

Table S1. Genes differentially expressed after treatments with methylglyoxal (MG), fructose (Fru), and glucose (Glc) relative to untreated controls. Results of H₂O₂ treatment was obtained from a previous study (1). These genes are discussed in the manuscript and organized based on functional categories. See Table S2 for the complete list. Red and green indicate increased and decreased expression, respectively, with shades denoting degrees of change.

SMU Number	Gene Name	Gene Function	MG	Fru	Glc	H ₂ O ₂
Thiol homeostasis/oxidative stress						
140	<i>gshR</i>	glutathione reductase		3.53	4.09	
141	<i>SMU_141</i>	conserved hypothetical protein	0.63	3.78	4.08	
		glutamate--cysteine ligase (gamma ECS)				
267	<i>gshAB</i>		1.14	1.29	1.00	
382	<i>SMU_382c</i>	possible oxidoreductase	3.67			
383	<i>SMU_383c</i>	undetermined reductase or epimerase	3.73			
463	<i>trxB</i>	thioredoxin reductase (NADPH)	1.90	1.31		1.75
629	<i>sodA</i>	superoxide dismutase	3.00	2.89	1.02	2.22
667	<i>nrdB</i>	ribonucleotide reductase, small subunit	3.50	1.31	0.66	1.54
668	<i>nrdA</i>	ribonucleotide reductase, large subunit	3.07	1.09		1.37
669	<i>nrdH</i>	glutaredoxin	2.63	0.83	-0.63	1.48
676	<i>gapN</i>	NADP-dependent G3P dehydrogenase	1.21	1.20	0.93	1.40
677	<i>rmeA</i>	transcriptional regulator, MerR family	2.46	1.01		
678	<i>ycgG</i>	aldo/keto oxidoreductase	3.15	1.21	0.96	
679	<i>ycgG</i>	aldo/keto oxidoreductase	3.24	1.49	1.12	
		carboxymuconolactone decarboxylase family protein				
680	<i>SMU_680</i>		3.20	1.22	0.71	
681	<i>SMU_681</i>	conserved hypothetical protein	3.14	1.14		
728	<i>SMU_728</i>	oxidoreductase		1.03		
764	<i>ahpC</i>	alkyl hydroperoxide reductase subunit C	3.76	2.18		2.33
765	<i>ahpF</i>	alkyl hydroperoxide reductase subunit F	4.22	2.30		2.24
837	<i>ycgG</i>	aldo/keto oxidoreductase			1.39	
838	<i>gor</i>	glutathione reductase	3.44	1.51	1.17	2.14
924	<i>tpx</i>	thiol peroxidase	3.01	2.48	1.06	2.72
991	<i>SMU_991</i>	possible ribonucleotide reductase	1.62	1.26		1.93
		oxidoreductase, short-chain				
1040	<i>ydfG</i>	dehydrogenase/reductase	1.34			
1117	<i>nox</i>	H ₂ O-forming NADH Oxidase	1.81	1.42	0.97	1.94
1296	<i>gst</i>	glutathione S-transferase	2.70	2.43	1.46	1.79
		oxidoreductase, short-chain				
1473	<i>SMU_1473c</i>	dehydrogenase/reductase family	1.21	1.05		
1602	<i>frp</i>	NAD(P)H-flavin oxidoreductase	1.78	1.19	1.16	
1603	<i>lguL</i>	lactoylglutathione lyase	2.14	1.78	1.70	

SMU Number	Gene Name	Gene Function	MG	Fru	Glc	H ₂ O ₂
1869	<i>trxA</i>	thioredoxin	1.63	2.28	1.34	2.25
2070	<i>SMU_2070</i>	conserved hypothetical protein	3.21			
2071	<i>nrdG</i>	ribonucleoside-triphosphate reductase activating protein	3.66			
2072	<i>SMU_2072c</i>	possible acetyltransferase, GNAT family	3.70			-1.22
2073	<i>SMU_2073c</i>	conserved hypothetical protein	3.59	-1.09	-1.61	
2074	<i>nrdD</i>	anaerobic ribonucleoside-triphosphate reductase	3.52	-1.40		
Metal homeostasis						
182	<i>sloA</i>	ABC transporter for iron/manganese	-1.87	-2.89	-1.51	-1.01
183	<i>sloB</i>	manganese ABC transporter permease element	-0.92	-1.20		-0.96
184	<i>sloC</i>	ABC transporter element, iron/manganese binding protein			-1.34	-1.14
185	<i>SMU_185</i>	hypothetical protein		-0.60	-1.51	-1.56
186	<i>sloR</i>	metal-dependent transcriptional regulator	-0.77			-1.01
247	<i>sufC</i>	ABC transporter, ATP-binding protein	2.24	0.98	0.72	1.89
248	<i>sufD</i>	ABC transporter permease	2.56	1.22	1.09	1.82
249	<i>sufS</i>	class-V aminotransferase, NifS protein homolog,	2.83	1.31	0.96	1.80
250	<i>sufU</i>	nitrogen fixation-like protein, NifU	2.91	1.01		1.90
251	<i>sufB</i>	ABC transporter permease	2.76	1.08	0.77	1.70
424	<i>copY</i>	negative transcriptional regulator, CopY	3.82	0.84	1.23	1.24
426	<i>copA</i>	copper-transporting ATPase	3.72	0.64	0.77	1.18
427	<i>copZ</i>	copper chaperone	3.47	0.82		1.09
540	<i>dpr</i>	peroxide resistance protein/iron binding protein	2.96	1.87		1.99
569	<i>feoA</i>	ferrous ion transport protein A	-2.44			-1.17
570	<i>feoB</i>	ferrous ion transport protein B	-1.65	-0.66	0.77	-1.00
1561	<i>trkB</i>	potassium uptake protein B	2.20	1.64		
1562	<i>trkA</i>	potassium uptake protein A	2.32	1.53		
1993	<i>adcB</i>	zinc ABC transporter, permease				1.08
1994	<i>adcC</i>	zinc ABC transport, ATP-binding protein				1.10
1995	<i>adcR</i>	zinc transport transcriptional repressor				1.04
2057	<i>zccE</i>	zinc/cadmium-efflux ATPase	-0.42	2.44	1.17	
DNA and protein repair						
80	<i>hrcA</i>	heat-inducible transcription repressor	-2.47			
81	<i>grpE</i>	co-chaperone protein GrpE	-2.12			
82	<i>dnaK</i>	chaperone protein, DnaK	-1.33			
561	<i>mutT</i>	mutator protein, Nudix hydrolase	2.46			
562	<i>clpE</i>	ATP-dependent protease	2.86	1.44		1.42
809	<i>uvrB</i>	excinuclease ABC subunit B			1.26	
956	<i>clpL</i>	ATP-dependent Clp protease	1.77	1.13		1.11
1649	<i>exoA</i>	exodeoxyribonuclease III	1.68	1.19	1.10	1.93
1650	<i>end3</i>	endonuclease III	1.82			1.56
1850	<i>pepP</i>	XAA-Pro aminopeptidase	1.78	1.16	0.89	1.45

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1851	<i>uvrA</i>	excinuclease ABC subunit A	1.34	1.03		1.70
1865	<i>mutY</i>	A/G-specific adenine glycosylase	2.41	1.24	0.66	1.66
2029	<i>clpC</i>	ATP-dependent Clp protease	1.11			
2036	<i>pepO</i>	endopeptidase O	1.61	1.18	1.07	1.42
2085	<i>recA</i>	recombinase A		1.18		
Transcription regulators						
61	<i>comR</i>	transcriptional regulator	1.01			1.55
363	<i>glnR</i>	glutamine synthetase repressor		-2.29		
381	<i>plcR</i>	transcriptional regulator	1.45			
486	<i>liaS</i>	two-component sensor histidine kinase				-1.00
487	<i>liaR</i>	two-component response regulator				-1.01
576	<i>lytT</i>	response regulator	-1.55	-1.58		
577	<i>lytS</i>	sensor histidine kinase	-2.26	-1.51		
593	<i>perR</i>	ferric uptake regulator protein	1.06	1.08		1.03
660	<i>spaK</i>	histidine kinase		-1.05		
661	<i>spaR</i>	transcriptional regulator	1.72			
928	<i>relS</i>	sensor histidine kinase	1.00			
1037	<i>phoR</i>	histidine kinase	2.12			
1038	<i>ycbL</i>	response regulator	1.79			
1065	<i>nagR</i>	transcriptional regulator, GntR family	-1.42			
1097	<i>SMU_1097c</i>	transcriptional regulator	1.37		-1.42	
1226	<i>SMU_1226c</i>	histidine protein kinase	1.03			
1287	<i>pmrA</i>	transcriptional regulator	-1.03		-1.48	1.12
1398	<i>irvR</i>	phage associated repressor protein	-1.60			
1515	<i>vicX</i>	<i>gtfB/C</i> regulator	1.28			
1516	<i>vicK</i>	two-component sensor histidine kinase	1.17			
1814	<i>scnK</i>	histidine kinase, ScnK homolog	2.50	1.37		1.58
1815	<i>scnR</i>	response regulator, ScnR homolog	2.26	1.37	0.59	1.72
1854	<i>hdrR</i>	high density responsive regulator		1.35		
1915	<i>comC</i>	competence stimulating peptide	2.15			
1916	<i>comD</i>	histidine kinase	2.95	1.01		1.24
1917	<i>comE</i>	response regulator	2.78			1.31
1924	<i>gcrR</i>	response regulator for glucan-binding protein		-1.77	-1.09	
1963	<i>levQ</i>	sugar-binding periplasmic protein		-1.02	-1.23	-1.07
1964	<i>levR</i>	two-component response regulator			-1.07	-1.20
1965	<i>levS</i>	histidine kinase				-1.12
1966	<i>levT</i>	ABC transport ribose-binding protein, periplasmic				-1.19
2027	<i>lexA</i>	transcriptional regulator/repressor	3.03	3.08	1.09	1.29
2084	<i>spxA2</i>	oxidative stress regulator		1.30		
Osmoprotection						
1057	<i>satE</i>	acid tolerance protein		1.05		
1058	<i>satD</i>	acid tolerance protein		1.26		
1060	<i>ffh</i>	signal recognition particle		1.13		

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1061	<i>ylxM</i>	DNA-binding protein		1.22		
1062	<i>busAB</i>	glycine-betaine binding ABC transporter permease	1.09	1.57		
1063	<i>opuAA</i>	amino acid ABC transporter, ATP-binding protein		1.68		
2116	<i>opuCa</i>	ABC transporter, ATP-binding protein		1.05		
2117	<i>opuCb</i>	ABC transporter permease		1.12		
2118	<i>opuCc</i>	ABC transporter, substrate-binding protein		1.13		
2119	<i>opuCd</i>	ABC transport permease		1.07		
F1F0 ATPase						
1527	<i>atpA</i>	ATPase epsilon subunit		-1.06		
1528	<i>atpB</i>	ATPase beta subunit		-1.13		
1529	<i>atpC</i>	ATPase gamma subunit		-1.31		
1530	<i>atpD</i>	ATPase alpha subunit		-1.20		
1531	<i>atpE</i>	ATPase delta subunit		-1.61	-1.25	
1532	<i>atpF</i>	ATPase b subunit		-1.35		
1533	<i>atpG</i>	ATPase a subunit		-1.40		
1534	<i>atpH</i>	ATPase c subunit		-1.26		
Fatty acid biosynthesis						
1735	<i>accD</i>	acetyl-CoA carboxylase beta subunit	0.72	-1.15		
1736	<i>accC</i>	acetyl-CoA carboxylase biotin carboxylase subunit	0.61	-1.29		
1737	<i>fabZ</i>	(3R)-hydroxymyristoyl-(acyl carrier protein) dehydratase	0.77	-1.38		
1738	<i>accB</i>	biotin carboxyl carrier protein of acetyl-CoA carboxylase	0.80	-1.46		
1739	<i>fabF</i>	3-oxoacyl-(acyl-carrier-protein) synthase	0.69	-1.51		
1740	<i>fabG</i>	3-oxoacyl-acyl-carrier-protein reductase		-1.78		
1741	<i>fabD</i>	[acyl-carrier-protein] S-malonyltransferase		-1.74		
1742	<i>fabK</i>	trans-2-enoyl-ACP reductase II		-1.56		
1743	<i>acp</i>	acyl carrier protein		-1.55	-1.56	
1744	<i>fabH</i>	3-oxoacyl-[acyl-carrier-protein] synthase III	-0.76	-1.39		
1745	<i>fabT</i>	transcriptional regulator, MarR family	-1.11	-1.06	-0.66	
Other stress/competence-related proteins						
20	<i>mreC</i>	cell shape-determining protein MreC	-2.19	-1.36	-1.45	
21	<i>mreD</i>	cell shape-determining protein MreD	-1.95	-2.02	-0.59	
150	<i>nImA</i>	non-lantibiotic mutacin IV A				-1.30
151	<i>nImB</i>	non-lantibiotic mutacin IV B				-1.13
152	<i>SMU_152</i>	immunity protein for NImAB			-1.88	-1.64
153	<i>SMU_153</i>	hypothetical protein				-1.75
284	<i>nImT</i>	transport and processing of non-lantibiotic mutacins		-1.24	-1.38	-1.05

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285	<i>nImE</i>	transport and processing of non-lantibiotic mutacins		-1.13	-1.16	-1.16
474	<i>luxS</i>	S-ribosylhomocysteine lyase (S-ribosylhomocysteinase)	-1.34			
503	<i>SMU_503c</i>	hypothetical protein	-1.86	-1.69	-1.58	-1.11
921	<i>rcrR</i>	transcriptional regulator	1.35		-1.31	1.21
922	<i>rcrP</i>	ABC transporter, ATPase component	1.75			1.07
923	<i>rcrQ</i>	AB transporter, ATPase component	1.87			1.08
1046	<i>relQ</i>	GTP pyrophosphokinase	-1.08	1.03		
574	<i>lrgB</i>	effector of murein hydrolase	-2.42	-2.46	-1.11	
575	<i>lrgA</i>	murein hydrolase regulator	-2.68	-3.00	-1.63	
1700	<i>cidB</i>	LrgB-like protein; possible murein hydrolase regulator	1.93	1.39		1.31
1701	<i>cidA</i>	conserved hypothetical protein	1.90	1.05		1.29
1702	<i>pgpB</i>	uncharacterized phosphatase	1.73	1.82		1.59
1703	<i>SMU_1703c</i>	conserved hypothetical protein	1.41	1.78		1.75
1980	<i>SMU_1980c</i>	conserved hypothetical protein	3.14	2.29	1.08	
1981	<i>comGF</i>	competence protein G	3.42	2.29		
1982	<i>SMU_1982c</i>	conserved hypothetical protein	2.76	1.96		
1983	<i>comYD</i>	late competence protein	2.20			
1984	<i>comYC</i>	late competence protein	2.50	1.26		
1985	<i>comYB</i>	late competence protein	2.19			
1987	<i>comYA</i>	late competence protein	2.28			
1988	<i>SMU_1988c</i>	probable DNA binding protein	2.80	1.43		2.19
1997	<i>comX</i>	competence-specific sigma factor	-1.57		-1.46	
2044	<i>relA</i>	GTP pyrophosphokinase				1.22

Carbohydrate metabolism

99	<i>fbaA</i>	fructose-bisphosphate aldolase		-1.25		
100	<i>nigB</i>	nigerose PTS system, IIB component		-1.52		
105	<i>nigR</i>	nigerose operon transcriptional repressor		-1.15		
113	<i>pfk</i>	fructose-1-phosphate kinase		1.39	1.13	
114	<i>fruC</i>	PTS system, fructose-specific IIBC component			1.08	
119	<i>adh</i>	alcohol dehydrogenase class III	1.02	1.74	1.76	
127	<i>adhA</i>	acetoin dehydrogenase E1 component alpha subunit	2.76			1.72
128	<i>adhB</i>	acetoin dehydrogenase E1 component beta subunit	3.33			1.88
129	<i>adhC</i>	dihydrolipoamide S-acetyltransferase	3.50			1.91
130	<i>adhD</i>	dihydrolipoamide dehydrogenase	3.30	1.27		1.96
131	<i>lplA</i>	lipoate-protein ligase	3.43	1.39		1.88
135	<i>mleR</i>	transcriptional regulator	-1.05			
137	<i>mleS</i>	malolactic enzyme	0.62	4.00	4.36	
138	<i>mleP</i>	malate permease/auxin efflux carrier		3.78	4.08	
139	<i>oxdC</i>	oxalate decarboxylase		3.80	4.33	
148	<i>adhE</i>	alcohol-acetaldehyde dehydrogenase	-1.11		1.26	

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270	<i>sgaT</i>	ribulose monophosphate PTS pathway enzyme IIC			1.36	
271	<i>ptxB</i>	L-ascorbate-specific PTS enzyme IIB component	1.88	1.00	0.96	1.19
272	<i>ptxA</i>	L-ascorbate-specific PTS enzyme IIA component	2.13	1.04	1.03	0.90
273	<i>rmpD</i>	hexulose-6-phosphate synthase	2.30	1.11	0.87	1.01
274	<i>rmpE</i>	hexulose-6-phosphate isomerase	2.48	1.17	1.01	1.16
275	<i>rmpF</i>	L-ribulose 5-phosphate 4-epimerase	2.59	1.66	1.06	1.11
276	<i>SMU_276c</i>	hypothetical protein	2.37		-2.62	
311	<i>srlA</i>	sorbitol PTS system enzyme IIC2		1.02		
312	<i>srlE</i>	sorbitol PTS system enzyme IIBC		1.36		
313	<i>srlB</i>	sorbitol PTS system enzyme IIA		1.68		
402	<i>pfl</i>	pyruvate formate-lyase		-1.49		
507	<i>sppR</i>	transcriptional regulator, DeoR family		4.56		
508	<i>sppA</i>	hexose-phosphate phosphohydrolase		4.56		
674	<i>ptsH</i>	PTS EI	-2.25			
675	<i>ptsI</i>	PTS HPr	-1.14			
754	<i>hprK</i>	HPr (serine) kinase/phosphatase		1.34	1.15	
870	<i>fruR</i>	transcriptional repressor of the fructose operon		1.68		
871	<i>fruK</i>	fructose-1-phosphate kinase		1.99		
872	<i>fruI</i>	fructose-specific PTS system enzyme IIBC component		1.87		
876	<i>msmR</i>	MSM operon regulatory protein	-1.93	-1.26		-1.28
877	<i>agaL</i>	alpha-galactosidase	-1.46	-1.73		-1.36
878	<i>msmE</i>	ABC transporter, sugar-binding protein		-1.79		-1.25
879	<i>msmF</i>	ABC transporter, sugar permease protein		-1.95		
880	<i>msmG</i>	ABC transporter permease		-1.78		
881	<i>gtfA</i>	sucrose phosphorylase		-1.64		
882	<i>msmK</i>	ABC transporter ATP-binding protein		-1.54		
883	<i>dexB</i>	glucan 1,6-alpha-glucosidase		-1.40		
886	<i>galK</i>	galactokinase		-1.46		
910	<i>gtfD</i>	glucosyltransferase-S		1.24	1.82	
1004	<i>gtfB</i>	glucosyltransferase-I			1.82	
1005	<i>gtfC</i>	glucosyltransferase-SI		-1.10		
1184	<i>mtlR</i>	transcriptional regulator	-1.05			
1185	<i>mtlA</i>	mannitol PTS EII	-1.73			
1396	<i>gbpC</i>	glucan-binding protein C	2.39	1.32	1.27	1.28
1451	<i>aldB</i>	alpha-acetolactate decarboxylase	2.86			1.66
1452	<i>alsS</i>	alpha-acetolactate synthase	2.33			1.54
1489	<i>lacX</i>	aldose 1-epimerase		1.13		
1492	<i>lacF</i>	PTS system, lactose-specific IIA component		1.85	1.92	
1493	<i>lacD</i>	tagatose-1,6-bisphosphate aldolase		1.39		
1494	<i>lacC</i>	tagatose-6-phosphate kinase		1.59	0.65	

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1495	<i>lacB</i>	galactose-6-phosphate isomerase	-0.78	1.59	0.98	
1496	<i>lacA</i>	galactose-6-phosphate isomerase		1.71	1.18	
1498	<i>lacR</i>	lactose phosphotransferase system repressor		3.11		
1537	<i>glgD</i>	glycogen biosynthesis protein		-1.06		
1564	<i>glg</i>	glycogen phosphorylase		-1.24		
1565	<i>malM</i>	4-alpha-glucanotransferase		-1.02		
1566	<i>malR</i>	maltose operon transcriptional repressor	1.53			1.57
1568	<i>malE</i>	maltose / maltodextrin-binding protein	-1.55	-2.32		
1569	<i>malF</i>	maltodextrin ABC transport system permease		-2.00		
1570	<i>malG</i>	maltose / maltodextrin ABC transport system (permease)		-2.06		
1571	<i>msmK</i>	ABC-type transport system ATP-binding protein (maltose)		-1.89		
1596	<i>celD</i>	cellobiose PTS system IIC	-1.59	-2.92	-1.02	
1597	<i>celX</i>	conserved hypothetical protein	-2.21	-3.06	-2.52	
1598	<i>celC</i>	cellobiose PTS system IIA component	-2.43	-3.00	-1.11	
1599	<i>celR</i>	cellobiose transcriptional regulator	-2.80	-3.62	-1.71	
1600	<i>celB</i>	cellobiose PTS system IIB	-3.15	-2.59	-1.18	
1664	<i>acoB</i>	acetoin utilization protein, acetoin dehydrogenase	1.66	0.76		
1692	<i>pflA</i>	pyruvate-formate lyase activating enzyme	1.36			1.81
1841	<i>scrA</i>	sucrose PTS system EIIBC components	-1.99	-2.13		
1843	<i>scrB</i>	sucrose-6-phosphate hydrolase	-1.65			
1844	<i>scrR</i>	sucrose operon repressor	-1.07	-1.24		
1867	<i>adhB</i>	alcohol dehydrogenase	1.75	2.12	1.97	1.85
1877	<i>manL</i>	mannose PTS system component IIAB	-2.50	-2.79	-0.85	
1878	<i>manM</i>	mannose PTS system component IIC	-1.76	-2.34		
1879	<i>manN</i>	mannose PTS system component IID	-1.24	-2.25	-0.92	
1956	<i>levX</i>	conserved hypothetical protein		2.07		
1957	<i>levG</i>	fructose-specific Enzyme IID component		2.16		
1958	<i>levF</i>	fructose-specific Enzyme IIC component		2.15		
1960	<i>levE</i>	fructose-specific Enzyme IIB component		1.58		
1961	<i>levD</i>	fructose-specific Enzyme IIA component		1.77		
2028	<i>ftf</i>	fructosyltransferase		1.48	1.72	
2047	<i>malT</i>	maltose PTS enzyme II		-1.71		
Amino acid metabolism						
261	<i>aguR</i>	transcriptional regulator	1.42	1.65		
262	<i>argF</i>	ornithine carbamoyltransferase	1.48	2.21	1.16	
263	<i>aguD</i>	amino acid permease /putrescine antiporter	1.49	2.13	1.41	

SMU Number	Gene Name	Gene Function	MG	Fru	Glc	H ₂ O ₂
264	<i>aguA</i>	agmatine deiminase		1.74	1.48	
265	<i>aguC</i>	carbamate kinase		1.18		
563	<i>argF</i>	ornithine carbamoyltransferase		1.00		
663	<i>argC</i>	N-acetyl-gamma-glutamyl-phosphate reductase	3.25	2.41	1.17	
664	<i>argJ</i>	ornithine acetyltransferase / N-acetylglutamate synthase	3.25	2.42	1.94	
665	<i>argB</i>	acetylglutamate kinase	3.32	2.24	1.68	
666	<i>argD</i>	N-acetylornithine aminotransferase	2.94	1.54	1.78	1.09
1665	<i>livF</i>	branched chain amino acid ABC transporter, ATP-binding protein	1.57	0.73		1.05
1666	<i>livG</i>	branched chain amino acid ABC transporter, ATP-binding protein	1.54	0.71	0.14	1.16
1667	<i>livM</i>	branched chain amino acid ABC transporter, permease	1.35			1.29
1668	<i>livH</i>	branched chain amino acid ABC transporter, permease	1.36			1.24
1669	<i>livK</i>	branched-chain amino acid ABC transporter, substrate-binding protein	1.06			1.34
2097	<i>ahrC</i>	arginine transcriptional repressor	-1.22			
Translation						
169	<i>rplM</i>	50S ribosomal protein L13	-1.22	-1.18		
170	<i>rpsI</i>	30S ribosomal protein S9		-1.32		
697	<i>infC</i>	translation initiation factor IF-3	-1.06			
818	<i>rpsU</i>	30S ribosomal protein S21		-1.38		
957	<i>rplJ</i>	50S ribosomal protein L10	-1.80	-1.89		
960	<i>rpl</i>	50S ribosomal protein L7/L12	-1.33	-1.77		
1127	<i>rpsT</i>	30S ribosomal protein S20	-1.03			
1200	<i>rpsA</i>	30S ribosomal protein S1	-1.21			
1288	<i>rplS</i>	50S ribosomal protein L19	-1.06			
1627	<i>rplK</i>	50S ribosomal protein L11	-1.11			
1860	<i>rpsF</i>	30S ribosomal protein S6	-1.16			
2000	<i>rplQ</i>	50S ribosomal protein L17	-1.66			
2002	<i>rpsK</i>	30S ribosomal protein S11	-1.27			
2003	<i>rpsM</i>	30S ribosomal protein S13, N-terminal fragment	-1.06			
2003a	<i>rl36</i>	50S ribosomal protein L36	-1.05		-1.22	
2024	<i>rplD</i>	50S ribosomal protein L4, N-terminal fragment		-1.01		
2025	<i>rplC</i>	50S ribosomal protein L3		-1.06		
2104a	<i>rl32</i>	50S ribosomal protein L32	-1.03			
2135	<i>rpsD</i>	30S ribosomal protein S4		-1.08	-1.03	
TnSmu1						
196	<i>SMU_196c</i>	immunogenic secreted protein (transfer protein)		1.35	1.60	
197	<i>SMU_197c</i>	hypothetical protein		1.09	1.35	
199	<i>SMU_199c</i>	hypothetical protein		1.20	1.14	
200	<i>SMU_200c</i>	hypothetical protein		1.98		

SMU Number	Gene Name	Gene Function	MG	Fru	Glc	H ₂ O ₂
201	SMU_201c	conserved hypothetical protein		1.12		
202	SMU_202c	conserved hypothetical protein		1.80	1.55	
204	SMU_204c	hypothetical protein		1.80	1.57	
205	SMU_205c	conserved hypothetical protein		1.91	1.28	
206	SMU_206c	hypothetical protein		1.48	1.27	
207	SMU_207c	transcriptional regulator			1.53	
		conserved hypothetical protein,				
208	SMU_208c	FtsK/SpoIIIE family		1.01	1.46	
209	SMU_209c	hypothetical protein		1.31	1.56	
210	SMU_210c	hypothetical protein		1.15	1.33	
211	SMU_211c	hypothetical protein		1.31	2.27	
212	SMU_212c	hypothetical protein		1.20	1.50	
213	SMU_213c	hypothetical protein		1.52	1.90	
214	SMU_214c	hypothetical protein		1.27		
215	SMU_215c	hypothetical protein		1.72	1.09	
216	SMU_216c	hypothetical protein		1.37		
217	SMU_217c	conserved hypothetical protein		1.34		
218	SMU_218	transcriptional regulator			-1.27	
CRISPR-Cas						
1402	<i>csn2</i>	conserved hypothetical protein	-1.28	-2.56	-1.95	
1403	<i>cas2</i>	conserved hypothetical protein	-1.49	-2.32	-0.85	
1404	<i>cas1</i>	conserved hypothetical protein	-1.30	-2.24	-1.22	
1405	<i>cas9</i>	conserved hypothetical protein	-1.50	-2.31	-1.74	
1406	SMU_1406c	possible oxidoreductase	-1.52	-1.15		
1753	<i>cas2</i>	conserved hypothetical protein		1.59		1.14
1754	<i>cas1</i>	conserved hypothetical protein		1.91	1.09	1.29
1755	<i>cas1</i>	conserved hypothetical protein		1.70		1.21
1757	<i>cas1</i>	conserved hypothetical protein		1.77		1.04
1758	<i>cas4</i>	conserved hypothetical protein		1.78		1.36
1760	<i>csd2</i>	conserved hypothetical protein	1.03	2.02		1.51
1761	<i>cas8c</i>	conserved hypothetical protein	1.48	1.79		1.63
1762	<i>csd1</i>	conserved hypothetical protein	1.43	1.88		1.87
1763	<i>cas5</i>	conserved hypothetical protein	1.47	1.94		1.88
1764	<i>cas3</i>	conserved hypothetical protein	1.22	1.90		2.09

Table S7. Expression of *fruRBA* in *S. sanguinis* SK36 (by RT-qPCR) and activities of the *fruR* promoter in UA159 (by CAT assay).

	SK36			UA159
	relative mRNA levels			<i>PfruR::cat</i> sp. act.
	<i>fruR</i>	<i>fruB</i>	<i>fruA</i>	
Control	1.00 ± 0.07	1.00 ± 0.10	1.00 ± 0.06	186.18 ± 13.87
20 µM fructose	9.70 ± 1.16	9.54 ± 3.15	7.98 ± 4.93	230.71 ± 7.22
50 mM fructose	10.67 ± 1.74	10.29 ± 1.92	8.83 ± 3.22	271.29 ± 3.59
25% human sera	1.27 ± 0.19	1.71 ± 0.54	2.04 ± 0.31	ND

Bacteria were cultured in FMC-glucose till exponential phase ($OD_{600} = 0.4$) and then treated for 30 min with fructose or 25% pooled human sera. Human sera were used at 25% instead of 100% to maintain comparability with the other samples of the experiment. Gene expression was measured by RT-qPCR or CAT assays.

17 **Table S8.** pH and final OD₆₀₀ of 20-h TV cultures of *S. mutans* WT isolates (n = 4).

Strains	Sugars	Resting pH			Final OD ₆₀₀		
		20 mM	100 mM	200 mM	20 mM	100 mM	200 mM
SMU-UA159	Glucose	4.92	4.93	4.93	0.83	0.72	0.57
	Fructose	4.76****	4.82**	4.81***	0.82	0.73	0.64****
SMU-UA101	Glucose	4.61	4.52	4.53	0.96	0.82	0.66
	Fructose	4.75***	4.55	4.61	0.86****	0.83	0.69*
SMU_GS-5	Glucose	4.73	4.65	4.64	0.93	0.80	0.64
	Fructose	4.62***	4.57**	4.62	0.86**	0.78	0.65
SMU_10449	Glucose	4.81	4.73	4.73	0.95	0.85	0.70
	Fructose	4.82	4.70	4.77	0.77****	0.75****	0.64**
SMU_OMZ175	Glucose	4.62	4.53	4.53	1.00	0.84	0.69
	Fructose	4.75***	4.76****	4.86****	0.88****	0.74****	0.64***
SMU_ST1	Glucose	4.77	4.72	4.75	0.86	0.74	0.61
	Fructose	4.88***	4.68	4.70	0.80***	0.76	0.69****
SMU_SM6	Glucose	4.73	4.72	4.72	0.68	0.57	0.49
	Fructose	4.90***	4.88**	5.03****	0.71	0.60	0.51

18 Results show average (standard deviation) of four independent cultures. Statistical significance
19 was determined relative to glucose cultures of the same concentration using Two-Way ANOVA
20 (*, $P < 0.05$; **, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$). Color red denotes decreased value, and
21 green for increased value, relative to glucose conditions.

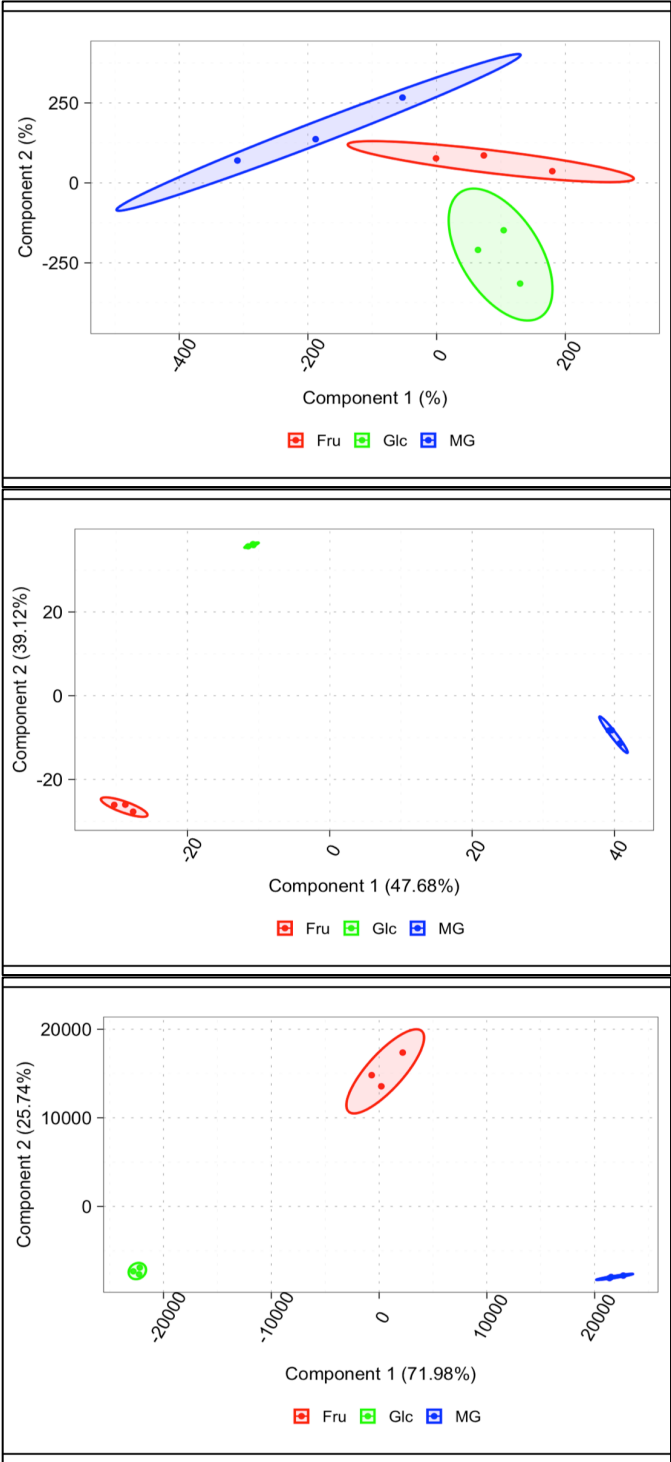
22 **Table S9.** Primers used in this study.

Primer name	Sequence	Purpose
frul-1	GGC GGT TTT ACT GGT AGG TT GCC ATT TAT TAT TTC CTT CCT CTT TTA GCC TGC	Δ frul
frul-2GA	AAG TCA AGC AAC A ATA TTT TAC TGG ATG AAT TGT TTT AGT AGA	Δ frul
frul-3GA	GCT GTT GGA GCA GTG ATT GCT	Δ frul
frul-4	AGC TGC TTG GAG ATA ATC TTT ACC T	Δ frul
SodpromF	CCGGAATTTCGATGTAGCTTTGC	sodA::gfp
SodpromR	CGCGGATCCTTCCTCTTTTC	sodA::gfp
SMU.phoR-S	AAACACGGCAAAAATCAAGC	RT-qPCR
SMU.phoR-AS	TTGTCAGCTGATCCAAATGC	RT-qPCR
nImA-S	TGGACAGCCAAACACTTTCA	RT-qPCR
nImA-AS	CTGCTGAAGCAGTTGCACAT	RT-qPCR
Sm_sloA-AS	ACG AGC CAA GAG CAT ACG TT	RT-qPCR
Sm_sloA-S	TGG CAA TGT GTT CAA GAA GC	RT-qPCR
SMU_sloC-S	AAG GAA AAG TCG GGT GTC TG	RT-qPCR
SMU_sloC-AS	TTT AGC GGC AAT TGG GAT AC	RT-qPCR
celB-S	CAAAAACGCATTGAAGCAGA	RT-qPCR
celB-AS	GCTGCATCAGCCAACTGTTT	RT-qPCR
mreC-AS	TTT TGC CCC TCA AAT TTT TC	RT-qPCR
mreC-S	AGC GCT GAT GAG ATC GTA CA	RT-qPCR
SMU.508-S	ATG GGG CTC TGA TTG TTG AG	RT-qPCR
SMU.508-AS	GCG GAA ACT GCT TCT TGA TT	RT-qPCR
SMU.127-AS	GCA TAG AAC CAC CAC GAC CT	RT-qPCR
SMU.127-S	TTT TCA AAT CAC CGT GGA CA	RT-qPCR
ahpF-S	GAA ACC ATG GGT GGT CAA GT	RT-qPCR
ahpF-AS	GAG CCA TTA ATT GGG GTC CT	RT-qPCR
copY-S	ACC AGT CAG CGT CAA GGA AG	RT-qPCR
copY-AS	ACA AAT GCG CGA GAA AAC TT	RT-qPCR
SMU.667-S	TGA CTT GGA TGA CTG GCG TA	RT-qPCR
SMU.667-AS	TGG GAT TGC ATG GTG TCT AA	RT-qPCR
feoA-S	ACG GTT GAA ACA TTG CCT TT	RT-qPCR
feoA-AS	CGG CGC TTA GCT TCA TTA AC	RT-qPCR
SMUsloC-S	AAG GAA AAG TCG GGT GTC TG	RT-qPCR
SMU_sloC-AS	TTT AGC GGC AAT TGG GAT AC	RT-qPCR
gbpC-S	AGC TCA AAA GGC AGC TTA CG	RT-qPCR
gbpC-AS	TCCTTGGGCTTTTTCAACAC	RT-qPCR
scnK-S	CAAACGGCTGATTTCAACAAG	RT-qPCR
scnK-AS	AAAGTGCGTTCCAATCTGCT	RT-qPCR

SMU.924-S	TCAGTTGATTTGCCATTTGC	RT-qPCR
SMU.924-AS	CCATAAGCCTTTCCAAACGA	RT-qPCR
SMU_phoR-S	AAACACGGCAAAAATCAAGC	RT-qPCR
SMU_phoR-AS	TTGTCAGCTGATCCAAATGC	RT-qPCR
SMU_vicK-S	TTTGGCACAGGAGAAAAACC	RT-qPCR
SMU_vicK-AS	TAATCTTTCCGCTGCGATCT	RT-qPCR
SMU.679-S	TTG GTG CTT ATC GTG CTC TG	RT-qPCR
SMU.679-AS	TGG AAT AAC CGA CAC CGT TT	RT-qPCR
SMU.1602-S	GTC GCG GTT TAA AGG ACA AA	RT-qPCR
SMU.1602-AS	TAG CGC CAA ATC GTT TTC TT	RT-qPCR
gshAB-S	GAGGCCCTCCGCTATTATTC	RT-qPCR
gshAB-AS	TTGTGACTGGCTGCTGTTTC	RT-qPCR
SMU.1603-S	GAA GAC GAC CCC GAC TAT GA	RT-qPCR
SMU.1603-AS	TCG CTT CAA GGT CAT CAA CA	RT-qPCR

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Fig. S1 Principal component analysis performed on transcriptomic datasets obtained from treatments of UA159 by 50 mM fructose (Fru), 5 mM methylglyoxal (MG), and the untreated control (Glc).



32 **Fig. S2** Gene Ontology (GO) term analyses performed on transcriptomes of UA159
33 impacted by (A) 50 mM fructose and (B) 5 mM methylglyoxal. Results shown are
34 derived from molecular function analysis only. Blocks filled with blue indicate functions
35 being repressed, whereas red colors indicate functions being activated by the treatment.
36 A



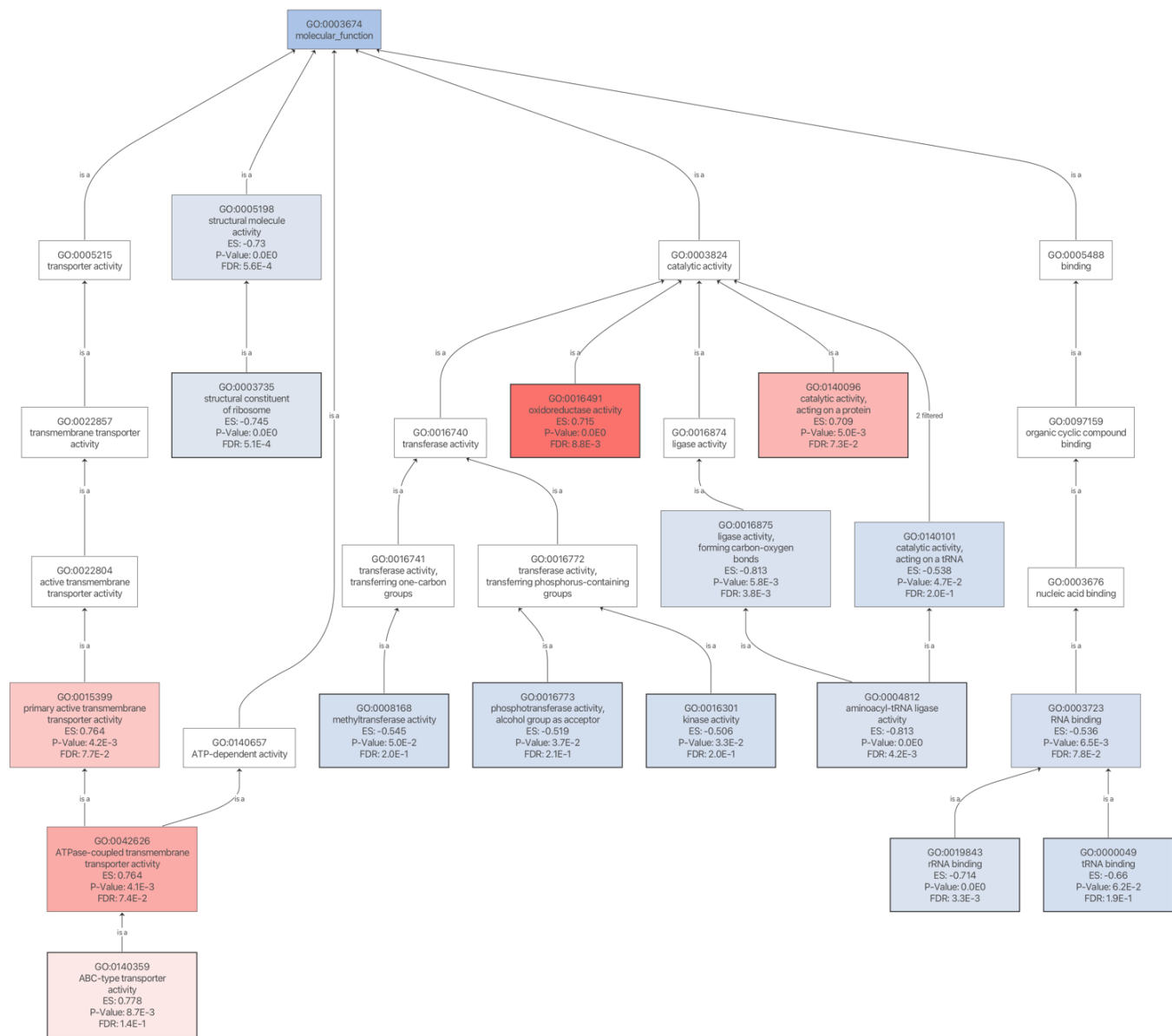


Fig. S3 Additional experiments measuring the expression of the *sodA* promoter fusion. UA159 and three mutant derivatives (*frul*, *levD*, and *spxA1*), each harboring a *PsodA::gfp* fusion, were cultured in FMC containing 10 mM glucose (A), 20 mM glucose (B), 10 mM fructose (C), or 20 mM fructose (D). The relative fluorescence units (RFU) of each culture were recorded as a measure of *sodA* promoter activity, subtracted of background fluorescence from a corresponding control strain cultured under the same condition, which was of the same genetic background but Gfp-negative, and normalized against OD₆₀₀ of the cultures. Results are the average from three biological replicates, each conducted in technical duplicates.

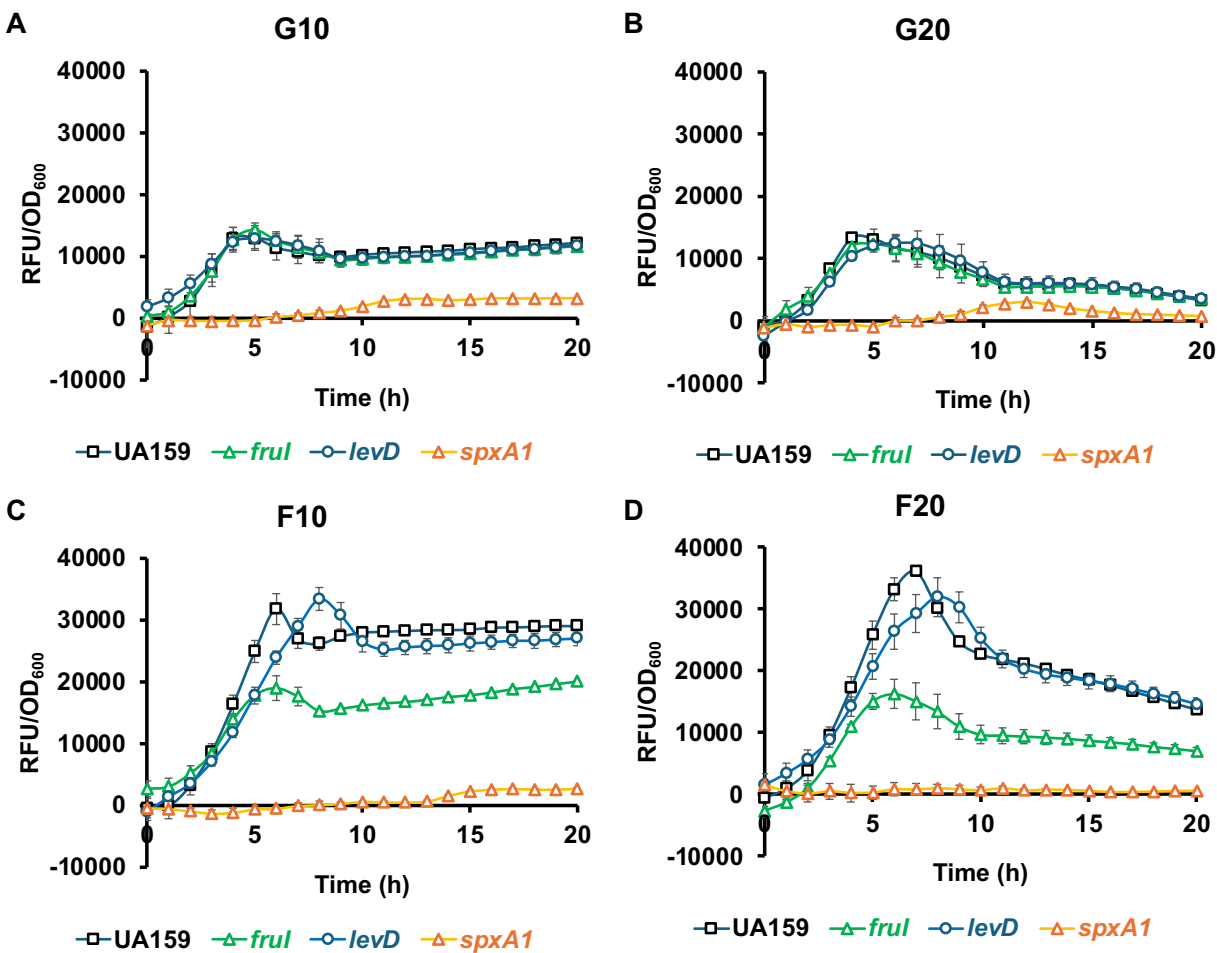


Fig. S4 Growth of UA159/*PsodA::gfp*. BHI cultures (n = 3) of the bacterium were diluted into FMC containing 20 mM glucose (G20), 19 mM glucose plus 1 mM fructose (G19/F1), 10 mM glucose plus 10 mM fructose (G10/F10), or 20 mM glucose plus 0.5 mM H₂O₂. Optical density (OD₆₀₀) of these cultures was monitored for 25 h.

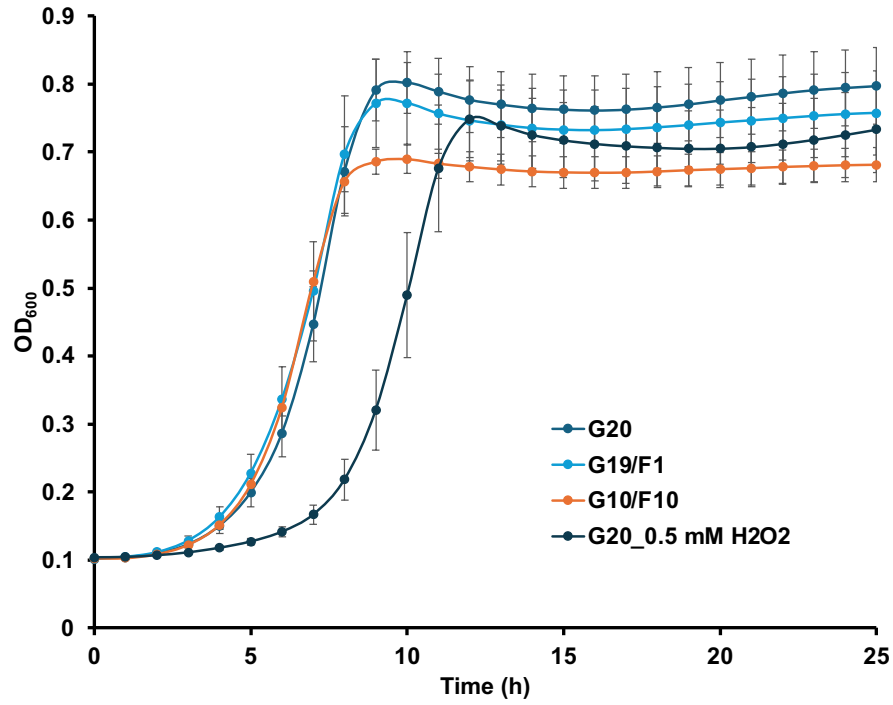


Fig. S5 pH drop assays performed with fructose. *S. mutans* UA159 was cultivated in TV supplemented with 20 mM fructose or glucose (controls), and then subjected to glycolytic profile analysis in the presence of 50 mM fructose or glucose, respectively. pH values monitored during 1-hour period from three separate experiments (**A**, **B**, **C**) were then converted to proton concentrations, followed by statistical analysis using area-under-the-curve values (**D**). The asterisk represents statistical significance according to Student's *t* test ($P < 0.05$).

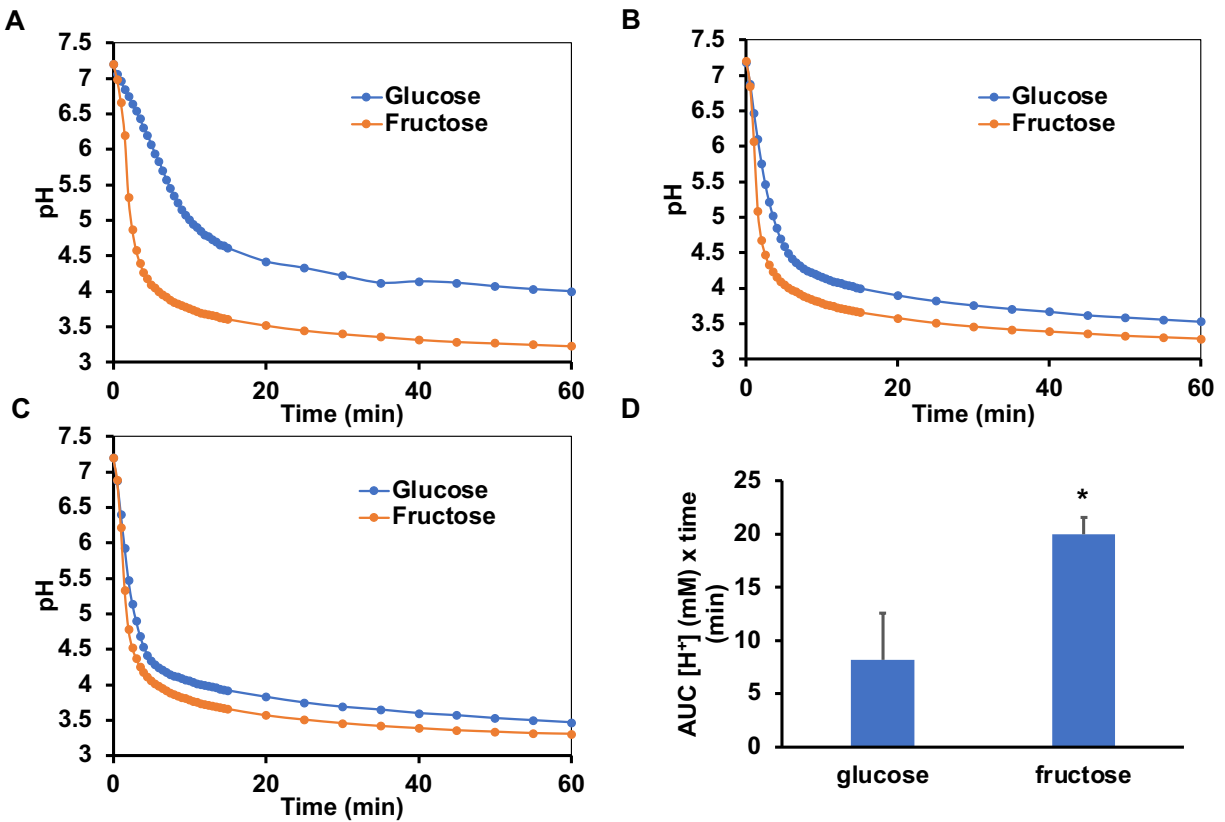
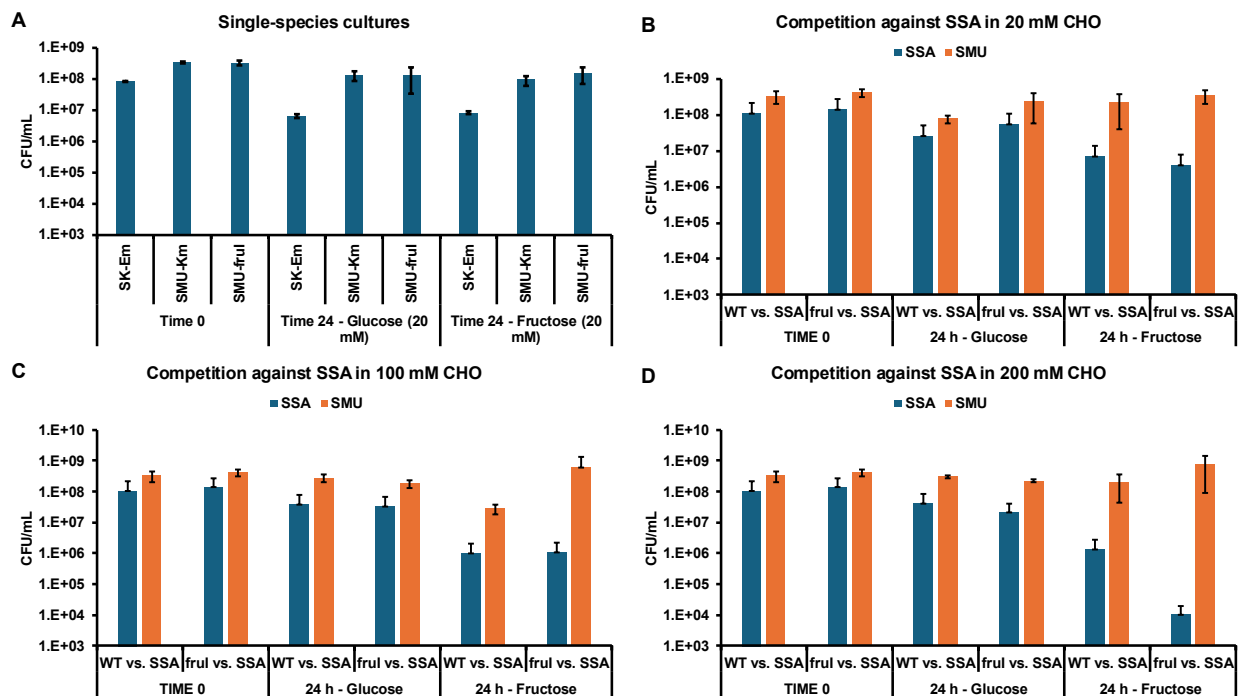
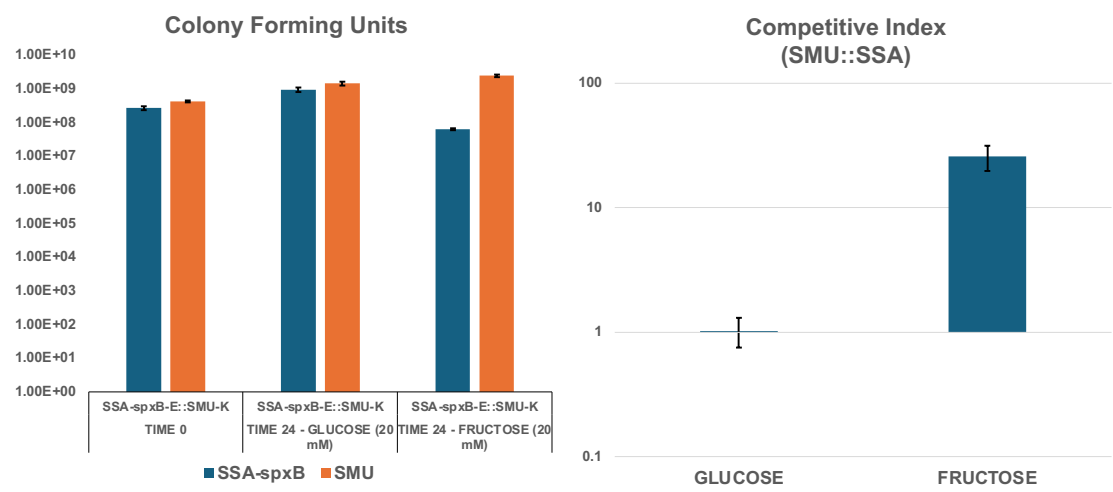


Fig. S6 CFU recovered during competitions between *S. mutans* (SMU) and *S. sanguinis* (SSA). Exponential-phase cultures in BHI (n = 3) from both species were mixed at 1:1 (v:v) ratio, or used singly, and diluted into a FMC medium supplemented with specified amounts of carbohydrates, followed by 24 h of incubation in a 5%-CO₂ atmosphere. CFU enumeration was carried out to assess bacterial viability. (A) controls run with only single species in 20 mM carbohydrates. (B, C, D) mixed-species cultures enumerated at time 0 and 24 h of competition. See Fig. 7B for the final competitive indices. (E) Competition between UA159 and SK36/*spxB* in 20 mM glucose or fructose.



79 E



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- 83 1. Kajfasz JK, Ganguly T, Hardin EL, Abranches J, Lemos JA. 2017. Transcriptome responses
84 of *Streptococcus mutans* to peroxide stress: identification of novel antioxidant pathways
85 regulated by Spx. Sci Rep 7:16018.
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