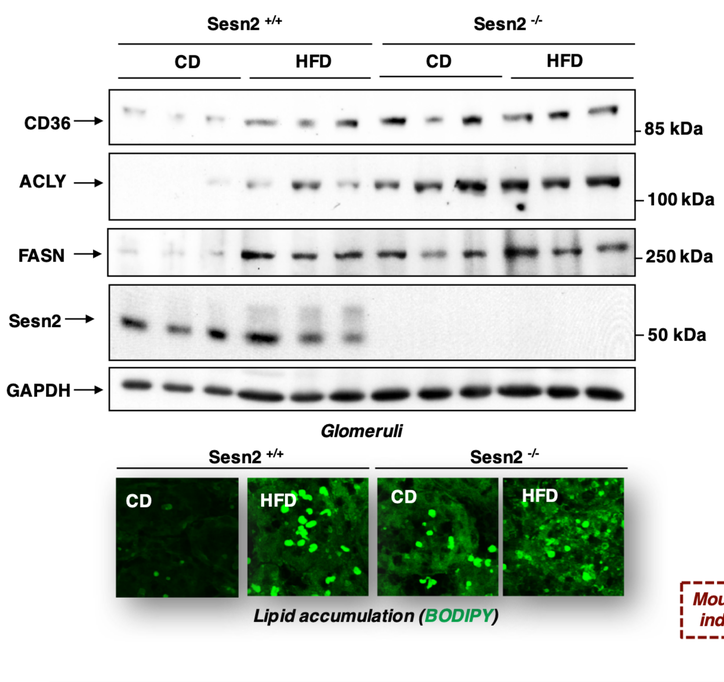
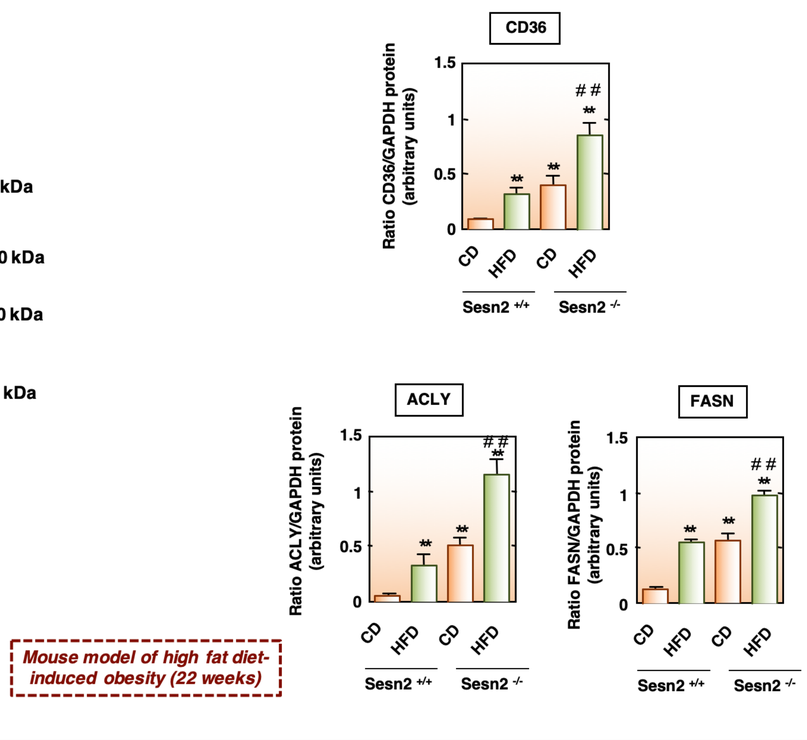


FIGURE 2 | Genetic deletion of Sesn2 exacerbated fibrotic injury in kidney of HFD-fed mice.





Mouse model of high fat diet-induced obesity (22 weeks)

FIGURE 3 | Genetic deletion of Sesn2 enhanced fatty acid translocase (CD36), ATP citrate lyase (ACLY), and Fatty Acid Synthase (FASN) expression and lipid accumulation in kidneys from HFD-fed mice.

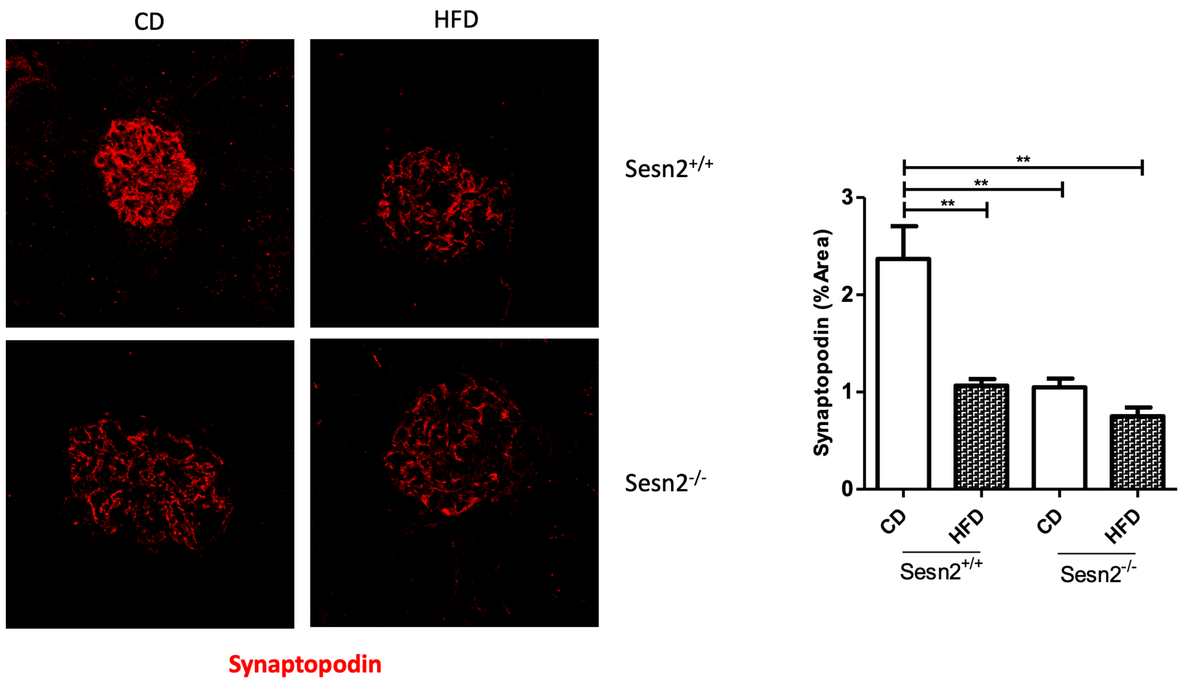


FIGURE 4 | Genetic deletion of Sesn2 damaged podocytes in HFD-fed mice.

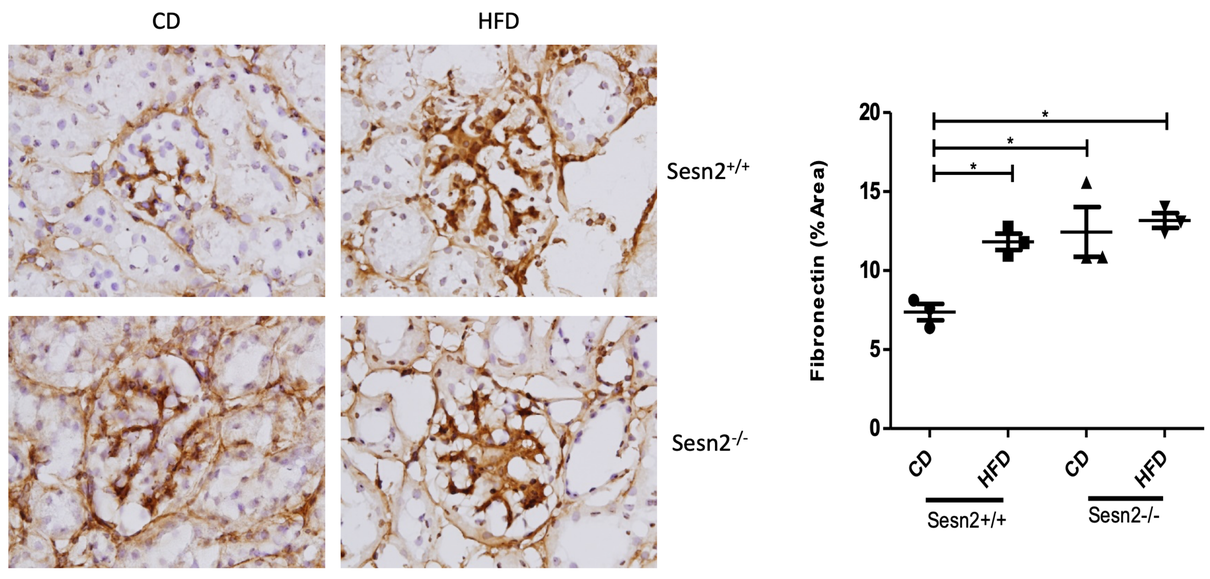


FIGURE 5 | Genetic deletion of Sesn2 aggravated renal fibrotic injury in HFD-fed mice.

Acknowledgements

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