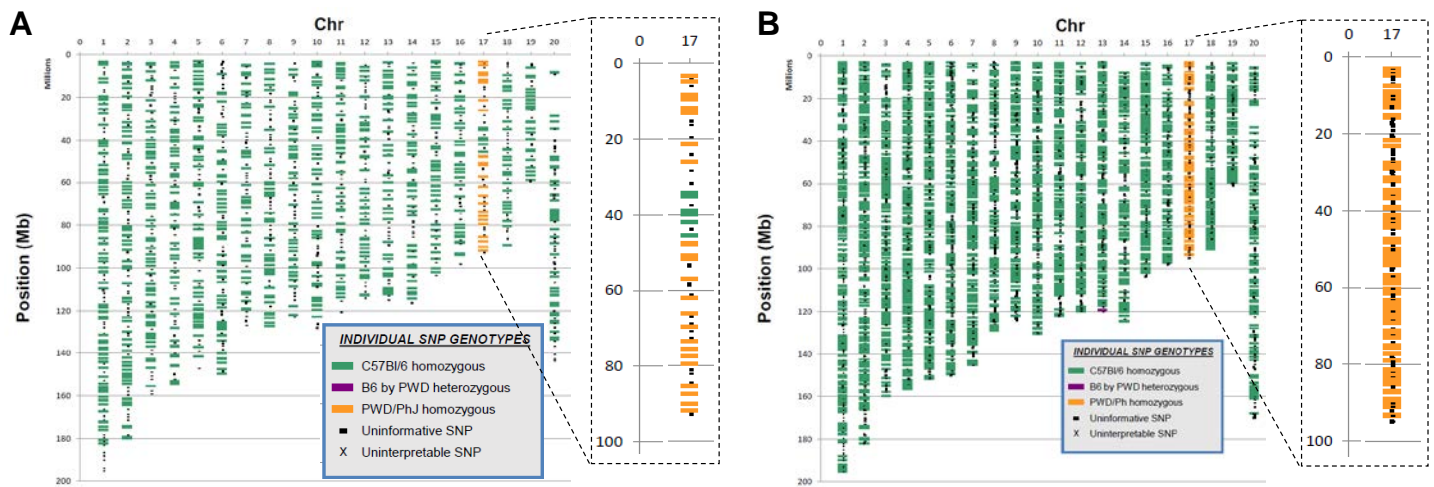
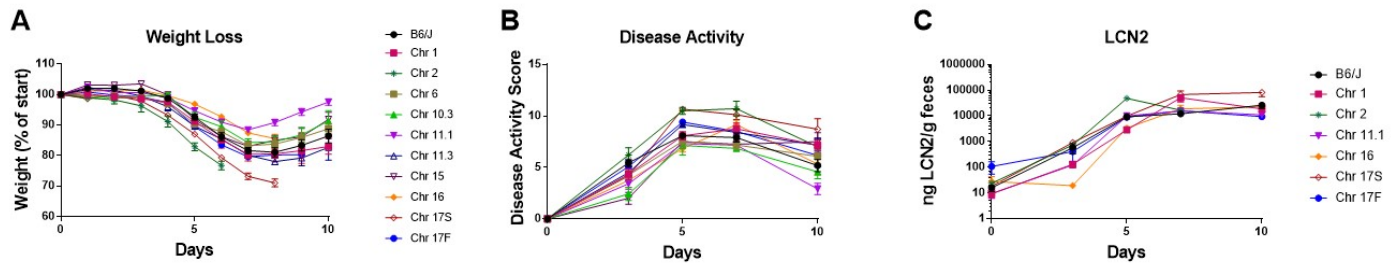


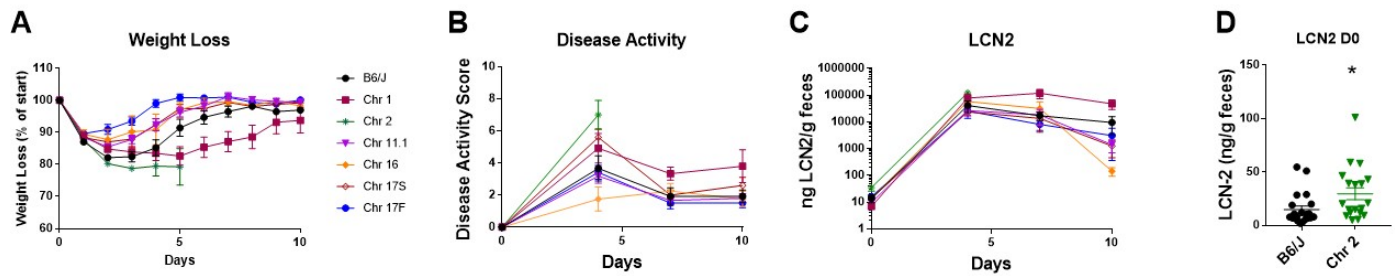
## Supplemental Figures



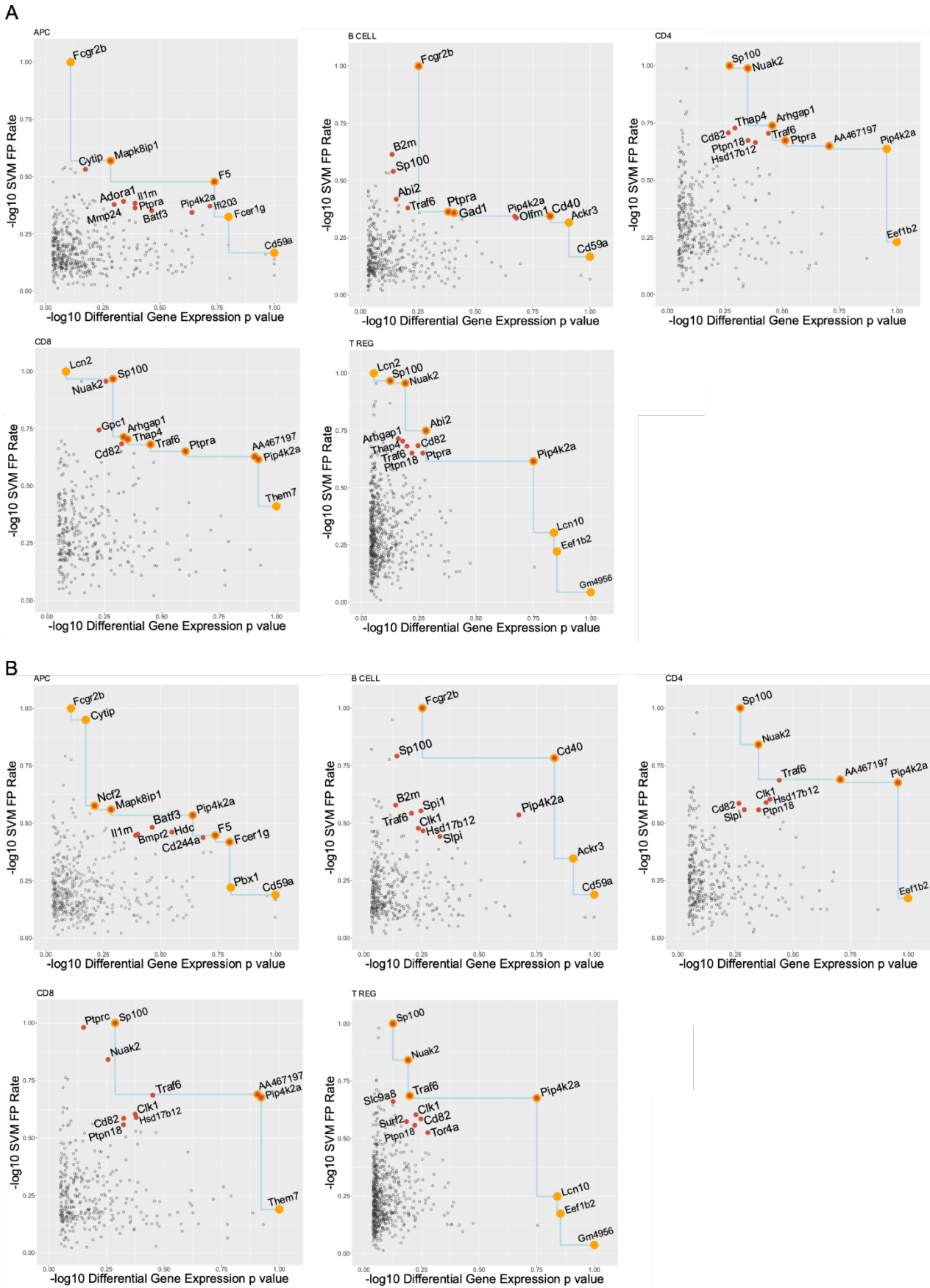
**Figure S1. Genetic comparison of Chr17S<sup>PWD</sup> and Chr17F<sup>PWD</sup> consomic strains.** DNA isolated from Chr17S<sup>PWD</sup> (**A**) and Chr17F<sup>PWD</sup> (**B**) consomic strains was subjected to genome-wide SNP-based genotyping as described in the Methods section. Note that the difference in SNP density is due to the fact that two different genotyping platforms were used, the 1449 SNP Illumina BeadChip in (**A**), and the 5307 SNP Illumina Infinium BeadChip in (**B**).



**Figure S2. Kinetics of DSS-induced colitis in B6.Chr<sup>PWD</sup> consomic strains.** DSS colitis was induced and evaluated in B6.Chr<sup>PWD</sup> consomic strains and B6 controls as described in **Fig. 3**. Weight loss (**A**) and disease activity (**B**) were evaluated as in **Fig. 3**. LCN2 was measured as in **Fig. 3**. For strains with significant mortality (Chr2<sup>PWD</sup> and Chr17S<sup>PWD</sup>), weight loss, and disease activity are shown up until the first mortality incidence.



**Figure S3. Kinetics of TNBS-induced colitis in B6.Chr<sup>PwD</sup> consomic strains.** (A-C) TNBS colitis was induced and evaluated in B6.Chr<sup>PwD</sup> consomic strains and B6 controls as described in **Fig. 4**. Weight loss (**A**) and disease activity (**B**) were evaluated as in **Fig. 3**. LCN2 was measured as in **Fig. 3**. For Chr2<sup>PwD</sup>, data are shown through D5, as only one mouse survived past this time point. (**D**) Fecal samples were collected from B6 and Chr2<sup>PwD</sup> mice prior to DSS or TNBS administration, and LCN2 levels were measured as in **Fig. 3**. Significance of differences was determined by T-test.



**Figure S4. Network-based functional scoring for five immune cell subtypes. (A) and (B)** The "Intestine" and "Hemolymphoid" network SVMs, respectively, were used to identify candidate genes associated with IBD susceptibility, as described in **Fig. 6B**. SVM results were integrated with the differentially expressed gene datasets from each of the five PWD and B6 cell types, indicated above each panel. Significantly differentially

expressed genes from chromosome 1 and 2 are plotted by normalized  $-\log_{10}(P)$  on the x-axis and normalized SVM  $-\log_{10}(\text{false positive rate}) (FPR)_{SVM}$  on the y-axis.  $FPR_{SVM}$  and P values were scaled/normalized by their maximum value (see Methods). Orange points denote genes located on the Pareto front, denoted by the blue line. Red points denote the top ten ranked genes based on the final score, which combines the count of the number of genes that have both a lower  $-\log_{10}(p\text{-value})$  and  $-\log_{10}(FPR)$ . Orange and red indicates top ranked genes that also fall on the Pareto front.