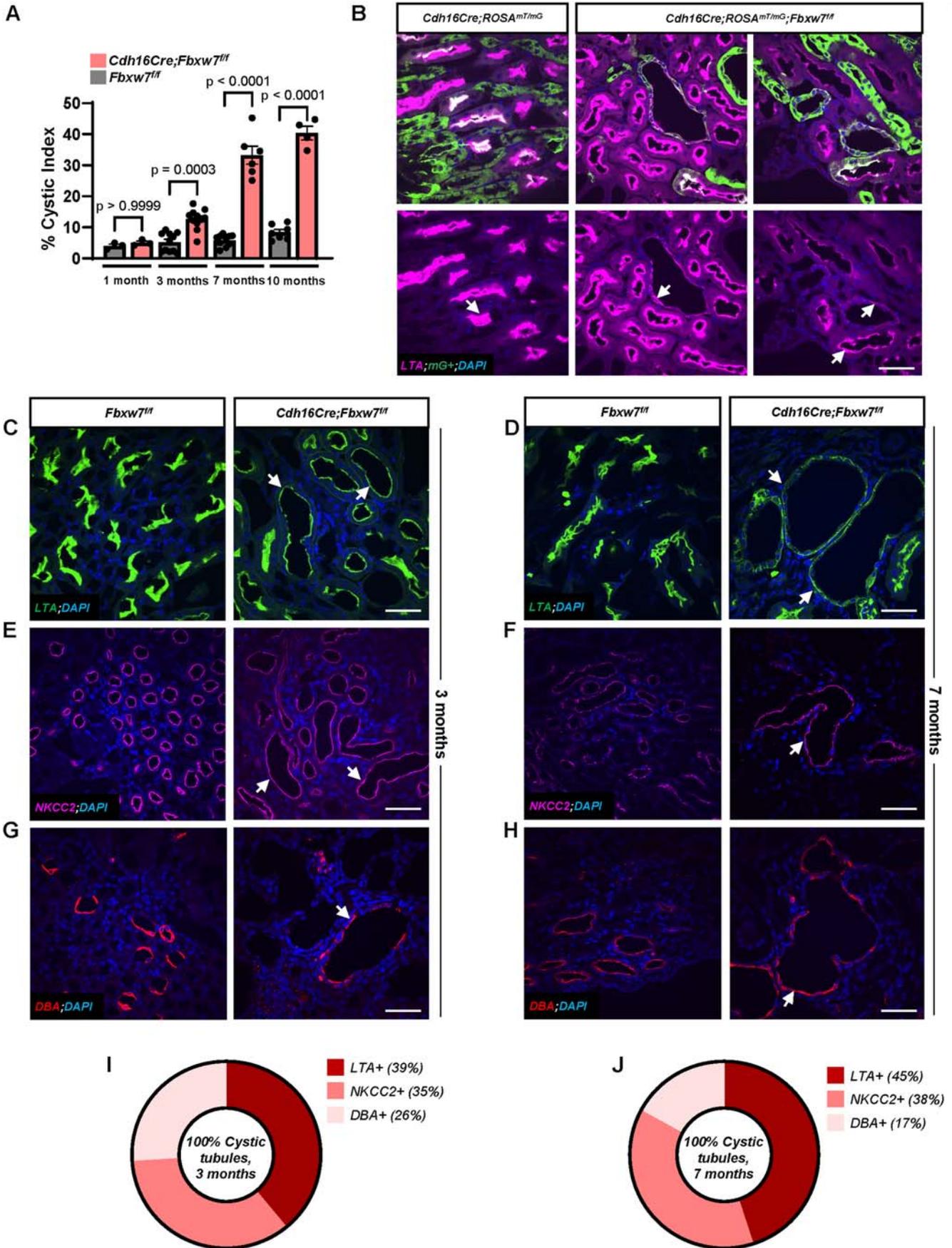
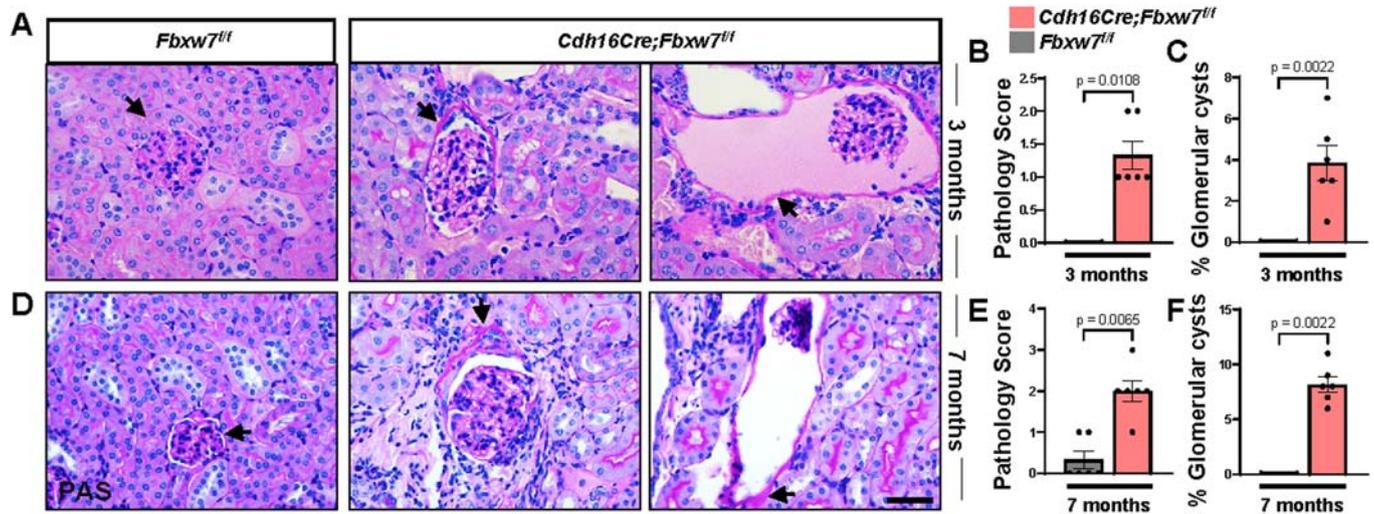


## Expanded View Figures

### Figure EV1. Deletion of *Fbxw7* results in cyst formation in different tubular segments of the kidney.

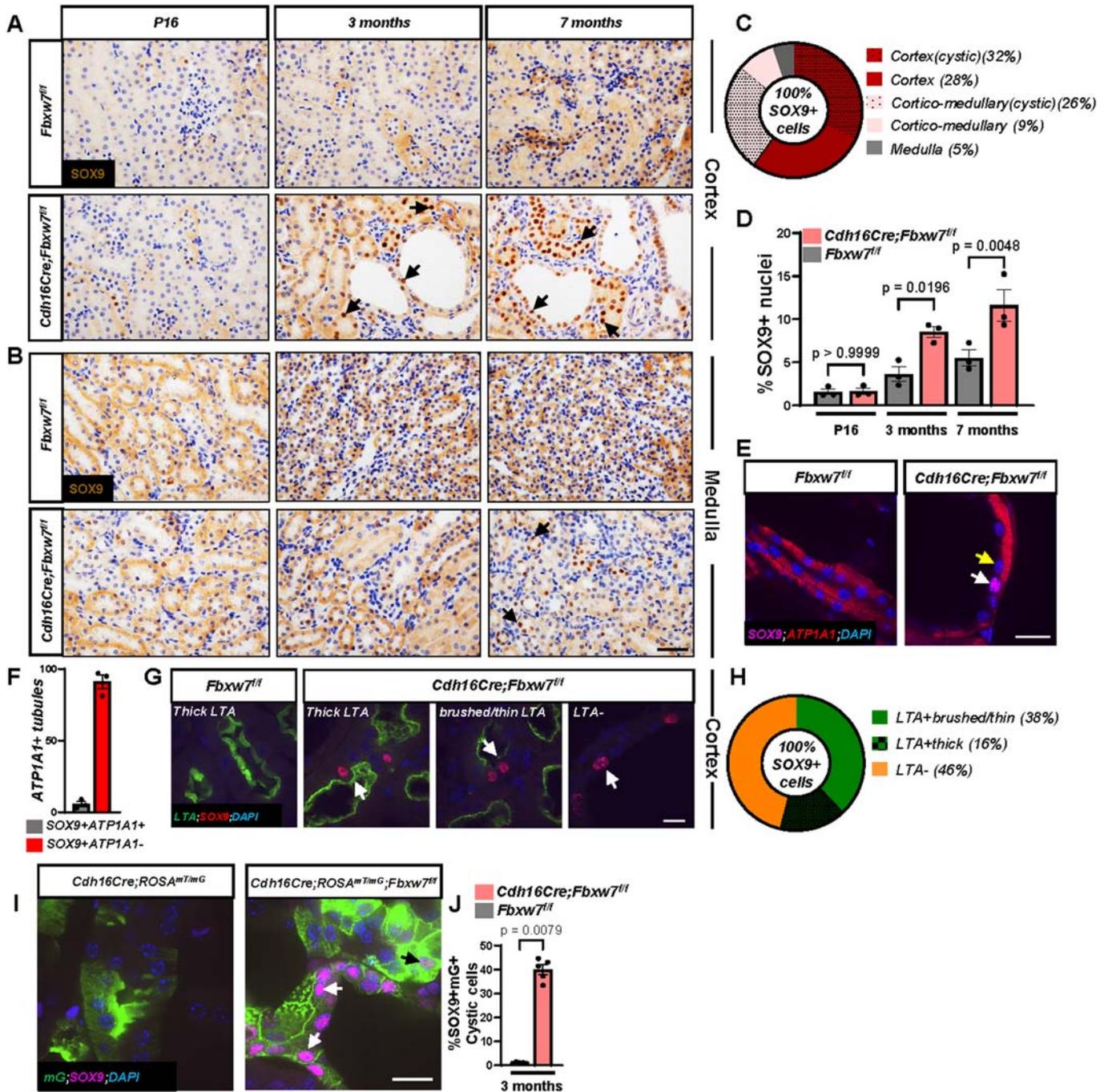
(A) Cystic index represented as the percentage of cystic area per kidney section from 1-, 3-, 7-, and 10-month-old *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice. Each data point represents one animal ( $n \geq 3$ ). Statistical analysis was performed using two-way ANOVA and is presented as the mean  $\pm$  SEM. (B) Representative images of LTA+ and mG+ cystic tubules in *Cdh16Cre;ROSA<sup>mT/mG</sup>;Fbxw7<sup>fl/fl</sup>* (middle and right panels) and *Cdh16Cre;ROSA<sup>mT/mG</sup>* (left panel) mice. White arrows show cystic mG+ tubules that are LTA+. Nuclei are stained with DAPI (blue). Scale bar: 50  $\mu$ m. (C–J) Representative images of immunofluorescence staining for (C, D) proximal tubule marker, Lotus tetragonolobus agglutinin (LTA), (E, F) thick ascending limb of the loop of Henle marker, NKCC2, and (G, H) collecting duct marker, Dolichos biflorus agglutinin (DBA) from 3- and 7-month-old kidneys of *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice. White arrows show dilated or cystic tubular segments of the kidney that are positive for (C, D) LTA (green), (E, F) NKCC2 (pink), and (G, H) DBA (red). Nuclei are stained with DAPI (blue). Scale bar: 50  $\mu$ m. (I, J) Pie chart displaying the percentage of cystic tubules distributed across different kidney segments from 3- and 7-month-old *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice ( $n \geq 3$ ).





**Figure EV2. Deletion of *Fbxw7* results in modest glomerular cysts and Bowman's capsule thickening.**

(A-F) Representative images and quantification of glomerular cysts and mild thickening of Bowman's capsule (black arrows) using PAS staining from 3- and 7-month-old kidneys of *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice. Nuclei are stained with Hematoxylin (blue). Scale bar: 200  $\mu$ m. (B, E) Pathology score for the mild thickening of Bowman's capsule and (C, F) percentage of glomerular cysts scored per animal ( $n = 6$ ). Statistical analysis was performed using the Mann-Whitney test and is presented as the mean  $\pm$  SEM.



**Figure EV3. Spatio-temporal characterization of increased SOX9 expression in *Fbxw7*-deletion-based NPHP-like mouse model.**

(A–D) SOX9 staining and quantification from different kidney regions from P16-, 3-, and 7-month-old *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice. (A, B) Black arrows show SOX9+ cells (brown). Nuclei are stained with Hematoxylin (blue). Scale bar: 100  $\mu$ m. (C) Pie chart displaying the percentage SOX9+ cells distributed across different kidney regions from 3-month-old *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice. (D) Each data point represents the percentage of SOX9+ cells scored per animal from P16-, 3-, and 7-month-old *Fbxw7<sup>fl/fl</sup>* and *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice ( $n = 3$ ). Statistical analysis was performed using two-way ANOVA and is presented as the mean  $\pm$  SEM. (E, F) Representative images and quantification of SOX9+ cells within ATP1A1+ tubules that have lost ATP1A1 expression. (E) The white arrow shows the SOX9+ATP1A1- cell, and the yellow arrow shows the SOX9-ATP1A1+ cell within the same cystic tubule. Nuclei are stained with DAPI (blue). Scale bar: 20  $\mu$ m. (F) Each data point represents the percentage of SOX9+ cells scored per animal from ATP1A1+ tubules of 3-month-old *Cdh16Cre;Fbxw7<sup>fl/fl</sup>* mice ( $n = 3$ ). (G, H) Representative images and distribution of SOX9+ cells in LTA+normal-looking, LTA+brushed proximal tubules, and LTA- tubules. (G) The white arrow shows SOX9+ cells in respective tubules. Nuclei are stained with DAPI (blue). Scale bar: 20  $\mu$ m. (I, J) SOX9 staining and quantification from 3-month-old kidneys of *Cdh16Cre;ROSA<sup>mT/mG</sup>* and *Cdh16Cre;ROSA<sup>mT/mG</sup>;Fbxw7<sup>fl/fl</sup>* mice. (I) The white and black arrows show nuclear SOX9 staining (pink) in mG+ cystic and non-cystic tubules (green), respectively. Nuclei are stained with DAPI (blue). Scale bar: 20  $\mu$ m. (J) Each data point represents the percentage of SOX9+ cells scored from mG+ cystic tubules per animal ( $n = 5$ ). Statistical analysis was performed using the Mann-Whitney test and is presented as the mean  $\pm$  SEM.