Supplementary Note

TIRAP spans 14500 base pairs on Chr11q24.2 and contains 8 exons, of which exons 4, 5 and 6 encode a protein 221 amino acids in length. We identified thirty-three single nucleotide polymorphisms (SNPs; **Supplementary Figure 1**) which span *TIRAP* and its flanking genes, using a combination of direct sequencing of all *TIRAP* exons, a 1500 base pair region immediately upstream of the transcription start site in exon 1, and the 3' untranslated region, as well as database searches (dbSNP and Ensembl).

In an initial screen, we genotyped the identified polymorphisms in two different case-control study groups to obtain an overall picture of the linkage disequilibrium and allele frequencies: the UK Invasive Pneumococcal Disease (IPD) study and a Gambian malaria group. Of the markers genotyped, polymorphisms -29144, +6032, S55N, S180L and +10122 were associated with IPD in UK individuals of European ancestry, whereas in the Gambian study, only markers R13W and S180L were associated with malaria (P<0.05, **Supplementary Tables 1** and **2**). As expected, the degree of linkage disequilibrium (LD) was more extensive in the UK population than in the Gambian population (**Supplementary Figure 1**). Variant S180L showed the only consistent association in the two populations studied, suggesting that this could be the functional variant, and was thus genotyped in the rest of the study populations.