**RESULTS**

**Figure 1.** Col4a5 mutant model, B6.Cg-*Col4a5tm1Yseq*/J, mating scheme with diversity outbred mice, J:DO. (A) 100 heterozygous female Col4a5 models, B6.Cg-*Col4a5tm1Yseq*/J, were crossed with 100 diversity outbred mice, J:DO. From each mating pairs we used one F1 female that was heterozygous to the Col4a5 mutation, and one F1 male that was hemizygous to the Col4a5 mutaiton for a total of 200 mice in the experimental cohort. Due to X-inactivation, F1 females will have a mosaic of Col4a5 knock out and wild-type cells. (B) Col4a5 mutation will contain residual 129X1/SvJ locus directly surrounding mutation site, due ES strain origin of the original knockout model.

**Figure 2.** Phenotyping of F1 females and males for renal function. 100 animals of each sex were phenotyped for (left panel) glomerular filtration rate (GFR) at 14 weeks of age, (middle panel) albumin to creatinine ratio (ACR) at 6, 10, and 15 weeks of age, and (right panel) correlation between GFR at 14 weeks and ACR at 15 weeks of age. (A1) Distribution of females at 14 weeks according to their GFR display higher functioning kidneys (n =, average GFR =, stderror = ) compared to the distribution of males (B1, n =, average GFR =, stderror = ). (A2) Distribution of females at 6, 10, and 15 weeks displayed in red, green, and blue respectively show increasing ACR with age (significant difference between ages?). (B2) Comparatively males also show increasing ACR with age (significant ACR with age), furthermore, ACR values in males show higher ACR values than females at their corresponding time points suggesting increase severity of renal disease in males. (A3) Correlation between ACR at 15 weeks and GFR at 14 weeks of age in females show very slight negative correlation (R2 = 0.048, p-val = ). (B3) Correlation between ACR at 15 weeks and GFR at 14 weeks of age in males show negative correlation (R2 = 0.411, p-val = ). Overall males show severe renal phenotype compared to their female counterparts.

**Figure 3.** Kinship maps showing heterogeneity of F1 experimental cohort before and after quality control (QC). (A1) Kinship map of samples pre-QC show blocks of samples that have nearly identical genomic back ground, suggesting either sample duplications or introduction of non-DO animals in cohort. (A2) Kinship map of samples post-QC show complete heterogeneity of data set. Previously identified incorrect GigaMUGA data were replaced with RNA reconstructed genome data and recovered GigaMUGA data.

**Figure 4. 1** GFR qtl

**Figure 4.** Haplotype QTL

**Figure 4.2** Albumin qtl 6wks

**Figure 4.3** Albumin qtl 10wks

**Figure 4.4** Albumin qtl 15wks

**Figure 5** Xce allele