ROLE OF EXTRACELLULAR MATRIX DEFECTS IN THE PROGRESSION OF THE POLYCYSTIC KIDNEY DISEASE

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INTRODUCTION AND OBJECTIVES

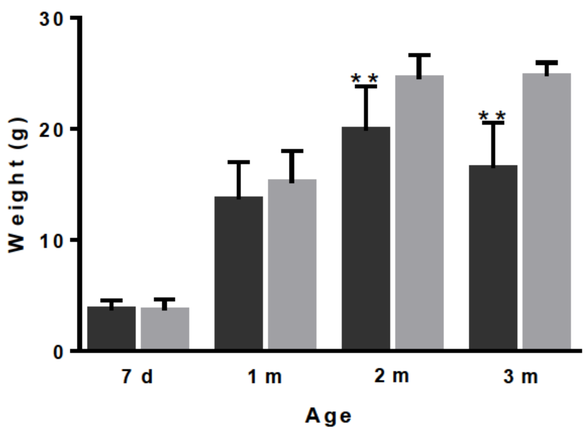
The role of the extracellular matrix (ECM) abnormalities in the development and the progression of the polycystic kidney diseases (PKD) remains poorly analyzed. Morphological defects and abnormal molecular composition of the basement membrane (BM) that surrounds tubular cysts have been however previously reported. The objective of the present study was to get insight into the potential deleterious role of primary tubular BM defects in the progression of PKD.

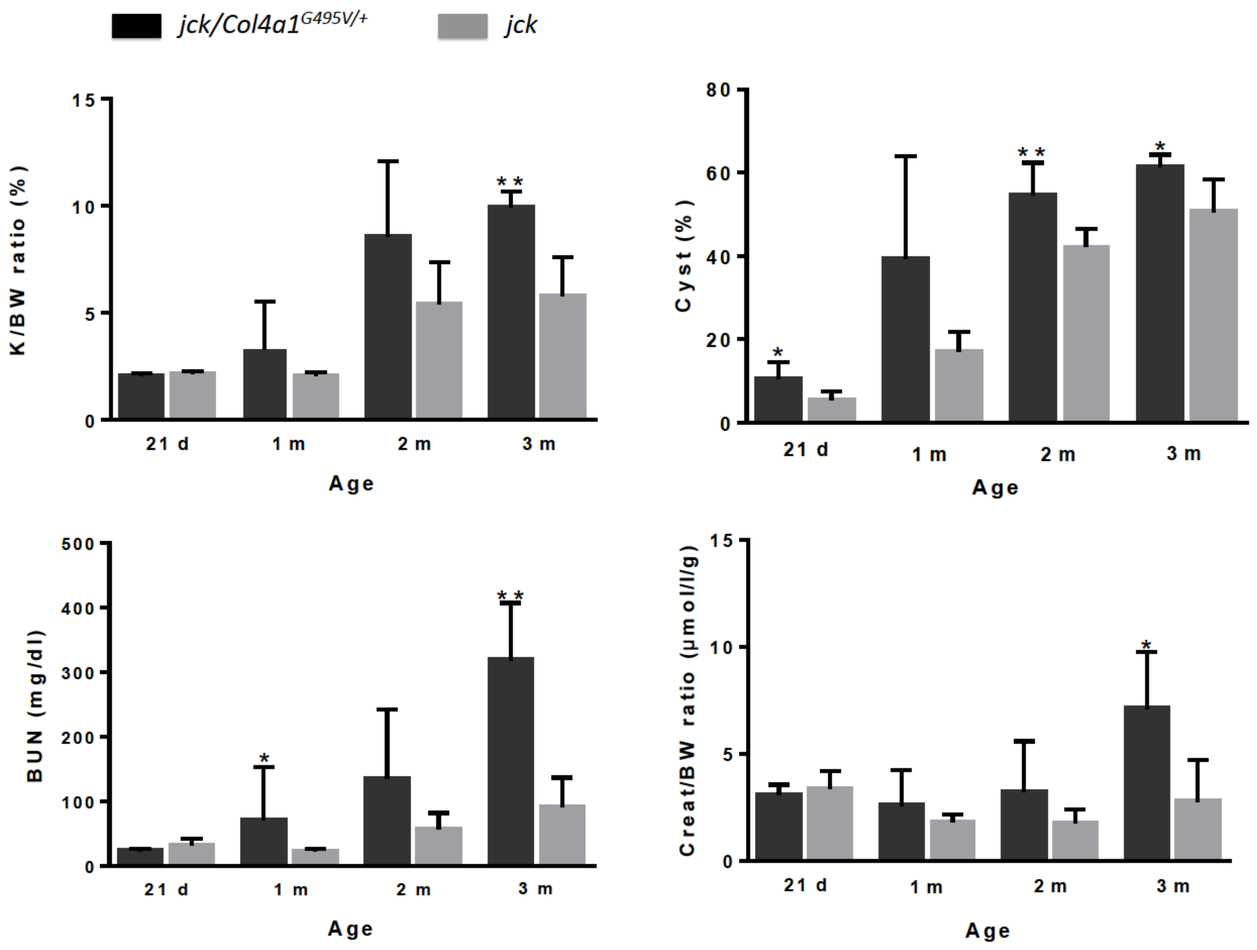
METHODS

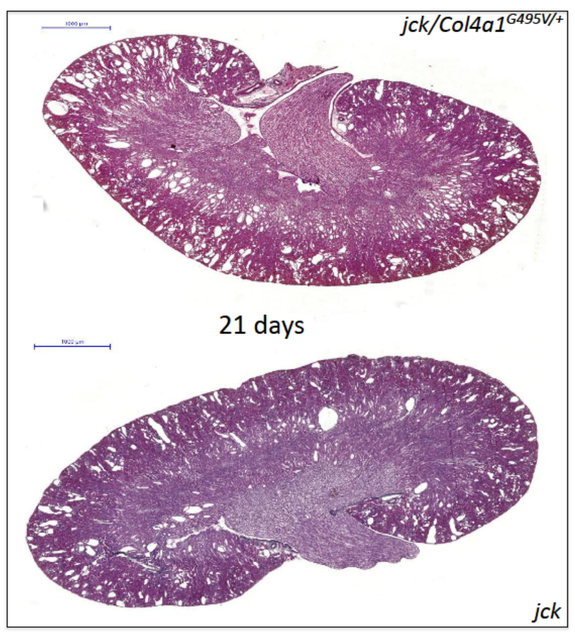
A double mutant mouse strain was generated by crossing *jck* mice, a well-described mouse model of typical PKD, with knock-in mice harboring a missense mutation of the Col4a1 gene, encoding for the collagen IV isoform expressed in the tubular BM. General, as well as functional and morphological renal parameters were assessed in *jck/Col4a1*$^{G495V/+}$ mice, and compared to *jck* animals.

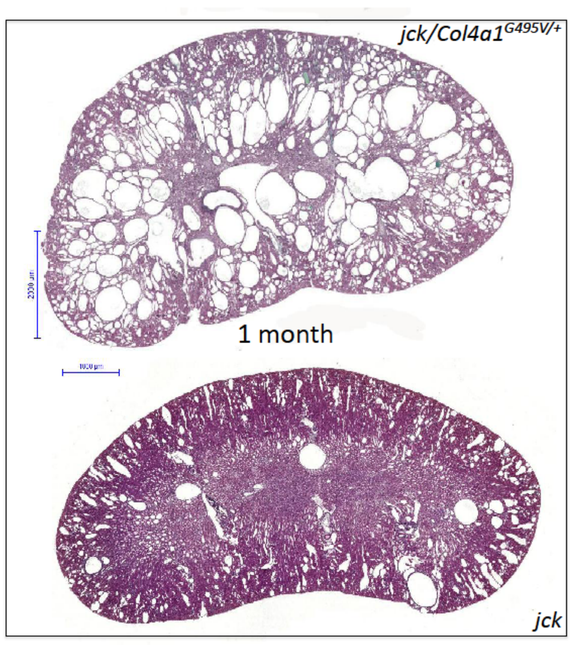
RESULTS

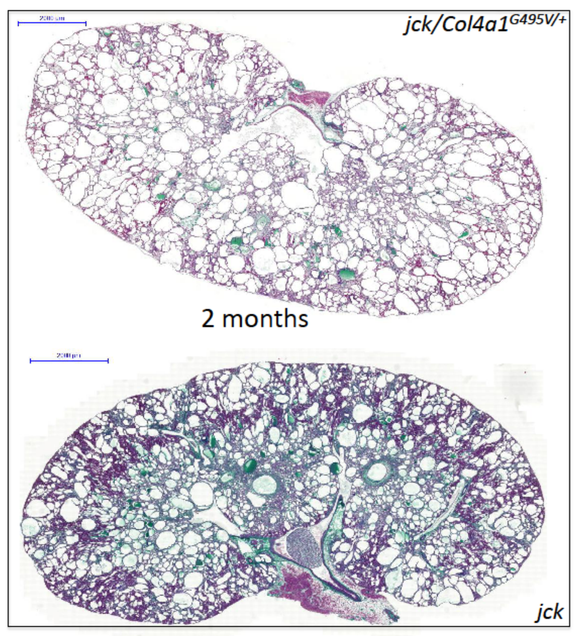
Median Survival (days)			
	jck/Col4a1$^{G495V/+}$	*jck*	*jck* §
Males	63 (range 14-88)		112
Females	88 (range 24-123)	134 (range 121-165)	133

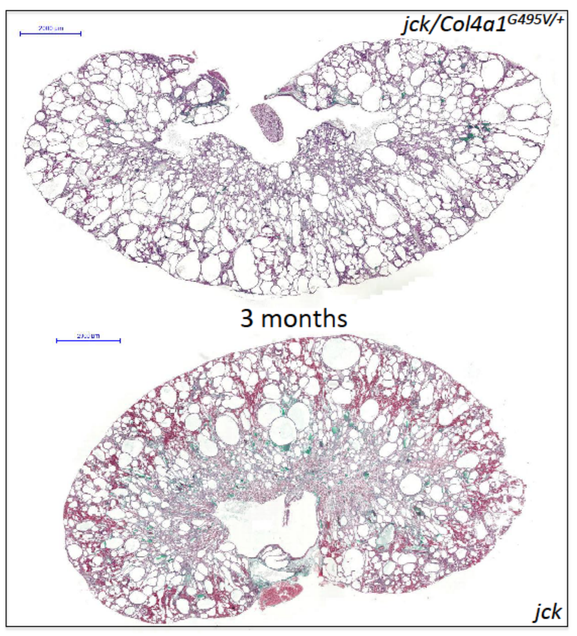












CONCLUSIONS

Our data highlight the role of tubular BM in PKD progression. Primary molecular abnormalities affecting the BM network may contribute to the faster progression of PKD, by promoting cysts growth. Deleterious impact of BM defects in PKD may be related to alterations of the mechanical properties of tubular BM, as well as to defective ECM-tubular cell signaling. Treatments that specifically target the ECM have to be considered in combination with the therapeutic strategies that are currently developed, to slow the progression of the renal failure in PKD.

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