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Supplemental information

**A functional genomics approach in Tanzanian
population identifies distinct genetic regulators of
cytokine production compared to European population**

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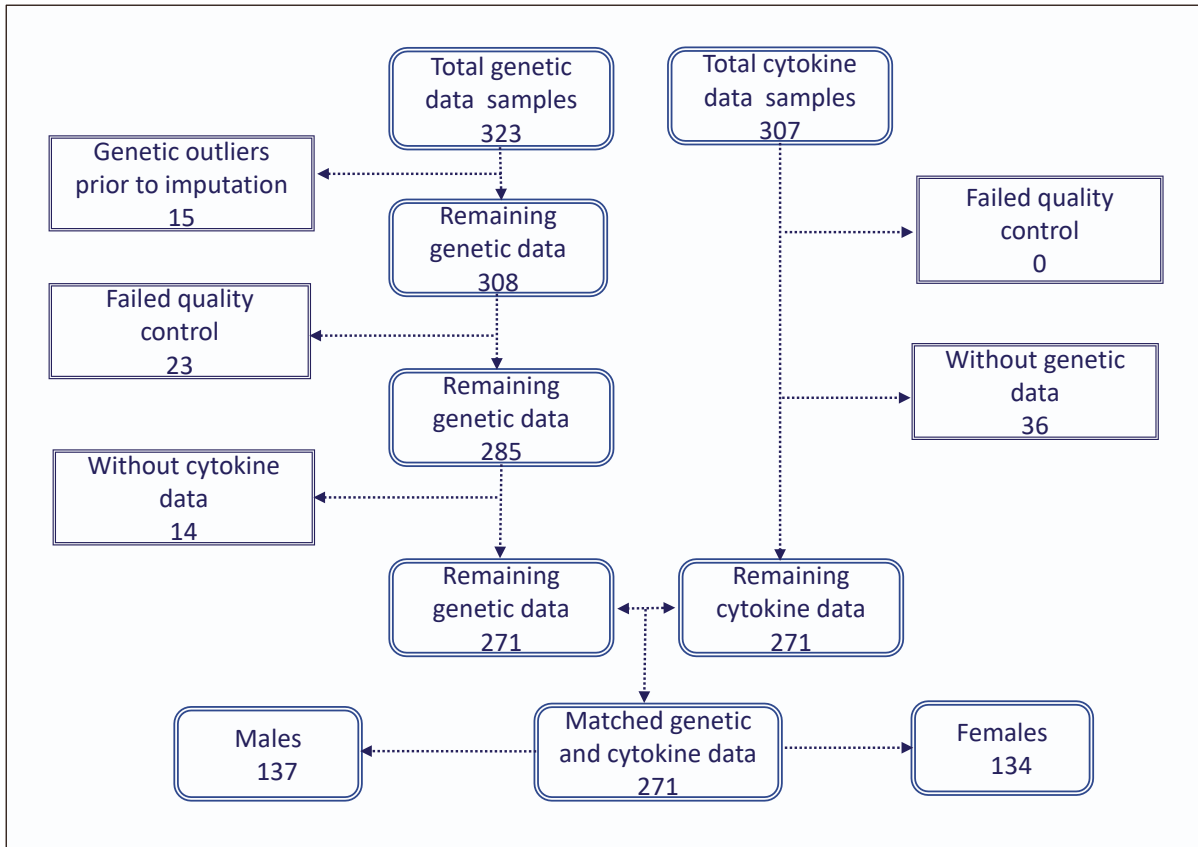


Figure S1. Schematic overview of Tanzania study cohort quality control.

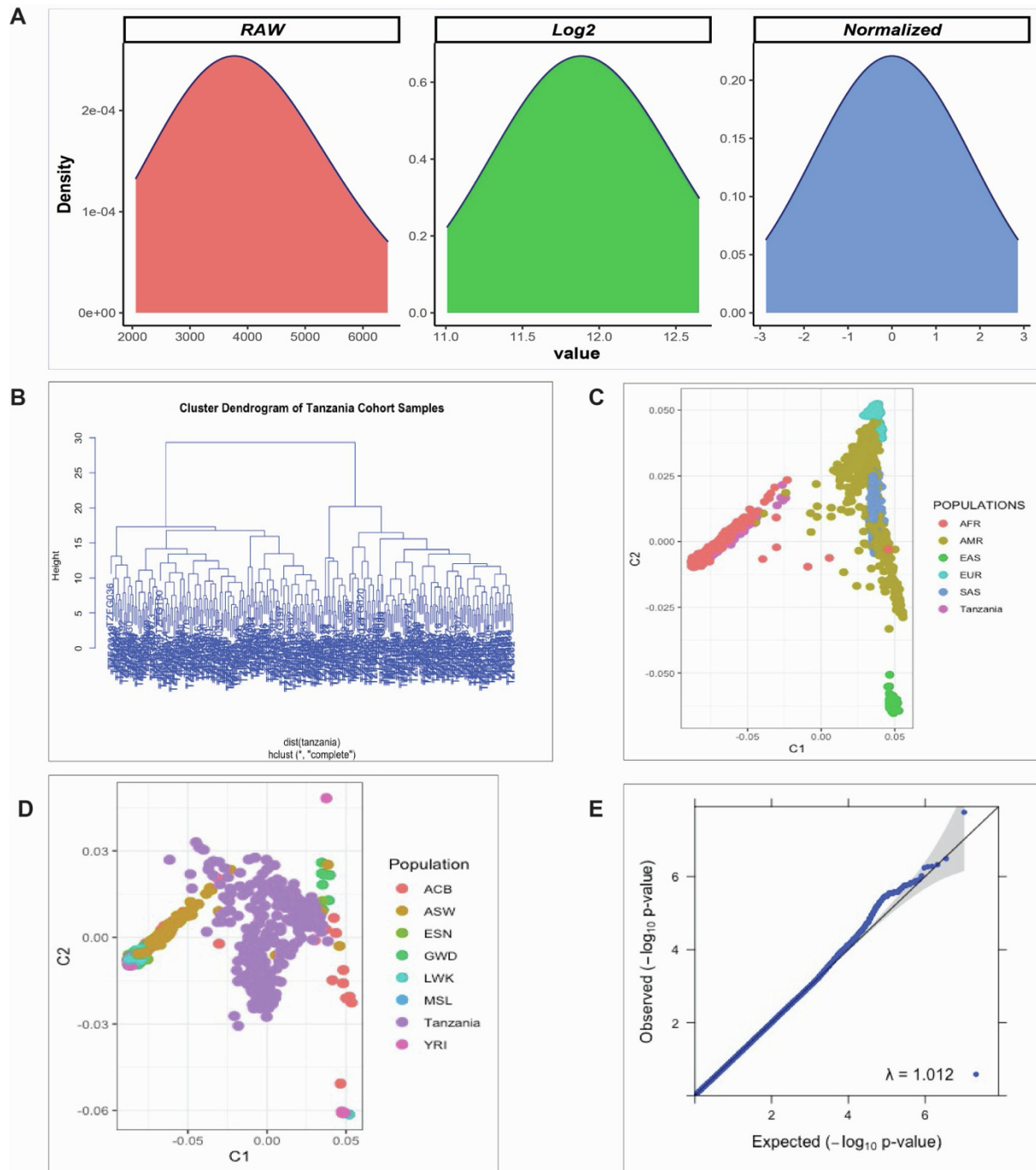


Figure S2. Quality control of genetic and cytokine data.

(A) Density plots depicting the distributions of *S. enteritidis* induced-IL-1 β concentrations. The density plot is faceted as follows: raw (RAW), Log2 transformed (Log2), and inverse-ranked normalization of IL-1 β distributions respectively. (B) Dendrogram visualization of unsupervised hierarchical clustering of individuals used for cQTL mapping. The “Euclidean” method in the “hclust” function was used for

computing distances. (C) Multi-dimensional scaling (MDS) plot of populations in the 1000 Genome project against individuals in Tanzania cohort. The first two MDS components (C1 and C2) are plotted against each other. Individuals representing various continental groups are color coded as shown in the color legend. The color legend populations in the 1000 Genome project are: AFR (Africans), AMR (American), EAS (East Asians), EUR (Europeans), and SAS (South Asians). Clustering of populations revealed genetically homogenous cluster of Tanzania cohort individuals with African ancestry individuals in the 1000 Genome project data. (D) MDS plot with Tanzanian data projected on only Africans (dominated by west Africans) in the 1000G data. (E) Quantile-Quantile (QQ) plot depicting association results of IL-1 β after *S. enteritidis* stimulation. Lambda (λ) value indicates lack of inflation of the test statistics.

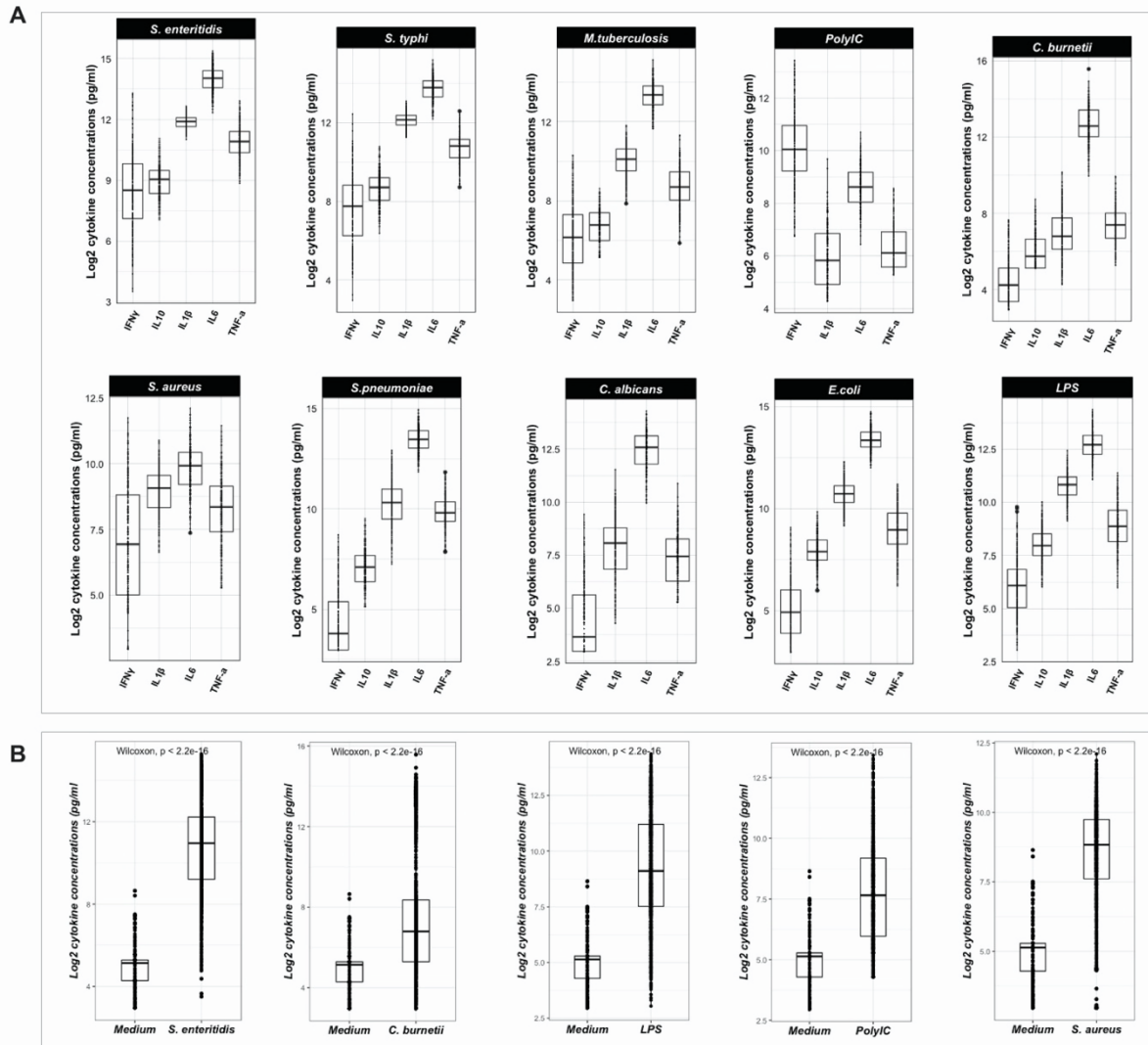


Figure S3: Interindividual variability of cytokine profiles upon stimulation. (A)

Boxplots indicating strong variation of IFN γ responses compared to other cytokines in most stimulations. (B) Boxplot of Wilcoxon test depicting the level of significant differences of cytokines response upon stimulation compared to unstimulated conditions (Medium).

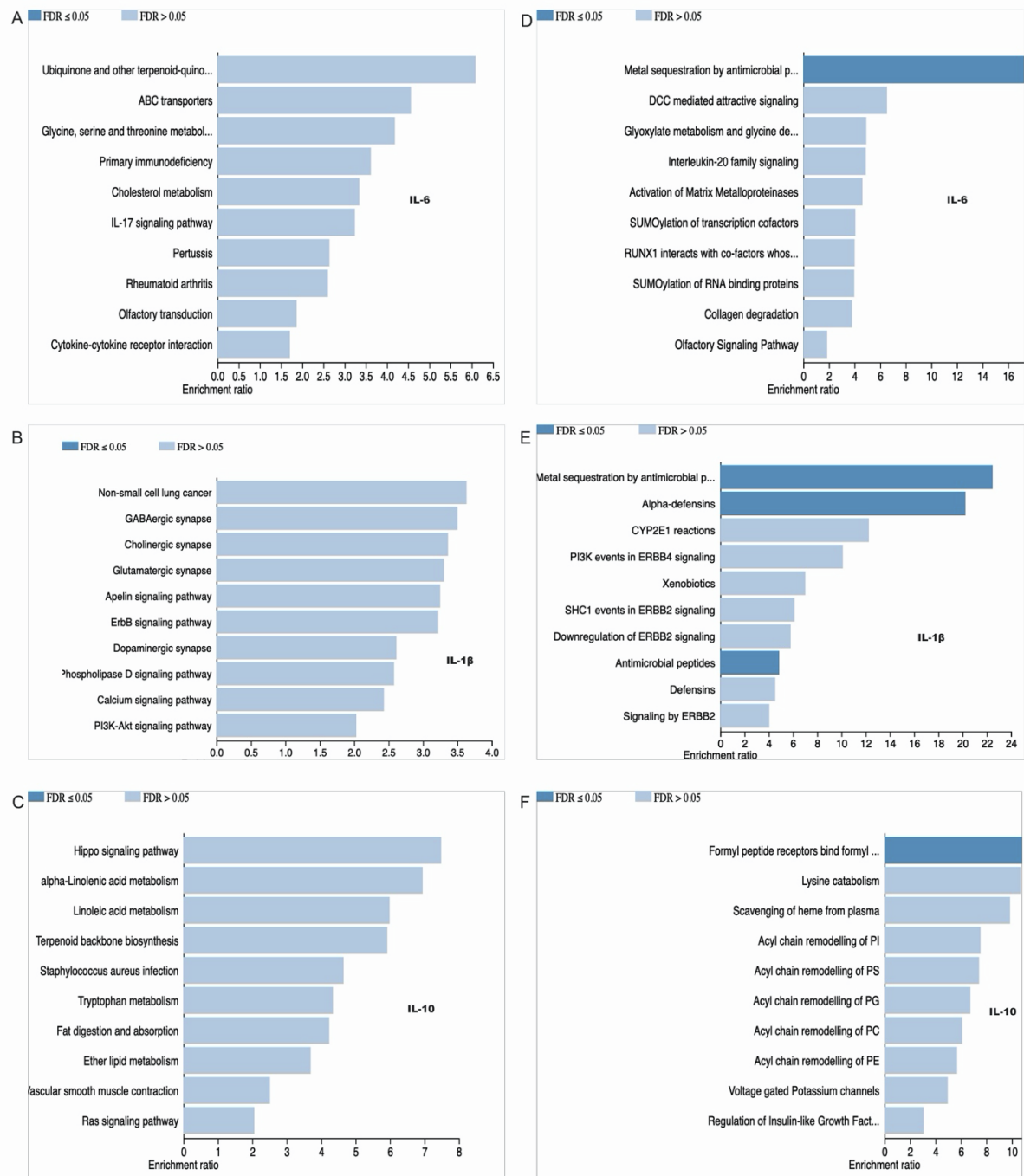


Figure S4. Bar chart representation of IL-6, IL-1β- and IL-10-based pathways.

(A , B and C) Top 10 enriched KEGG pathways for IL-6, IL-1β and IL-10 respectively.

(D , E and F) Top 10 enriched Reactome pathways for IL-6, IL-1β and IL-10 respectively. Darker blue bars represent statistically significant pathways and lighter blue bars represent non-significant pathways after multiple testing. We set the false discovery rate (FDR)-adjusted P-value to 0.05 as significance level.

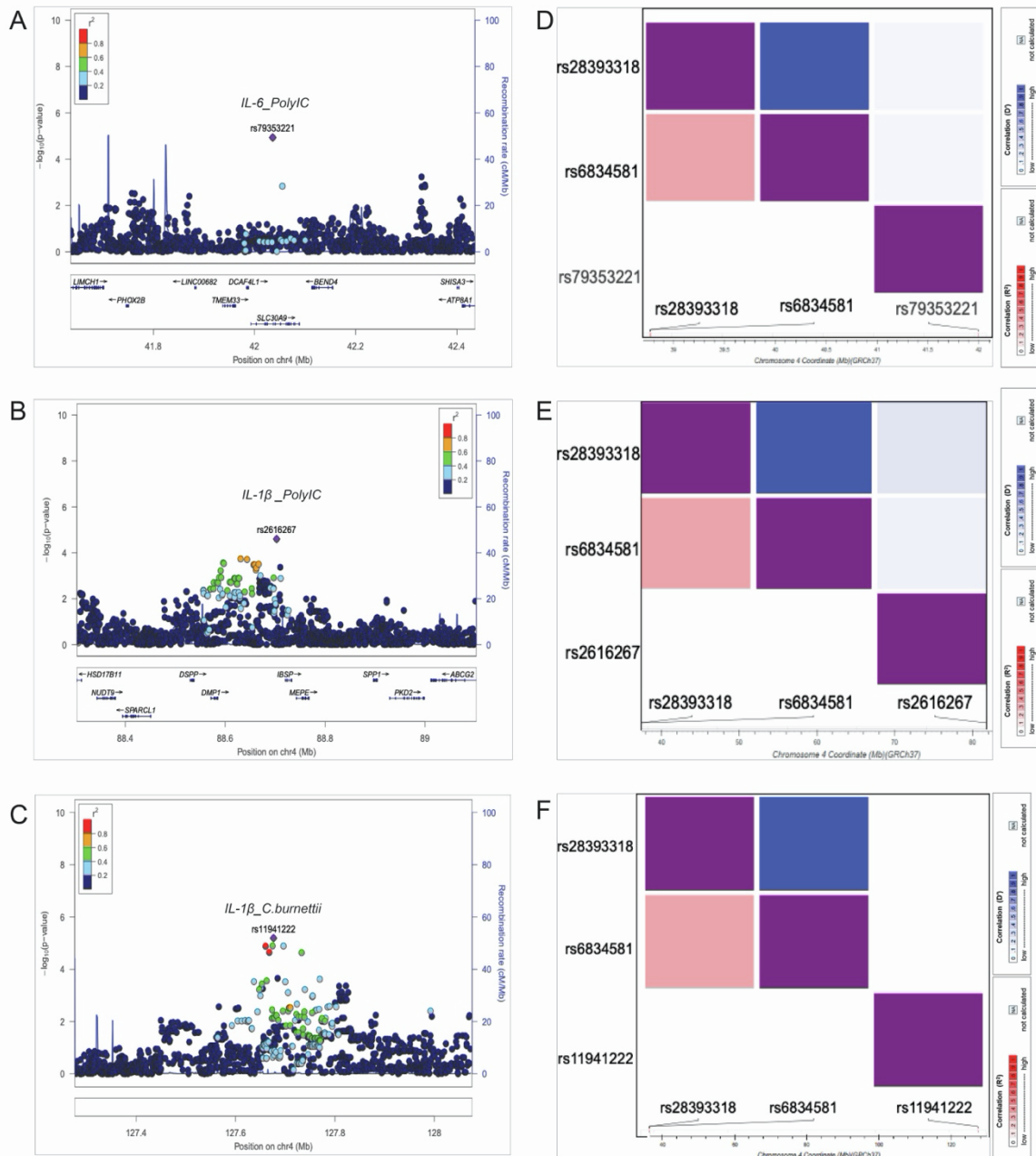


Figure S5. Different haplotypes regulate cytokine production between Africans and Europeans.

(A, B and C) Regional association plots of SNPs flanking genomic window of 400kb around top SNPs: rs79353221, rs2616267 and rs11941222 associated with IL-6 and IL-1 β concentrations at *TLR10-TLR1-TLR6* locus. None of these variants are in linkage disequilibrium with the top variants identified in this locus in the European

population. (D, E and F) Heatmaps showing lack of correlation between lead SNPs in the African and the European dataset at the *TLR10-TLR1-TLR6* locus.