

Table S1: Primer Sequences used in this study

Primer Name	Sequence	Purpose
<i>copYFor</i>	5' CTTATTGCTGGTCCGCTTCAAC 3'	qRT-PCR
<i>copYRev</i>	5' CGACACTTGCTGCTCTAATGCCTC 3'	qRT-PCR
<i>copAFor</i>	5' GGGTCAATCAATGGTCAGGGAAG 3'	qRT-PCR
<i>copAFor</i>	5' CAGCAATCTTGGCAATGGGTG 3'	qRT-PCR
<i>copZFor</i>	5' GACAATGTCACCAAACGC 3'	qRT-PCR
<i>copZFor</i>	5' TGGTTCCTTTCAGTGCTCG 3'	qRT-PCR
<i>GtfB-For</i>	5' ACACTTTCGGGTGGCTTG 3'	qRT-PCR
<i>GtfB-Rev</i>	5' GCTTAGATGTCACTTCGGTTG 3'	qRT-PCR
<i>GtfC-FOR</i>	5' CCAAAATGGTATTATGGCTGTCTG 3'	qRT-PCR
<i>GtfC-REV</i>	5' TGAGTCTCTATCAAAGTAACGCAG 3	qRT-PCR
<i>16SrRNA-FOR</i>	5' CTTACCAGGTCTTGACATCCCG 3'	qRT-PCR
<i>16SrRNA-REV</i>	5' ACCCAACATCTCACGACACGAG 3'	qRT-PCR
<i>comS-For</i>	5' TTTTGATGGGTCTTGACTGG 3'	qRT-PCR
<i>comS-Rev</i>	5' TTTATTACTGTGCCGTGTTAGC 3'	qRT-PCR
<i>comX-For</i>	5' ACTGTTTGTCAAGTGGCGG 3'	qRT-PCR

<i>comX-Rev</i>	5' TGCTCTCCTGCTACCAAGCG 3'	qRT-PCR
<i>GbpB-For</i>	5' AGCAACAGAAGCACAACCATCAG 3'	qRT-PCR
<i>GbpB-Rev</i>	5' CCACCATTACCCAGTAGTTTCC 3'	qRT-PCR
<i>copYAZ P1</i>	5' AGTATGTTTGTAGTCAGTTGCG 3'	Gene Deletion
<i>copYAZ P2</i>	5' <u>GCGCGCCT</u> AATCGTTGAAGCGGACC 3'	Gene Deletion
<i>copYAZ P3</i>	5' <u>GGCCGGCC</u> CAGGAAATCCAAGCAAGTGG 3'	Gene Deletion
<i>copYAZ P4</i>	5' ATACCAGACTCGCATCATAAGC 3'	Gene Deletion
<i>Ermcst- F</i>	5' <u>GCGCGCC</u> CCGGGCCAAAATTTGTTTGAT 3'	Gene Deletion
<i>Ermcst- B</i>	5' <u>GGCCGGCC</u> AGTCGGCAGCGACTCATAGAAT 3'	Gene Deletion
<i>compForE</i>	5' <u>GAATTCGAATTC</u> AATGTAGATGAAAGGAGC 3'	Cloning in pIB166
<i>compRevX</i>	5' <u>CTCGAGCTCGAG</u> GGTATATGAAGCCTACTT 3'	Cloning in pIB166
<i>compRevX</i>	5' <u>CTCGAGCTCGAG</u> GGTATATGAAGCCTACTT 3'	Cloning in pJET
<i>compForP</i>	5' <u>CTGCAGCTGCAG</u> AATGTAGATGAAAGGAGC 3'	Cloning in pJET

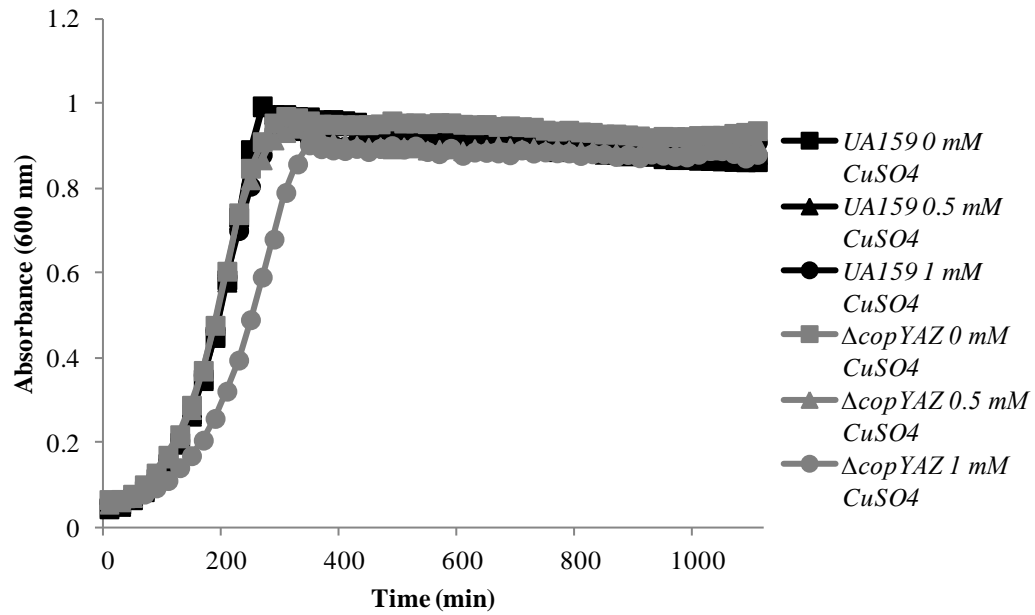


Figure S1: Growth Kinetics under copper stress: UA159 and $\Delta copYAZ$ strains cultivated under varying concentrations of $CuSO_4$. Results are the representative of six independent experiments conducted with duplicates for each strain.

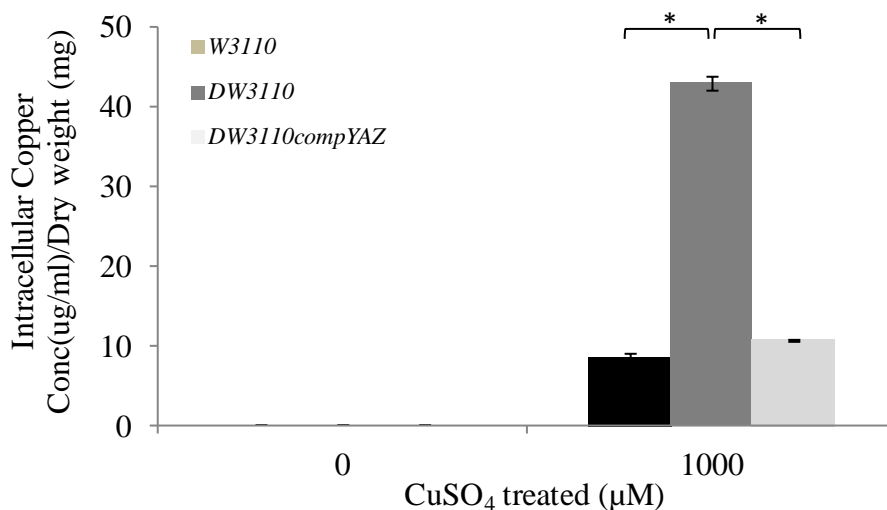
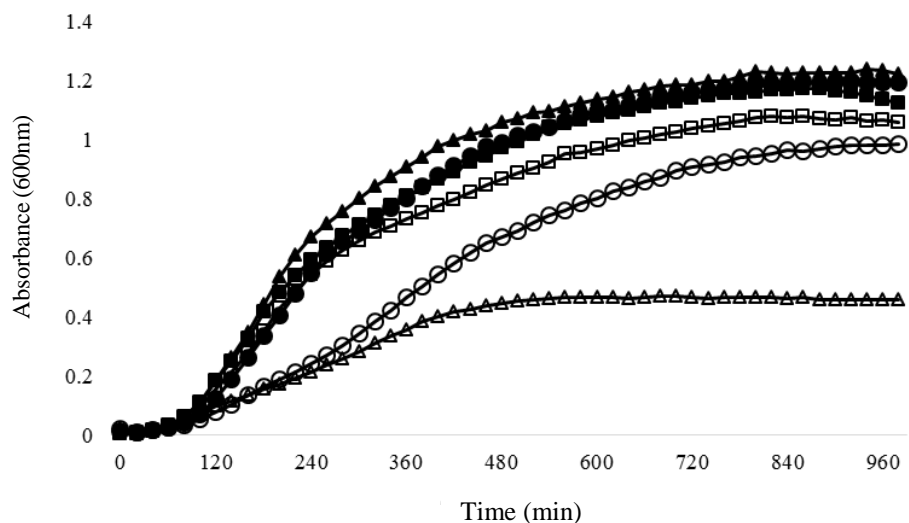


Figure S2 Growth kinetics and transport studies using *E. coli* strains. A) *E. coli* strains cultivated in the presence or absence of 2 mM CuSO₄. Results are representative of six independent experiments conducted with duplicates for each strain. Legend: squares indicate wild type, triangles indicate *cop* mutant, circles indicate complemented strain of *E. coli* strains, solid-filled indicate strains grown in the absence of CuSO₄, and hollow icons indicate strains grown in the presence of 2 mM CuSO₄. B) Intracellular copper concentration normalized to dry weight of cells of *E. coli* wild type W3110 (black bar), DW3110 (grey bar), and DW3110*compYAZ* (white bar) was quantified using ICP-AES. Cells were grown in the presence or absence of 1 mM CuSO₄ until the mid-logarithmic growth phase. Cells were lysed and intracellular copper concentration was normalized with cell dry weight. Results shown here are the mean values obtained from three independent experiments \pm standard error (**P* < 0.05).

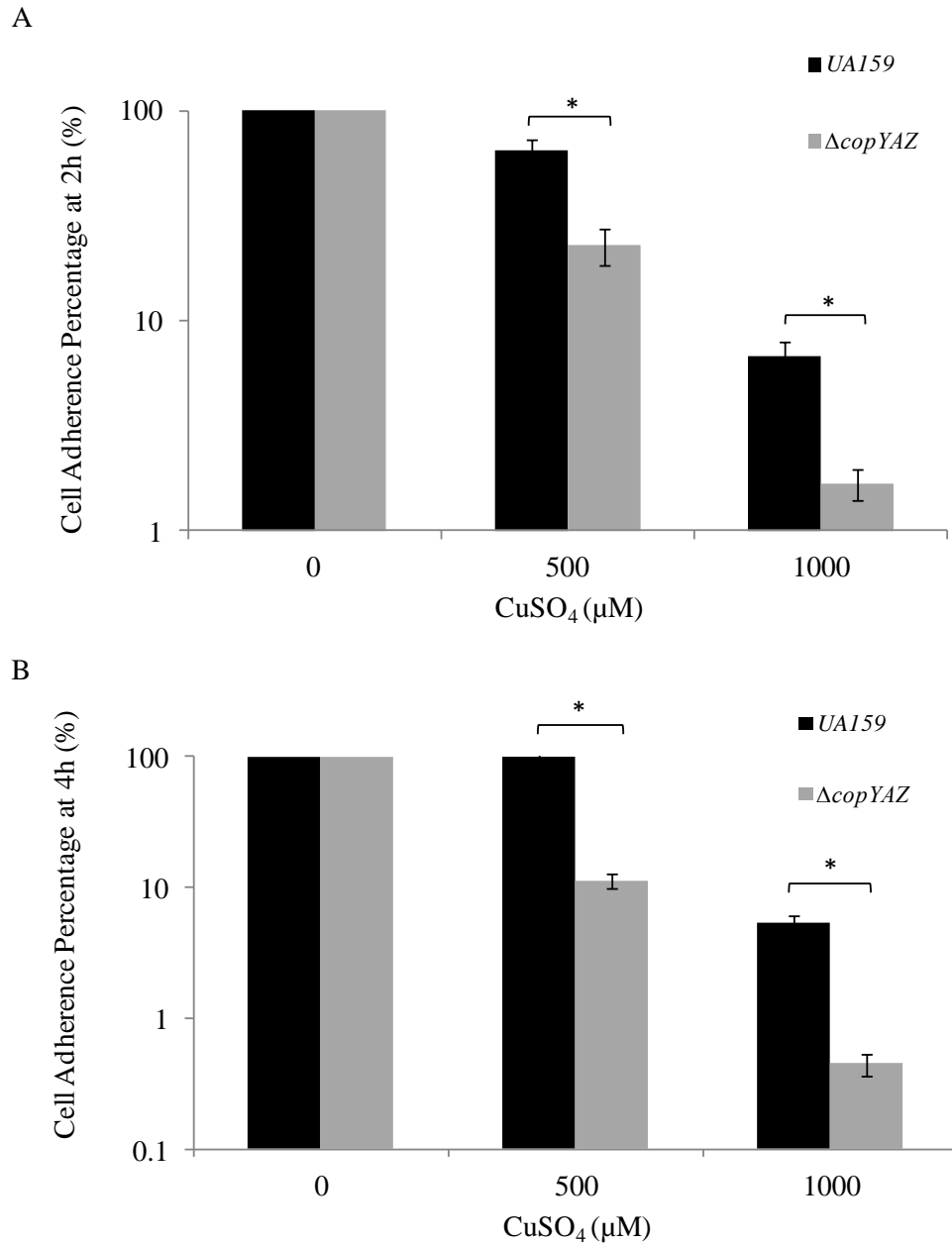


Figure S3 Cell adherence assays. Percentage of the cells (log scale) adhered to the polystyrene surface after A) 2h and B) 4h incubation using UA159 (black bars) and $\Delta copYAZ$ (grey bars) in the presence of varying concentrations of $CuSO_4$ relative to no copper. Results shown represent the mean values obtained from three independent experiments with three replicates for each strain \pm standard error ($*P < 0.05$).

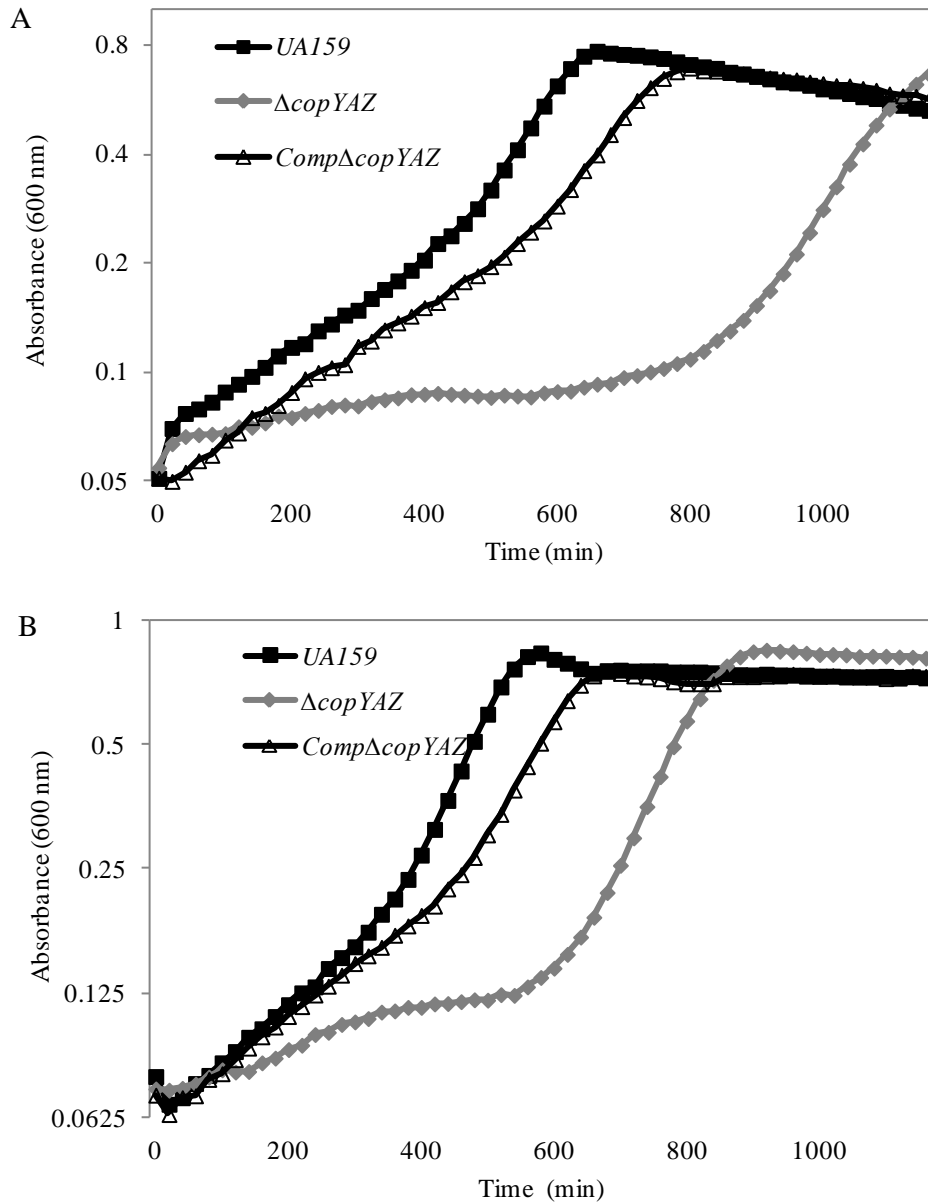


Figure S4 Growth Kinetics under oxidative stressors: UA159, $\Delta copYAZ$ and $comp\Delta copYAZ$ to grown in the presence of the oxidative stressors A) paraquat (25 mM) paraquat and B) H₂O₂ (0.0045%). Results are the representative of six independent experiments conducted with duplicates for each strain.

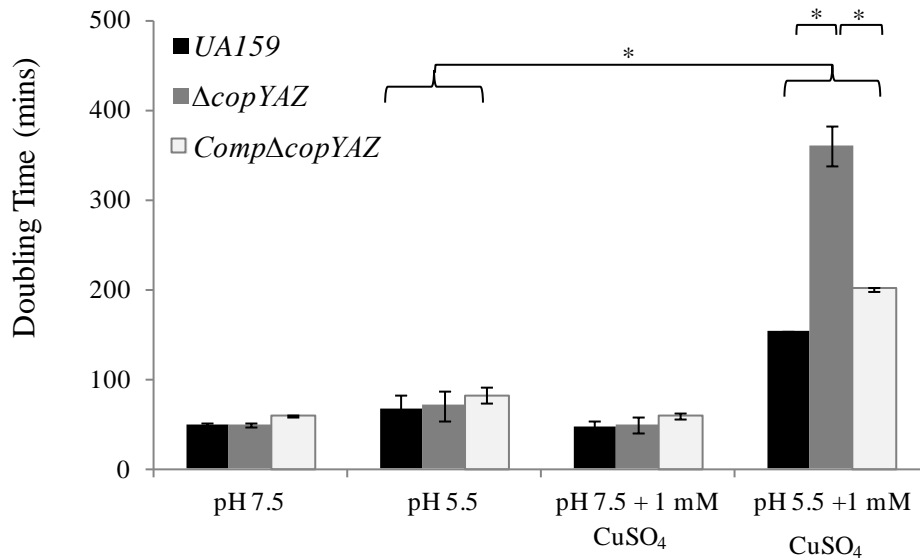


Figure S5 Doubling times under acid stress with or without copper. Evaluation of *S. mutans* doubling time in the presence of various stressors using wild type UA159 (black bars), $\Delta copYAZ$ (grey bars), and *comp* $\Delta copYAZ$ (light grey bars). Results are the mean of three independent experiments with duplicate samples of each strain \pm standard error (* $P < 0.05$).

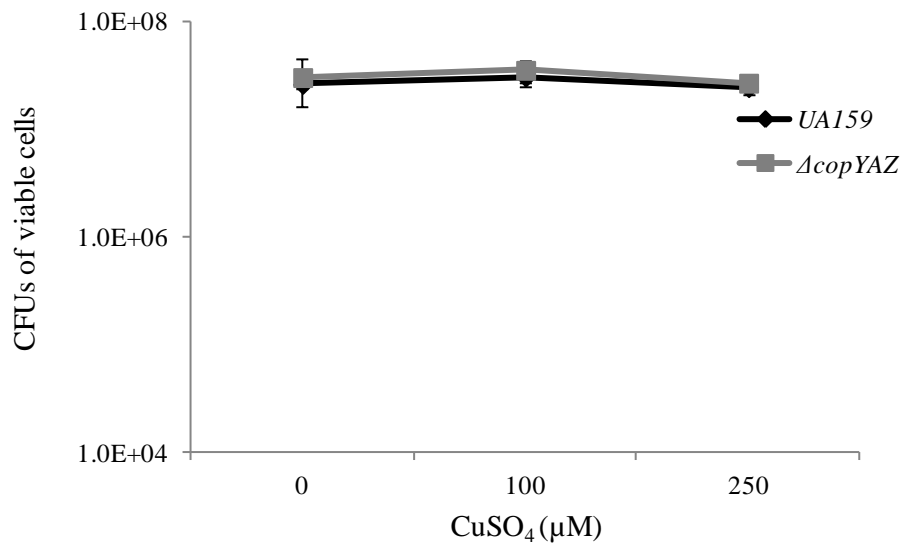


Figure S6 Colony forming units of viable cells at different copper concentrations. *S. mutans* colony forming unit of the total viable cells (during the transformation frequency assays) in the presence of varying copper concentrations using wild type UA159 (black line), $\Delta copYAZ$ (grey line). Results are the mean of three independent experiments with duplicate samples of each strain \pm standard error (* $P < 0.05$).