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.

Myh3$^{tm1b(EUCOMM)Wtsi}$

Genetic Background: C57BL/6N

ES Cell Clone: EPD0780_2_F11

Affected genotypes

Homozygous (*Myh3*$^{tm1b(EUCOMM)Wtsi}$).

Alternative breeding strategy

Following initial welfare observations, wild-type x heterozygous mating strategy was employed to ensure no more homozygous mice were produced.

Welfare observations

Homozygous mice exhibit:

- Whole Body > General > Abnormal Gait = 70% affected (7 out of 10 Homs)
- Abdomen > Urogenital > Penile prolapse = 75% of males affected (3 out of 4 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]*

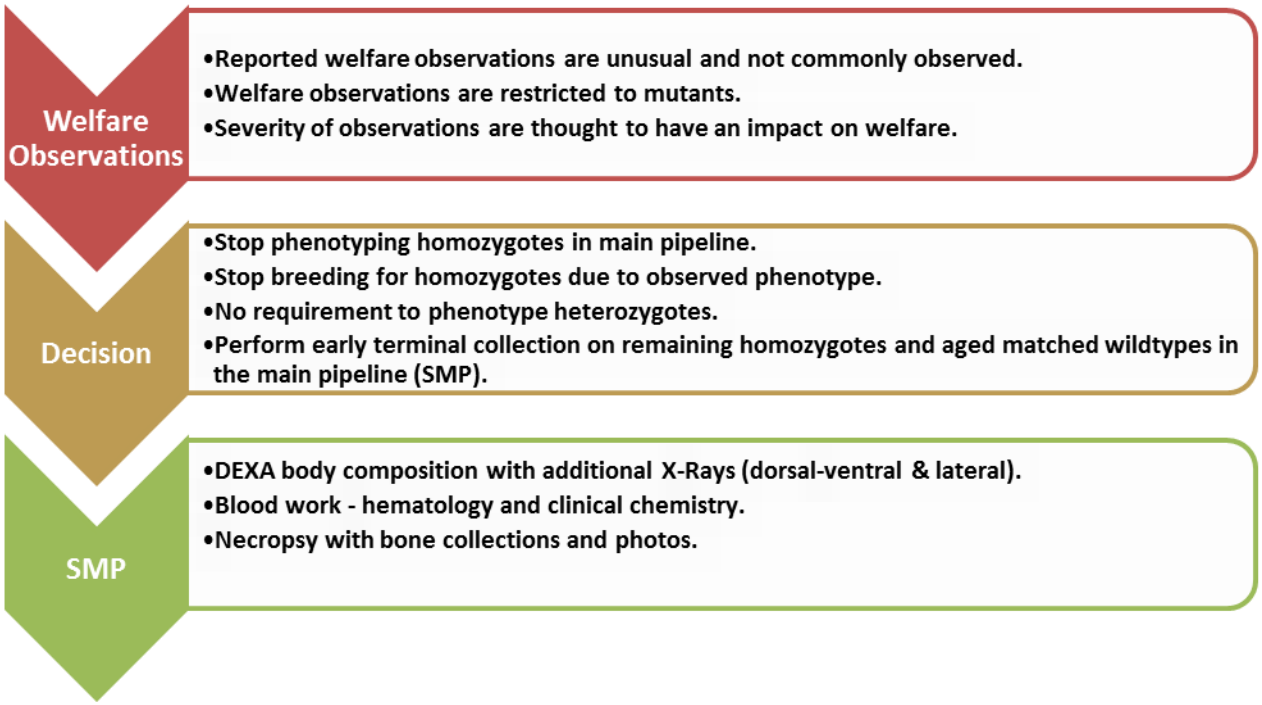
- **Subviable** : 9 Homs / 115 Total = 7.82 %

Sick Mouse Procedure (SMP)

Myh3$^{tm1b(EUCOMM)Wtsi}$ shows partial lethality. Of mice that enter the phenotyping pipeline, the mice are generally alert and active, but have a grossly abnormal posture and gait, probably caused by a misalignment of the spine over the pelvis which appears to progress in severity with age. Some mice that have been X-rayed have shown some degree of spinal twist on X-rays.

From a welfare perspective, the mice have lower than normal body weight and we consider that these mice may be in some discomfort. Therefore it was decided to discontinue breeding and phenotyping this colony and to perform an early terminal collection on the remaining 2 male and 2 female mice in the pipeline with the same number of aged matched wild-type controls.

Schematic Outline of Bespoke SMP Pipeline

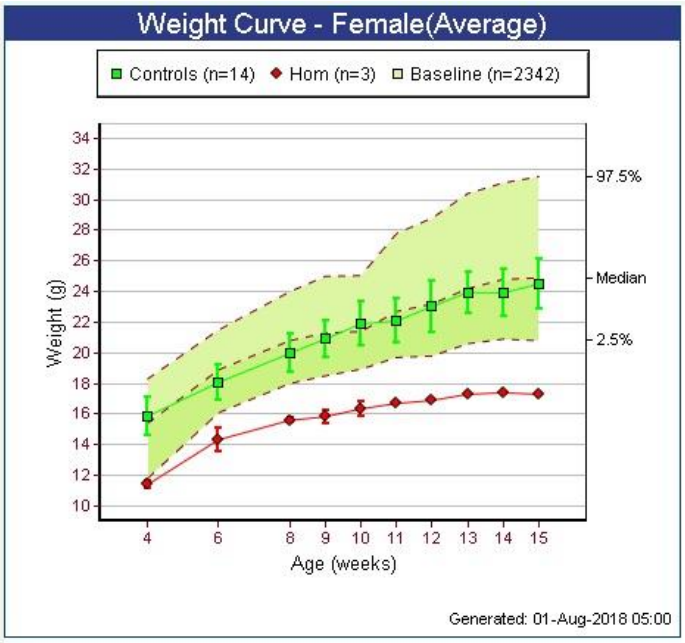


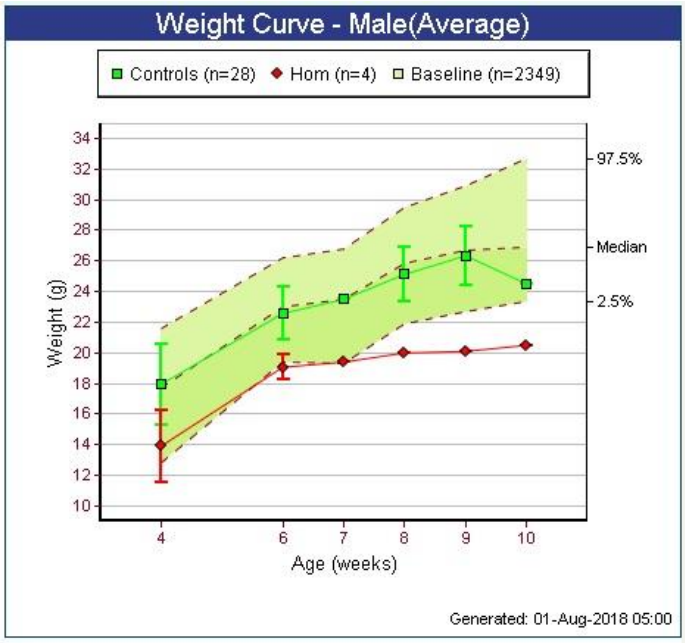
Phenotyping data of interest (significant changes)

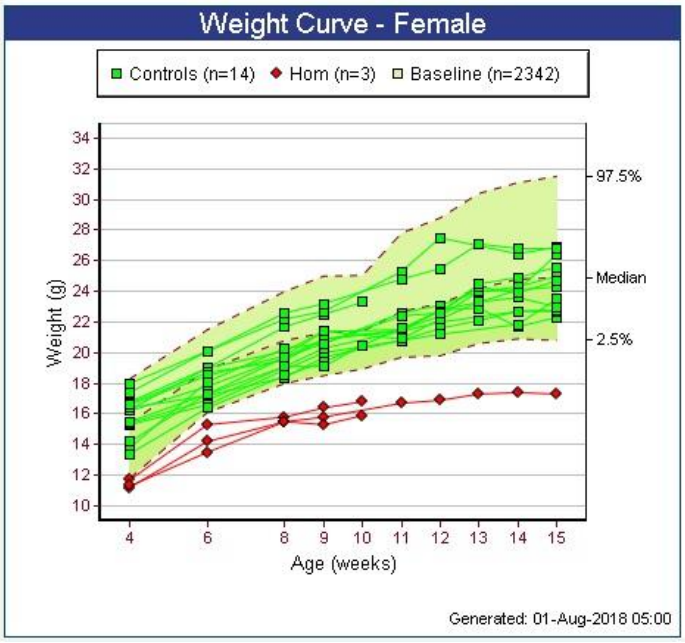
Due to some mice being culled before the end of the pipeline and the early terminal collection of the remaining homozygous mice, the following data sets include mice of varying ages plotted on the same graphs.

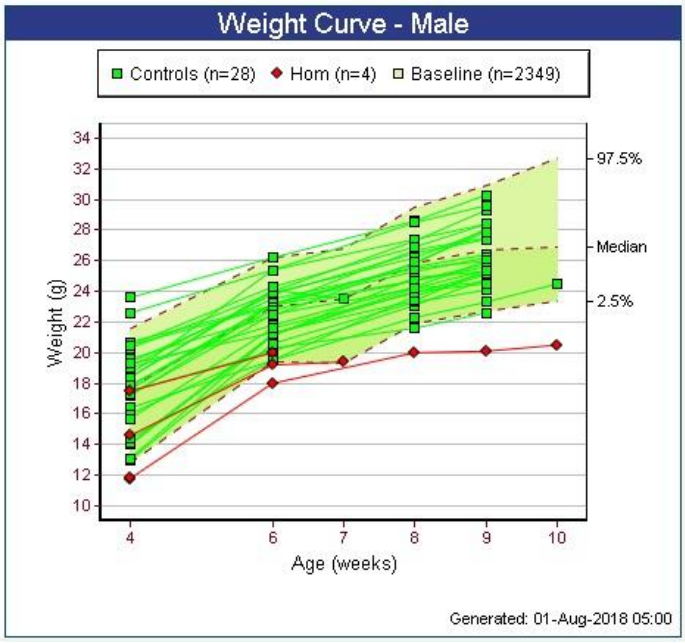
In life phenotyping

Body weights





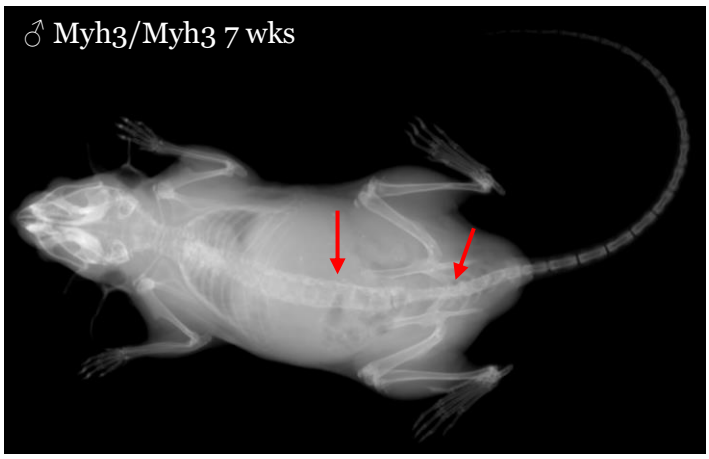


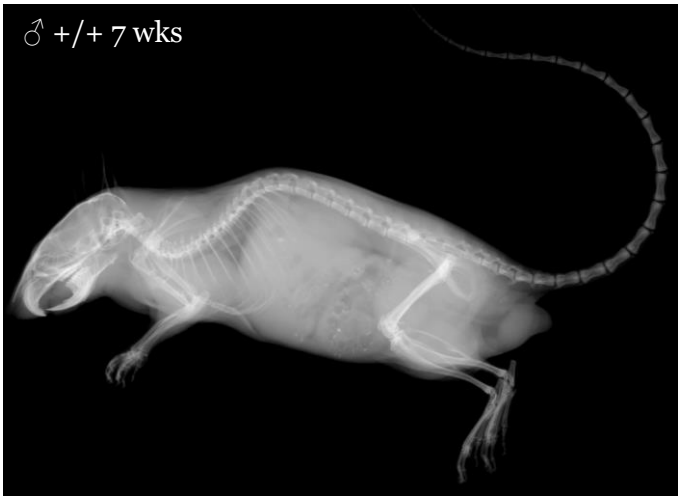


Males and Females – reduced body weight (MP:0001262)

X-Rays


♂ +/+ 7 wks

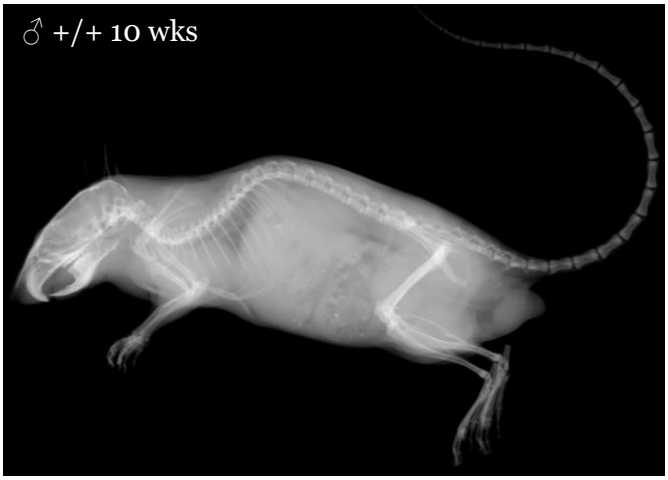

♂ Myh3/Myh3 7 wks

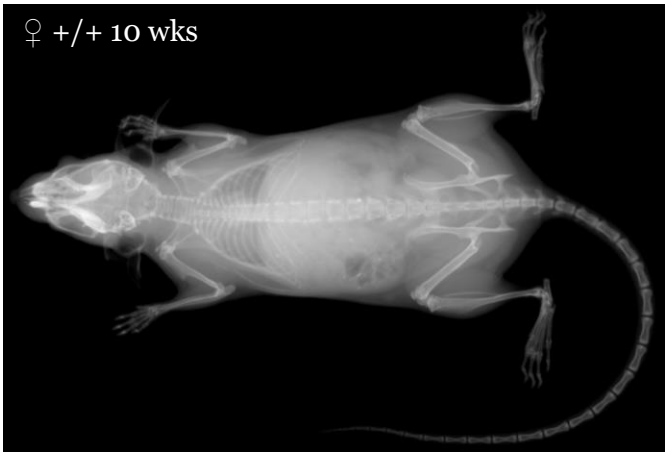

♂ +/+ 7 wks


♂ Myh3/Myh3 7 wks


♂ +/+ 10 wks

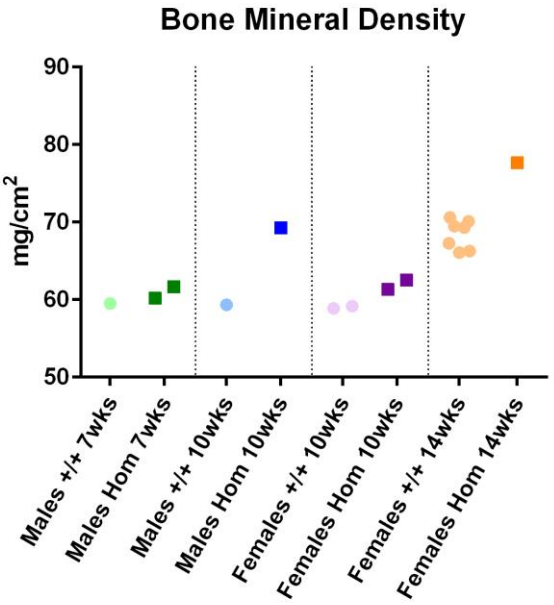

♂ Myh3/Myh3 10 wks



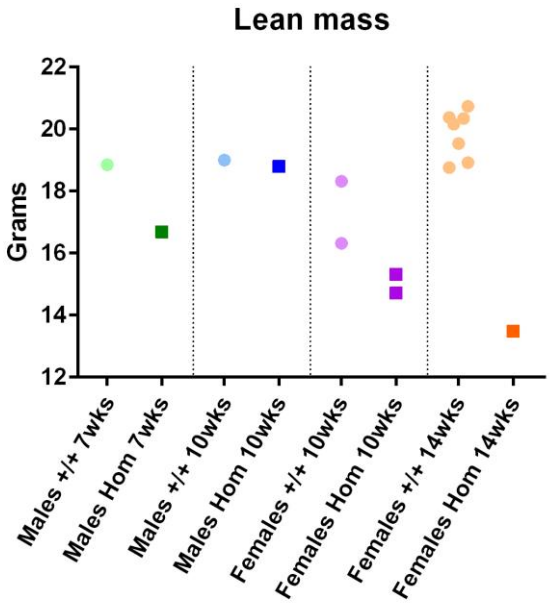


Males and Females – All homozygous *Myh3* mice showed signs of marked scoliosis (MP:0000161) from circa C7 to circa S4, apical vertebra circa L4 with vertebral fusion (MP:0004609); marked pelvic deviation and increased kyphosis (MP:0000160).

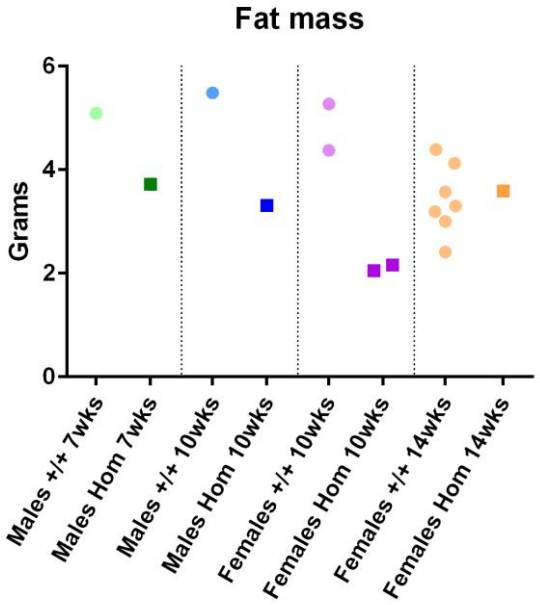
Body Composition (DEXA)



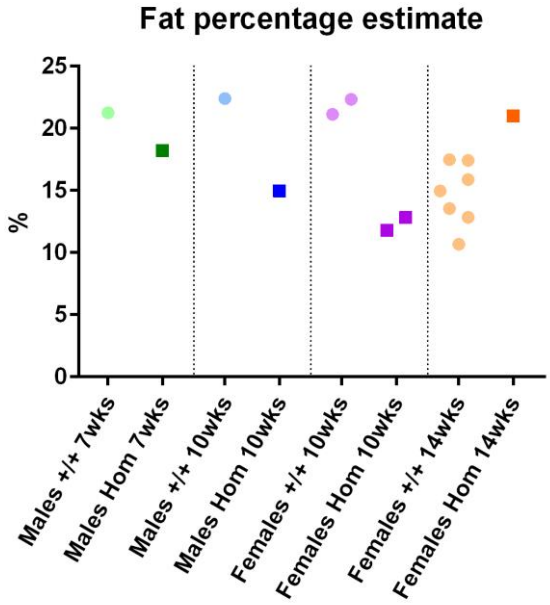
Males and Females - increased bone mineral density (MP:0000062)



Males and Females – decreased lean body mass (MP:0003961)

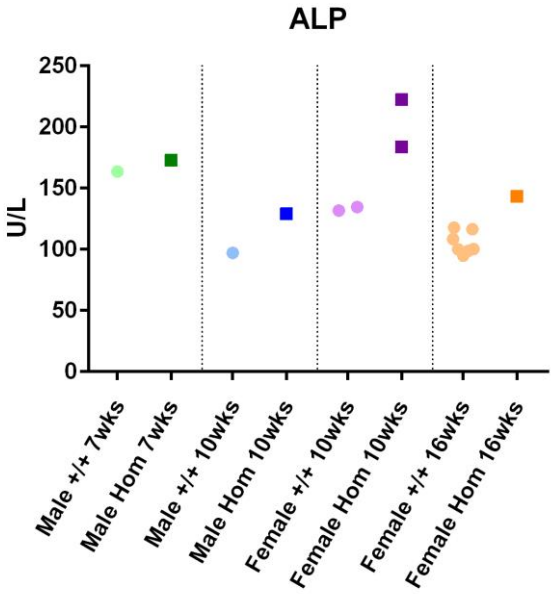


Males and Females – decreased total body fat amount (MP:0010025)



Ex vivo phenotyping

Plasma Chemistry



Males and Females – increased circulating alkaline phosphatase level (MP:0002968)

Necropsy observations

All 5 *Myh3* homozygous mice (3 females 2 males) collected for necropsy displayed severely curved spines, some vertebral fusion and abnormal tail angles with one male mouse showing a less severe spinal curvature than the others.