Histopathology of the Tubule

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The functional unit of the kidney is the nephron, which consists of a renal corpuscle or glomerulus and its associated tubule. The tubular portion of the nephron is composed of three major subdivisions : The proximal convoluted tubule (PCT), the loop of Henle, and the distal convoluted tubule (DCT). The latter continues into the collecting duct system, which is derived from the ureteric bud and, strictly speaking, is not part of the nephron. The loop of Henle includes the proximal straight tubule (PST) (pars recta of the proximal tubule), the thin limb segments, and the thick ascending limb (TAL) (pars recta of the distal tubule).

Each human kidney contains approximately 1.2 million nephrons. Those originating from outer and midcortical glomeruli have short loops of Henle that bend in the inner stripe of the outer medulla. Juxtamedullary nephrons originating from glomeruli located near the corticomedullary junction have long loops of Henle that reach into the inner medulla. In the human kidney 10-15% of the glomeruli belong to long-looped nephrons.

The complex multicellular composition of the kidney reflects the complicated nature of its functional properties. The kidney is responsible for maintaining both the volume and composition of the body fluids, excreting fixed or nonvolatile metabolic products such as creatinine, urea and uric acids and eliminating exogenous drugs and toxins. The kidney is a major endocrine organ producing renin, erythropoietin, 1,25-dihydroxycholecalciferol, prostaglandins and kinins, and it also serves as a target organ for many hormones. The kidney also catabolizes small molecular weight proteins and is responsible for a host of metabolic functions, e.g., ammoniagenesis and gluconeogenesis.

Proximal Tubule

1. Structure

The proximal tubule includes an initial pars convoluta, or PCT, and a pars recta, or PST, which is located in the medullary ray. The PCT has numerous lateral cell processes that extend from the apical to the basal surface of the cell and interdigitate with similar cell processes from adjacent cells. Mitochondria are located in these processes in close proximity to the cell membrane. The presence of these lateral cell processes and interdigitations gives rise to a complex extracellular compartment between the cells. This intercellular space is separated from the tubule lumen by the tight junction or zonula occludens. A prominent endocytic-lysosomal system is present in the cells and plays an important role in the reabsorption and catabolism of proteins from the tubule fluid. Based on morphologic differences, the proximal tubule can be subdivided into three distinct segments. The S_1 segment corresponds to the initial PCT; the S_2 segment corresponds to the terminal PCT and the initial PST; and the S_3 segment constitutes the remainder of the PST.

2. Function

The main function of the proximal tubule is the reabsorption of sodium, chloride, bicarbonate, potassium, phosphate, water, and organic solutes such as glucose and amino acids, and the secretion of organic acids and bases, including common drugs such as salicylates, barbiturates, penicillin, and many diuretics. Much of the sodium reabsorption is an active process mediated by the Na-K-ATPase or sodium pump located in the basolateral plasma membrane. The transport of the various anions and organic solutes across the luminal membrane is coupled to the reabsorption of sodium down its concentration gradient. Fluid reabsorption is accomplished primarily by isosmotic water flow through the cell and the intercellular spaces.

Thin Limb of Henle's Loop

1. Structure

The thin limb of Henle's loop extends from the proximal tubule to the TAL. Short-looped nephrons have only a short descending thin limb segment that is located in the inner stripe of the outer medulla. Long-looped nephrons have both a long descending and a long ascending thin limb. Four morphologically distinct segments can be identified in the thin limb. All are lined by a flat epithelium containing few cell organelles.

2. Function

The thin limb of Henle's loop plays an important role in the countercurrent multiplication mechanism. The descending limb is permeable to water but impermeable to sodium, whereas the ascending limb is almost impermeable to water but highly permeable to sodium and modestly permeable to urea. Accordingly, water diffuses out of the descending limb and, subsequently, sodium exits the ascending limb down its concentration gradient. Thus, the countercurrent mechanism plays a role in the maintenance of a hypertonic medullary interstitium and in the formation of a dilute tubule fluid.

Distal Tubule

1. Structure

The distal tubule consists of the TAL which can be subdivided into a medullary and a cortical segment, the macula densa, and the distal convoluted tubule (DCT). The transition from the TAL to the DCT occurs shortly after the macula densa. The cells of both the TAL and the DCT possess extensive invaginations of the basolateral plasma membrane and interdigitations of cell processes between adjacent cells. Numerous elongated mitochondria are located in the lateral cell processes in close proximity to the plasma membrane. In contrast to the proximal tubule, the luminal membrane of the distal tubule does not possess a brush border.

2. Function

The ultrastructural composition of the distal tubule is characteristic of an epithelium involved in active transport. Both the TAL and the DCT are responsible for active reabsorption of sodium chloride, which plays an important role in the countercurrent multiplication process and the urinary concentrating and diluting mechanism. Since the TAL is relatively impermeable to water, the active reabsorption of sodium chloride creates a hypertonic interstitium and ensures the delivery of a hypotonic tubule fluid to the DCT. The TAL is the site of action of the loop diuretics (e.g., furosemide), whereas thiazide diuretics exert their effect mainly on the DCT.

The connecting segment is located between the distal tubule and the collecting duct. It is a transition region where a mixture of cells from adjacent regions can be encountered including DCT cells, connecting tubule cells, and collec-

ting duct cells (intercalated and principal cells).

Collecting Duct

The collecting duct system can be divided into the cortical (CCD), outer medullary (OMCD), and inner medullary collecting duct (IMCD). The CCD consists of the initial collecting tubule and the segment located in the medullary ray. The epithelium of both the CCD and OMCD is composed of two distinct cell types, principal cells and intercalated cells, the latter constituting approximately one third of the cells. Principal cells have a light cytoplasm with few cell organalles and a relatively smooth luminal surface, whereas intercalated cells have a dark staining cytoplasm with many mitochondria and numerous small tubulovesicles. The luminal surface of intercalated cells is covered with microprojections that are either microvilli or microplicae. Two different configurations of intercalated cells have been observed, type A cells which are involved in hydrogen ion secretion and type B cells which secrete bicarbonate. A main function of principal cells in the CCD is potassium secretion.

Intercalated cells gradually disappear in the early portion of the IMCD and are absent in the papillary portion. The cells in the terminal two thirds of the IMD are believed to constitute a distinct cell type that is called the IMCD cell. The IMCD cells have a very light cytoplasm and few organelles. They increase in height as the collecting duct descends toward the papillary tip. The principal cells and the IMCD cells are responsive to antidiuretic hormone (ADH). In the presence of ADH water is reabsorbed from the collecting duct which leads to the formation of a hypertonic urine. In the absence of ADH the collecting duct is relatively impermeable to water and a hypotonic urine is formed.

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