

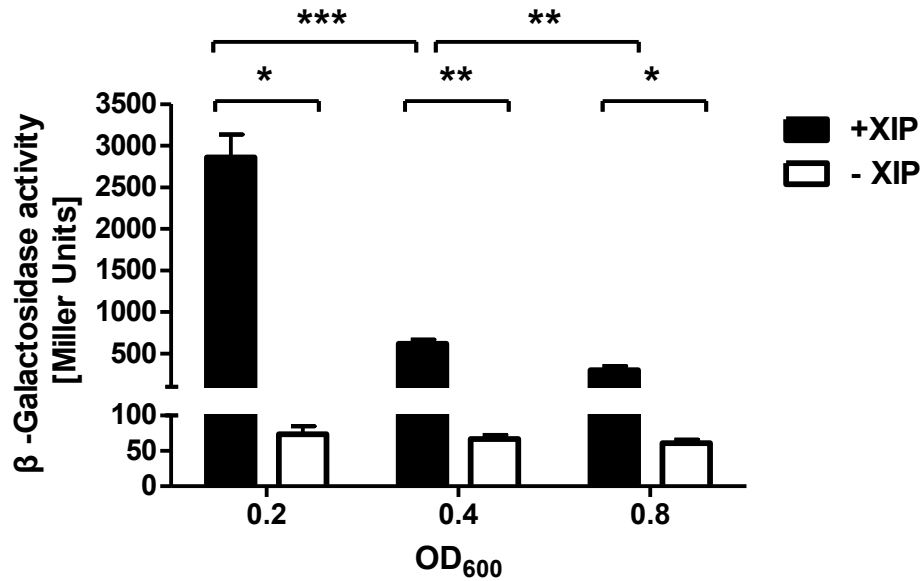
		1% DMSO	0.2 μM XIP	2 μM XIP	20 μM XIP
beginning	Doubling time (min)	85.2 \pm 1.3	194.2 \pm 6.0	252.7 \pm 33.1	423.8 \pm 24.9
	Final OD	1.01 \pm 0.05	0.99 \pm 0.01	0.71 \pm 0.03	0.37 \pm 0.01
OD₆₀₀=0.2	Doubling time (min)	85.6 \pm 0.9	89.5 \pm 2.7	114.9 \pm 8.5	131.3 \pm 2.2
	Final OD	1.14 \pm 0.04	0.99 \pm 0.07	0.84 \pm 0.06	0.87 \pm 0.03
OD₆₀₀=0.4	Doubling time (min)	84.7 \pm 12.5	83.5 \pm 2.8	93.3 \pm 2.5	102.2 \pm 3.6
	Final OD	1.17 \pm 0.01	1.17 \pm 0.01	0.96 \pm 0.02	1.02 \pm 0.01
OD₆₀₀=0.8	Doubling time (min)	N.D.	N.D.	N.D.	N.D.
	Final OD	1.02 \pm 0.05	1.06 \pm 0.03	1.06 \pm 0.04	1.11 \pm 0.02

1

2 **N.D. = Not determined**

3 **Table S1. Doubling times and final OD of wild-type UA159 cultures, with the addition of sXIP at the beginning of the incubation period,**

4 **or at different optical densities of 0.2, 0.4, or 0.8.**



5

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

13

14

15

16

17

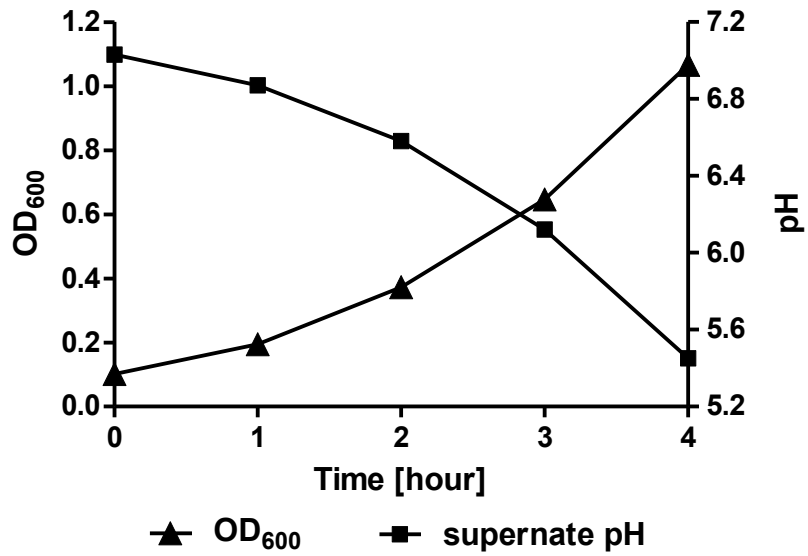
18

19

20

21

22



23

24 **Fig. S2. Growth curve and supernatant pH.** *S. mutans* UA159 was grown in FMC
 25 medium containing 25 mM glucose. OD₆₀₀ values and pH values of the cultures were
 26 measured starting from OD₆₀₀ = 0.1 (0 h) at 1h intervals. Data points are the averages
 27 of triplicate samples.

28

29

30

31

32

33

34

35

36

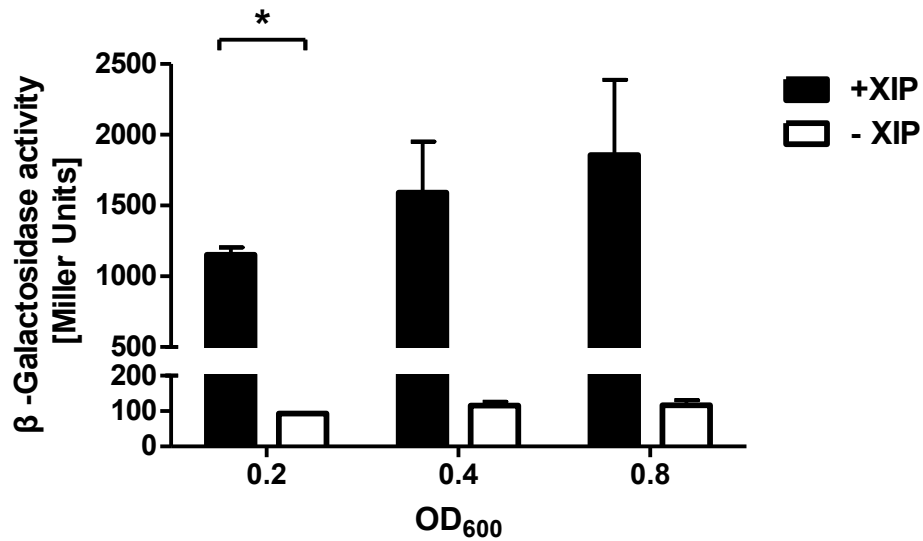
37

38

39

40

41



42

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

49

50

51

52

53

54

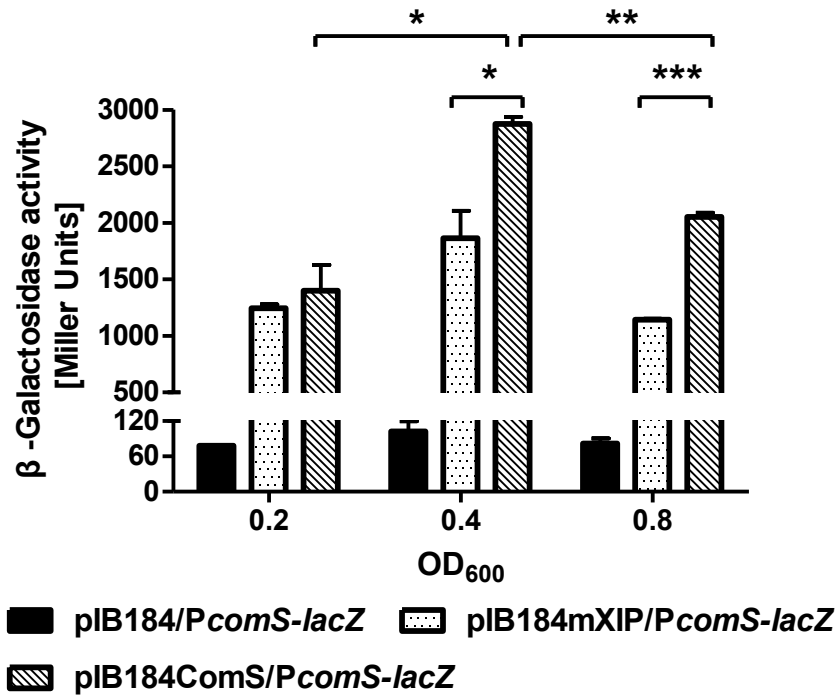
55

56

57

58

59



60

61 **Fig. S4. Induction of *comS* in cells endogenously overproducing ComS or mXIP.**

62 The strains, including pIB184ComS/*PcomS-lacZ* (ComS overexpressing),

63 pIB184mXIP/*PcomS-lacZ* (mXIP overexpressing), and pIB184/*PcomS-lacZ* (vehicle

64 control), were grown to optical densities of 0.2 (early-), 0.4 (mid-), or 0.8

65 (late-exponential phase) in FMC and then expression of *comS* was measured by LacZ

66 assays. The data shown are means \pm standard deviations (error bars) of three

67 biological replicates conducted in triplicate. Statistical analyses were performed using

68 Student's *t* test: **P* < 0.05, ***P* < 0.01, ****P* < 0.001.

69

70

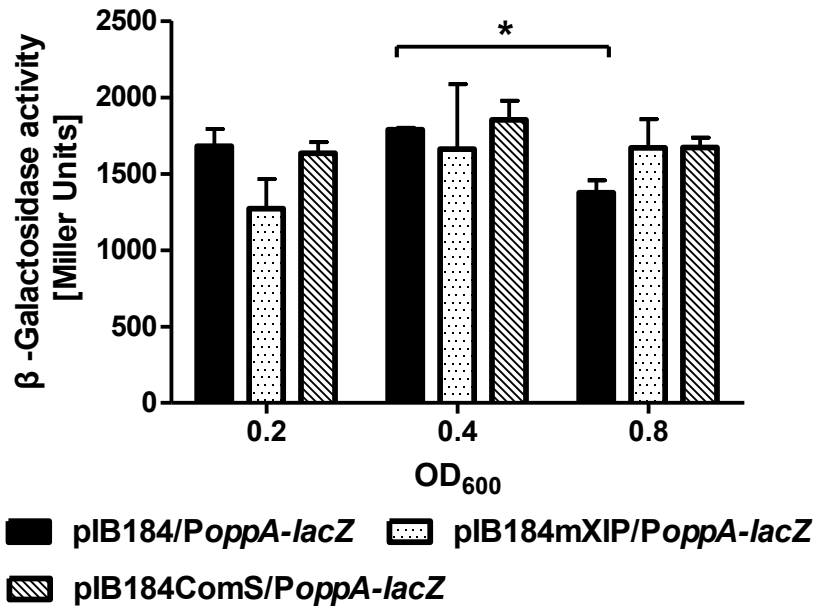
71

72

73

74

75



76

77 **Fig. S5. Expression of the *oppA* gene in strains endogenously overproducing**

78 **ComS or mXIP.** The strains, including pIB184ComS/*P_{oppA}-lacZ* (ComS

79 overexpressing), pIB184mXIP/*P_{oppA}-lacZ* (mXIP overexpressing), and

80 pIB184/*P_{oppA}-lacZ* (vehicle control), were grown to optical densities of 0.2 (early-), 0.4

81 (mid-), or 0.8 (late-exponential phase) in FMC, and then expression of *oppA* was

82 measured by LacZ assays. The data shown are means \pm standard deviations (error

83 bars) of three biological replicates conducted in triplicate. Statistical analyses were

84 performed using Student's *t* test: **P* < 0.05.

85

86

87

88

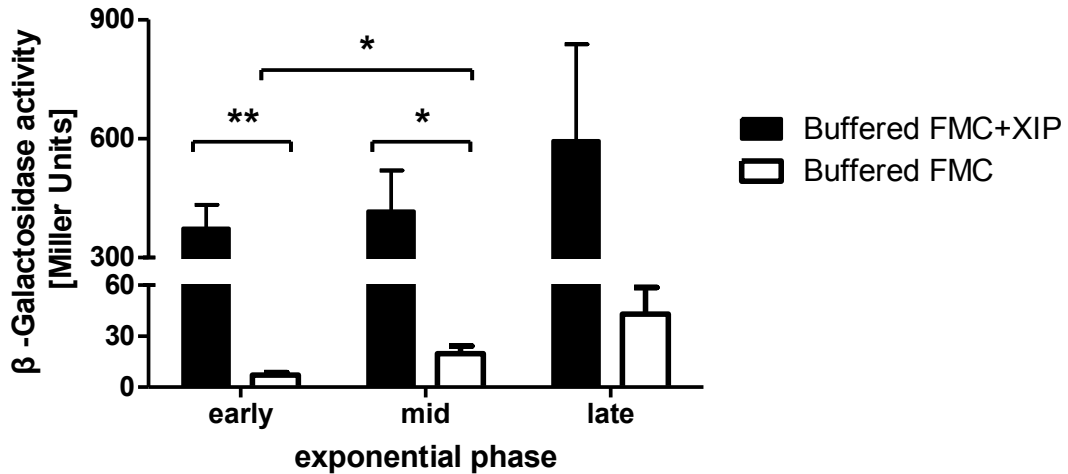
89

90

91

92

93



94
 95 **Fig. S6. Induction of *comX* by exogenously-added XIP in FMC buffered with the**
 96 **same concentration of K- and Na-phosphates as CDM. 2 μ M synthetic XIP (sXIP)**
 97 **was added to cultures at optical densities of 0.2 (early-), 0.4 (mid-), or 0.6**
 98 **(late-exponential phase) in FMC that was buffered at 7.0 with K- (8.5 mM) and Na-**
 99 **(74.9 mM) phosphates to mimic CDM. Expression of *comX* was measured by LacZ**
 100 **assays. The data shown are means \pm standard deviations (error bars) of three**
 101 **biological replicates conducted in triplicate. Statistical analyses were performed using**
 102 **Student's *t* test: **P* < 0.05, ***P* < 0.01.**