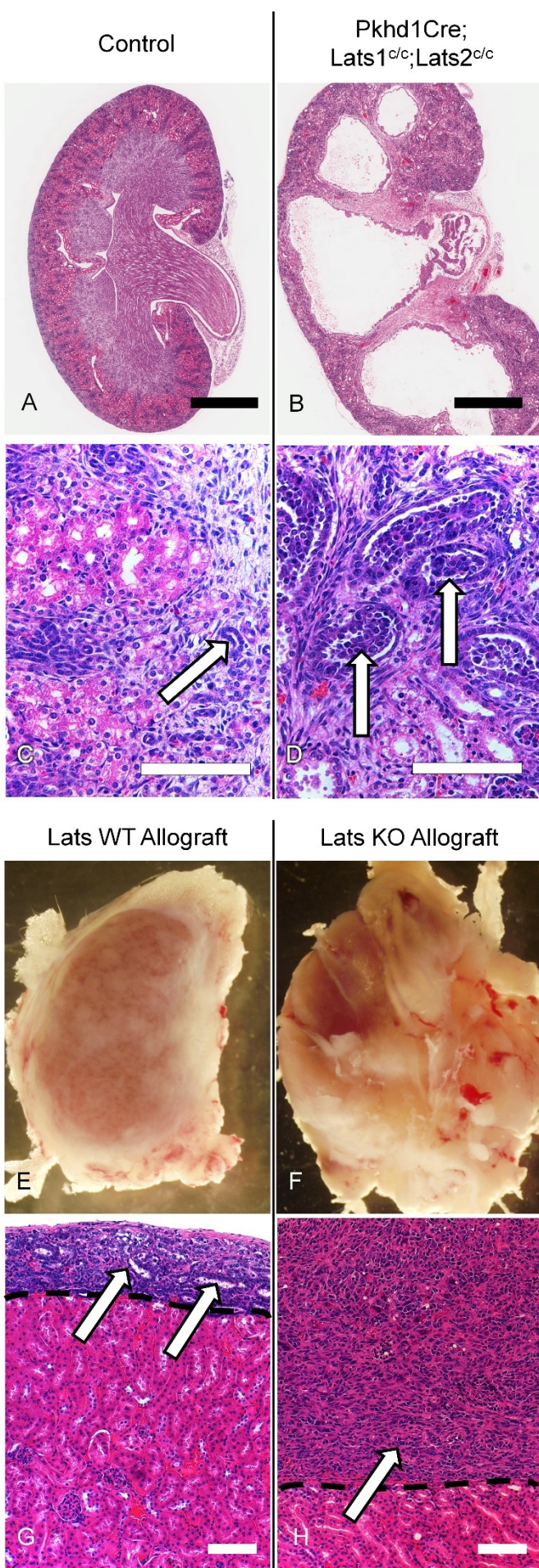
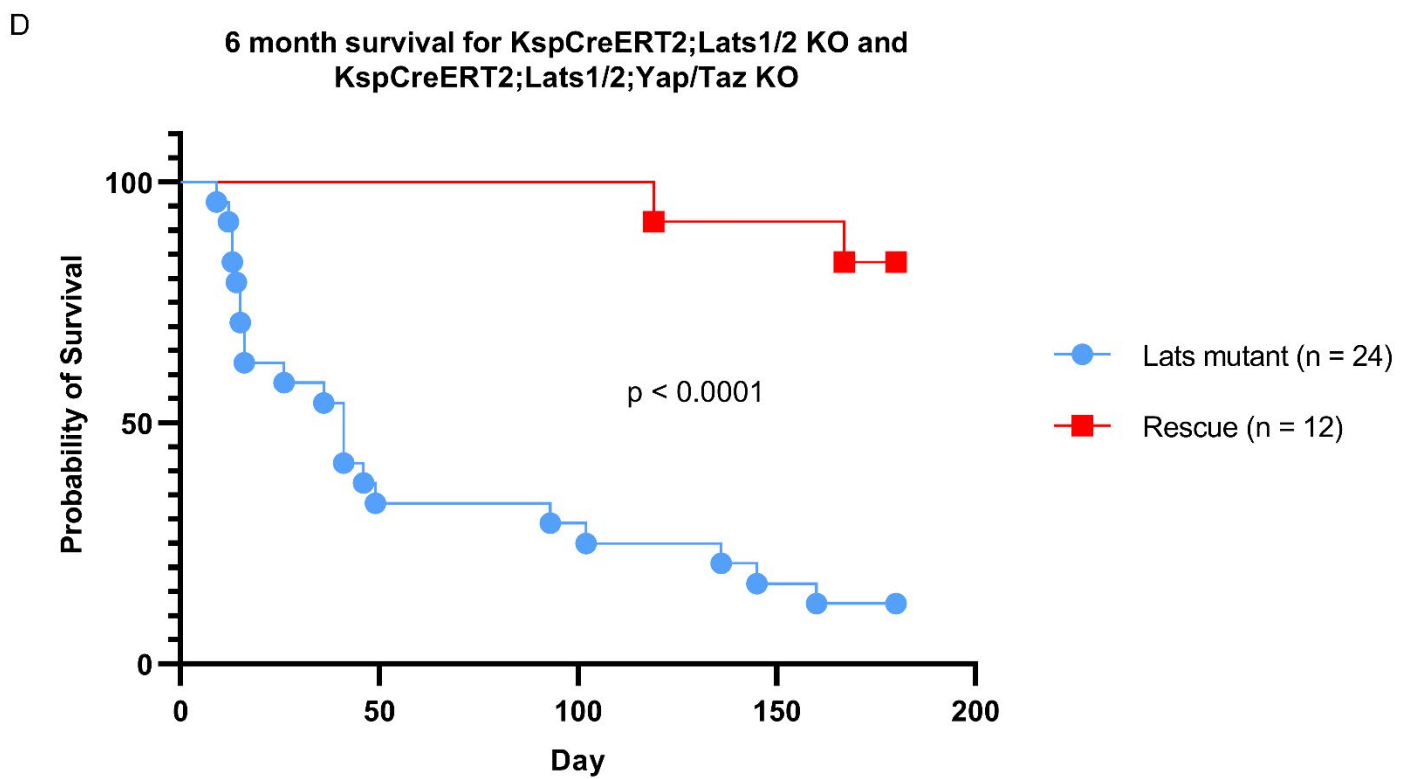
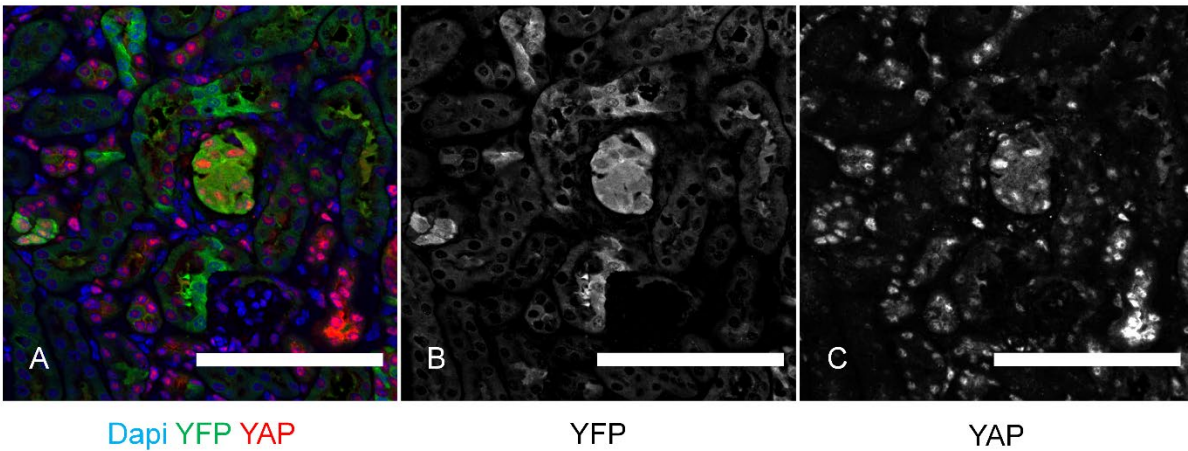


**Supplemental figure 1: Neoplastic cells in kidney are derived from the KspCre-lineage. Cells in lung represent metastases.** Immunofluorescence staining of YFP expression (red) in kidney (A-B) and lung (C-D) in control animal (A,C) or in KspCreERT2;Lats1/2<sup>cl/c</sup>;RosaYFP animal (B,D) 4 months after tamoxifen (n=3 for control and mutant). A) Green= E-cadherin, red=YFP, white=cytokeratin, blue=dapi. B-D) Green=pYap, red=YFP, white=cytokeratin, blue=dapi. E-H) H&E stained sections of KspCreERT2;Lats1/2<sup>cl/c</sup>;RosaYFP kidneys 4 (E, n=4), 7 (F, n=11), 14 (G, n=8) or 28 (H, n=4) days post tamoxifen. Immunofluorescence staining on section of KspCreERT2;Lats1/2<sup>cl/c</sup>;Rosa26mT/mG kidney 5 months post tamoxifen (I-L, n=5). I) Green= GFP, red= tomato, white=sm22a, blue= dapi. J-L are single channel images of the image in I showing Tomato, GFP and Sm22a, respectively. All scale bars= 100um.



**Supplemental Figure 2: Lats1/2 ablation in collecting ducts leads to EMT and Lats1/2 mutant allografts form RCC.** H and E stained sections of kidneys from 7 day old control (A,C, n=3) or Pkhd1Cre;Lats1/2<sup>cl/c</sup> (B,D, n=4) mice. Mutants show transformed cells in the lumens of collecting ducts (arrows, D) which are absent in control (arrow, C). Whole mount kidneys injected with control (E,G, n=15) or Lats1/2 KO (F,H, n=12) IMCD cells. While control cells give rise to a thin layer of cells with epithelialized structures (arrows, G), Lats1/2 KO cells yield large sarcomatoid tumors (arrow, H). Scale bars- A-B: 900um, C-D, G-H: 100um.

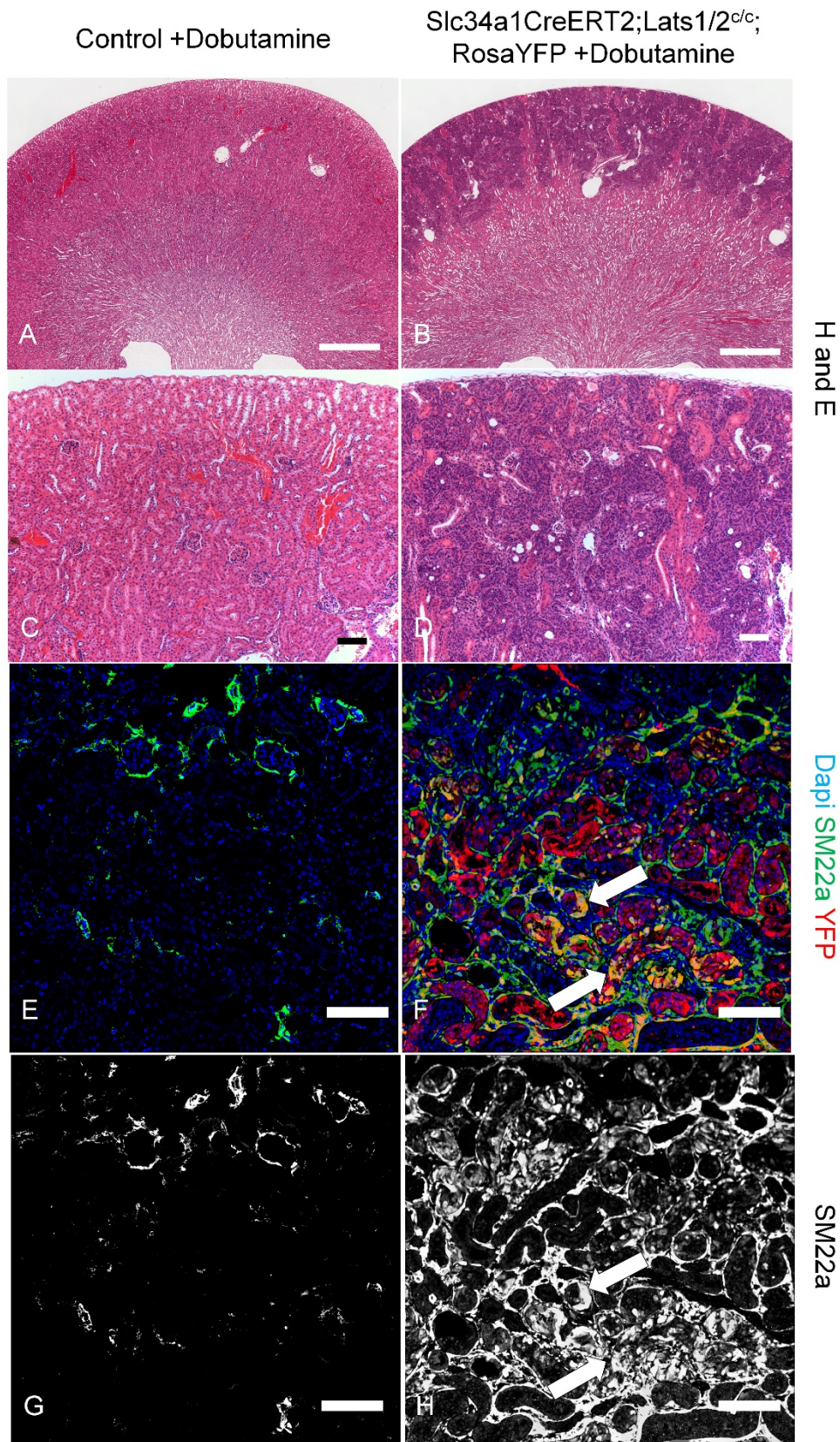
KspCreERT2; Lats1<sup>cl/c</sup>;Lats2<sup>cl/c</sup>;Yap<sup>cl/c</sup>;Taz<sup>cl/c</sup>;RosaYFP



**Supplemental figure 3: Yap and Taz deletion rescues Lats1/2 deletion phenotype. A-C)**

Immunofluorescence staining on sections of KspCreERT2; Lats1<sup>cl/c</sup>;Lats2<sup>cl/c</sup>;Yap<sup>cl/c</sup>;Taz<sup>cl/c</sup>;RosaYFP kidneys shows that remaining lesions are YFP and YAP positive (A, Green= YFP, red= YAP, blue= dapi, n=3). B and C are single channel images of YFP and YAP, respectively, from A. D) Survival curve of KspCreERT2;Lats1/2 KO and KspCreERT2;Lats1/2;Yap;Taz KO mice (n=24 mutant, n=12 rescue). P value determined by log-rank (Mantel-Cox) test. Scale bars- A-C: 100um.





**Supplemental Figure 5: Dobutamine treatment does not rescue Lats KO phenotype.** H and E stained sections of control (A, C, n=3) or Slc34a1CreERT2;Lats1/2<sup>cl/c</sup>;RosaYFP kidney 2 weeks after tamoxifen and dobutamine treatment (B,D, n=2 survived to 14 days). C and D are high magnification images of the sections in A and B, respectively. Immunofluorescence staining on sections of control (E,G) or Slc34a1CreERT2;Lats1,2<sup>cl/c</sup>;RosaTomato kidneys 2 weeks after tamoxifen and Dobutamine (F,H)(blue=dapi, green=sm22a, red=GFP). G-H show single channel (Sm22a) corresponding with E and F, respectively. Mutant lesions co-express sm22a and YFP (Arrows, F and H). Scale bars- A-B: 900um, C-H: 100um.