

Molecular regulation of kidney

- Involves epithelial mesenchymal interactions.
- Epithelium of utereric bud from the mesonephros interacts with mesenchyme of the metanephric blastema

Mesenchyme expresses WT1- transcription factor that makes this tissue competent to respond to induction by the ureteric bud.

WT1 also regulates production of **GLIAL-DERIVED NEUROTROPHIC FACTOR (GDNF)** and **HEPATOCYTE GROWTH FACTOR (HGF/SCATTER FACTOR)** by the mesenchyme, these proteins stimulate branching and growth fo the ureteric buds.

The **TYROSINE KINASE RECEPTOR RET** for GDNF and MET for HGF are synthesized by the epithelium of the ureteric buds. This establishes a signalling pathways between the 2 tissues

Buds induce the mesenchyme via **FIBROBLAST GROWTH FACTOR 2 (FGF2)** and **BONE MORPHOGENIC PROTEIN 7 (BMP7)**

Both of these growth factors block apoptosis and stimulate proliferation in the metanephric mesenchyme while maintaining production of WT1.

Conversion of mesenchyme to epithelium for nephron formation is also mediated by ureteric buds thorough expression of WNT9B and WNT6 which upregulate PAX2 and WNT4 in the metanephric mesenchyme.

PAX2 promotes condensation of mesenchyme to epithelialize and form tubules. Because of these interactions, modifications in the extracellular matrix also occur.

Fibronectin, collagenI collagen III are replaced by laminin and type IV collagen, which is a characteristic of an epithelial basal lamina.

The cell adhesion molecules **SYNDECAN** and **E CADHERIN**, which are essential for condensation of the mesenchyme into an epithelium, are synthesized.

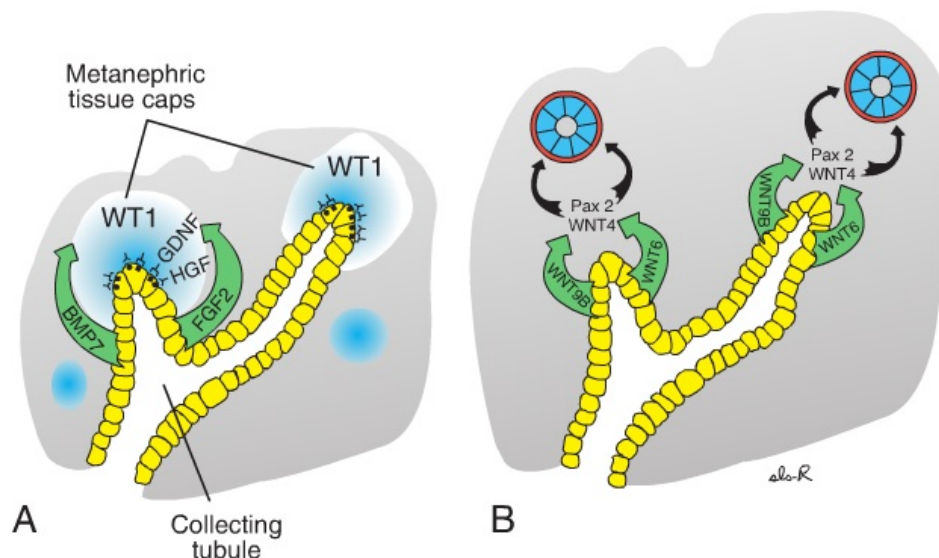


Figure 15.7 Genes involved in differentiation of the kidney. **A.** *WT1*, expressed by the mesenchyme, enables this tissue to respond to induction by the ureteric bud. GDNF and HGF, also produced by the mesenchyme, interact through their receptors, RET and MET, respectively, in the ureteric bud epithelium, to stimulate growth of the bud and maintain the interactions. The growth factors FGF2 and BMP7 stimulate proliferation of the mesenchyme and maintain *WT1* expression. **B.** WNT9B and WNT6 secreted by branches of the ureteric bud epithelium cause upregulation of *PAX2* and *WNT4* in the surrounding mesenchyme. In turn, these genes cause the mesenchyme to epithelialize (*PAX2*) and to then form tubules (*WNT4*). Changes in the extracellular matrix also occur, such that laminin and type IV collagen form a basement membrane for the epithelial cells.

Bibliography

SADLER, Thomas, et al. Langman's Medical Embryology. 10. edition. Lippincott Williams & Wilkins, 2006. 371 pp. ISBN 978-0781794855.

