Figure S1: Violin plot of the antimicrobial susceptibility profiles of all four populations against amikacin, meropenem, piperacillin-tazobactam, ciprofloxacin, tobramycin, and ceftazidime as measured by zone of inhibition in a standard disc diffusion assay. This plot displays the same data as Fig. 3, displayed in clusters by antibiotic rather than by population. Black horizontal bars indicate the cut-off values for susceptibility (top bar) and resistance (bottom bar) for each antibiotic as determined by the Clinical and Laboratory Standards Institute (CLSI).

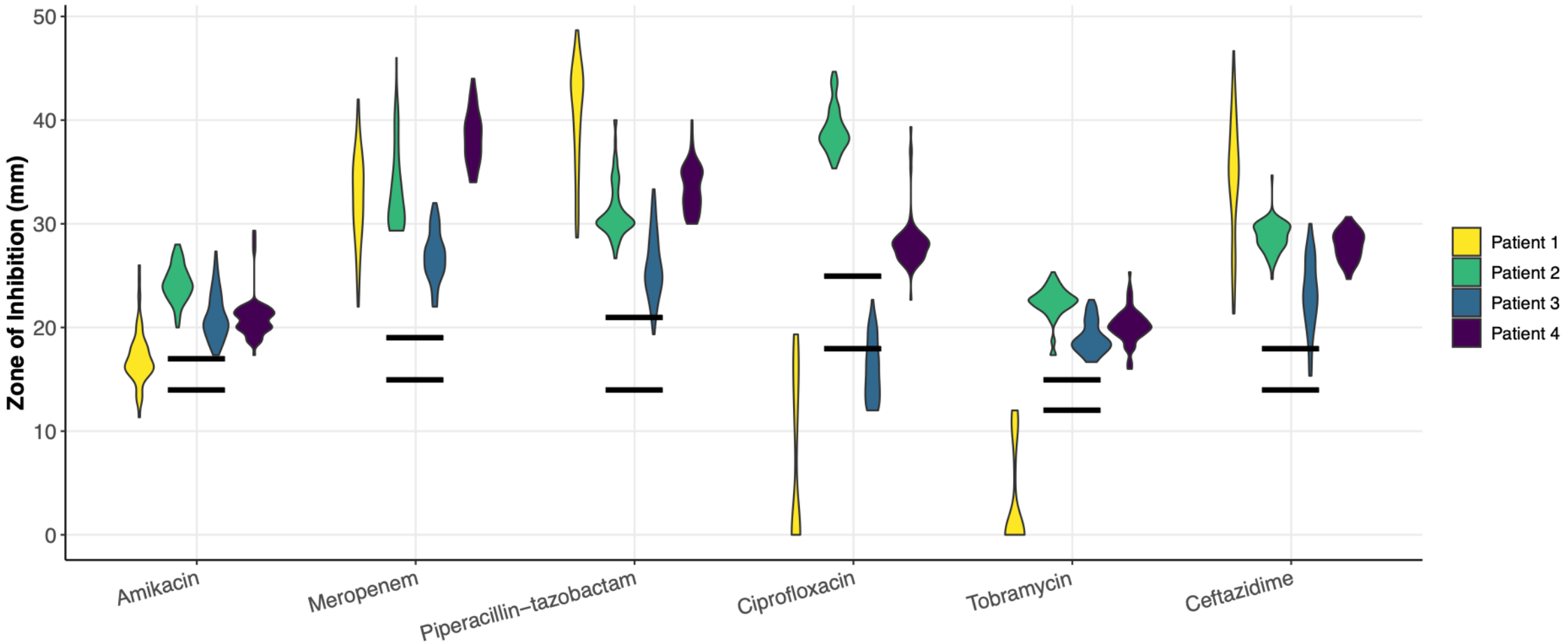


Figure S2: Phylogeny of Patients 1-4 with PAO1 and PA14. Patients 1, 2, and 4 cluster with PAO1, while Patient 3 clusters with PA14.

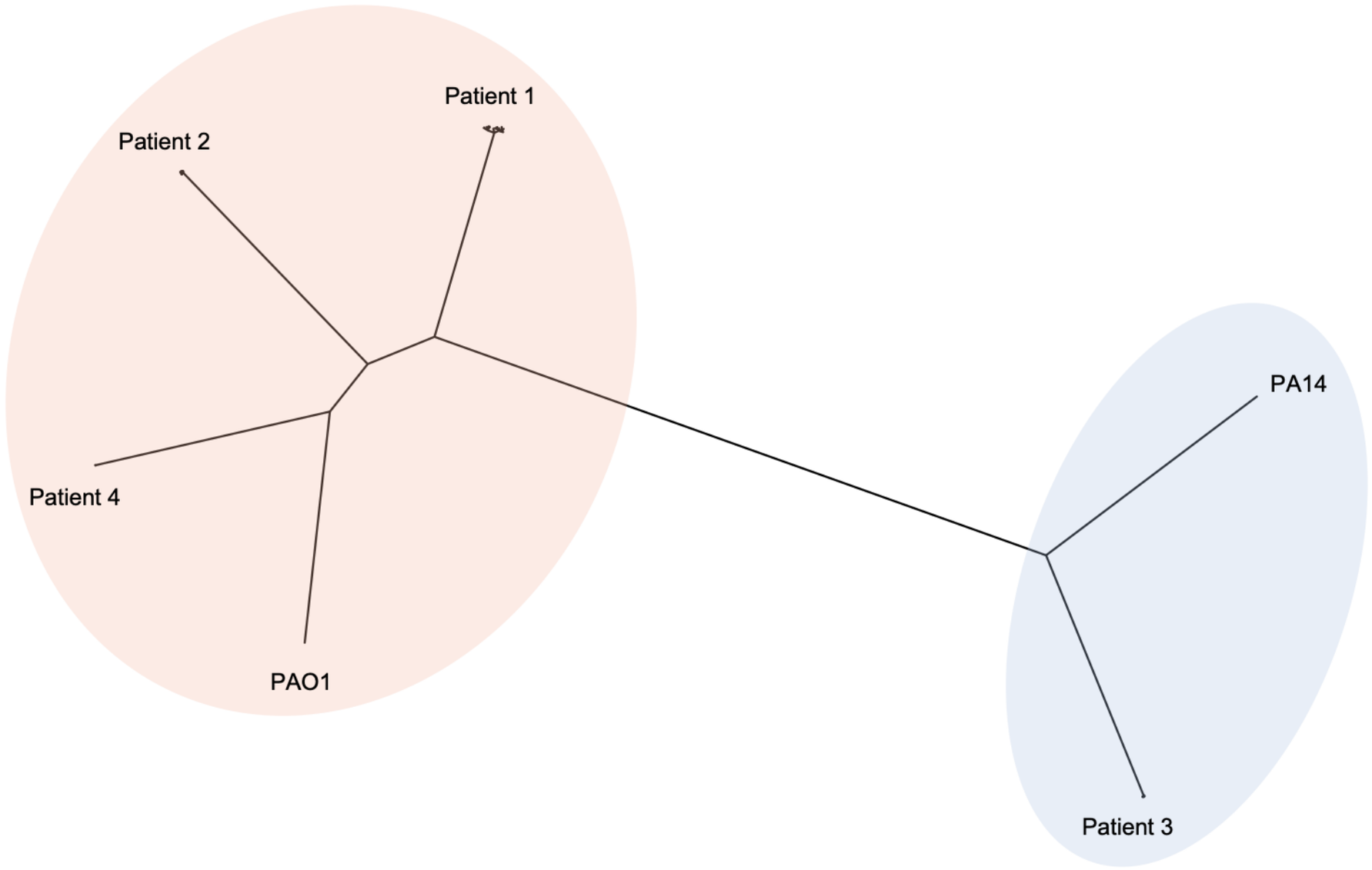


Fig. S3. Enrichment analysis of the frequency of functional categories in which non-synonymous SNPs and microindels are found in each of the four populations relative to the proportions of these functional categories in the PAO1 genome shows that protein secretion/ export apparatuses and transcriptional regulators are enriched for such variants, while phage/ transposon/ plasmid and non-coding RNA are less likely to be impacted by such variants. Donut plot of the relative frequencies of genes categorized within each of the 27 different PseudoCAP functional categories in the PAO1 genome (A). Donut plots of the relative frequencies of non-synonymous SNPs and indels located in each of the 27 different PseudoCAP functional categories in Patient 1 (B), 2 (C), 3 (D), and 4 (E).

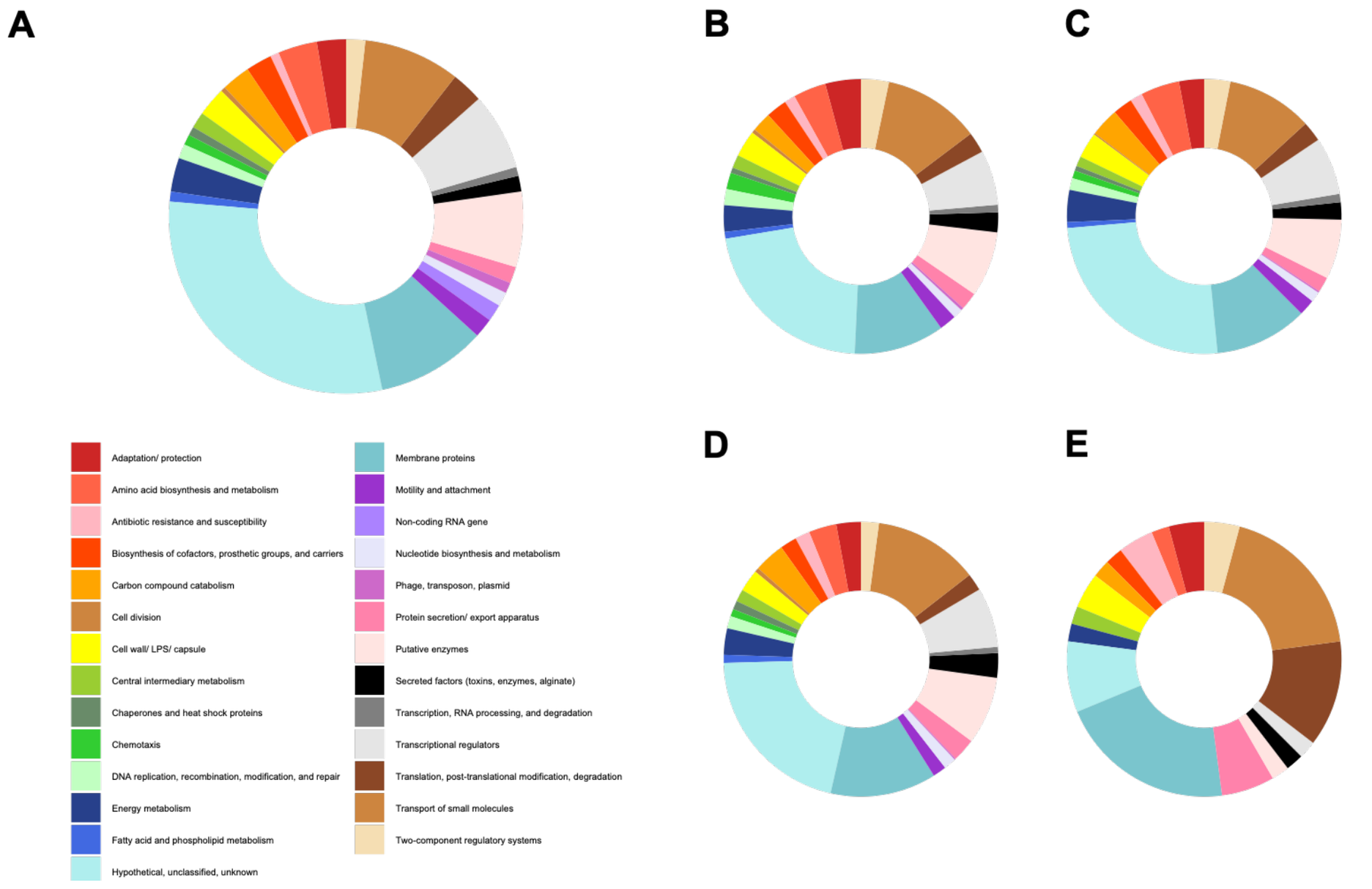
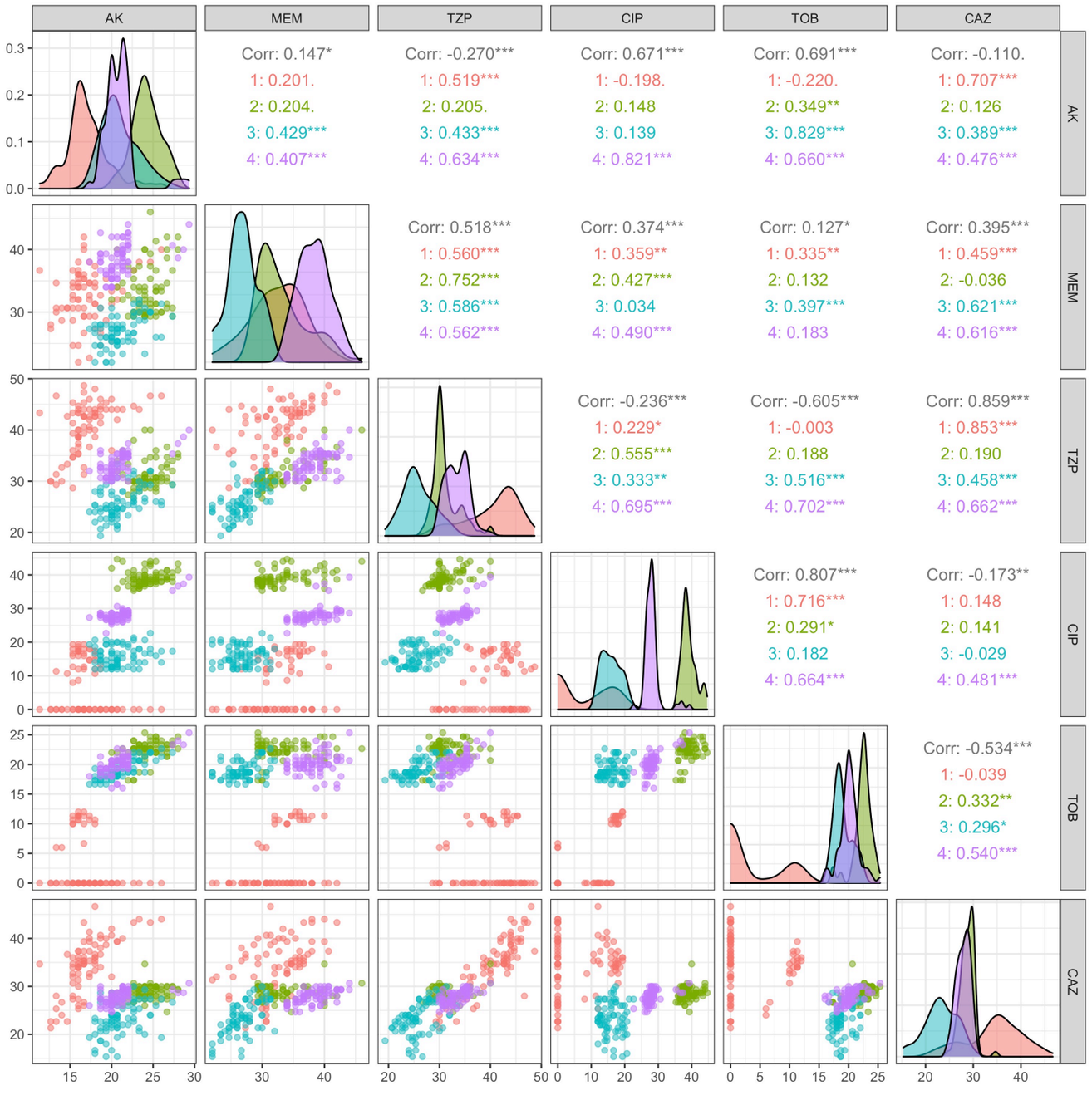


Fig. S4. Lack of statistically significant negative correlations between any two antimicrobial susceptibility profiles provides no evidence for collateral sensitivity trade-offs. Pearson's correlation coefficient (upper right quadrant), scatterplots (lower left quadrant), and density plots (diagonal) for pairwise comparisons of susceptibility profiles across all six tested antimicrobials: amikacin (AK), meropenem (MEM), piperacillin-tazobactam (TZP), ciprofloxacin (CIP), tobramycin (TOB), and ceftazidime (CAZ).



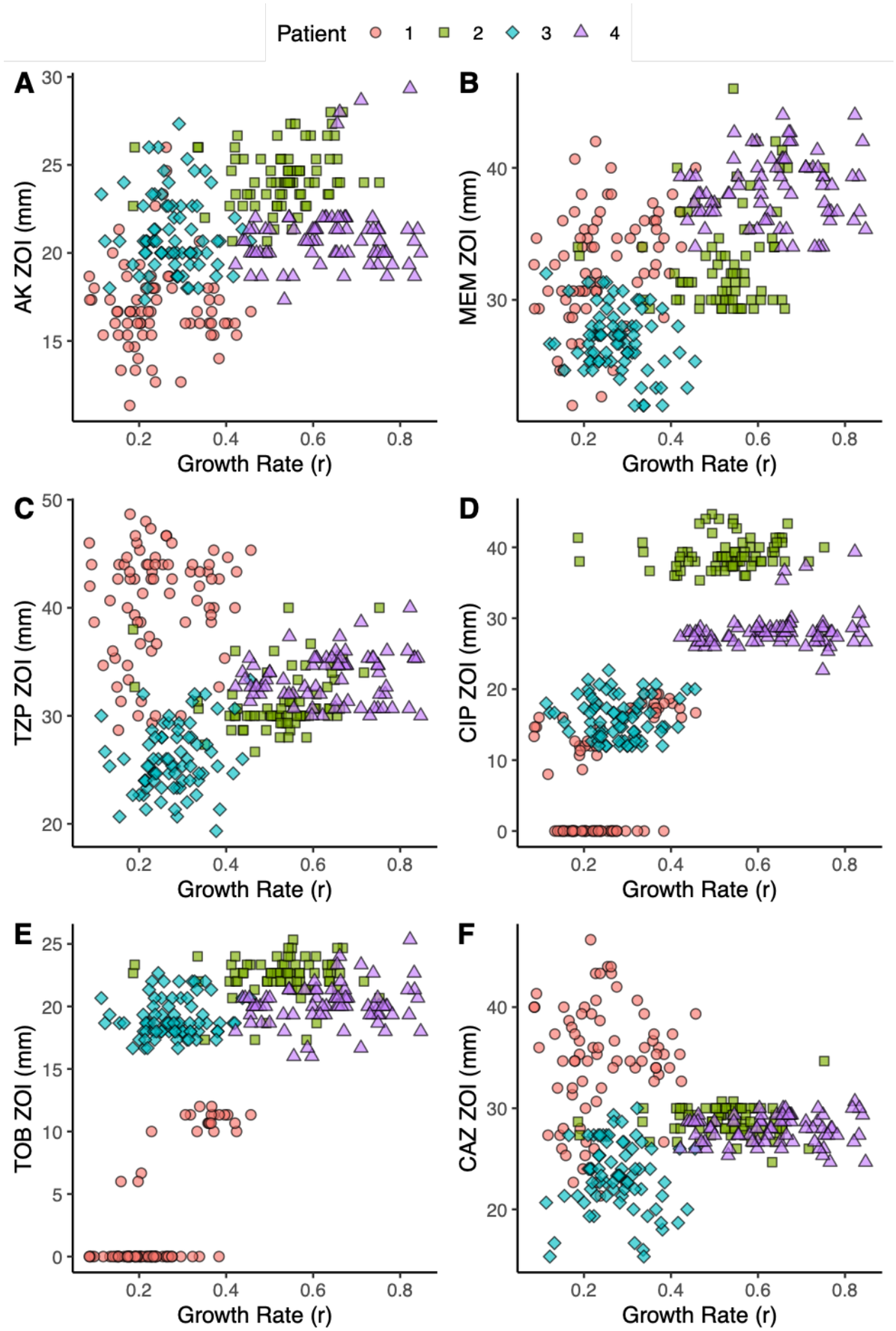


Fig. S5. Scatterplots of zone of inhibition (ZOI) versus growth rate (r) in SCFM for all six tested antibiotics: amikacin (AK), meropenem (MEM), piperacillin-tazobactam (TZP), ciprofloxacin (CIP), tobramycin (TOB), and ceftazidime (CAZ). Linear mixed model, with growth rate in SCFM as a fixed effect and patient as a random effect, demonstrates that there is no significant effect of growth rate on resistance, and therefore, no evidence for trade-offs between growth rate and resistance in these four populations.