

# 5<sup>th</sup> World Congress on **Cell & Stem Cell Research**

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## Modeling renal progenitor development using the zebrafish kidney

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Chronic kidney disease (CKD) affects 300 million people world-wide, representing the 12<sup>th</sup> leading cause of death. Understanding how nephrons, the simplest functional unit of the kidney, develop from renal progenitors can lend insight into the processes that go awry during disease. The zebrafish pronephros provides an excellent in vivo system to study the mechanisms of vertebrate nephrogenesis. When and how renal progenitors in the zebrafish embryo undergo tubulogenesis to form nephrons is poorly understood, but is known to involve a mesenchymal to epithelial transition (MET) and the acquisition of polarity. We determined the precise timing of these events in pronephros tubulogenesis. As the ternary polarity complex is an essential regulator of epithelial cell polarity across tissues, we performed gene knockdown studies to assess the roles of the related factors atypical *protein kinase C* iota and zeta (*prkci*, *prkcζ*). We found that *prkci* and *prkcζ* serve partially redundant functions to establish pronephros tubule epithelium polarity. Further, the loss of *prkci* or the combined knockdown of *prkci/ζ* disrupted proximal tubule morphogenesis and podocyte migration due to cardiac defects that prevented normal fluid flow to the kidney. Surprisingly, tubule cells in *prkci/ζ* morphants displayed ectopic expression of the transcription factor *pax2a* and the podocyte-associated genes *wt1a*, *wt1b*, and *podxl*, suggesting that *prkci/ζ* are needed to maintain renal epithelial identity. Interestingly, knockdown of *pax2a*, but not *wt1a*, was sufficient to rescue ectopic tubule gene expression in *prkci/ζ* morphants. These data suggest a model in which the redundant activities of *prkci* and *prkcζ* are essential to establish tubule epithelial polarity and also serve to maintain proper epithelial cell type identity in the tubule by inhibiting *pax2a* expression. These studies provide a valuable foundation for further analysis of MET during nephrogenesis, and have implications for understanding the pathways that affect renal progenitors during kidney development, disease, and regeneration.

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