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Promoting Sustainable Kidney Health: The Asia-Pacific and Beyond

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Cell states and niches in diabetic kidneys identified by spatial mapping of targeted gene panel at single cell resolution

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Objectives : Technical advance in single-cell genomics ushers into deeper understanding of kidney disease. As kidney is an elaborately organized structure, single-cell research at spatial context in this organ is highly required but few of researches have been tried. Here, we investigated spatial organization of various types of cells in diabetic kidney disease using Xenium In Situ.
Methods : Using Xenium In Situ, we generated single-cell spatial datasets for 475 targeted genes from 4 formalin-fixed, paraffin-embedded human kidney tissues obtained by renal biopsy, which were pathologically diagnosed as advanced stage of diabetic kidney disease.
Results : We created an atlas composed of 168,904 cells and identified major cell types in the kidneys by supervised annotation of marker gene expressions, such as WT1 for podocyte, AQP1 for proximal tubular cells and descending limb of Loop of Henle, CXCL12 for fibroblast, and PTPRC for immune cells. Most of proliferating cells belonged to B cells and macrophages were classified into $LYVE^{high}$, $CCL2^{high}$, $LGMN^{high}$, and others. We defined 12 spatial cellular niches, some of which corresponded to nephron and collecting duct comparment and injury-associated specific cell-enriched comparments such as myofibroblast, B cells, T cells, and plasma cells. These pathologic niches were in close promixity each other, of which forms tertiary lymphoid tissues in which plasma cell niches were surrounded outwardly by B cell and fibroblast niches.
Conclusions : Targeted spatial datesets defines normal and pathologic cellular niches in diabetic kidneys, the latter of which are thought to be the hub for disease propagation.

Figure 1.jpg

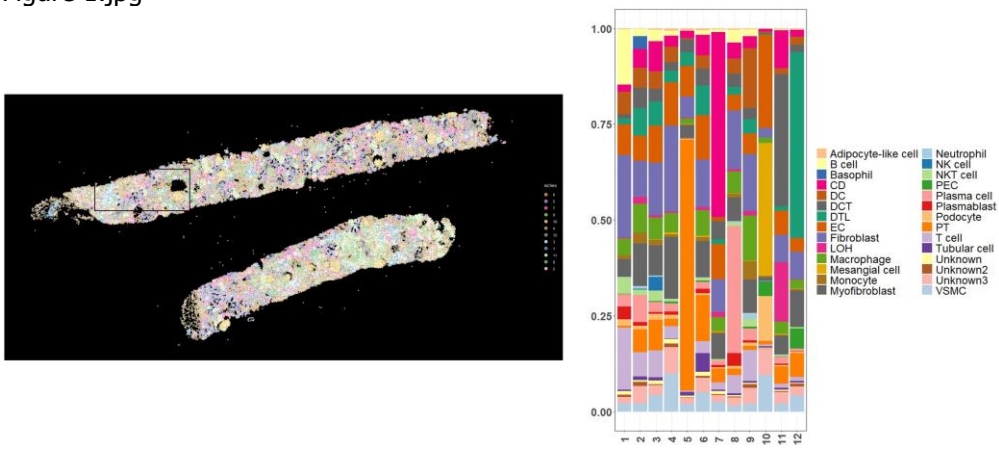
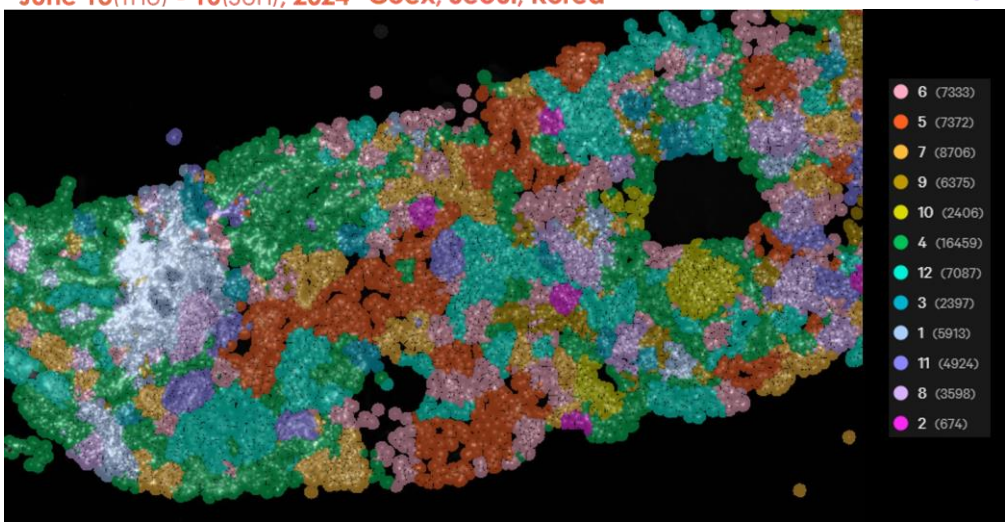


Figure 1.jpg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