

**Fig E1. Distribution of Airway gene signature. Airway gene signature is positively associated with (A) Airway wall thickness, (B) Wall area percent and (C) P110. (D) Airway gene signature score is significantly different between non-COPD and COPD (Wilcoxon test,  $p < 5 \times 10^{-11}$ )**

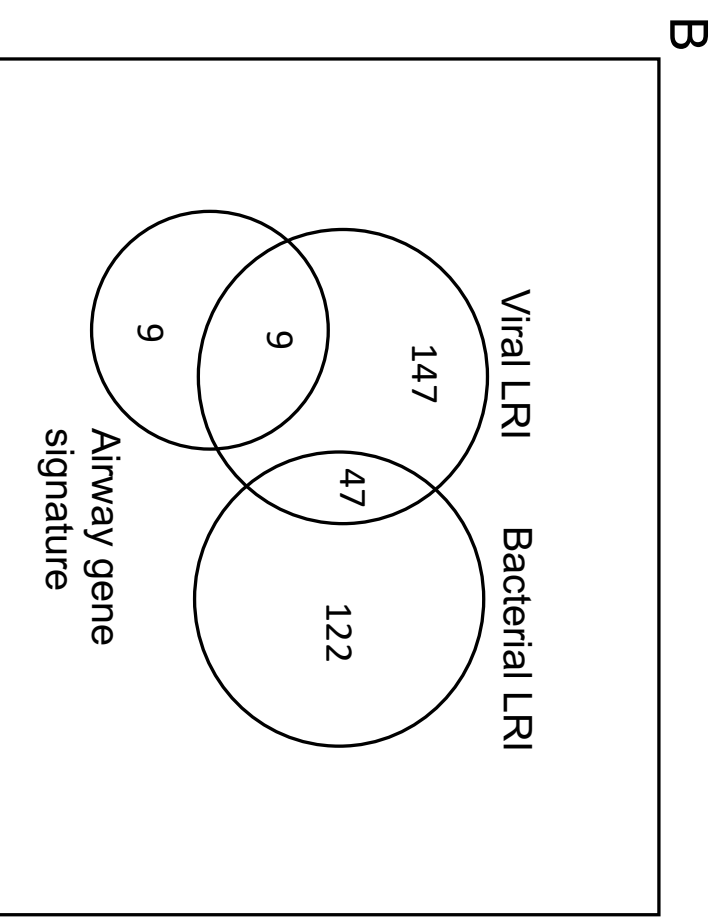
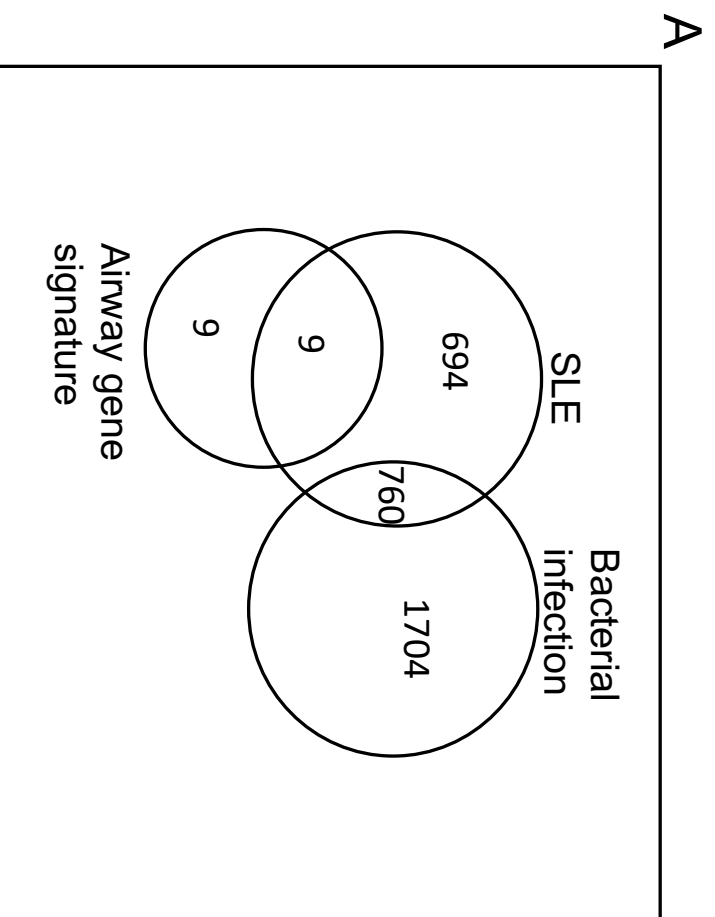


Fig E2. Overlap of airway gene signature with publicly available gene expression of autoimmune disease and respiratory infections. (A) Airway gene signature overlaps with SLE gene expression but not with bacterial infection. (B) Airway gene signature overlaps with viral lower respiratory infection gene expression but not with bacterial lower respiratory infection. LRI: lower respiratory infection.

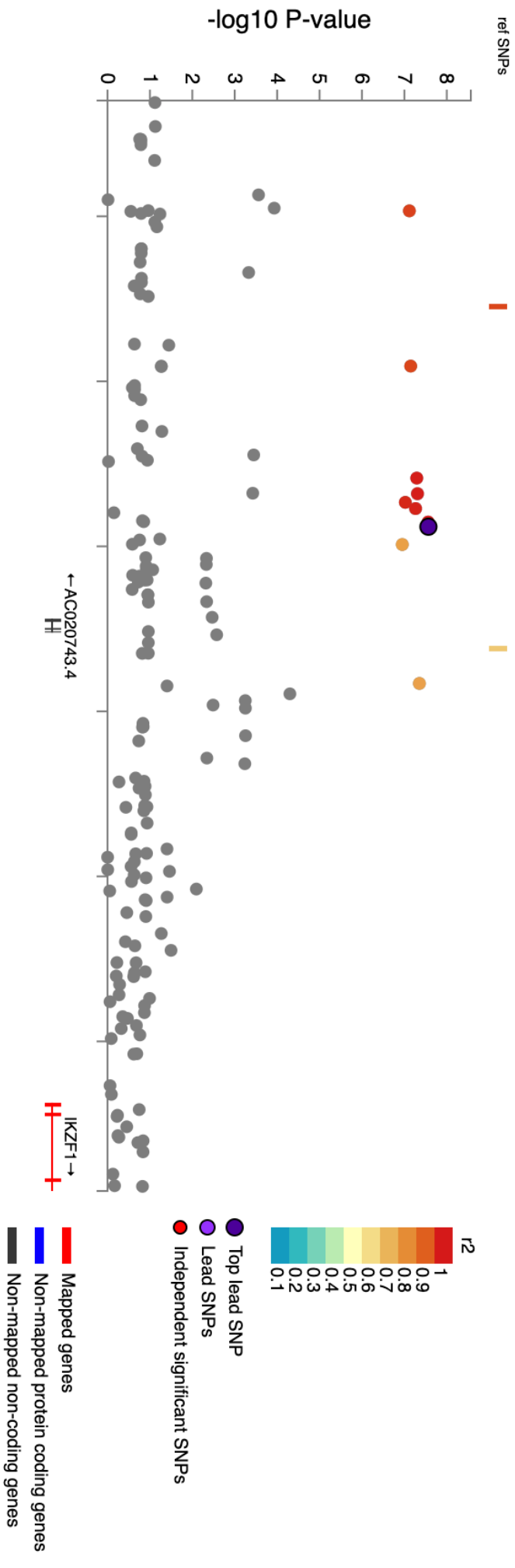


Fig E3. Genome wide association study of airway gene signature score. Regional association plot showing locus near *IKZF1*

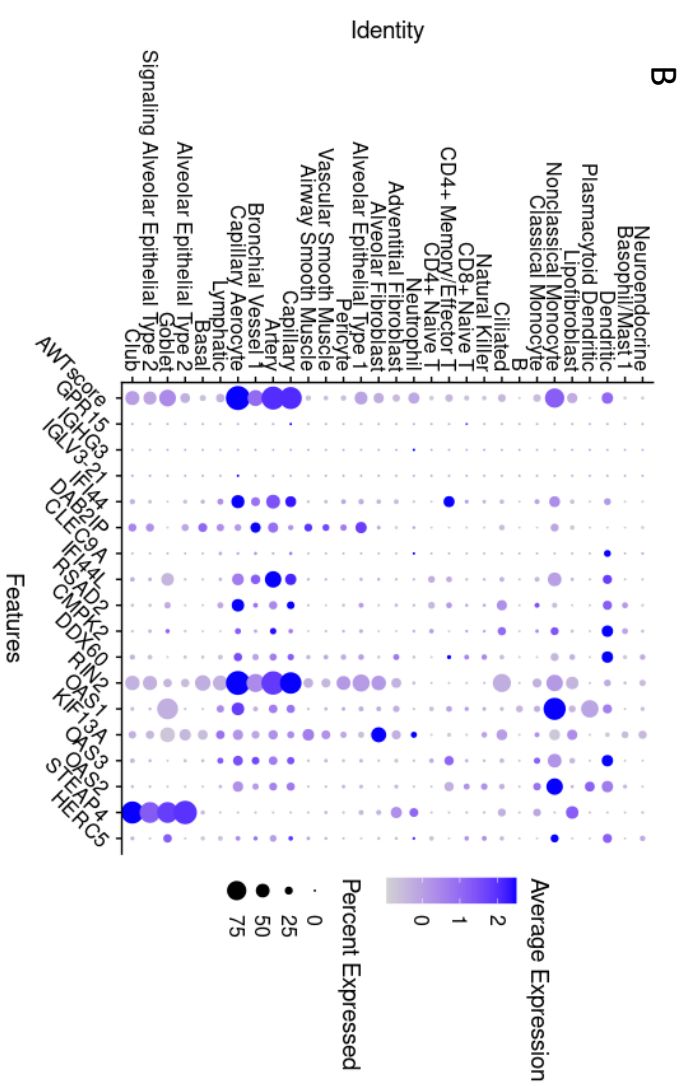
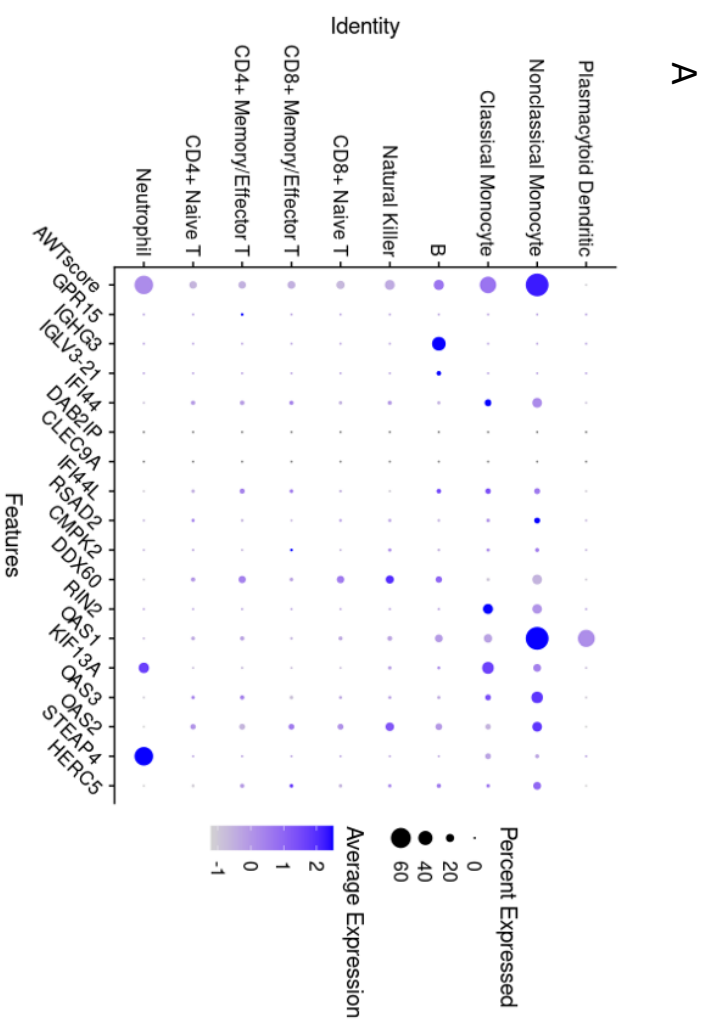


Fig E4. Normalized expression of AWT score genes. (A) peripheral blood (Smart-Seq2 single cell RNA sequencing) (B) lung. 17 of 18 genes (except CTD-2083E4.5) are expressed. AWT score composite expression was calculated by the average expression of each genes on a single cell level, subtracted by the aggregate expression of randomly selected control features