SIGNIFICANCE STATEMENT

The nephrogenic niche of the developing kidney contains distinct progenitor cell types for nephron, interstitial, and collecting duct lineages. Mouse studies have defined these progenitor cell compartments and identified key regulatory mechanisms acting within and between progenitor types to coordinate developmental programs. Here, we used a variety of molecular and cellular approaches to characterize the nephron- and interstitial-forming compartments within the developing human kidney. These studies reveal significant differences between their global transcriptional profiles and distinct human and mouse differences in gene expression patterns pointing to a likely evolutionary divergence in their developmental programs. The insights and data resources generated here will facilitate efforts to generate appropriate progenitor types for *in vitro* engineering of human kidney structures. Unlike many organ systems where long-lived stem cell populations generate and regenerate functional mature cell types, the mammalian metanephric (definitive, adult) kidney forms from a small subset of lineage-restricted progenitor cell types that undergo expansion and commitment over a limited period of fetal and neonatal development.[1] Molecular, cellular, and genetic studies in the mouse have demonstrated that the transcription factors Foxd1 and Six2 demarcate self-renewing, lineage-restricted interstitial and nephron progenitor cells, respectively.[2,3] Each population occupies a unique position within the nephrogenic niche; nephron progenitors closely associate with underlying collecting duct progenitor cells, whereas interstitial progenitors localize between the nephron progenitors and the renal capsule.[1] Interactions among these progenitor pools drive the process of kidney organogenesis.[1]