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Single Cell Analysis of Human Organoid Models

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Single cell RNA sequencing (scRNA-seq) is a powerful tool that allows researchers to analyze the gene expression profiles of individual cells within a complex tissue or organoid. In the case of kidney organoids, scRNA-seq can provide important insights into the development, function, and disease mechanisms of the kidney. To test the effect of kidney decellularized extracellular matrix (dECM) on kidney organoid development, we performed scRNAseq for kidney organoid cells from different methods. Single-cell transcriptomics reveal that the vascularized kidney organoids cultured using the kidney dECM have more mature patterns of glomerular development and higher similarity to human kidney than those cultured without the kidney dECM. Using gene regulatory network analysis, key transcription factors of off-target cells were identified. TWIST1 was identified as a regulator of neuron cells, and TWIST1 inhibition significantly reduced neuronal cells without alteration in the kidney organoids. Furthermore, we applied this comparative analysis at the single cell level to systematically evaluate kidney organoids that were generated by different groups and methods. In summary, scRNAseq is a valuable tool for studying the heterogeneity of kidney organoids, identifying the novel factors to improve the organoids culture methods, and evaluating organoid maturation as a critical step towards their potential clinical application.