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Essential Function of Wnt-4 for Tubulogenesis in the *Xenopus* Pronephric Kidney

Didier M.E. Saulnier [1] … André W. Brändli [2]

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Abstract

In the vertebrate embryo, development of the excretory system is characterized by the successive formation of three distinct kidneys: the pronephros, mesonephros, and metanephros. While tubulogenesis in the metanephric kidney is critically dependent on the signaling molecule Wnt-4, it is unknown whether Wnt signaling is equally required for the formation of renal epithelia in the other embryonic kidney forms. We therefore investigated the expression of Wnt genes during the pronephric kidney development in *Xenopus*. Wnt4 was found to be associated with developing pronephric tubules, but was absent from the pronephric duct. Onset of pronephric Wnt-4 expression coincided with mesenchyme-to-epithelium transformation. To investigate Wnt-4 gene function, we performed gain- and loss-of-function experiments. Misexpression of Wnt4 in the intermediate and lateral mesoderm caused abnormal morphogenesis of the pronephric tubules, but was not sufficient to initiate ectopic tubule formation. We used a morpholino antisense oligonucleotide-based gene knockdown strategy to disrupt Wnt-4 gene function. *Xenopus* embryos injected with antisense Wnt-4 morpholinos developed normally, but marker gene and morphological analysis revealed a complete absence of pronephric tubules. Pronephric duct development was largely unaffected, indicating that ductogenesis may occur normally in the absence of pronephric tubules. Our results show that, as in the metanephric kidney, Wnt-4 is critically required for tubulogenesis in the pronephric kidney, indicating that a common, evolutionary conserved gene regulatory network may control tubulogenesis in different vertebrate excretory organs.

Keywords

Wnt-4; pronephric kidney; tubulogenesis; morpholinos; *Xenopus*

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1 These authors contributed equally to this work.

2 To whom correspondence should be addressed. Fax: +41-1-635 6882. E-mail: brandli@pharma.anbi.ethz.ch.