

March 1, 2024

Yong-sun Maeng, PhD
Special Issue Editor
International Journal of Molecular Sciences

Dear Dr. Maeng,

I hope this letter finds you well.

My co-authors and I are pleased to submit an article "***Renal endothelial single-cell transcriptomics reveals spatiotemporal regulation and divergent roles of differential gene transcription and alternative splicing in murine diabetic nephropathy***" for consideration for publication in the special issue "Molecular Research in Vascular Disease" in *International Journal of Molecular Sciences*.

Understanding the underlying disease drivers of diabetic kidney disease (DKD) is a large challenge due to the many factors involved in the pathophysiology and progression of disease. We have built an extensive single-cell renal endothelial cell transcriptomics atlas characterizing different endothelial cell populations during evolution of murine diabetic kidney disease. This provides an integrated and comprehensive view of their spatial and temporal regulation in diabetic kidney disease at the single cell level. We discovered differential regulation of glomerular endothelial cell and peritubular capillary endothelial cells including EIF2 inactivation, mitochondrial dysfunction, and dysregulated IGF signalling. This highlights the importance of a changed intrarenal microcirculation during disease progression.

Moreover, we have taken advantage of the full-length sequencing of Smart-seq2 and evaluated alternative splicing within the endothelial cell subsets. Hereby we submit our data as a first demonstration of glomerular and peritubular endothelial cell displaying aberrant and dynamic alteration of alternative splicing associated with DNA repair. Strikingly, genes displaying differential transcription or alternative splicing participate in divergent biological processes.

Our data are meant to be a resource for all scientists and are therefore available for further review:

1. Plots for single cell transcriptomics (login: reviewer; password: reviewer):
<https://betsholtzlab.org/Publications/MouseKidenyOB/database.html>
2. Sashimi plots for genes displaying differential splicing: links in Supplementary file 6

This manuscript reports original work and is not published or under consideration for publication elsewhere. The manuscript is approved by all the authors, each of whom meets the ICMJE authorship criteria.

Thank you for considering this submission and please let me know if you have any queries.

Kind Regards,
Pernille

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