Knockout mouse lines presenting with welfare issues affecting their survival (abnormal survival [MP:0010769]) are processed through a bespoke sub-pipeline known as the "sick mouse procedure" (SMP) to maximise information collected on that mouse line. Matched wild-type controls are also processed to identify phenotypic abnormalities arising from the targeted allele.

Upk1b$^{tm1b(KOMP)Wtsi}$

Genetic Background: C57BL/6NTac

ES Cell Clone: EPD0854_2_E05

Affected genotypes

Homozygous (*Upk1b*$^{tm1b(KOMP)Wtsi}$).

Alternative breeding strategy

Following initial welfare observations, a wild-type x heterozygous mating strategy was employed to complete phenotyping work in standard pipeline using heterozygous mice only.

Heterozygous mice showed no significant phenotypic findings on the primary screen.

Welfare observations

Homozygous mice exhibit:

- Abdomen > General > Swollen = 6.6% (5 out of 76 Homs)
- Observation > Observation > Observation (culled as Hom's suspected to have kidney problems - internal observations showed one/both kidneys to be enlarged) = 11.8% (9 out of 76 Homs)

Homozygous Viability:

All genotyped mice from het x het intercross considered. When at least 28 mice are available, viability is calculated. *[>13% = Homozygous viable; >0% and <13% = Sub-viable; 0% = Lethal]*

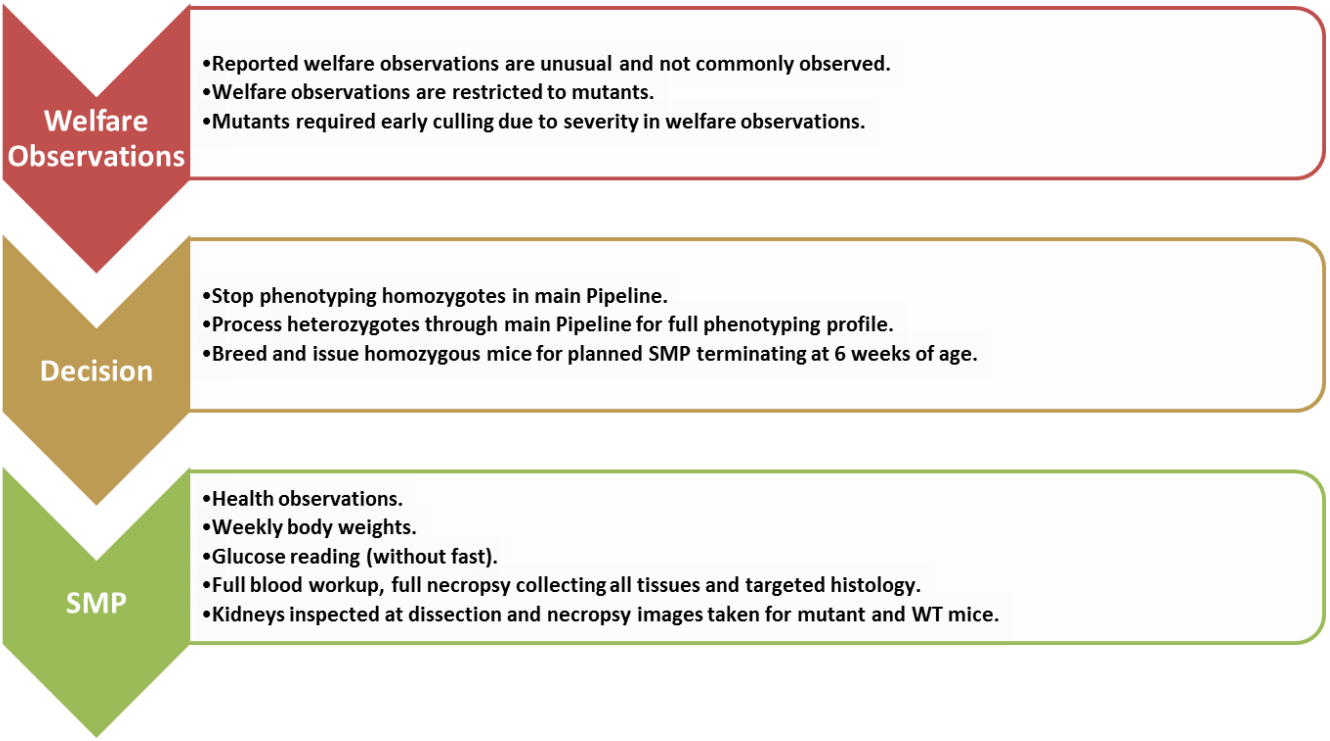
- **Viable** : 76 Homs / 393 Total =19.3%

Sick Mouse Procedure (SMP)

In generating and processing mice for our primary pipeline, 4 Homs were found to be presenting with distended abdomen (x3 at 13 weeks and x1 at 18 weeks). Basic necropsy reports revealed enlarged fluid-filled kidneys (either on one or both sides); a pathology termed hydronephrosis. Extending investigation to the rest of the colony, 9 out of the 13 remaining Hom mice culled were found with enlarged kidneys (again either on one or both sides). 8 out of the 9 affected were ≤ 6 weeks of age and both males and females were affected.

Welfare observations in homozygotes described above progressed to moderate severity at 6 weeks of age upon which SMP (see schematic below) was initiated. 7 male and 2 female homozygotes were processed alongside 7 male and 2 female matched wild-types. No further homozygotes were phenotyped due to the aforementioned alternative breeding strategy employed to reduce further welfare implications.

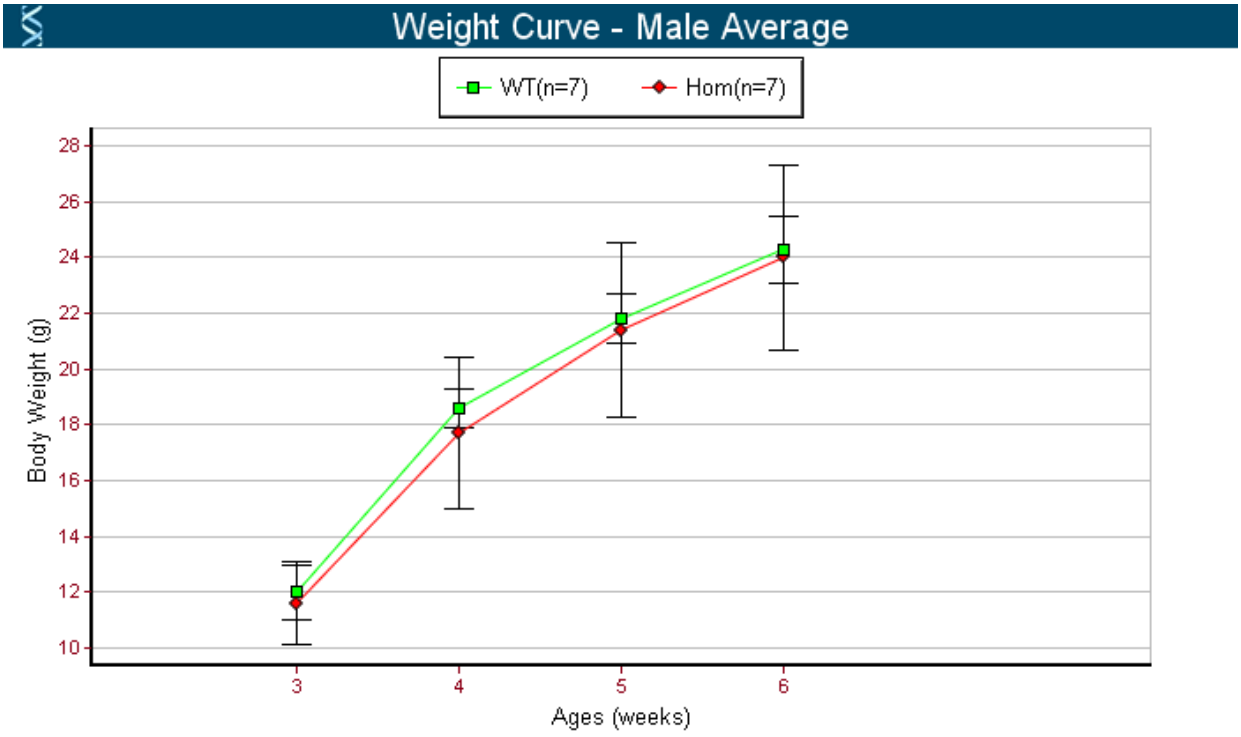
Schematic Outline of Bespoke SMP Pipeline

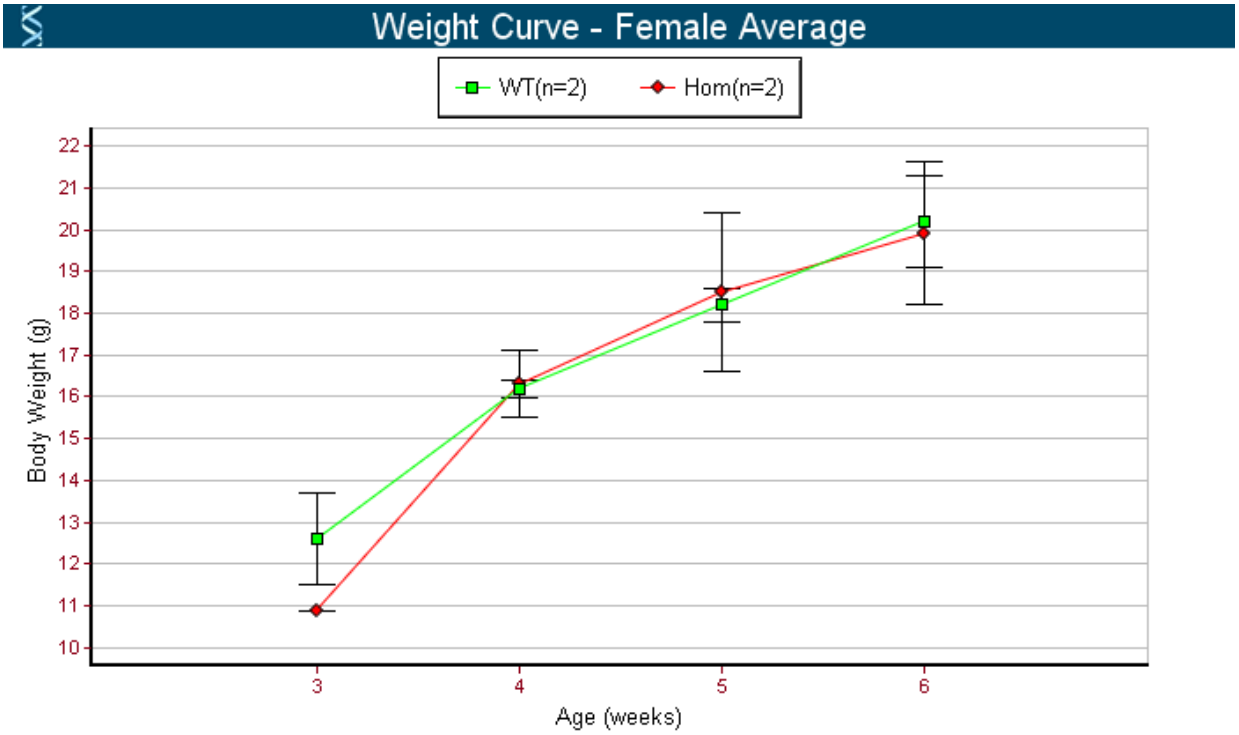


Phenotyping data of interest

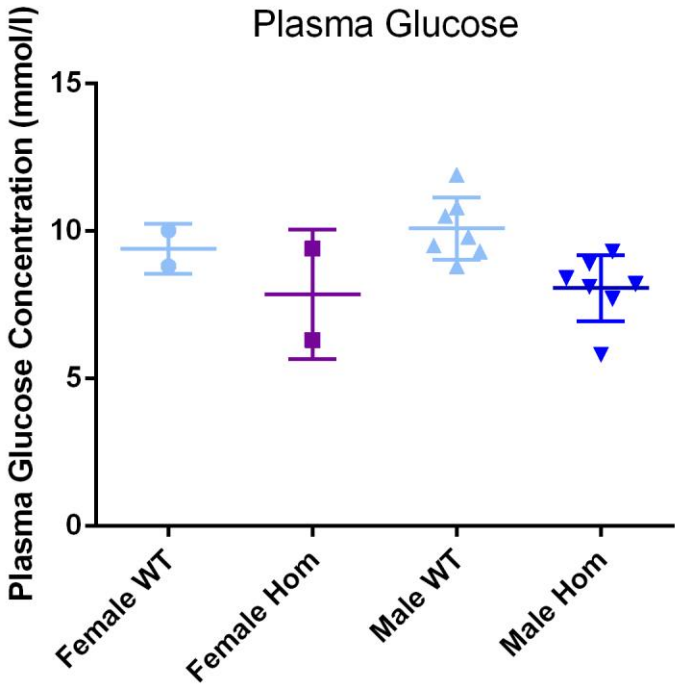
In life phenotyping

Body Weights





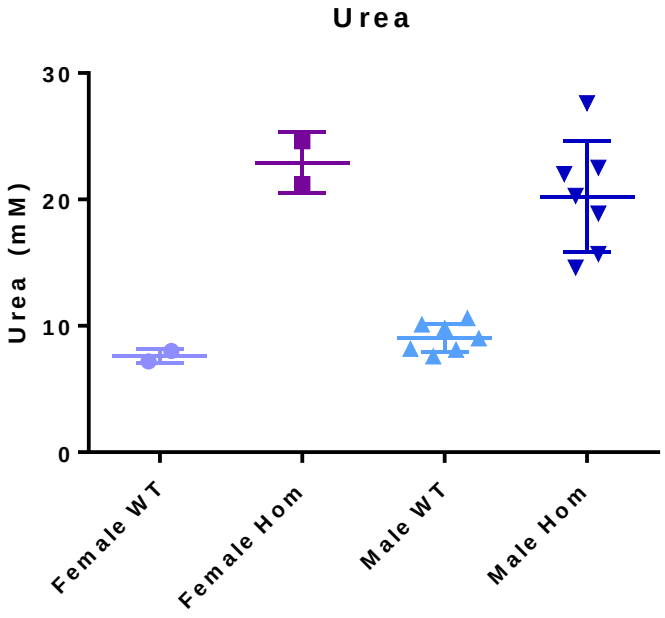
Plasma Glucose (without fast)



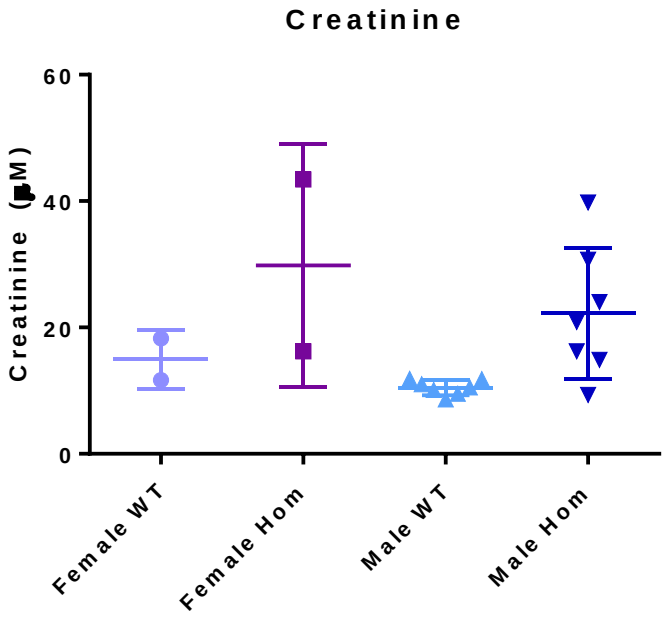
Males and Females - Decreased circulating glucose level (MP:0005560)

Ex vivo phenotyping

Plasma Chemistry



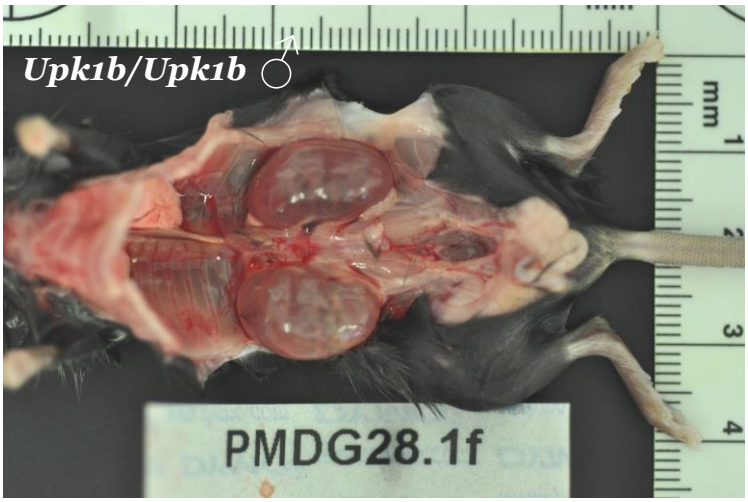
Males and Females - Increased circulating urea level [MP: 0005565]

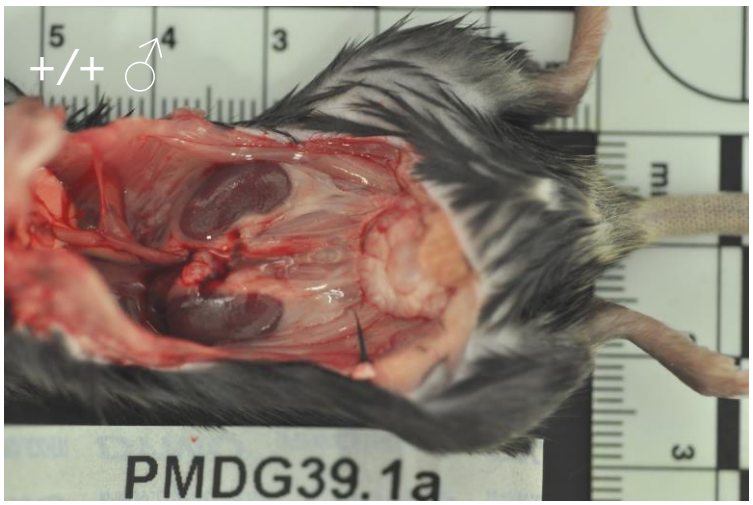


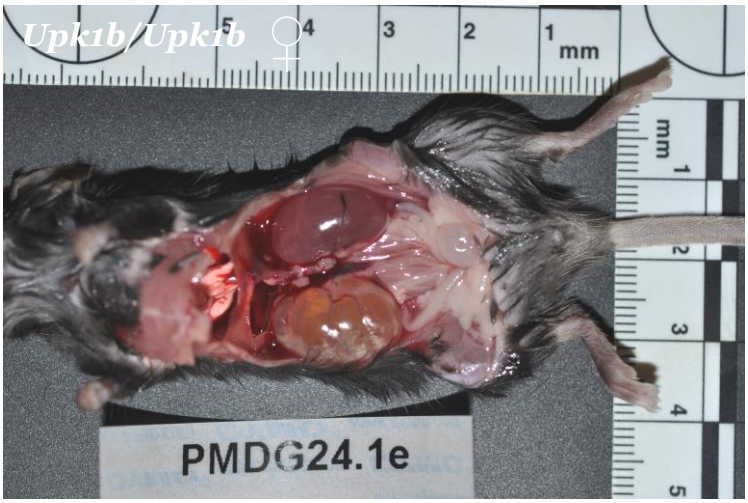
Males and Females – Increased circulating creatinine level [MP: 0005553]

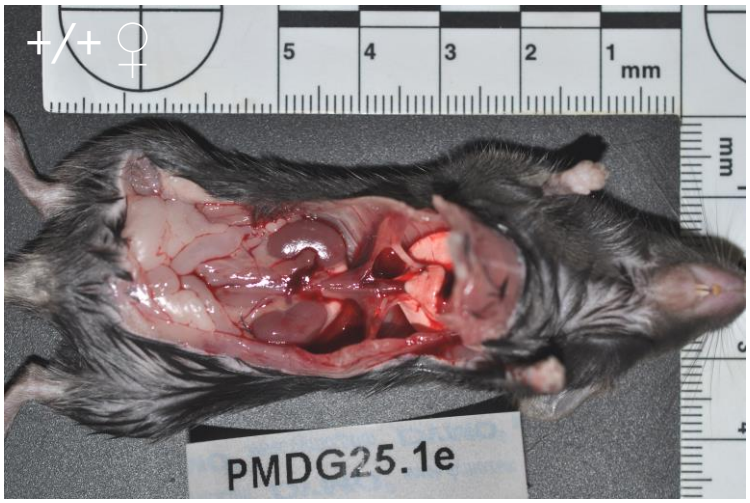
Necropsy observations

Dysmorphology



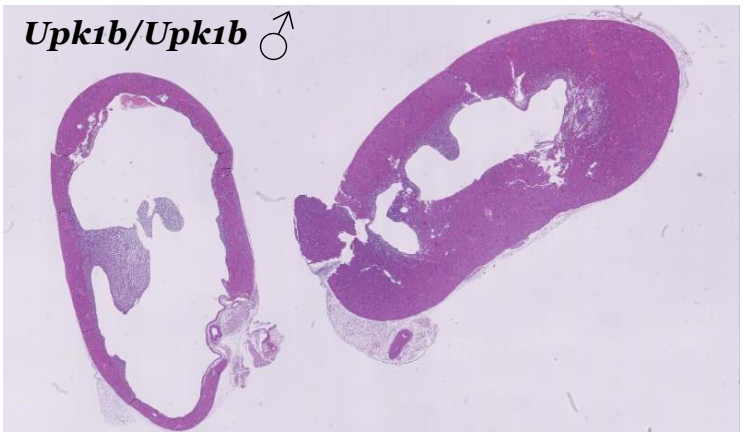




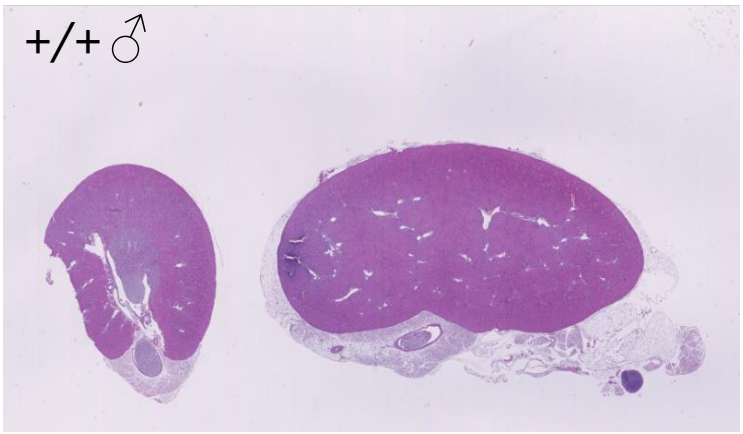


Transverse and longitudinal kidney sections H & E stained

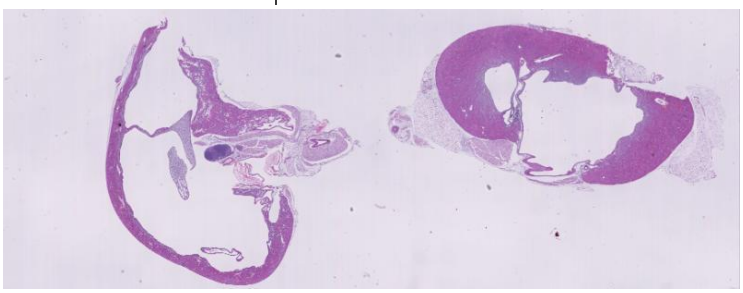
Upk1b/Upk1b ♂



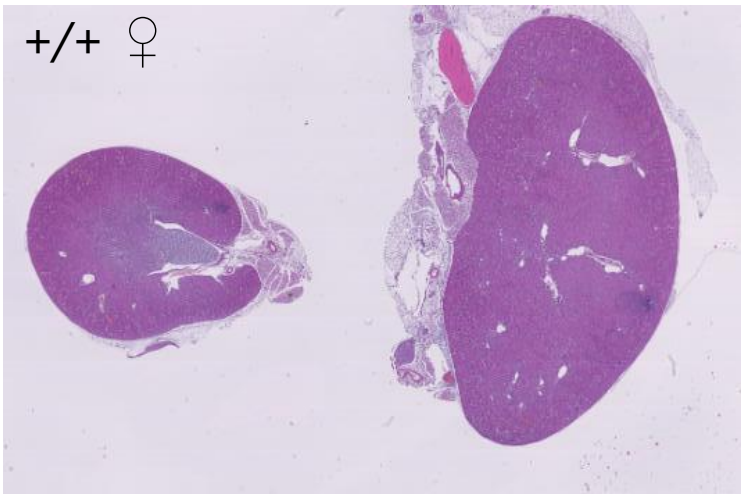
+/+ ♂



Upk1b/Upk1b ♀



+/+ ♀



Males and Females – All 9 homozygous mice displayed hydronephrosis [MP:0000519] with either one or both kidneys affected at necropsy.