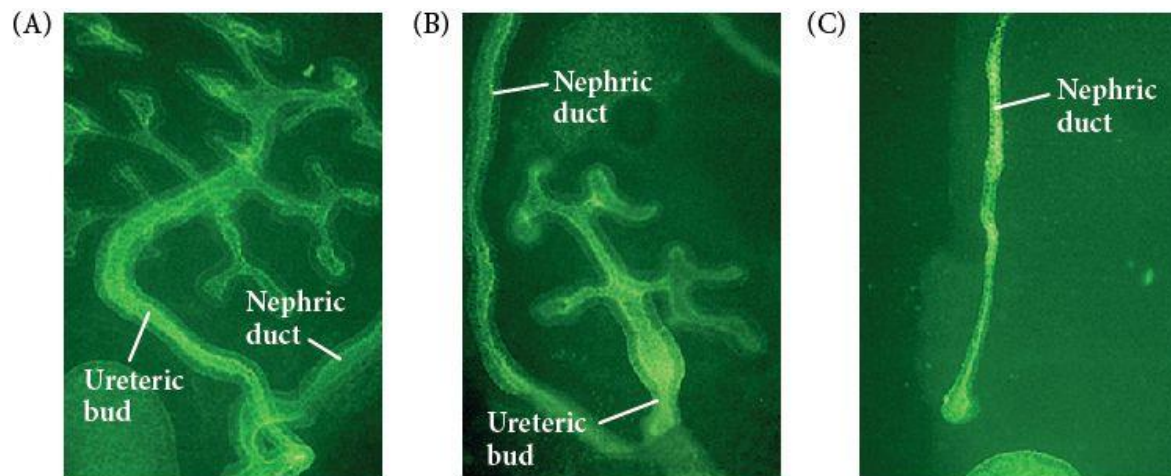


# The Metanephric Mesenchyme Secretes

The stage is now set for the secretion of paracrine factors that can induce the ureteric buds to emerge. Under the influence of retinoic acid (which is made in many of the surrounding tissues), the nearby nephric duct is instructed to express the Ret receptor on its cell surfaces (Rosselot et al. 2010). Ret is the receptor for glial-derived neurotrophic factor (GDNF), and GDNF is now secreted from the metanephric mesenchyme. GDNF secreted from the metanephric mesenchyme causes the outgrowth of the ureteric bud from the nephric duct. Indeed, during formation of the ureter, a subset of nephric duct cells (those in which the Ret receptor is most active) migrate to positions closest to the source of GDNF and thus form the tip of the emerging ureteric bud (see Figure 20.7; Chi et al. 2009). Mice whose genes for either GDNF or its receptor are knocked out die soon after birth from renal agenesis (lack of kidneys) (Figure 1; Moore et al. 1996; Pichel et al. 1996; Sánchez et al. 1996). The ability of other regions of the nephric duct to proliferate appears to be suppressed by activin, and one of the major mechanisms of GDNF action may be to locally suppress this inhibitory activin; when activin was experimentally inhibited, numerous ureteric buds formed (Maeshima et al. 2006).



From J. G. Pichel et al. 1996. Nature 382: 73–76, courtesy of J. G. Pichel and H. Sariola

**FIGURE 1** (A) The ureteric bud from an 11.5-day wild-type mouse kidney cultured for 72 hours has a characteristic branching pattern. (B) In embryonic mice heterozygous for a mutation of the gene encoding GDNF, both the size of the kidney and the number and length of its ureteric bud branches are reduced. (C) In mouse embryos missing both copies of the *Gdnf* gene, the ureteric bud does not form. (From Pichel et al. 1996, courtesy of J. G. Pichel and H. Sariola.)

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