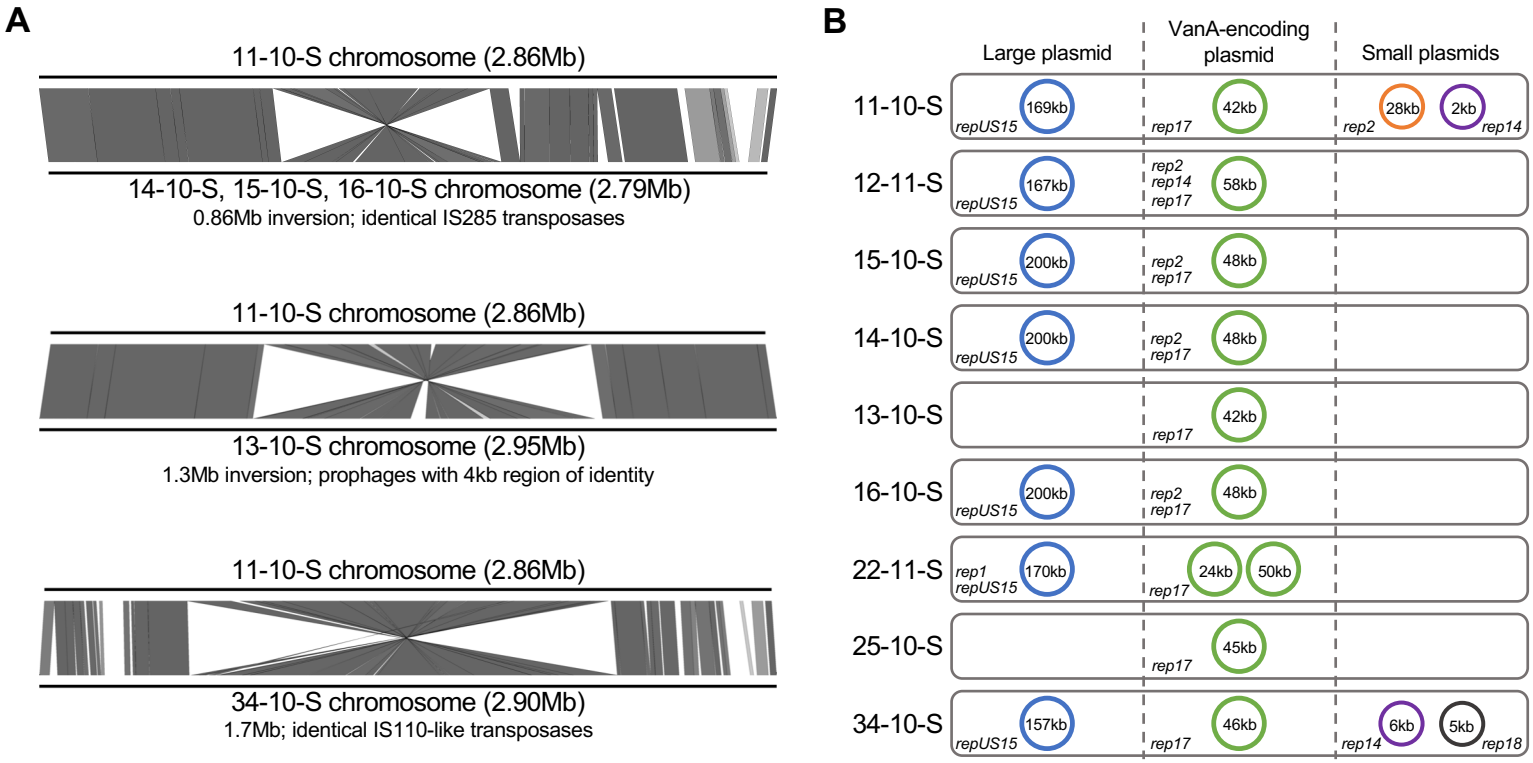

Figure S1. Genomic diversity of ST412 reference isolates. (A) Chromosome alignments of ST412 isolates showing three different chromosomal inversions in ST412 isolates from different patients. Horizontal lines represent nucleotide sequences across closed circular chromosomes, and vertical shading indicates regions of nucleotide homology. Nucleotide sequences greater than 5kb having greater than 98% identity are connected, with darker shading corresponding to higher identity. The size of each inversion and the flanking genes are listed below each plot. (B) Plasmid diversity among nine ST412 reference isolates. Plasmid sizes are indicated inside each circle, and *rep* genes are noted to the side. Plasmids colors correspond to *rep* types: blue = *repUS15*, green = *rep17*, orange = *rep2*, purple = *rep14*, black = *rep18*.

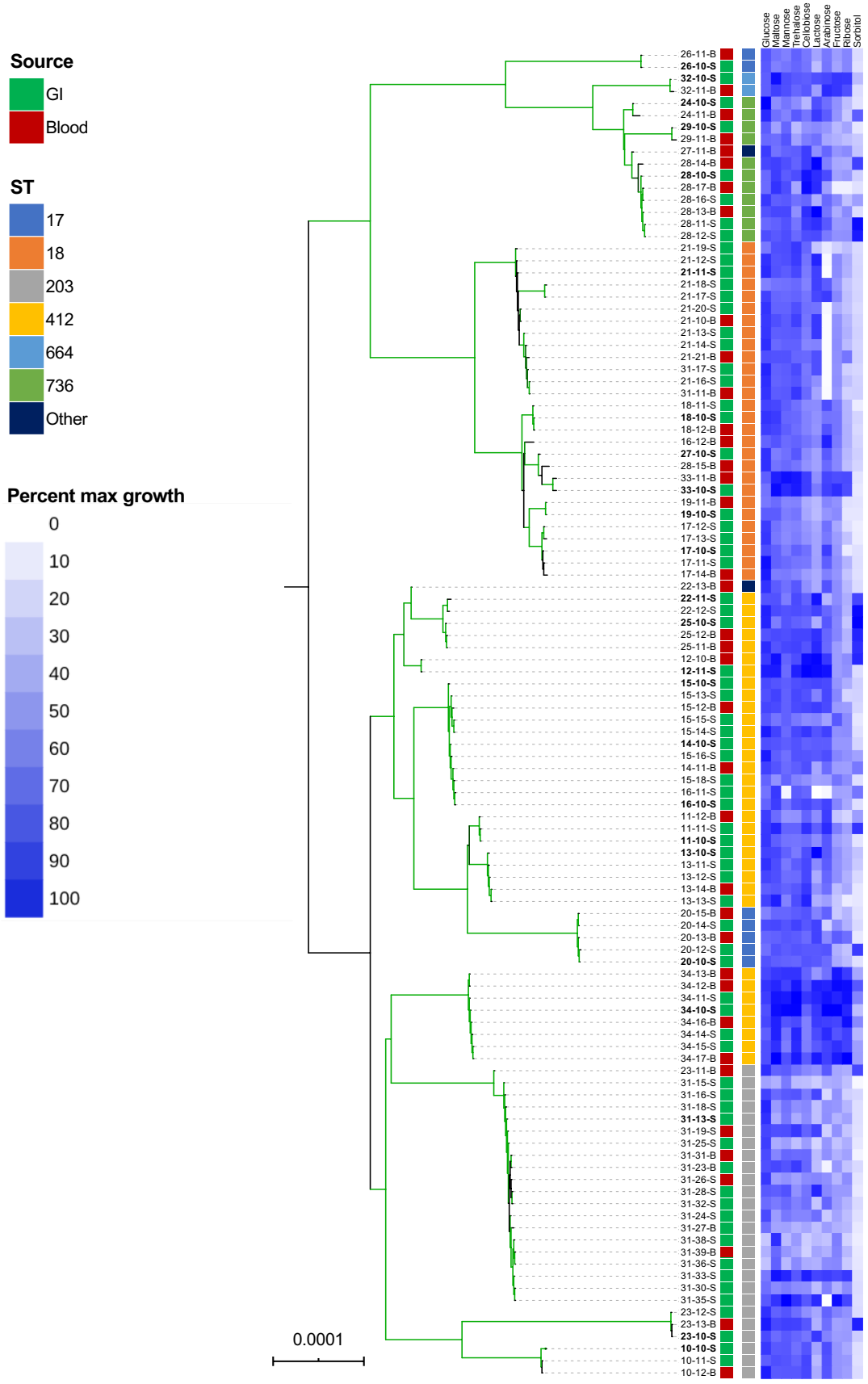

Figure S2. Differential growth of VREfm isolates in different carbon sources. 110 VREfm study isolates were screened for their ability to grow in a complete defined minimal medium supplemented individually with the following carbohydrates (all 0.5%): glucose, maltose, mannose, trehalose, cellobiose, lactose, arabinose, fructose, ribose and sorbitol. The genome phylogeny from Fig. 1C is shown, isolates are annotated by source and ST, and the heatmap to the right shows the percentage of maximum growth of each isolate in each sugar. Results are averaged over three biological replicates.

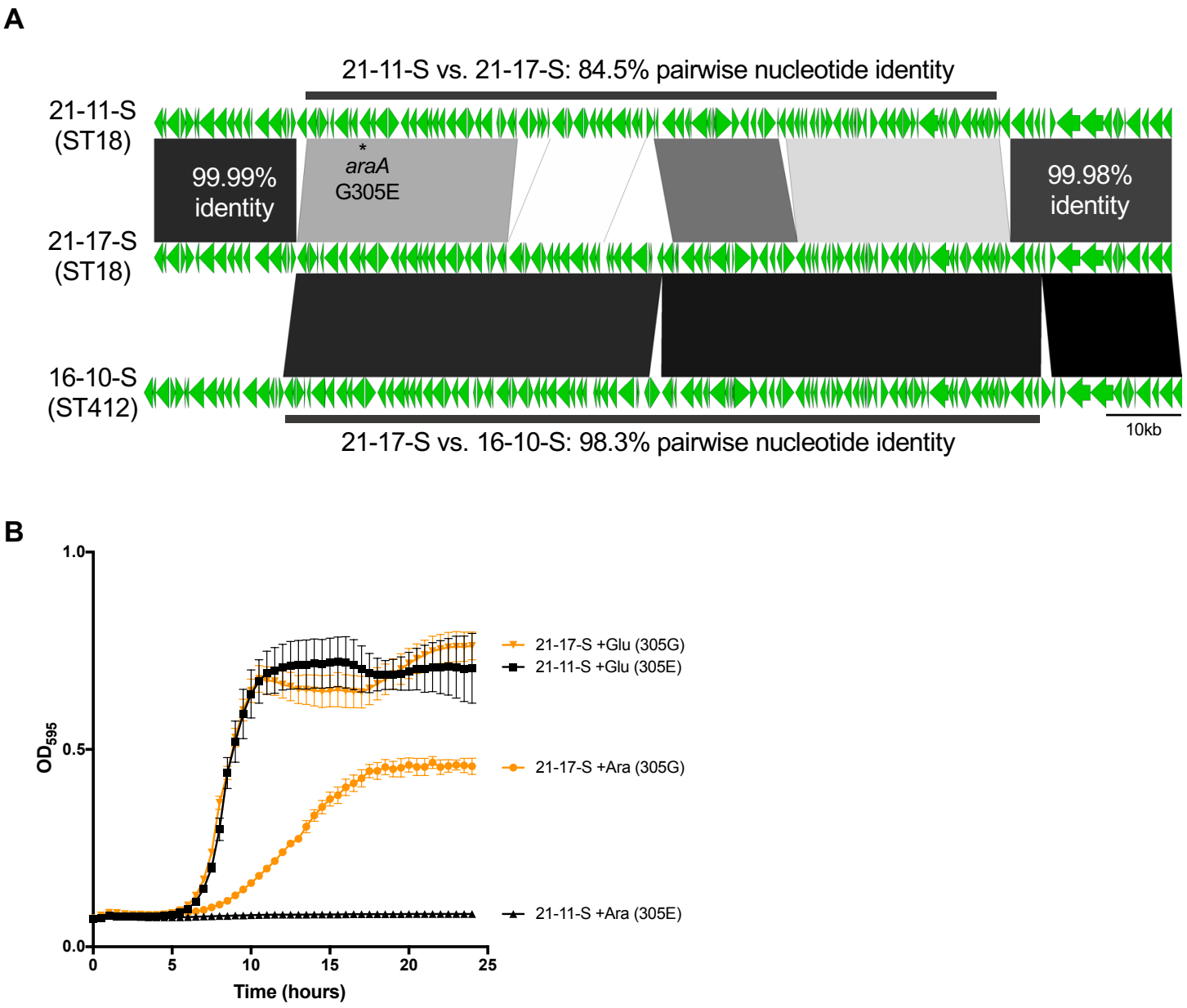

Figure S3. Recombination with a genetically distinct isolate is associated with restored arabinose growth in ST18 isolates harboring a G305E mutation in the L-arabinose isomerase *araA.* (A) Nucleotide alignment of a 152kb chromosomal region in isolates 21-11-S (ST18), 21-17-S (ST18) and 16-10-S (ST412). An approximately 97kb region of recombination, in which the 21-17-S sequence more closely resembles the sequence of 16-10-S, is marked with horizontal lines above and below the figure. Pairwise nucleotide identities are indicated for the recombined and flanking regions. Green arrowheads indicate coding sequences, and greyscale shading indicates nucleotide identity of at least 99% over 1kb, with darker shading corresponding to higher identity. The approximate location of a G305E mutation in the L-arabinose isomerase *araA* is marked with an asterisk. (B) Kinetic growth curves of the 21-11-S (*araA* G305E) and 21-17-S (*araA* wild type) isolates in complete defined medium supplemented with glucose (+Glu) or arabinose (+Ara). Optical density at 595nm (OD_{595}) was measured every 30 minutes during growth at 37°C, and mean values +/- standard deviations are plotted for at least three replicates of each isolate. The *araA* allele of each isolate is listed to the right of the growth curves.

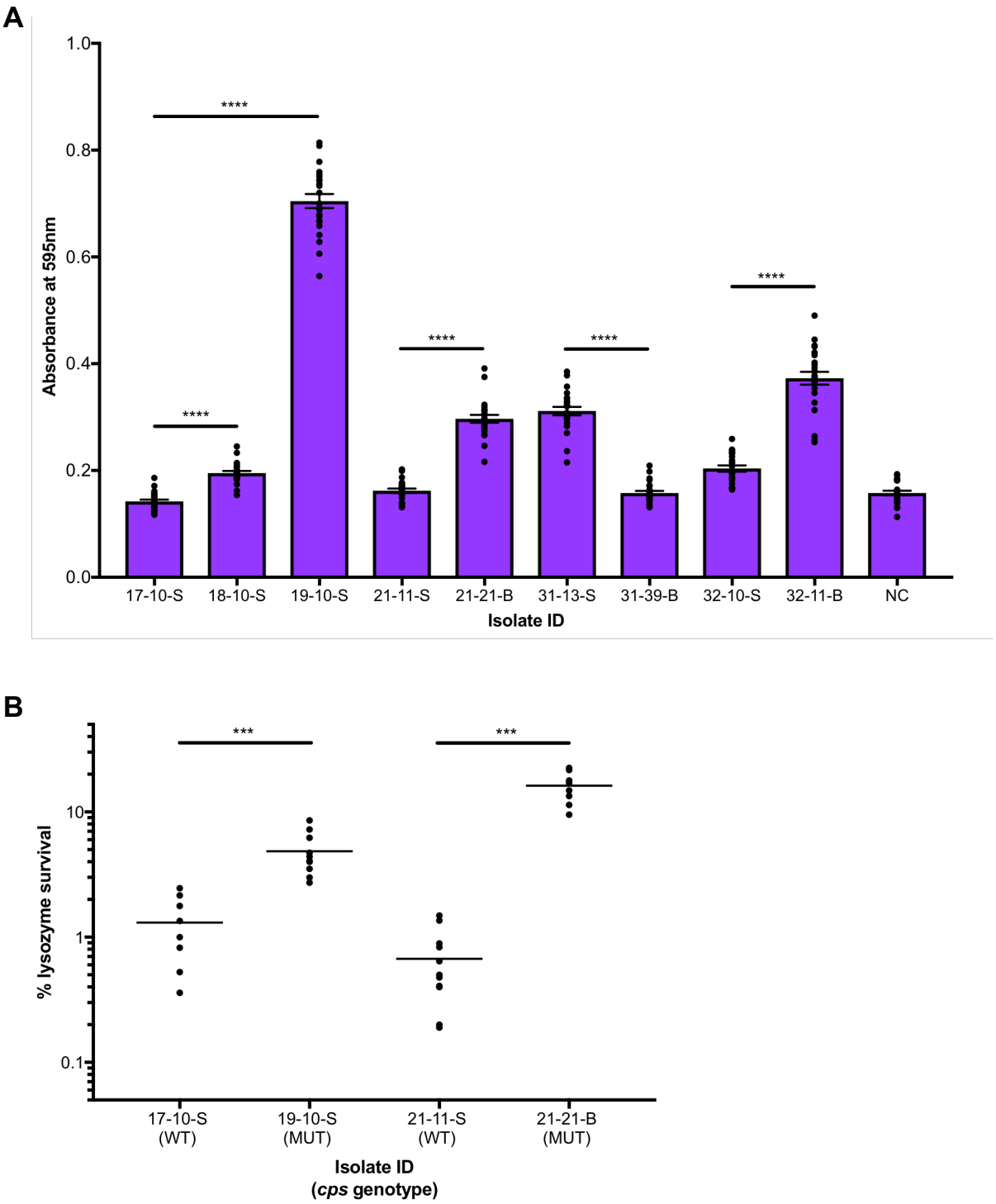

Figure S4. Isolates with *cps* locus mutations form more biofilm when grown on fibronectin, and are more resistant to lysozyme treatment when grown in biofilms. (A) Biofilm formation measured in the nine VREfm isolates tested in Fig. 4B and 4C, grown in fibronectin-coated wells. Bars shown mean crystal violet absorbance values and error bars show standard errors of biological triplicate experiments, each with eight technical replicates. NC = negative control. **** = $p<0.0001$ by two-tailed t-test. (B) Lysozyme survival among two pairs of matched *cps* wild type (WT) and mutant (MUT) isolates grown in a biofilm. Biofilms were grown for 24 hours and were treated for 30 minutes with 10mg/mL lysozyme. Biofilm cells were resuspended and were then plated to determine CFU/mL. Percentage survival is shown versus no-lysozyme controls. Horizontal lines showing mean values of at least eight replicate experiments. *** = $p<0.001$ by two-tailed t-test.