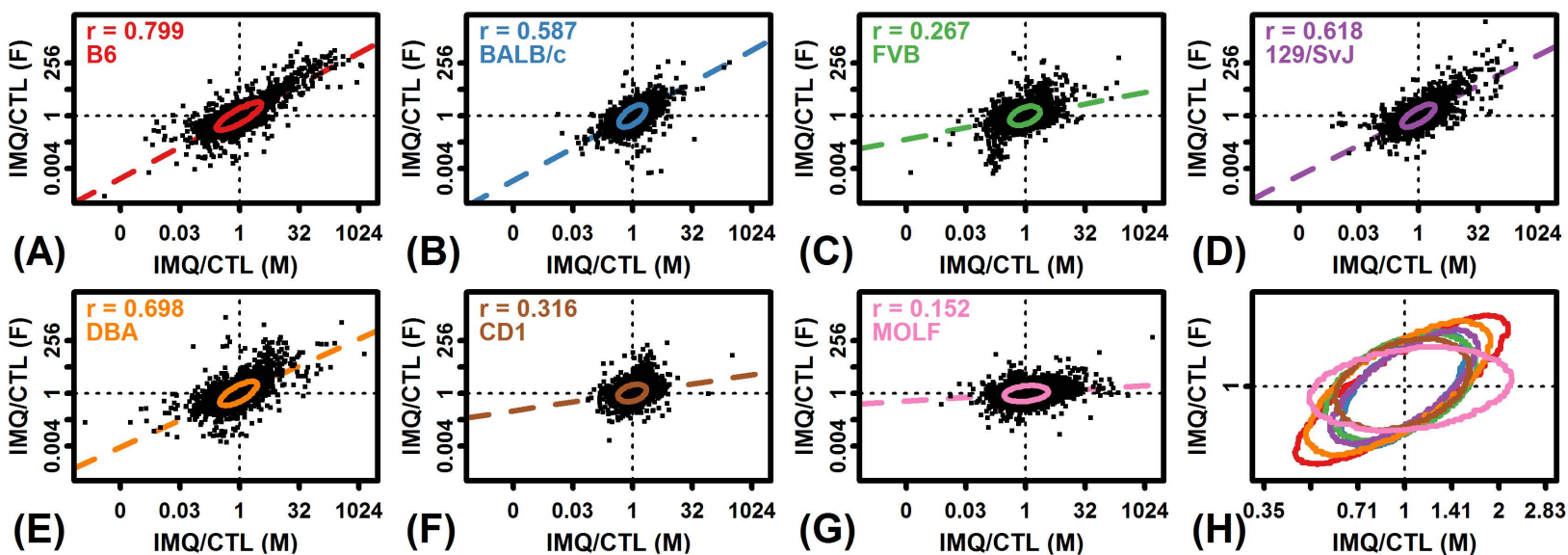
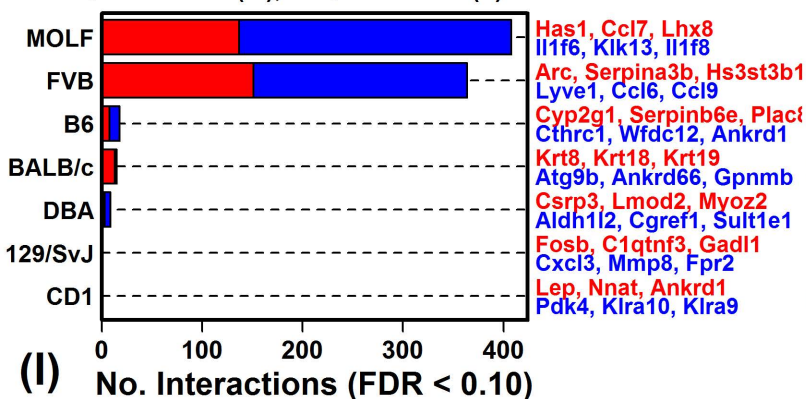


**Additional File 5. Comparison of IMQ responses between males and females. (A – G)**

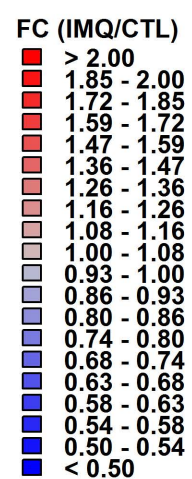
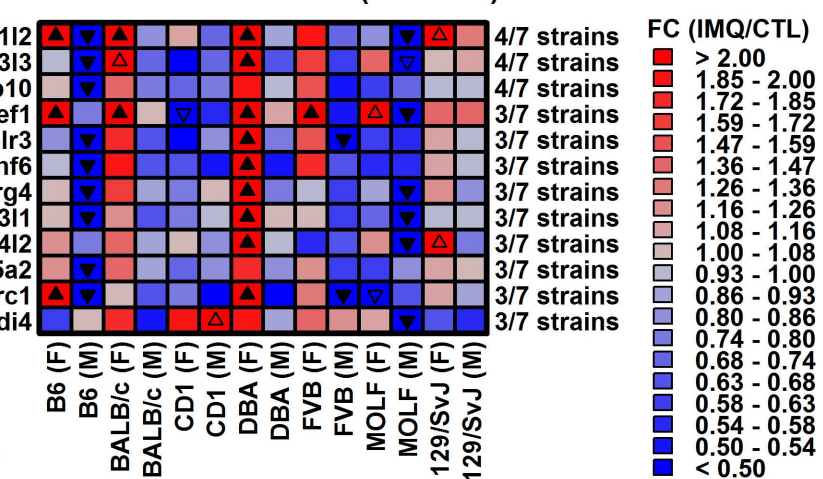
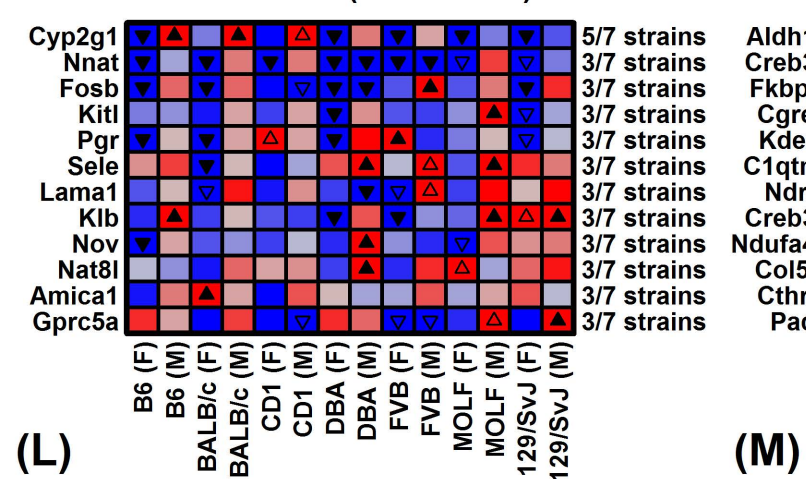
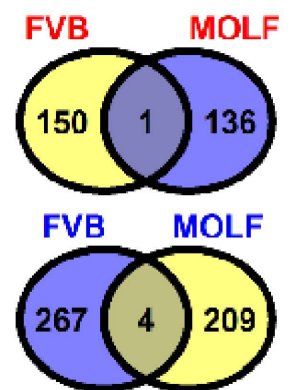
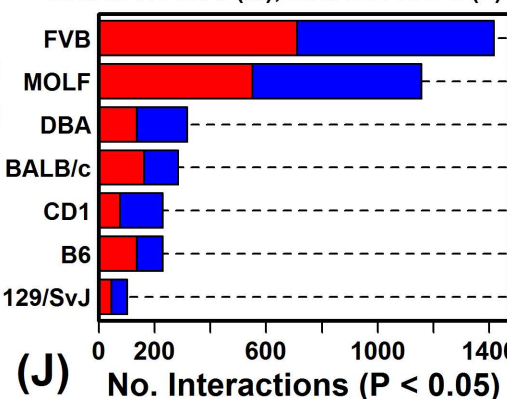
IMQ response comparison between males and females for each strain ( $r$  = Spearman rank correlation; dashed lines: robust linear regression estimates; ellipses: 90% of genes closest to the bivariate mean based on Mahalanobis distance). (H) Overlap of Mahalanobis distance ellipses for each strain. (I) Number of genes with significant sex-by-treatment interaction effects (FDR < 0.10; right margin: example genes with most significant interactions). (J) Number of genes with significant sex-by-treatment interaction effects (without FDR correction,  $P < 0.05$ ). (K) Overlap of genes with sex-by-treatment interaction effects in FVB and MOLF strains (FDR < 0.10; top: IMQ-increased (males) and IMQ-decreased (females); bottom: IMQ-decreased (males) and IMQ-increased (females)). (L, M) Genes with the most consistent sex-by-treatment interaction patterns across strains (right margin: number of strains with shared pattern, without FDR correction,  $P < 0.05$ ). (N – P) RT-PCR analysis of (N) *Cyp2g1*, (O) *Fosb* and (P) *Aldh1l2* expression ( $n = 5$  per strain/sex/treatment group;  $n = 40$  mice total). Groups without the same letter differ significantly ( $P < 0.05$ , Tukey honest significant difference; Error bars: standard error of the mean; p-values: sex-by-treatment interaction effects). *Rn18s* was used as an endogenous control to estimate relative gene expression.



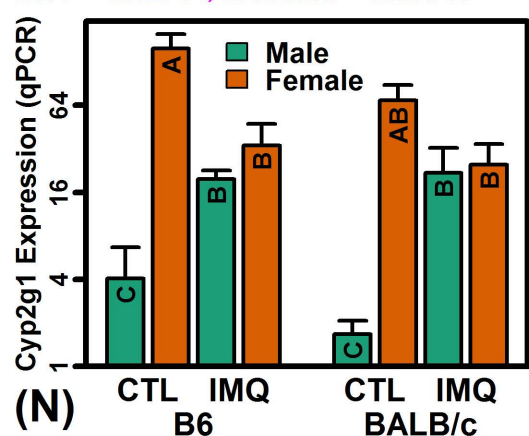
■ IMQ-increased (M), IMQ-decreased (F)  
 ■ IMQ-decreased (M), IMQ-increased (F)



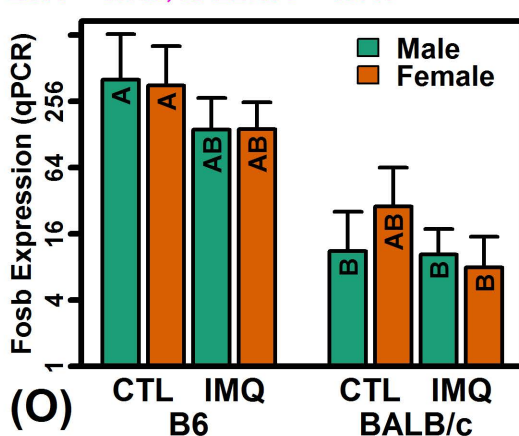
■ IMQ-increased (M), IMQ-decreased (F)  
 ■ IMQ-decreased (M), IMQ-increased (F)



B6:  $P = 2.28e-04$ , BALB/c:  $P = 2.05e-05$



B6:  $P = 0.932$ , BALB/c:  $P = 0.411$



B6:  $P = 3.82e-03$ , BALB/c:  $P = 0.466$

