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Review

Coordinated cell behaviours in early urogenital system morphogenesis

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ABSTRACT

The elaboration of functional kidneys during embryonic development proceeds in a stepwise manner, starting with the formation of the embryonic pro- and mesonephros, followed by the induction and growth of the final metanephric kidney. These early stages of urinary tract development are critical for the embryo as a failure in pro/mesonephros morphogenesis leads to major developmental defects, often incompatible with life. The formation of the pro/mesonephros and its central component the nephric duct, is also interesting as it offers a relatively simple system to study cell biological behaviours underlying tissue morphogenesis. This system is especially well adapted to study the questions of cell lineage specification, epithelial integrity and plasticity, tissue interactions, collective cell migration/guidance and programmed cell death. In this review, we establish the link between these cell behaviours, their molecular regulators and early genitourinary tract development.

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1. Introduction

The study of mammalian urogenital system development has focused mainly on the importance of metanephric (adult) kidney formation. Arguably, however, the earlier events of nephric duct specification and formation are as important for urinary system morphogenesis. The entire renal lineage is derived from the intermediate mesoderm, which epithelializes bilaterally at the level of the 6th to 8th somites to generate the nephric ducts [1]. These paired ducts elongate caudally along the anterior–posterior axis until they reach and fuse with the cloaca, which serves as the precursor of the adult bladder and urethra. During its development the nephric duct gives rise to three distinct renal structures, the pronephros, mesonephros and metanephric kidney, by induction of nephric cord mesoderm adjacent to the nephric duct [2]. Only the metanephric kidney is maintained to adulthood in vertebrates, whereas the pro/mesonephros become part of the genital system in males (vas deferens and epididymis), and degenerate in females.

The metanephric kidney arises from the posterior nephric duct through reciprocal inductive signalling between the metanephric mesenchyme and the nephric duct, causing a budding of the duct known as the ureteric bud. The ureteric bud invades the metanephric mesenchyme, whereupon iterative cycles of branching and mesenchymal-to-epithelial differentiation will give rise to the entire glomerular-nephron-collecting duct system of the adult kidney (reviewed in [3] and Blake and Rosenblum this issue).

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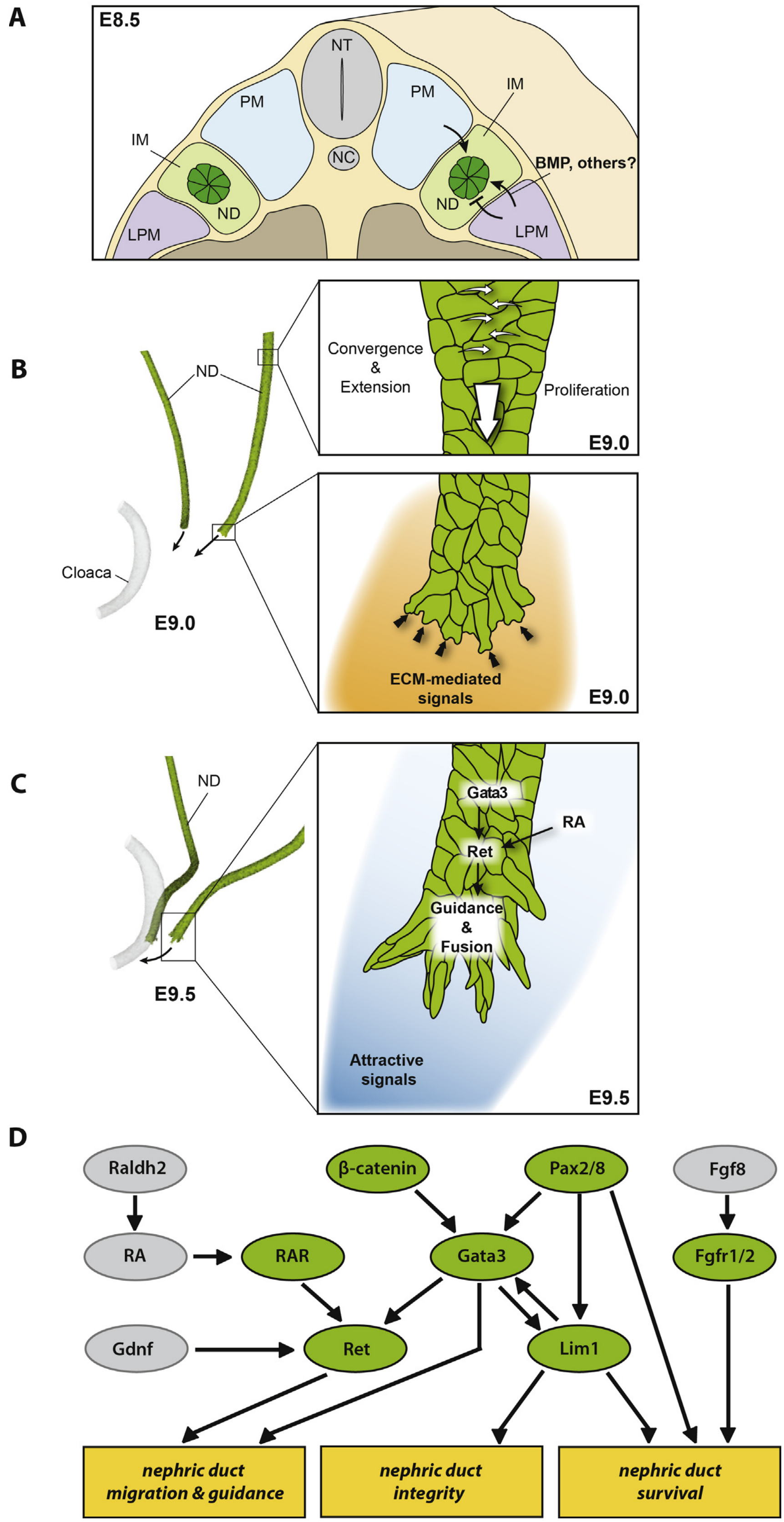

Fig. 1. Early urogenital system development involves coordinated signalling between mesenchymal and epithelial tissues to form and elongate the nephric ducts. (A) Delineation of the renal field is achieved by positive and negative signals emanating from the paraxial mesoderm and lateral plate mesoderm. Bmp signalling from the lateral plate mesoderm and unknown positive signals from the paraxial mesoderm interact to specify the renal field, while negative signals from the lateral plate mesoderm are thought to repress the renal fate laterally. (B) Initial elongation of the nephric duct in amphibian and avian systems involves convergence and extension cell movements (white arrows), as well as proliferation, to drive extension towards the cloaca. Early guidance cues are provided via lamellipodia-like cellular extensions (black arrows) that sense the underlying extracellular matrix. (C) Later guidance cues from the cloacal region are interpreted by the Ret receptor tyrosine kinase activated and maintained by both Gata3

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