Conserved and Divergent Molecular and Anatomic Features of Human and Mouse Nephron Patterning.

Journal: J Am Soc Nephrol

Publication Year: 2018

Authors: Nils O Lindstrom, Tracy Tran, Jinjin Guo, Elisabeth Rutledge, Riana K Parvez, Matthew E Thornton, Brendan Grubbs, Jill A McMahon, Andrew P McMahon

PubMed link: 29449451

Funding Grants: Repair and regeneration of the nephron

Public Summary:
The long, tubular nephron is the functional unit of the kidney. The adult human kidney is made up of approximately 1,000,000 nephrons. How nephrons form in the human kidney is not well understood. We conducted a detailed analysis of nephron development comparing the human kidney with its well-studied mouse counterpart. The data show significant conservation in how different regions of the nephron form between mouse and man. Analyzing different time points in the nephron forming program, we identified different gene sets that demarcate emerging cell complexity in the maturing structure that may play a role in these events. These findings have conceptual implications for the evolutionary processes driving the diversity of mammalian organ systems. Furthermore, these findings provide practical insights beyond those gained with mouse and rat models to guide efforts to harness the developmental programs necessary to build human kidney structures in the laboratory.

Scientific Abstract:
The nephron is the functional unit of the kidney, but the mechanism of nephron formation during human development is unclear. We conducted a detailed analysis of nephron development in humans and mice by immunolabeling, and we compared human and mouse nephron patterning to describe conserved and divergent features. We created protein localization maps that highlight the emerging patterns along the proximal-distal axis of the developing nephron and benchmark expectations for localization of functionally important transcription factors, which revealed unanticipated cellular diversity. Moreover, we identified a novel nephron subdomain marked by Wnt4 expression that we fate-mapped to the proximal mature nephron. Significant conservation was observed between human and mouse patterning. We also determined the time at which markers for mature nephron cell types first emerge-critical data for the renal organoid field. These findings have conceptual implications for the evolutionary processes driving the diversity of mammalian organ systems. Furthermore, these findings provide practical insights beyond those gained with mouse and rat models that will guide in vitro efforts to harness the developmental programs necessary to build human kidney structures.