

WIDESPREAD KALLIKREIN EXPRESSION DURING HUMAN KIDNEY DEVELOPMENT BECOMES RESTRICTED TO TUBULES WITH A REDUCED NUMBER OF PRIMARY CILIA IN POSTNATAL KIDNEYS

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Introduction

The primary cilium is a signalling organelle present in most cell types and it has a crucial role in the regulation of development and homeostasis. Kallikrein is an enzyme that is part of the kallikrein-kinin system involved in regulation of natriuresis and blood pressure. Our goal was to determine the relationship between primary cilia and kallikrein expression in the developing human mesonephros and metanephros and postnatal kidneys.

Materials and Methods

We used double immunofluorescence to analyze kallikrein and acetylated α -tubulin (primary cilia marker) expression in 5- to 16-week-old human conceptuses and postnatal kidneys. The density of primary cilia was calculated using ImageJ as the ratio of the number of cilia counted and the length of the apical surface of tubules in mm. Statistical analysis was performed in GraphPad Prism.

Results

Our preliminary results show that, during development, diffuse kallikrein expression characterized both podocytes and parietal epithelial cells (PECs) of renal corpuscles, while only PECs retained primary cilia past the embryonic period (Figure 1). In the postnatal kidney, the entire corpuscle became devoid of kallikrein, while only some tubules, morphologically resembling proximal tubules, demonstrated strong apical expression (Figure 1). When comparing postnatal kidney tubules with and without kallikrein expression, a noticeable reduction in the number of primary cilia in kallikrein-positive tubules was observed (Figure 2). Statistical analysis showed a significant difference ($p < 0.0001$) in the average density of primary cilia between kallikrein-positive (4.2 cilia/mm) and kallikrein-negative (21 cilia/mm) tubules.

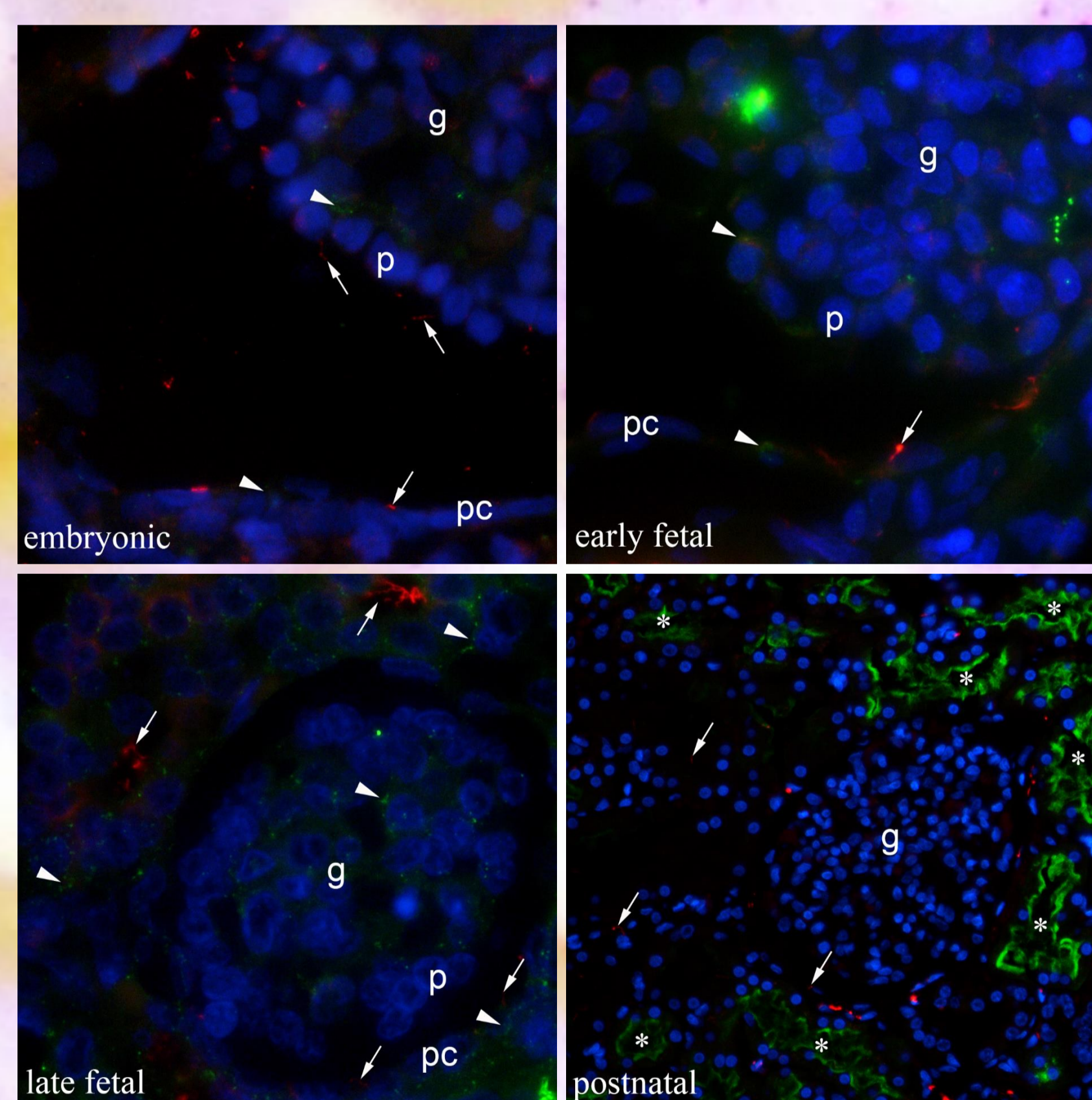


Figure 1. Double immunofluorescent staining to acetylated- α -tubulin and kallikrein in developmental stages of renal corpuscles. g – glomerulus, p – podocytes, pc – parietal epithelial cells, arrows – primary cilia, arrowheads – kallikrein expression, asterisks – kallikrein-positive tubules.

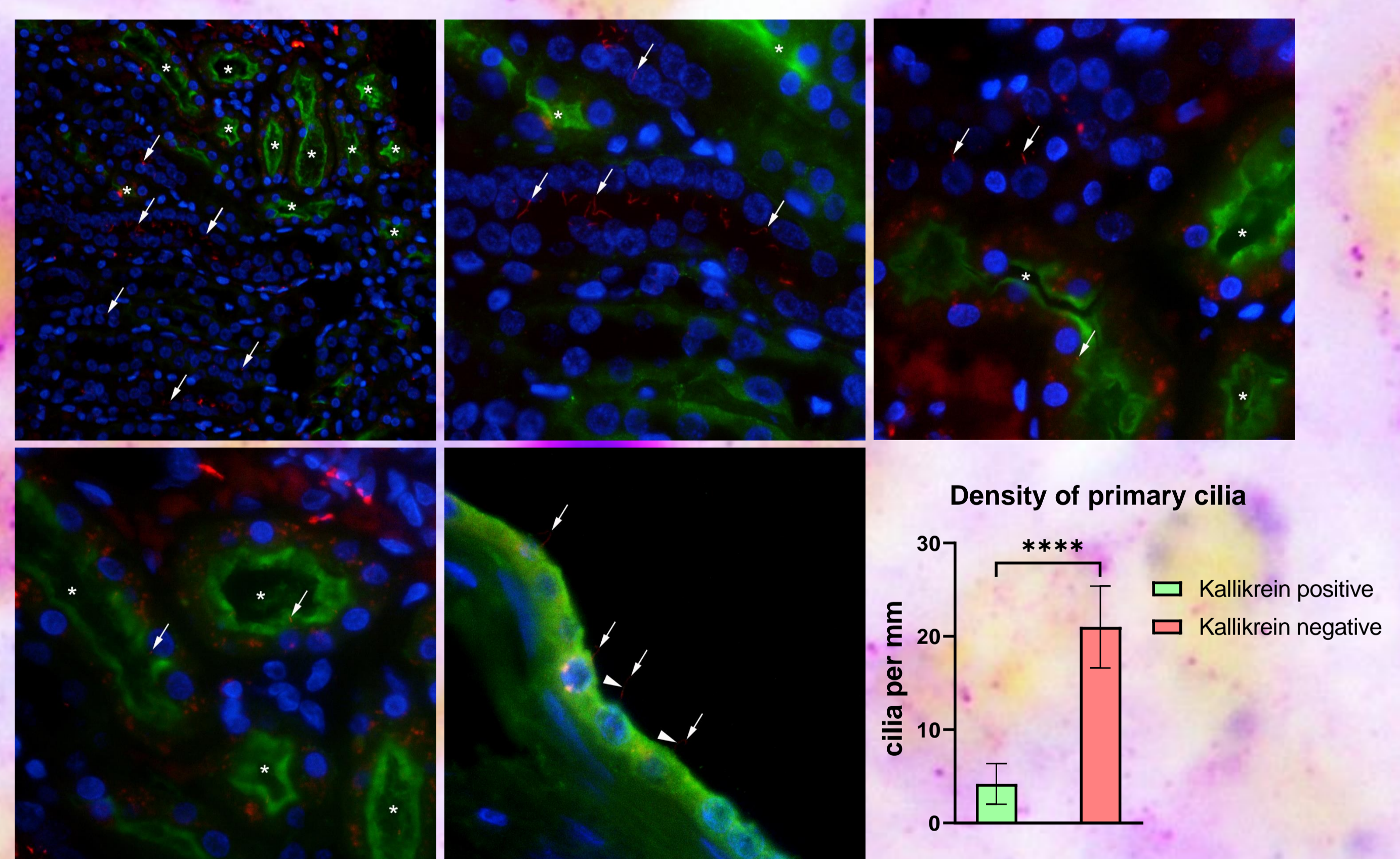


Figure 2. Double immunofluorescent staining to acetylated- α -tubulin and kallikrein in postnatal kidney tubules. arrows – primary cilia, arrowheads – kallikrein expression, asterisks – kallikrein-positive tubules. The graph represents the mean values of primary cilia density; error bars represent the standard deviation; **** $p < 0.0001$.

Conclusions

Extensive kallikrein expression present during nephrogenesis becomes limited to certain tubules in the mature kidney and those tubules have comparatively less primary cilia than the rest. This implies an inverse relationship between kallikrein expression and primary cilium signalling.

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