Seminars in Cell & Developmental Biology xxx (2014) xxx–xxx

Contents lists available at ScienceDirect

Seminars in Cell & Developmental Biology

journal homepage: www.elsevier.com/locate/semcdb

Review

Patterning the renal vascular bed

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ARTICLE INFO

Article history:
Available online xxx

Keywords:
Kidney development
Vascular patterning
Angiogeneis
Vasculogenesis

ABSTRACT

The renal vascular bed has a stereotypic architecture that is essential for the kidney's role in excreting metabolic waste and regulating the volume and composition of body fluids. The kidney's excretory functions are dependent on the delivery of the majority of renal blood flow to the glomerular capillaries, which filter plasma removing from it metabolic waste, as well as vast quantities of solutes and fluids. The renal tubules reabsorb from the glomerular filtrate solutes and fluids required for homeostasis, while the post-glomerular capillary beds return these essential substances back into the systemic circulation. Thus, the kidney's regulatory functions are dependent on the close proximity or alignment of the post-glomerular capillary beds with the renal tubules. This review will focus on our current knowledge of the mechanisms controlling the embryonic development of the renal vasculature. An understanding of this process is critical for developing novel therapies to prevent vessel rarefaction and will be essential for engineering renal tissues suitable for restoring kidney function to the ever-increasing population of patients with end stage renal disease.

Contents

1. Introduction

The vascular bed of the kidney exhibits unique structural features that are essential for its function. Although the kidneys comprise less than 0.08% of body weight, they receive 20% of cardiac output. This magnitude of blood flow is not required for metabolic purposes. Rather, it reflects the kidney's role in clearing the blood of metabolic waste, substances that are harmful or foreign, as well as fluids and ions that are in excess to body economy. Blood flows into the kidney via the renal artery, which enters the organ in a central fissure called the hilum. Although the renal artery is in close proximity to the medulla, less than 10% of arterial blood flow is delivered to this central region of the kidney. Instead, the major branches of the arterial tree conduct greater than 90% of renal blood flow directly to the glomerular capillary bed located in the peripheral, cortical region of the organ [1] (Fig. 1A).

Each of the approximately 1,000,000 nephrons that comprise the human kidney has a glomerular capillary composed of 6–8 loops embedded into its blind end (Fig. 1D–F). The glomerular endothelium is relatively permeable to fluids and low, but not high molecular weight solutes. The extended length of the glomerular capillary and its permeability properties, along with the location of the glomerular capillary between two high resistance arterioles, enables the glomeruli to produce a plasma ultrafiltrate that flows into urinary space at a rate of 125 ml/min. Notably, the tone of the two high resistance arterioles that flank the glomerulus plays a fundamental role in modulating this high rate of fluid flow out of the glomerular capillaries, which is approximately 50× greater

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http://dx.doi.org/10.1016/j.semcdb.2014.08.002
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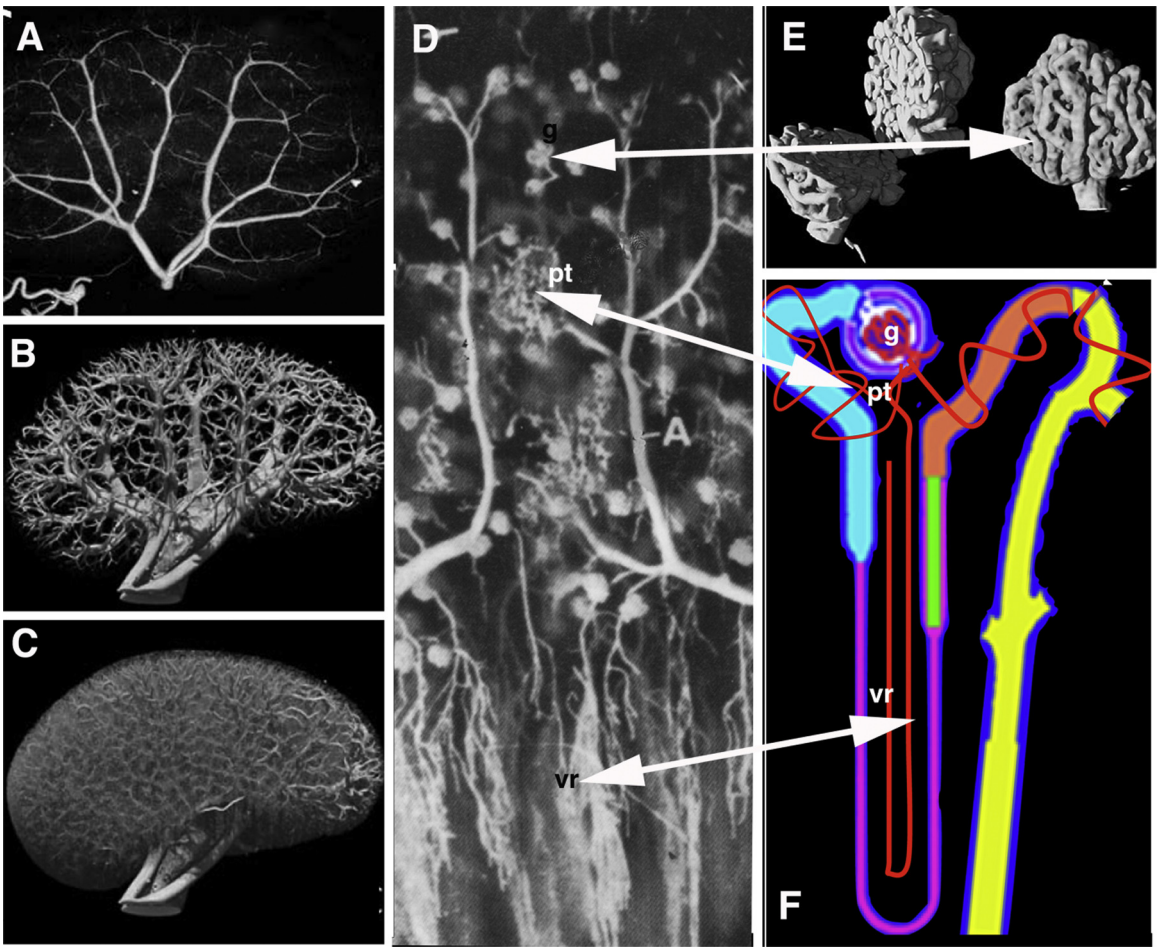

Fig. 1. Anatomy of the renal vascular bed. Reconstructed scan of an entire mouse kidney corrosion cast by nano-CT (A–C) [42]. Thresholding for large vessels (A) illustrates the stereotypic architecture of the renal artery and its major branches. As thresholding is adjusted to visualize smaller vessels, the cortical arterial tree up to the level of the intralobular arteries is detected (B). Finer thresholding allows for the visualization of the complex architecture of the cortical microvasculature (C). Corrosion cast of rat kidney imaged by scanning electron microcroscopy (kindly provided by Dr. Wilhelm Kriz). The glomerului (g), peritubular capillaries (pt) and vasa recta (vr) are easily visualized. (E) A corrosion cast of an isolated glomerulus imaged by nano-CT illustrating the complexity of the capillary loops [42]. (F) Representation of a single nephron and its associated glomerulus (g), peritubular capillaries (pt) and vasa recta (vr).

than the rate of fluid flow out of any other systemic capillary beds.

After being filtered by the glomerulus, blood flows via the efferent arteriole into the peritubular capillaries. Blood entering the peritubular capillaries has a high oncotic pressure, due to the loss of fluids by glomerular filtration and retention of high molecular weight solutes. The relatively high oncotic pressure in the peritubular capillaries, exceeds the hydrostatic pressure across this capillary bed. Thus, the peritubulars are poised for the reabsorption of solutes and fluids lost by glomerular filtration, a function that is dependent on their close alignment with the cortical renal tubules (Fig. 1D and F). Specifically, the transporting epithelia of the renal tubules rebsorb from the glomerular filtrate, solutes and ions essential for homeostasis and then, the peritubular capillaries return these essential substances to the systemic circulation.

The renal vasculature also includes a third capillary bed, termed the vasa recta, which is in close alignment with the medullary renal tubules. The vasa recta emanate from the post-glomerular capillary bed and deliver oxygen and nutrients to the medullary region of the kidney. In addition, they return ions and solutes reabsorbed by the medullary renal tubules to circulation. The vasa recta follow the contours of the medullary renal tubules, descending deep into the medullary zone of the kidney and then back up to the cortex. The looped architecture and permeability of the renal medullary tubules and closely aligned vasa recta generate a gradient of increasing osmolarity in the medullary region of the kidney which is essential for conserving water during times of fluid deprivation. Thus, the vasa recta are essential for concentrating the urine, as well as for perfusing the medulla and returning to systemic circulation ions and water reabsorbed by the medullary renal tubules. After all these steps, blood is collected into a venous system at the cortical-medullary junction of the kidney and flows out of the kidney via the renal vein. It is likely that the renal lypmphatics also play a role draining plasma fluids out of the kidney although they remain rather poorly characterized. Studies by Lee et al. demonstrate that vessels expressing the lymphatic maker LYVE-1 are embedded in cortical, periarterial loose connective tissue, while studies by Madsen demonstrate that the medulla lacks lymphatics altogether [1,2].

This brief description of the mature renal vascular bed well illustrates several of the architectural challenges that must be met as the kidney is vascularized during embryogenesis. These challenges include:

- Formation of an arterial tree that conducts blood directly to the glomerular capillaries.
- Formation of the glomerular capillaries and their specialized features required for filtration.

Please cite this article in press as: Herzlinger D, Hurtado R. Patterning the renal vascular bed. Semin Cell Dev Biol (2014), http://dx.doi.org/10.1016/j.semcdb.2014.08.002