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Advances in Anatomy Embryology and Cell Biology

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Factors Influencing Mammalian Kidney Development: Implications for Health in Adult Life

With 12 Figures

Springer

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Abstract

There are many reasons why it is timely to review the development of the mammalian kidney. Perhaps the most important of these is the increasing amount of evidence to demonstrate that factors which impinge on/alter the normal developmental processes of this organ can have lifelong consequences for the health of the adult. The 'Developmental Origins of Health and Adult Disease' (DOHaD) hypothesis, proposes that changes in the environment during the development of an organ or system, can have permanent deleterious effects leading to increased risk of cardiovascular and/or metabolic disease. The permanent metanephric kidney has been shown to be very vulnerable to such influences with many factors shown to alter both the permanent structure and the level of expression of important functional genes. Thus it is important to understand the precise timing of kidney development in terms of both structure and the genes involved at each stage. Such knowledge has been gained by significant advances in technology, which allow quantification of the number of nephrons by unbiased stereology, detections of both levels and site of gene expression, 'knock-out' and knock-in' of genes in animal (mainly mouse) models and by the ability to examine nephron development, in real time, in culture systems.

1
Introduction

There are many reasons why it is timely to review the development of the mammalian kidney. Perhaps the most important of these is the increasing amount of evidence demonstrating that factors which impinge on or alter the normal developmental processes of this organ can have lifelong consequences for the health of the adult. The original Barker hypothesis, more recently termed developmental origins of health and adult disease (DOHaD) hypothesis, proposed that changes in the environment (such as level of nutrition [total, protein, mineral, vitamin] or exposure to stress hormones) during the development of an organ or system, could have permanent deleterious effects leading to increased risk of cardiovascular and/or metabolic disease (Barker and Bagby 2005; Barker 2007; Gluckman and Hanson 2006; Hoy et al. 2005; Moritz et al. 2003, 2005a; Moritz and Bertram 2006).

The permanent metanephric kidney has been shown to be very vulnerable to such influences, with many factors shown to be able to alter both the permanent structure and the level of expression of important functional genes, most likely by the process of epigenetics (Moritz et al. 2003; Bagby 2006; Zandi-Nejad et al. 2006). Thus it has become increasingly important to understand the precise timing of kidney development in terms of both structure and the genes involved at each stage. Such knowledge has been gained by significant advances in technology, which allow quantification of the number of branching points and whole nephrons by unbiased stereology, detections of both levels (microarray, real-time PCR) and site (hybridization histochemistry) of gene expression, and by the ability to examine nephron development, in real time, in culture systems (3D, 4D microscopy) (Caruana et al. 2006b; Sanna-Cherchi et al. 2007; Jain et al. 2007; Bertram 1995, 2001). In addition, knowledge of the relative importance of individual genes in kidney development has been gained from knock-out and knock-in of genes in animal (mainly mouse) models.

The purpose of this review is to examine recent progress in the field of renal development and the long-term impact that poor renal development has on adult health.

2
Morphological Development of the Mammalian Kidney

In mammals, three pairs of excretory organs form from the intermediate mesoderm in a cranial to caudal direction. These are the pronephroi, mesonephroi and metanephroi, respectively. The pronephroi and mesonephroi are transient organs, but their existence is required for the development of the metanephroi or permanent kidneys. The development of these three excretory organs is shown diagrammatically in Fig. 1.