

Expression of Keratin 17 in renal injury indicates tubular stress and dedifferentiation

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Introduction

- Keratins (K) are the intermediate filaments of epithelial cells
- Keratins (K) K7, K8, K18, K19 are the main renal keratins in humans and mice (Moll et al., *Lab Invest* 1991; Djudjaj et al., *Kidney Int* 2016)
- K17 was mentioned to be expressed in the injured human kidney (Moll et al., *Lab Invest* 1991)
- K17 is robustly upregulated during organ stress e.g. in skin (Paladini et al., *J Cell Biol* 1996)
- K17 is expressed by "reserved cells" in the cervix epithelium (Martens et al., *Anticancer research* 2004)

AIM: To comprehensively analyse the expression and regulation of K17 in human and murine healthy and diseased renal tissue.

Summary & Conclusion

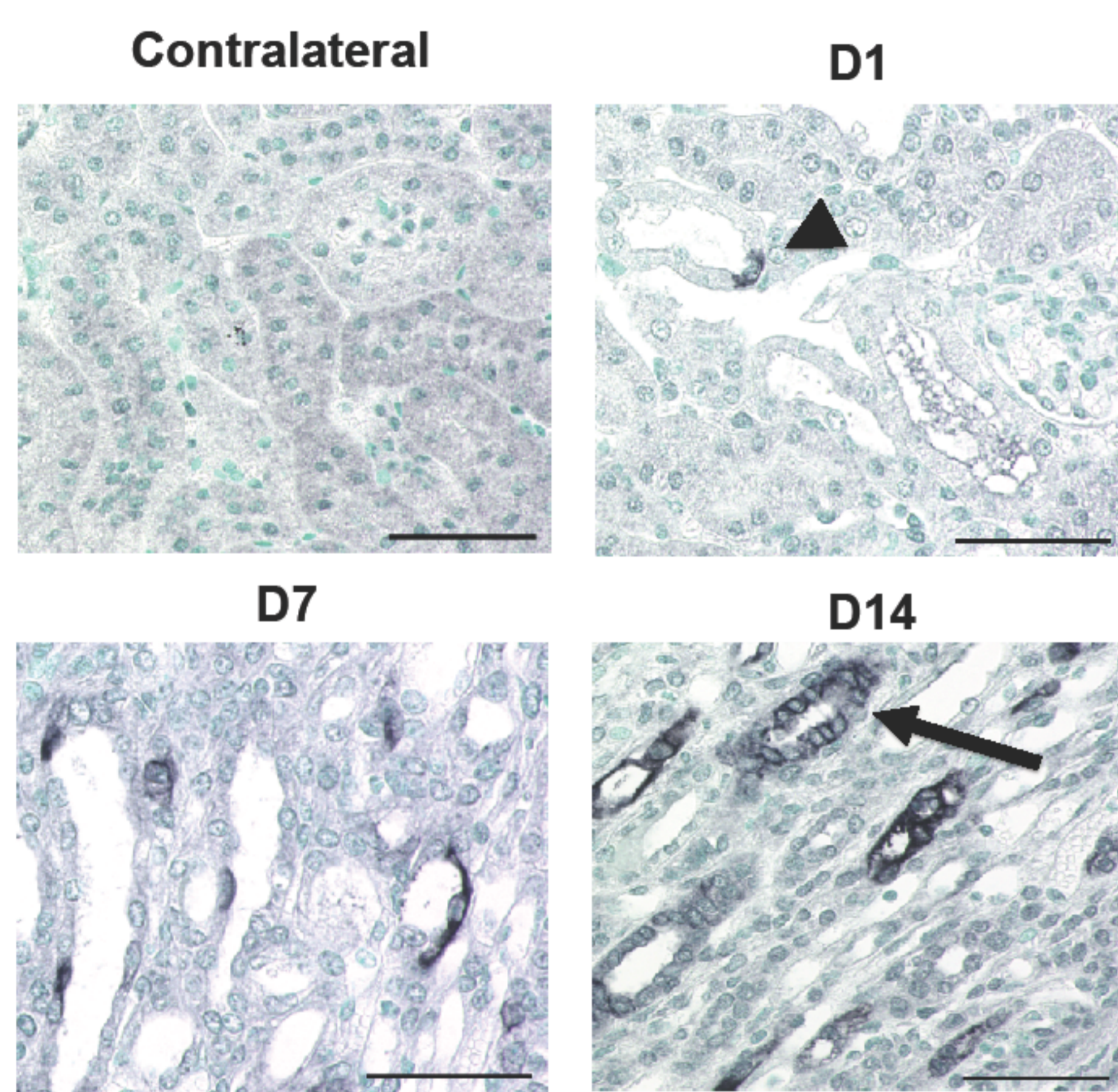
- K17 is not expressed in healthy murine kidneys, in contrast to basolateral expression of K17 in collecting ducts of healthy human kidneys
- K17 is expressed *de novo* in five different murine models of renal disease and marks a subpopulation of tubular cells which expand with severity of injury
- K17 cell subpopulation is not proliferating nor injured, but expresses vimentin and shows similar subcellular localization as embryonic K17
- K17 is not found in healthy PECs, neither murine nor human, but is found in human PECs in glomeruli with prominent periglomerular fibrosis

K17 marks a distinct subpopulation of tubular cells during kidney injury, showing some aspects of dedifferentiation towards embryonic phenotype.

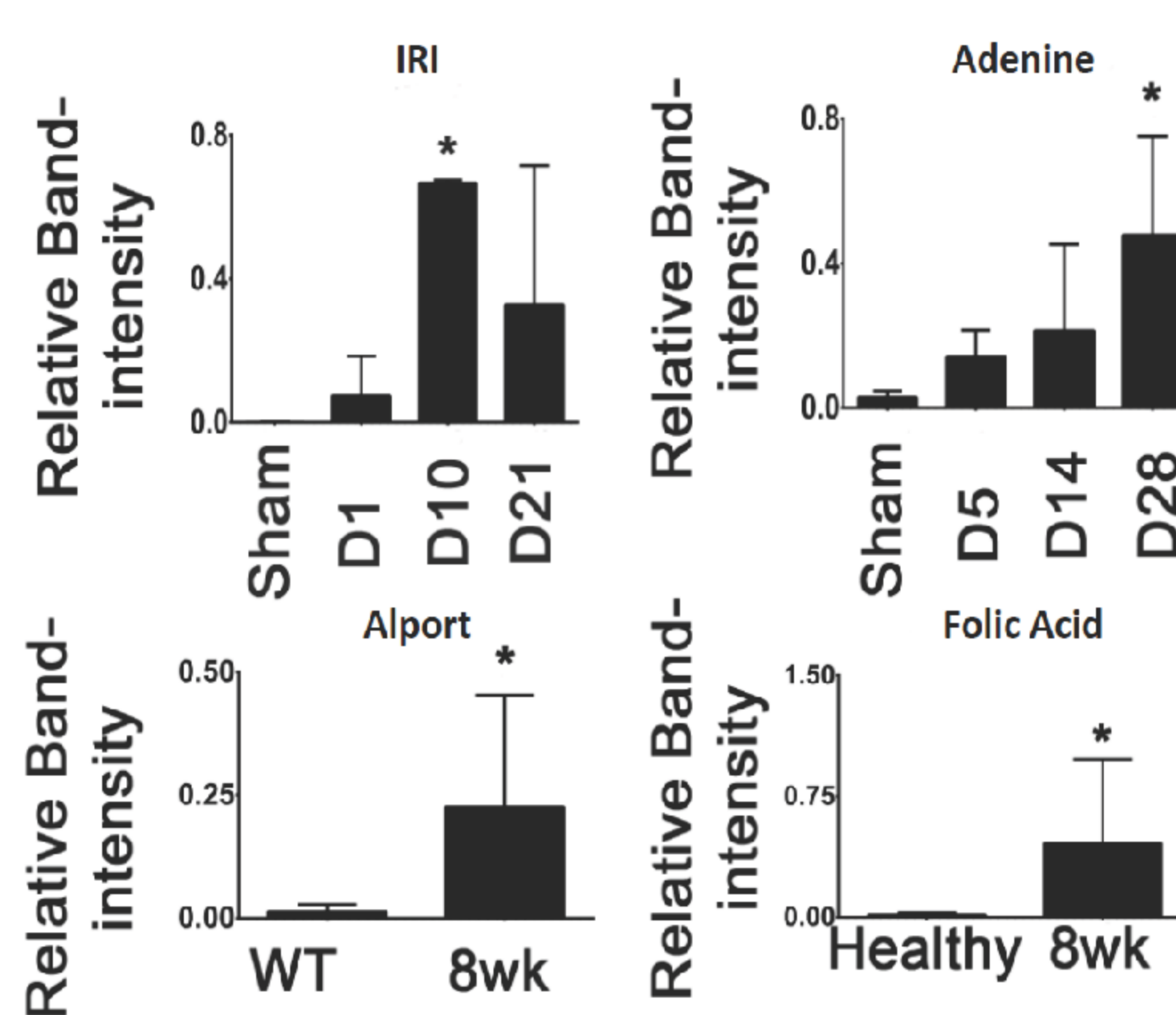
Methods & Results

Five murine models (UUO: unilateral ureteral obstruction, IRI: ischemia-reperfusion injury, FA: folic acid nephropathy, the adenine-model and the alport model) were analyzed for K17-expression by means of immunohistochemistry, immunofluorescence, qRT-PCR and Western blotting. Additionally, both human non-fibrotic and fibrotic renal tissue was investigated using immunohistochemistry and immunofluorescence. A tissue microarray representing major renal tumors (RCC: renal cell carcinoma) was also stained for K17.

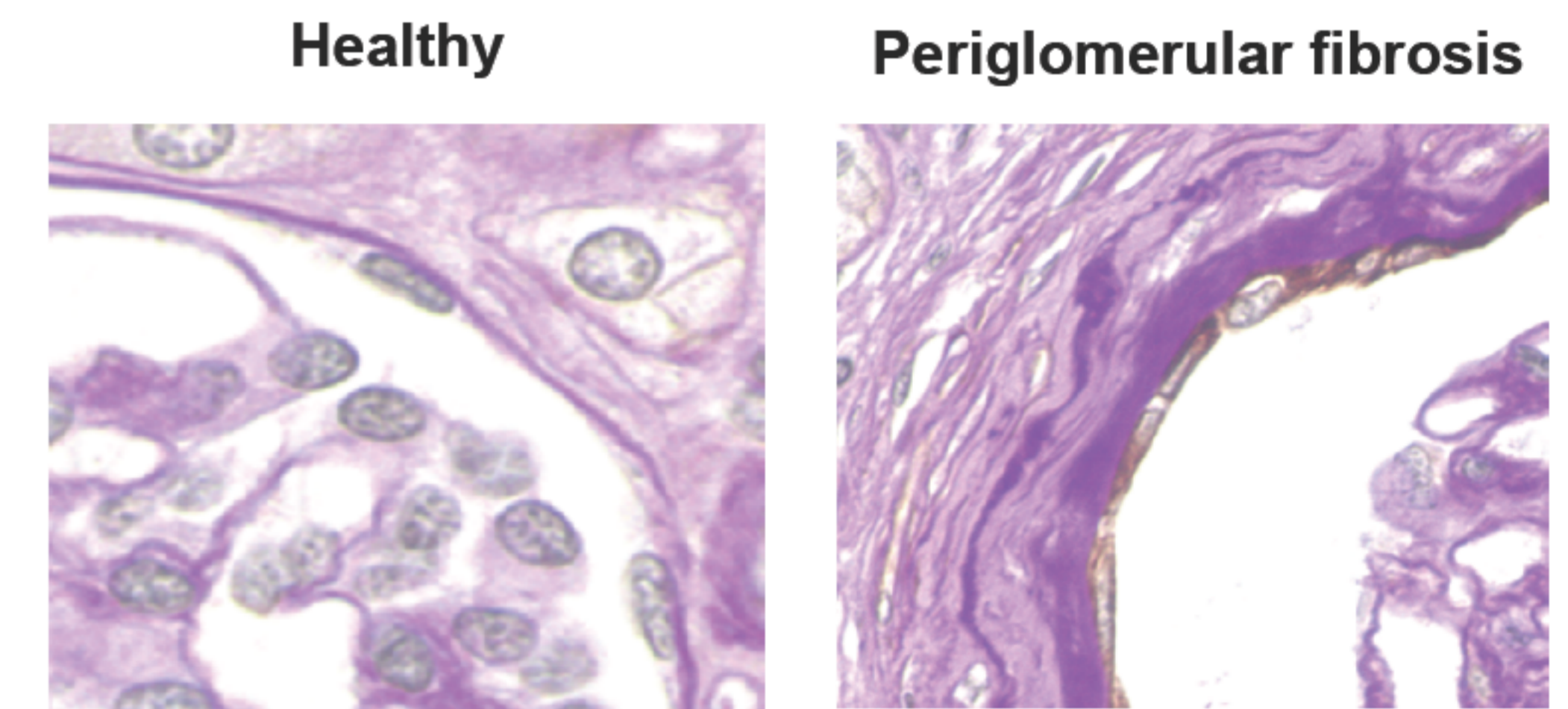
K17 is *de novo* expressed in UUO



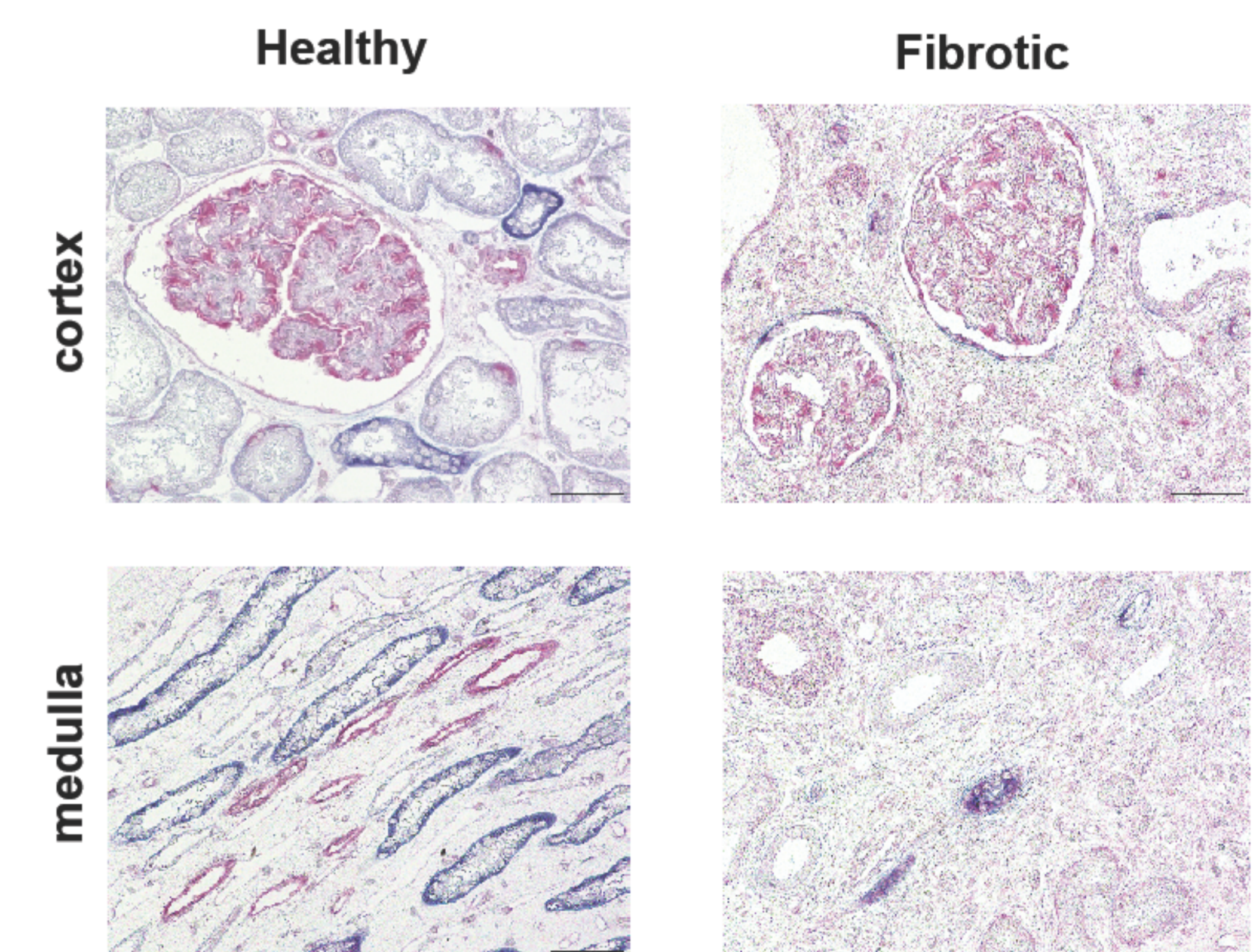
Western Blot confirmation



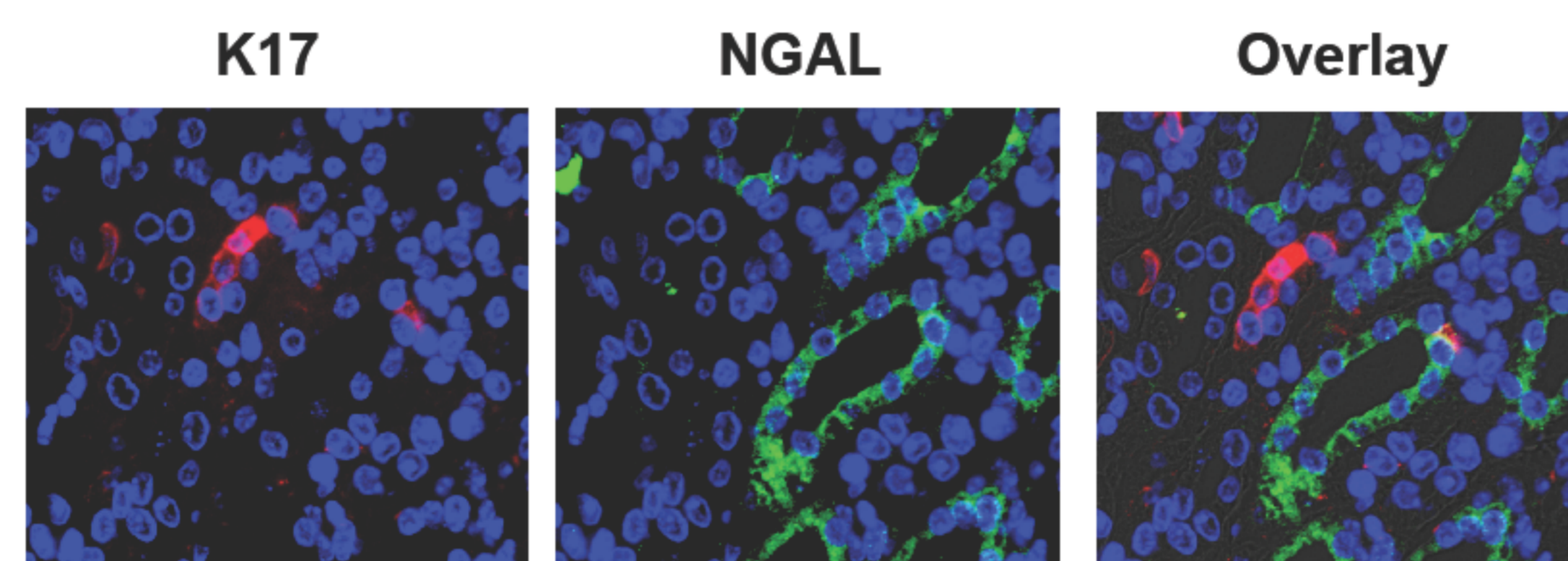
K17 is expressed *de novo* in human PECs



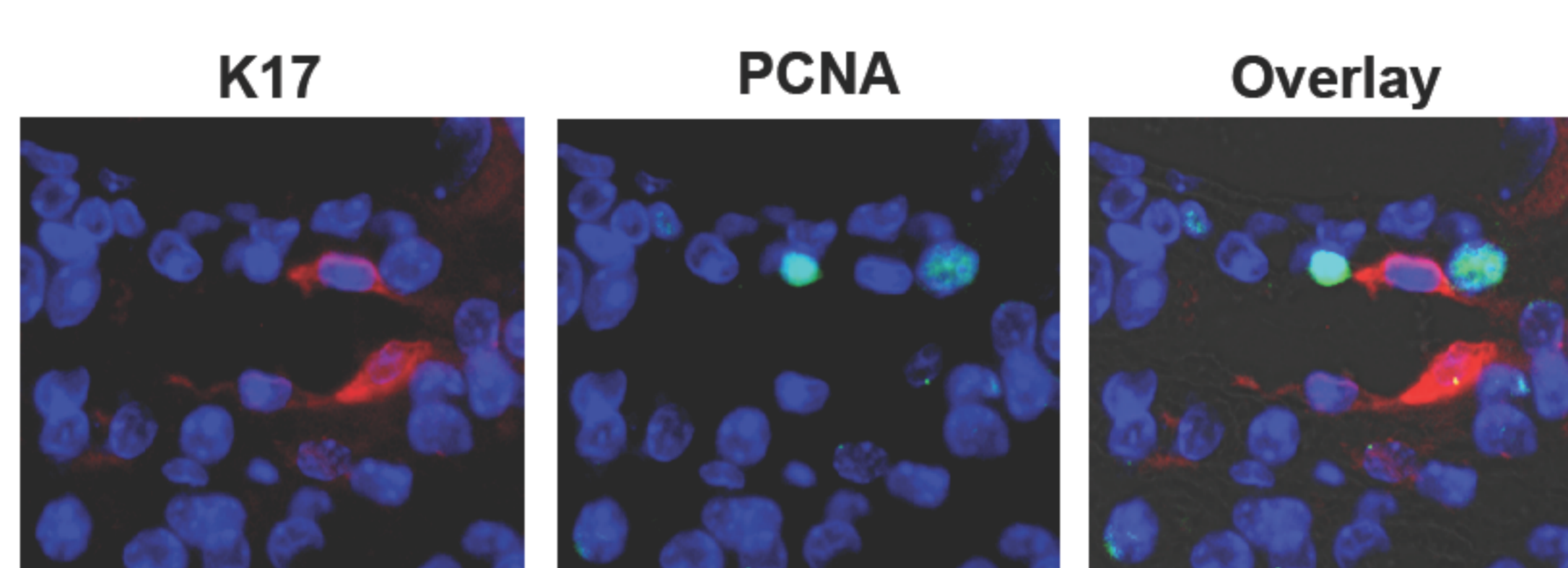
K17⁺ cells colocalize with vimentin



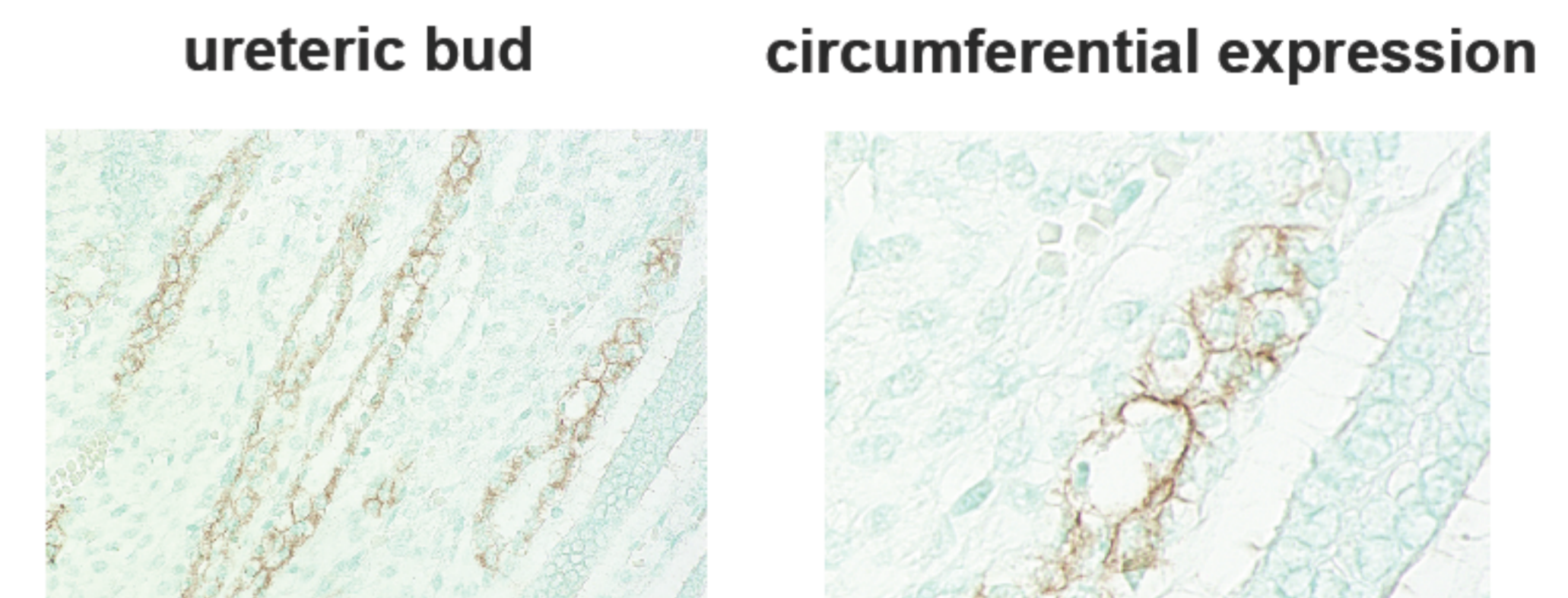
K17⁺ cells are NGAL⁻



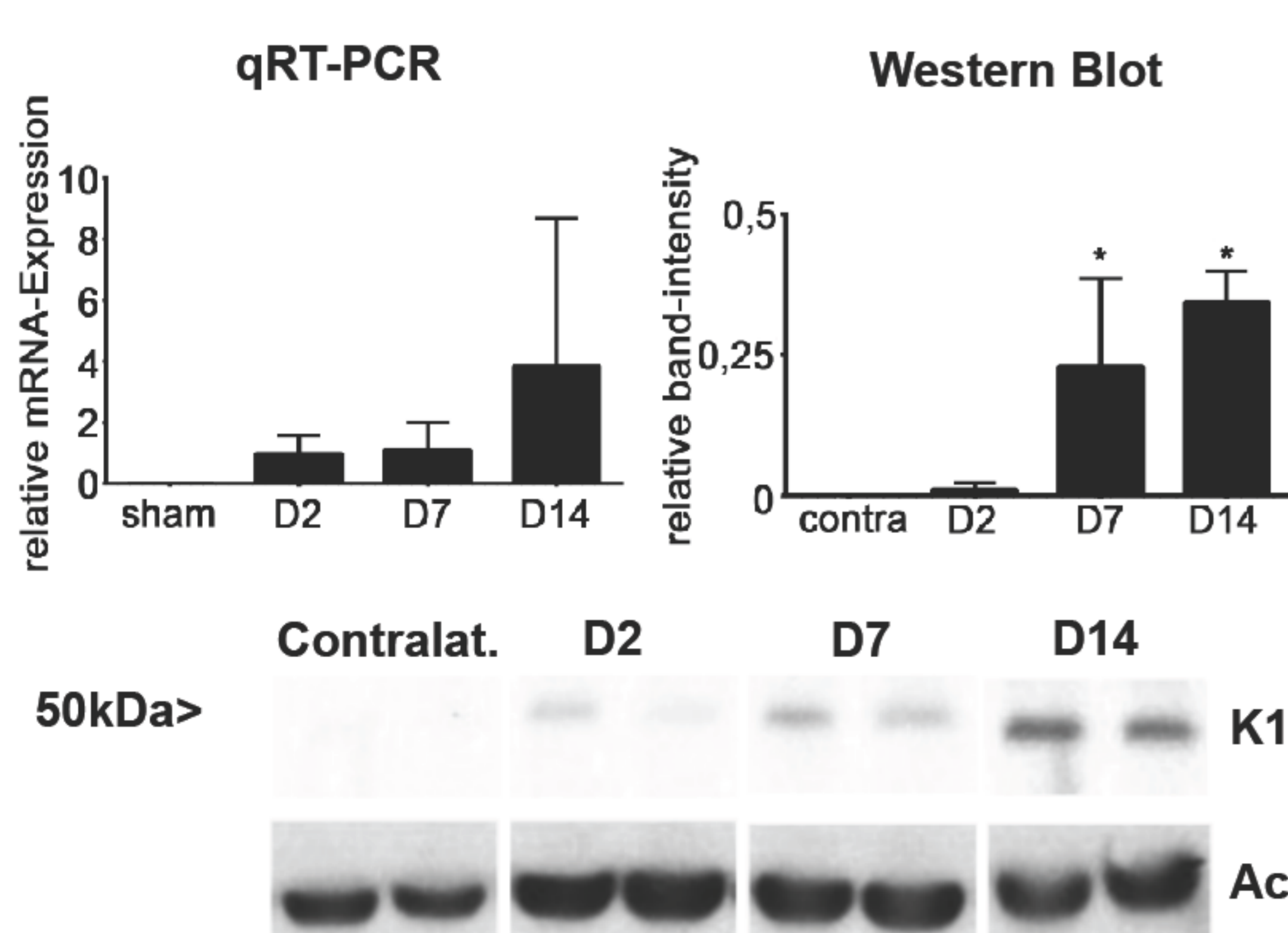
K17⁺ cells are PCNA⁻



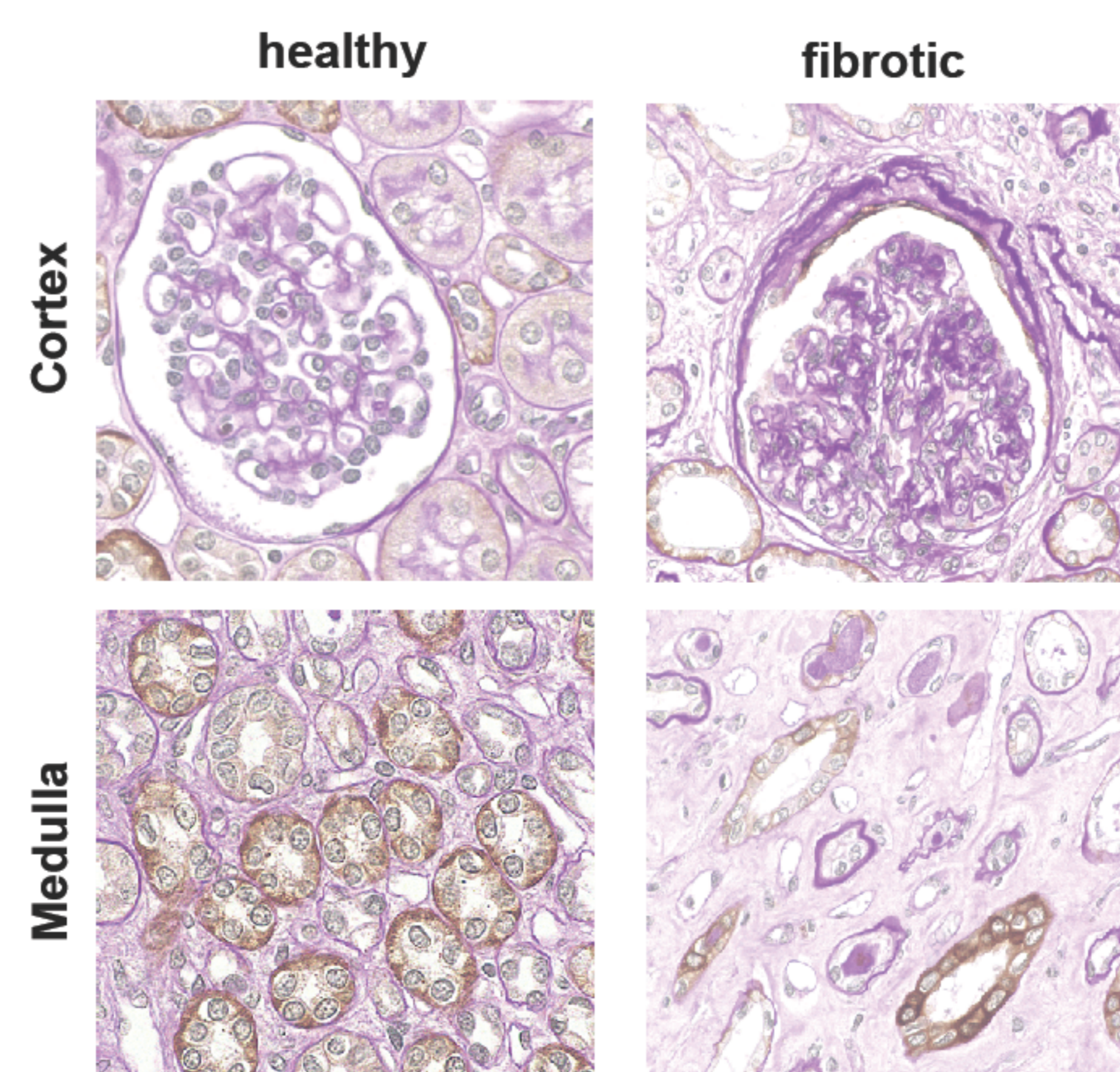
K17 is expressed in the fetal human kidney



Confirmation of IHC data in UUO model



Human expression of K17



K17 expression in renal tumors

Entity	Positive K17 Staining
Papillary RCC, type 1	1/3
Papillary RCC, type 2	0/3
Clear Cell RCC, Grade 1	0/15
Clear Cell RCC, Grade 2	0/2
Clear Cell RCC, Grade 3	0/2
Oncocytoma	0/3
Metanephric Adenoma	2/2
Angiomyolipoma	0/1
Chromophobe RCC	0/4
Juxtaglomerular Tumor	0/1
Ductus Bellini-Carcinoma	0/1

