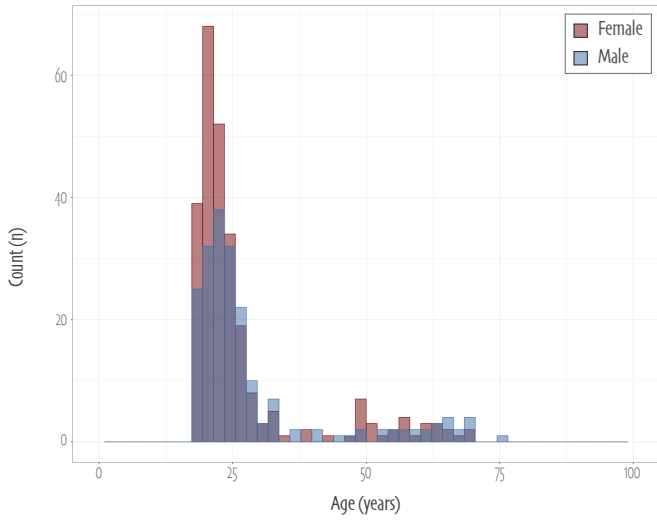


A.



B.

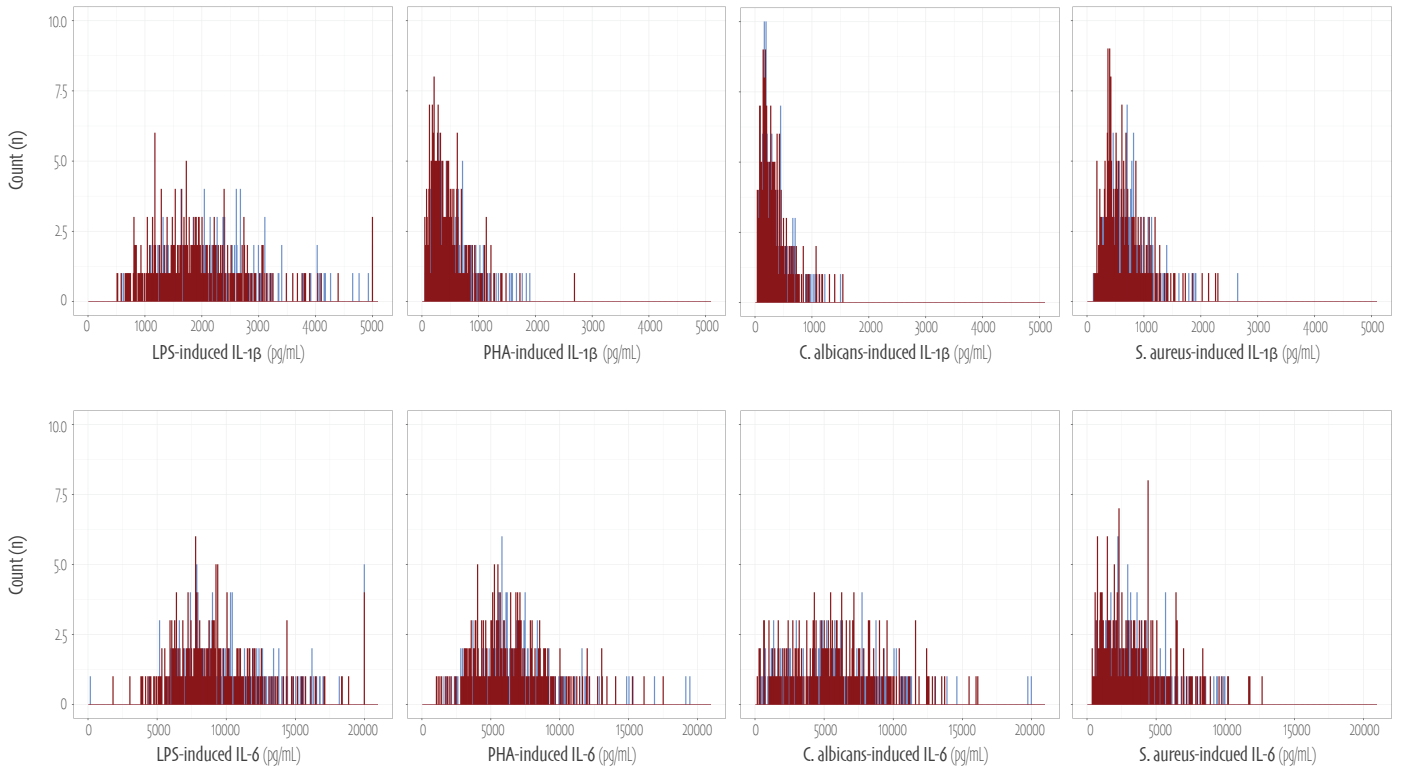


Fig. S1: Baseline characteristics of healthy individuals (n=463) included in analysis. (A) Shows the age distribution of all individuals included in analyses classified by gender (mean age - Female=26.66, Male=28.84; median age - Female=22, Male=24). (B) Shows the IL-1 β and IL-6 in vitro cytokine production in response to LPS (100ng/mL), PHA (10 μ g/mL), *C. albicans* (10⁶ CFU/mL), *S. aureus* (1x10⁶/mL), classified by gender.

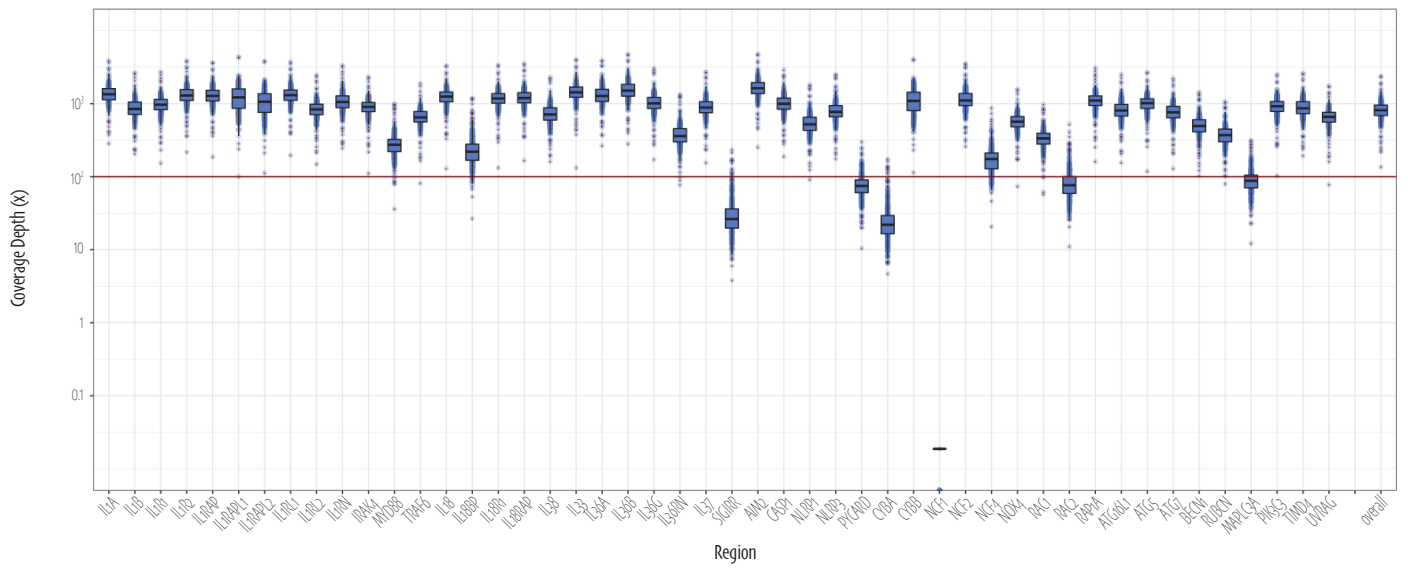


Fig. S2: Average coverage depth for healthy individuals (n=463) included in analysis. The average coverage for each individual per gene (and overall on the most right) is visualized in separate jitter plots, overlaid by boxplots, where boxes contain a median line, edges at 25th and 75th percentile, and default whiskers (1.5 * InterQuartileRange). Logarithmic y-axis, with a horizontal red line representing the analysis inclusion coverage cut-off of 100x.

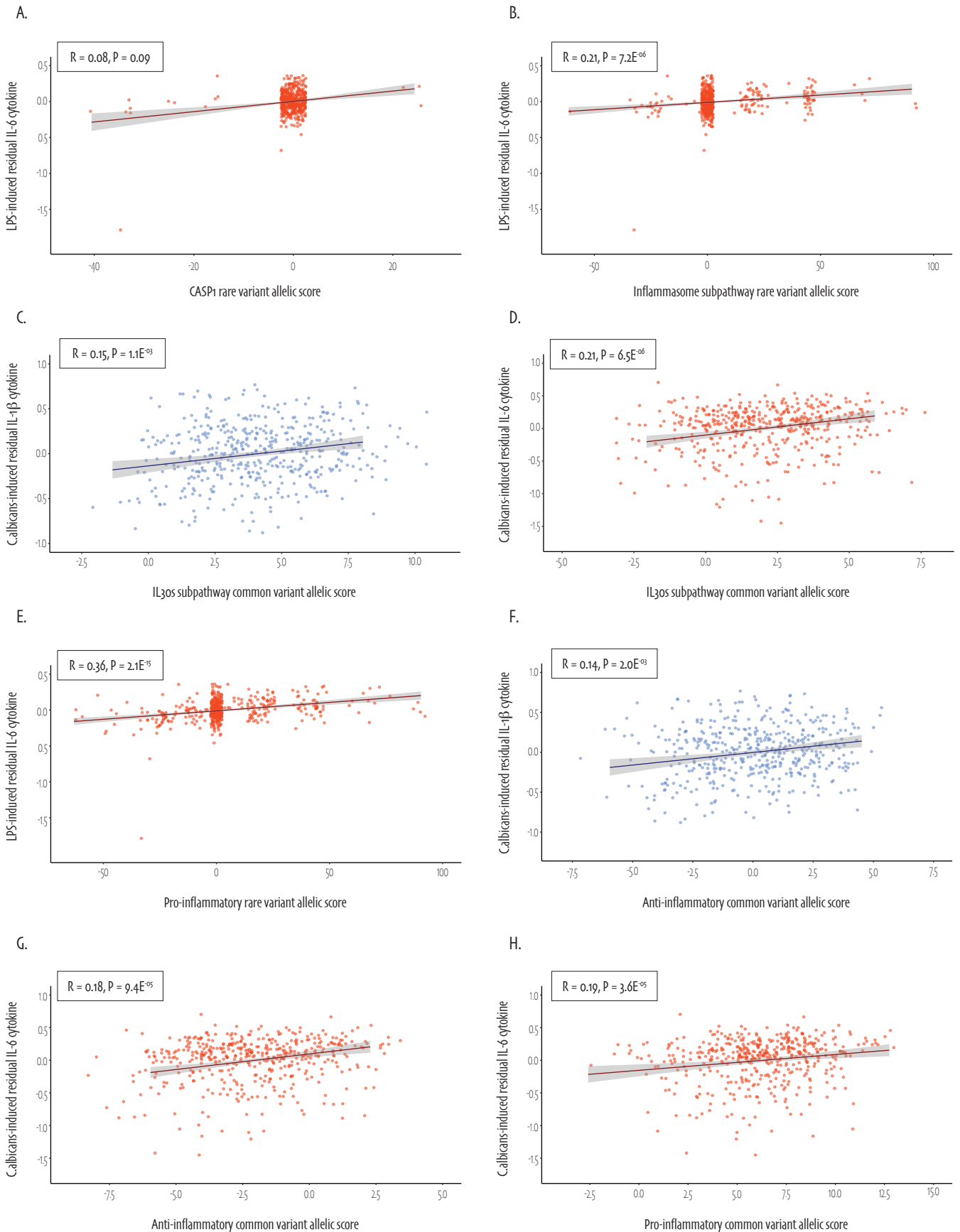


Fig. S3: Correlation plots of significantly associated sets. Stimulation-induced residual (corrected for age and sex) cytokine production in correlation with set-based, directional, allele frequency weighted allelic scores for significant bi-directional rare variant and common variant (variant $n > 2$) associations. **(A)** LPS-induced IL-6 residual cytokine production in correlation with CASP1 rare variant ($n=5$) allelic score. **(B)** LPS-induced IL-6 residual cytokine production in correlation with inflammasome subpathway rare variant ($n=42$) allelic score. **(C)** C. albicans-induced IL-1 β residual cytokine production in correlation with IL3os subpathway common variant ($n=7$) allelic score. **(D)** C. albicans-induced IL-6 residual cytokine production in correlation with IL3os subpathway rare variant ($n=7$) allelic score. **(E)** LPS-induced IL-6 residual cytokine production in correlation with pro-inflammatory rare variant ($n=102$) allelic score. **(F)** C. albicans-induced IL-1 β residual cytokine production in correlation with anti-inflammatory common variant ($n=10$) allelic score. **(G)** C. albicans-induced IL-6 cytokine production in correlation with anti-inflammatory common variant ($n=10$) allelic score. **(H)** C. albicans-induced IL-6 residual cytokine production in correlation with pro-inflammatory common variant ($n=16$) allelic score.