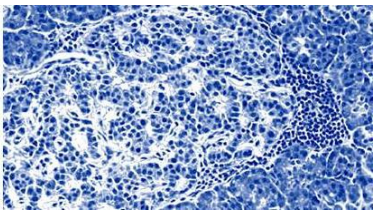
nPOD
Network for Pancreatic Organ Donors with Diabetes



nPOD-Kidney: Mapping the pathology of Diabetic Kidney Disease

AUTHORS

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PURPOSE

Diabetic kidney disease (DKD) is the most common complication of diabetes; yet DKD remains poorly understood. The nPOD-Kidney (nPOD-K) pilot project was initiated to assess the feasibility of collecting kidney from organ donors with and without diabetes, with the long-term goal of improving our understanding of DKD pathogenesis. To date, 47 of the planned 48 kidneys have been collected. The tissue integrity of the current cohort was evaluated, and key pathways published in high profile preclinical publications were selected for validation.

METHODS

Two-µm renal FFPE sections from the nPOD-K cohort were stained for kidney-specific cell markers and kidney disease markers. Slides were imaged at a 20x magnification using an Axioscan Z1 whole slide scanner and quantitative image analyses were performed using Visiopharm software.

SUMMARY OF RESULTS

Various multiplex immunofluorescent stainings were optimized, followed by a periodic acid-Schiff (PAS) staining. We developed an automatic segmentation of kidney compartments using PAS images and the neural network DeepLabV3+, allowing for an in-depth whole-slide image analysis. We observed the expected loss of the podocyte marker WT1 and endothelial marker CD31 with concomitant increases in expression of FSP1 and other fibrotic markers in diseased kidneys. Interestingly, approximately one fifth of the cohort displayed no overt sign of kidney disease despite long-standing diabetes (8+ years).

CONCLUSIONS

This cohort provides an exceptional opportunity to study DKD physiopathology through the analyses of large, CKD stage-specific areas of the kidney. Similar to previously published observations from the nPOD pancreas cohort, all stages of the disease can be detected in affected kidneys. Thus, the nPOD-K cohort establishes a unique and valuable window into the development and progression of DKD and support the identification and development of novel therapeutic targets.