		1% DMSO	0.2 µM XIP	2 µM XIP	20 µM XIP
beginning	Doubling time (min)	85.2 ± 1.3	194.2 ± 6.0	252.7 ± 33.1	423.8 ± 24.9
	Final OD	1.01 ± 0.05	0.99 ± 0.01	0.71 ± 0.03	0.37 ± 0.01
OD_{600}=0.2	Doubling time (min)	85.6 ± 0.9	89.5 ± 2.7	114.9 ± 8.5	131.3 ± 2.2
	Final OD	1.14 ± 0.04	0.99 ± 0.07	0.84 ± 0.06	0.87 ± 0.03
OD_{600}=0.4	Doubling time (min)	84.7 ± 12.5	83.5 ± 2.8	93.3 ± 2.5	102.2 ± 3.6
	Final OD	1.17 ± 0.01	1.17 ± 0.01	0.96 ± 0.02	1.02 ± 0.01
OD_{600}=0.8	Doubling time (min)	N.D.	N.D.	N.D.	N.D.
	Final OD	1.02 ± 0.05	1.06 ± 0.03	1.06 ± 0.04	1.11 ± 0.02

N.D. = Not determined

Table S1. Doubling times and final OD of wild-type UA159 cultures, with the addition of sXIP at the beginning of the incubation period, or at different optical densities of 0.2, 0.4, or 0.8.

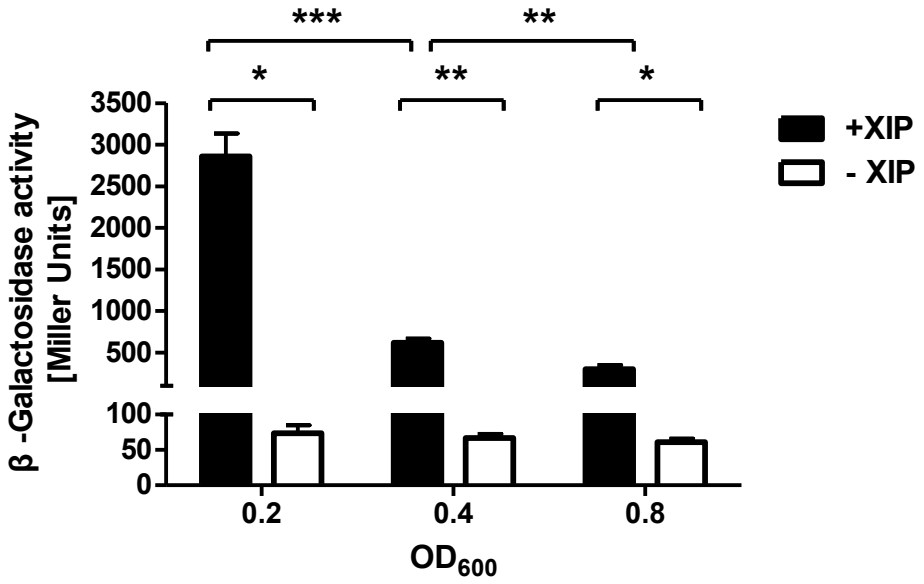

Fig. S1. Response of *comS* to exogenously-added XIP at different growth phases in FMC medium. The P_{comS}-*lacZ* strain was grown to optical densities of 0.2 (early-), 0.4 (mid-), or 0.8 (late-exponential phase) in FMC and then incubated with 1% DMSO or 2 μM synthetic XIP (sXIP) for 1 h. Expression of *comS* was measured by LacZ assays. The data shown are means ± standard deviations (error bars) of three biological replicates conducted in triplicate. Statistical analyses were performed using Student's *t* test: **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

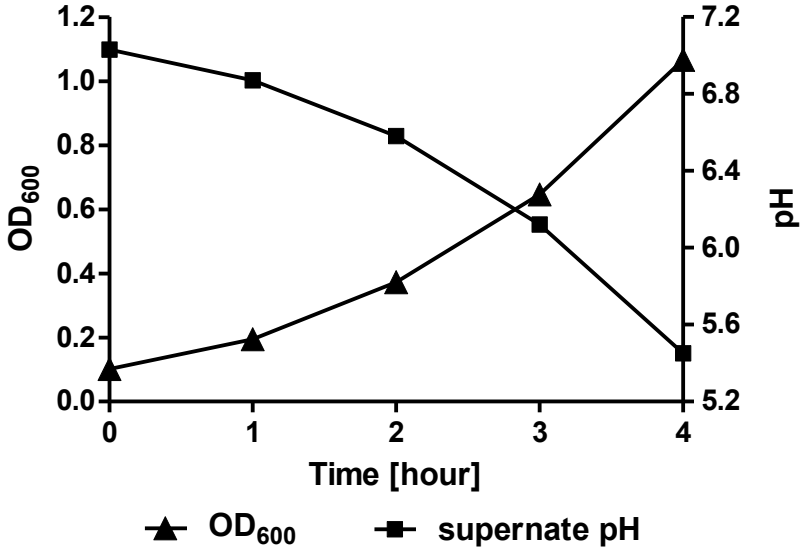

Fig. S2. Growth curve and supernatant pH. *S. mutans* UA159 was grown in FMC medium containing 25 mM glucose. OD_{600} values and pH values of the cultures were measured starting from OD_{600} = 0.1 (0 h) at 1h intervals. Data points are the averages of triplicate samples.

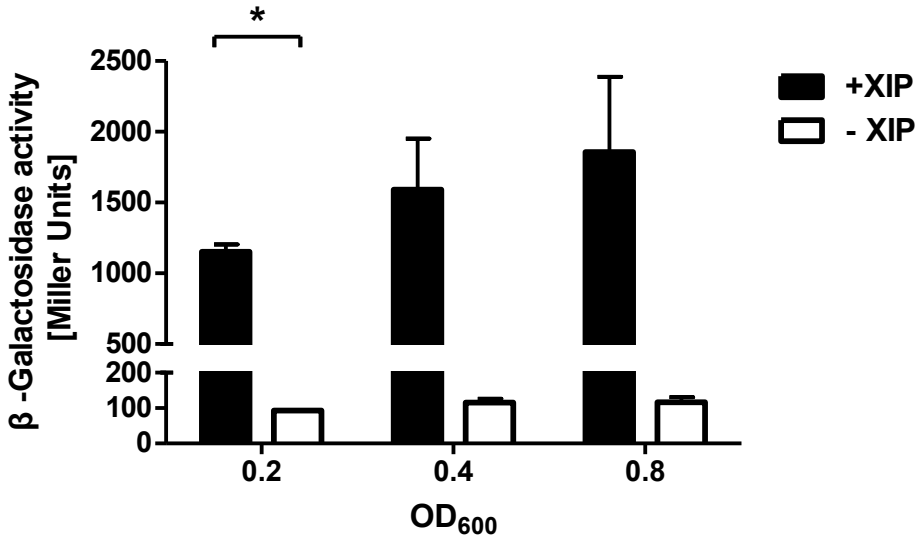

Fig. S3. Induction of *comS* by exogenously-added XIP in buffered FMC. 2 μM synthetic XIP (sXIP) was added to cultures at optical densities of 0.2 (early-), 0.4 (mid-), or 0.8 (late-exponential phase) in FMC that was buffered at 7.0 with 100 mM K-phosphate. Expression of *comS* was measured by LacZ assays. The data shown are means ± standard deviations (error bars) of three biological replicates conducted in triplicate. Statistical analyses were performed using Student's *t* test: ***P* < 0.05.

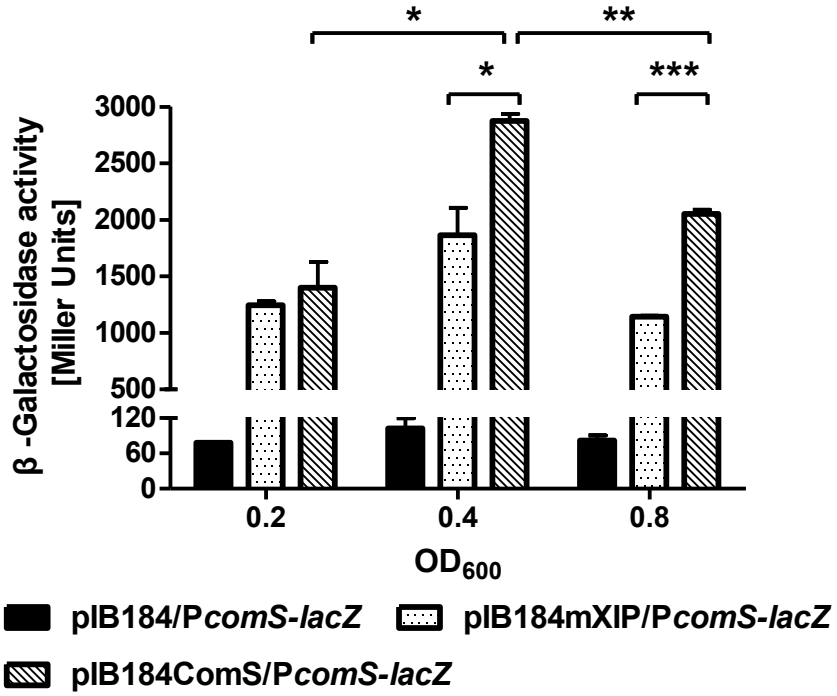

Fig. S4. Induction of *comS* in cells endogenously overproducing ComS or mXIP. The strains, including pIB184ComS/P_{comS}-*lacZ* (ComS overexpressing), pIB184mXIP/P_{comS}-*lacZ* (mXIP overexpressing), and pIB184/P_{comS}-*lacZ* (vehicle control), were grown to optical densities of 0.2 (early-), 0.4 (mid-), or 0.8 (late-exponential phase) in FMC and then expression of *comS* was measured by LacZ assays. The data shown are means ± standard deviations (error bars) of three biological replicates conducted in triplicate. Statistical analyses were performed using Student's *t* test: **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

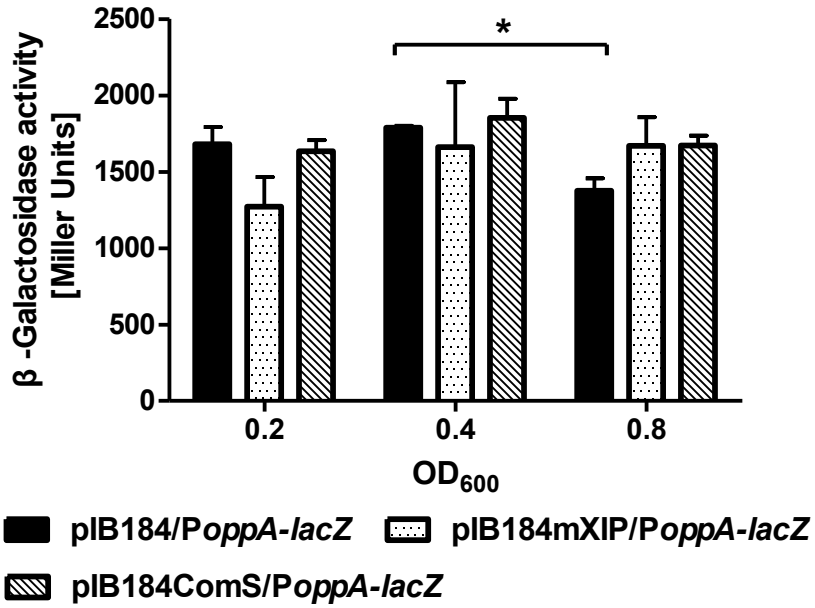

Fig. S5. Expression of the *oppA* gene in strains endogenously overproducing ComS or mXIP. The strains, including pIB184ComS/P_{oppA}-*lacZ* (ComS overexpressing), pIB184mXIP/P_{oppA}-*lacZ* (mXIP overexpressing), and pIB184/P_{oppA}-*lacZ* (vehicle control), were grown to optical densities of 0.2 (early-), 0.4 (mid-), or 0.8 (late-exponential phase) in FMC, and then expression of *oppA* was measured by LacZ assays. The data shown are means ± standard deviations (error bars) of three biological replicates conducted in triplicate. Statistical analyses were performed using Student's *t* test: $*P < 0.05$.

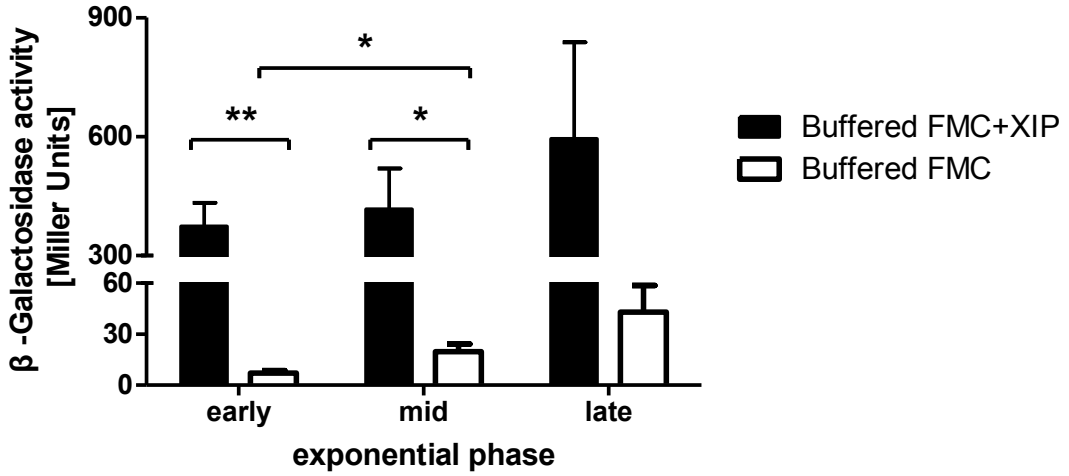

Fig. S6. Induction of *comX* by exogenously-added XIP in FMC buffered with the same concentration of K- and Na-phosphates as CDM. 2 µM synthetic XIP (sXIP) was added to cultures at optical densities of 0.2 (early-), 0.4 (mid-), or 0.6 (late-exponential phase) in FMC that was buffered at 7.0 with K- (8.5 mM) and Na- (74.9 mM) phosphates to mimic CDM. Expression of *comX* was measured by LacZ assays. The data shown are means ± standard deviations (error bars) of three biological replicates conducted in triplicate. Statistical analyses were performed using Student's *t* test: **P* < 0.05, ***P* < 0.01.