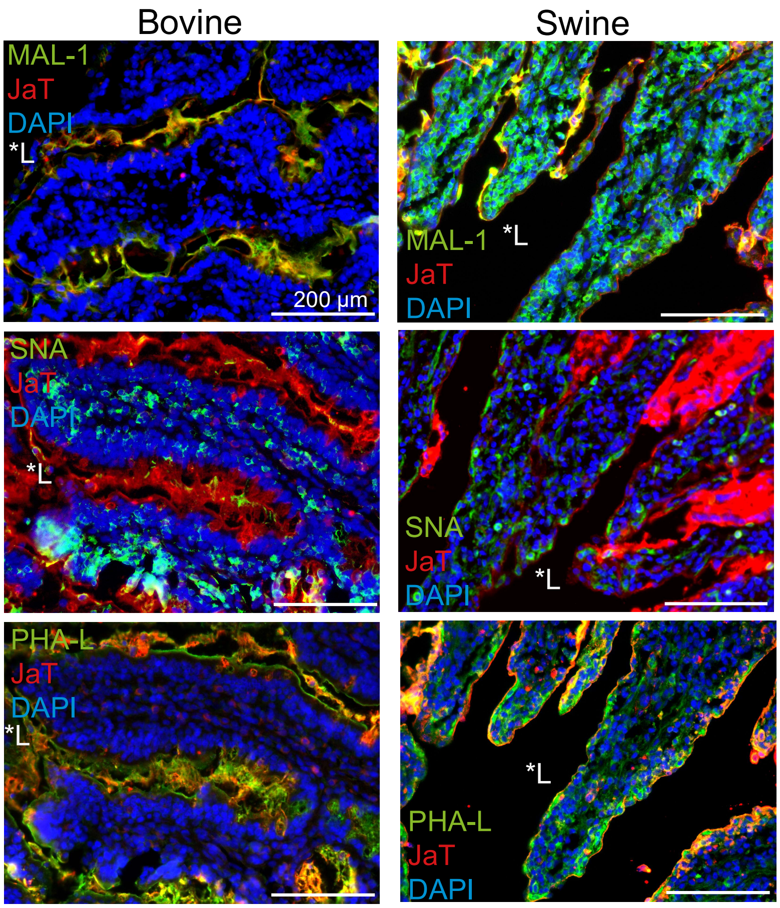

Figure S1. Lectin-assisted mapping of glycans expressed in the bovine and swine intestines, related to Fig. 3A. Bovine and swine intestinal tissue sections (Zyagen) were stained with MAL-1 conjugated to fluorescein (FITC), SNA conjugated to FITC, PHA-L conjugated to FITC, Javiana toxin conjugated to Alexa Fluor 555, and DAPI (DNA). *L, Lumen.

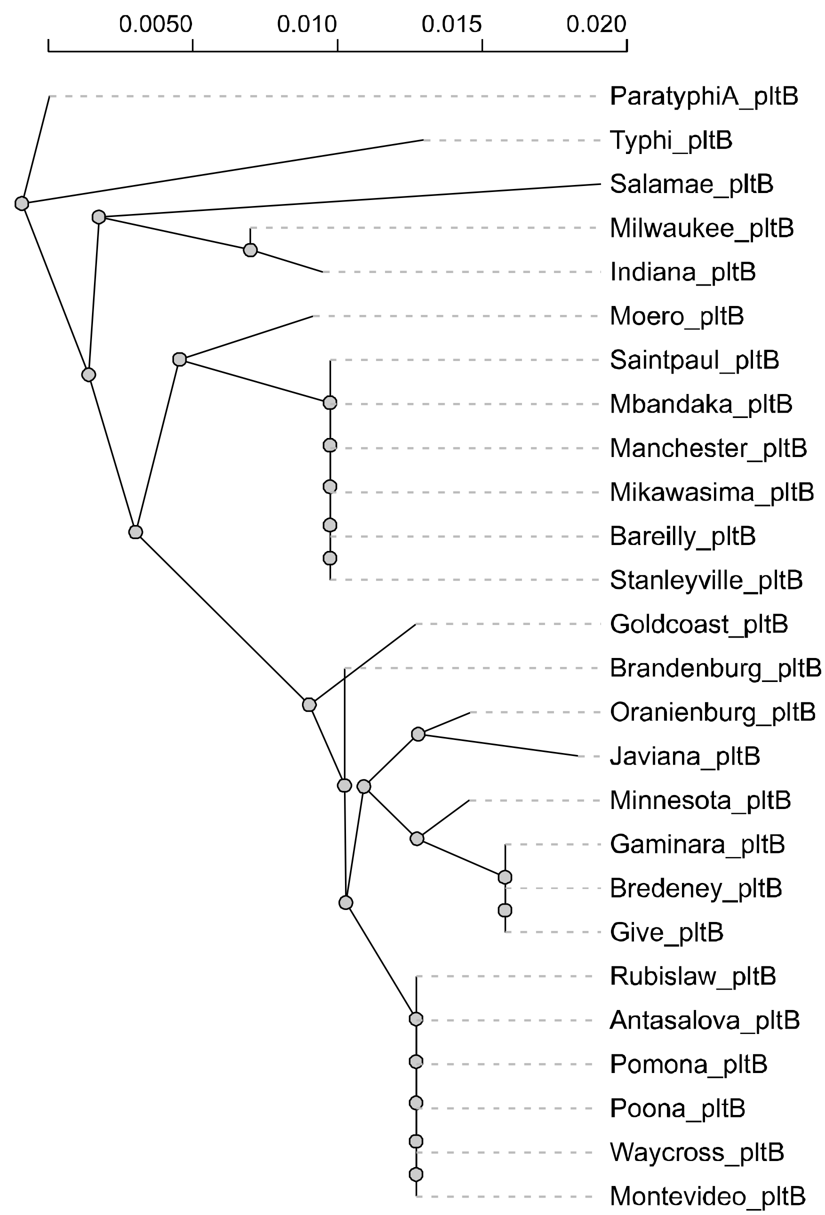

Figure S2. Phylogram of *S.* Typhi *pltB* and its orthologues, related to Figs. 4A-C. *Salmonella* serovars and their *pltB* sequences used in this analysis are summarized in Table S3. Distance scale is shown on the top of the figure. Note that, as shown in Table S2, *S.* Typhi *pltB* sequences are identical across the *S.* Typhi isolates identified thus far. The first hundred hits from the BLAST search using *S.* Typhi CT18 *pltB* are shown in Table S2.

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Typhi_mPltB               EWTGDNTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
ParatyphiA_mPltB          EWTGDNTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Goldcoast_mPltB           EWTGDNTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Pomona_mPltB              EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Antasalova_mPltB          EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Bareilly_mPltB            EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Stanleyville_mPltB        EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Mikawasima_mPltB          EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Manchester_mPltB          EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Mbandaka_mPltB            EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Saintpaul_mPltB           EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Brandenburg_mPltB         EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Waycross_mPltB            EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Montevideo_mPltB          EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Rubislaw_mPltB            EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Poona_mPltB               EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Javiana_mPltB             EWTGDKTNAYYSDEVISELHVGQIDTGPYFCIKTVKANGSGIPVVACAVSKQSIWAPSFK
Oranienburg_mPltB         EWTGDKTNAYYSDEVISELHVGQIDTGPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Bredeney_mPltB            EWTGDKTNAYYSDEVISEIHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Give_mPltB                EWTGDKTNAYYSDEVISEIHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Gaminara_mPltB            EWTGDKTNAYYSDEVISEIHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Minnesota_mPltB           EWTGDKTNAYYSDEVISEIHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Milwaukee_mPltB           EWTGDNTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Indiana_mPltB             EWTGDNTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Moero_mPltB               EWTGDKTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAVSKQSIWAPSFK
Salamae_mPltB             EWTGDNTNAYYSDEVISELHVGQIDTSPYFCIKTVKANGSGTPVVACAIAKQSIWAPSFK
                          *****:************:*******.************** ******::**********

Typhi_mPltB               ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
ParatyphiA_mPltB          ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Goldcoast_mPltB           ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Pomona_mPltB              ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Antasalova_mPltB          ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Bareilly_mPltB            ELFDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Stanleyville_mPltB        ELFDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Mikawasima_mPltB          ELFDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Manchester_mPltB          ELFDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Mbandaka_mPltB            ELFDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Saintpaul_mPltB           ELFDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Brandenburg_mPltB         ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Waycross_mPltB            ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Montevideo_mPltB          ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Rubislaw_mPltB            ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Poona_mPltB               ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Javiana_mPltB             ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Oranienburg_mPltB         ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNAFSANALVGLSSCSATQCFGPK
Bredeney_mPltB            ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Give_mPltB                ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Gaminara_mPltB            ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
Minnesota_mPltB           ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNAFSANALVGLSSCSATQCFGPK
Milwaukee_mPltB           ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSTTQCFGPK
Indiana_mPltB             ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSTTQCFGPK
Moero_mPltB               ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSTTQCFGPK
Salamae_mPltB             ELLDQARYFYSTGQSVRIHVQKNIWTYPLFVNTFSANALVGLSSCSATQCFGPK
                          **:*****************************:*************:*******
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Figure S3. Mature PltB amino acid sequence comparison analysis of *S.* Typhi PltB and its orthologues, related to Figs. 4A-C. Amino acid residues evaluated in this study are highlighted in bold red. Amino acid variations that are seen in *S.* Javiana PltB are indicated in grey, while amino acid variations that are not seen in *S.* Javiana PltB are indicated in green.

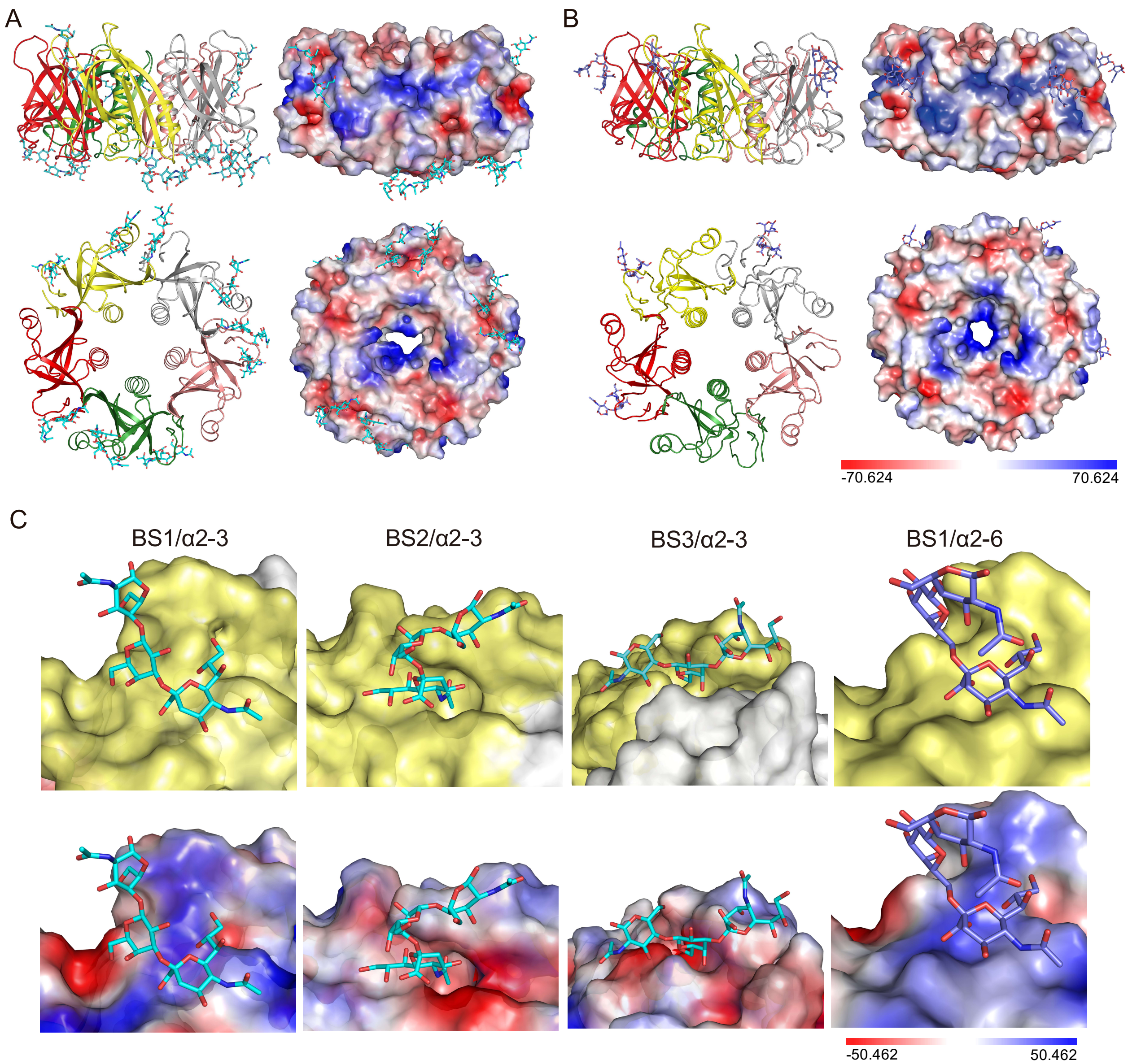

Figure S4. Crystal structures of *S.* Typhi PltB bound to specific glycan moieties, related to Figs. 5A-H. A, Crystal structure of typhoid toxin PltB pentamer in complex with Neu5Ac-α2-3-Gal-β1-4-GlcNAc (Cyan sticks, sugar carbon atoms; blue sticks, nitrogen atoms; red sticks, oxygen atoms) is shown as a ribbon cartoon with each protomer depicted in a different color (side view, top left; bottom view, bottom left in A). Surface charge distribution of the PltB pentamer structure and Neu5Ac-α2-3-Gal-β1-4-GlcNAc (side view, top right; bottom view, bottom right in A). **B**, Ribbon diagrams (left) and surface charge distributions (right) of crystal structure of typhoid toxin PltB pentamer in complex with Neu5Ac-α2-6-Gal-β1-4-GlcNAc (Purple sticks, sugar carbon atoms; blue sticks, nitrogen atoms; red sticks, oxygen atoms). **C**, Close-up views (top panels) and surface charge distributions (bottom panels) of the binding sites 1-3 (BS1-3) of PltB in complex with Neu5Ac-α2-3-Gal-β1-4-GlcNAc or Neu5Ac-α2-6-Gal-β1-4-GlcNAc.

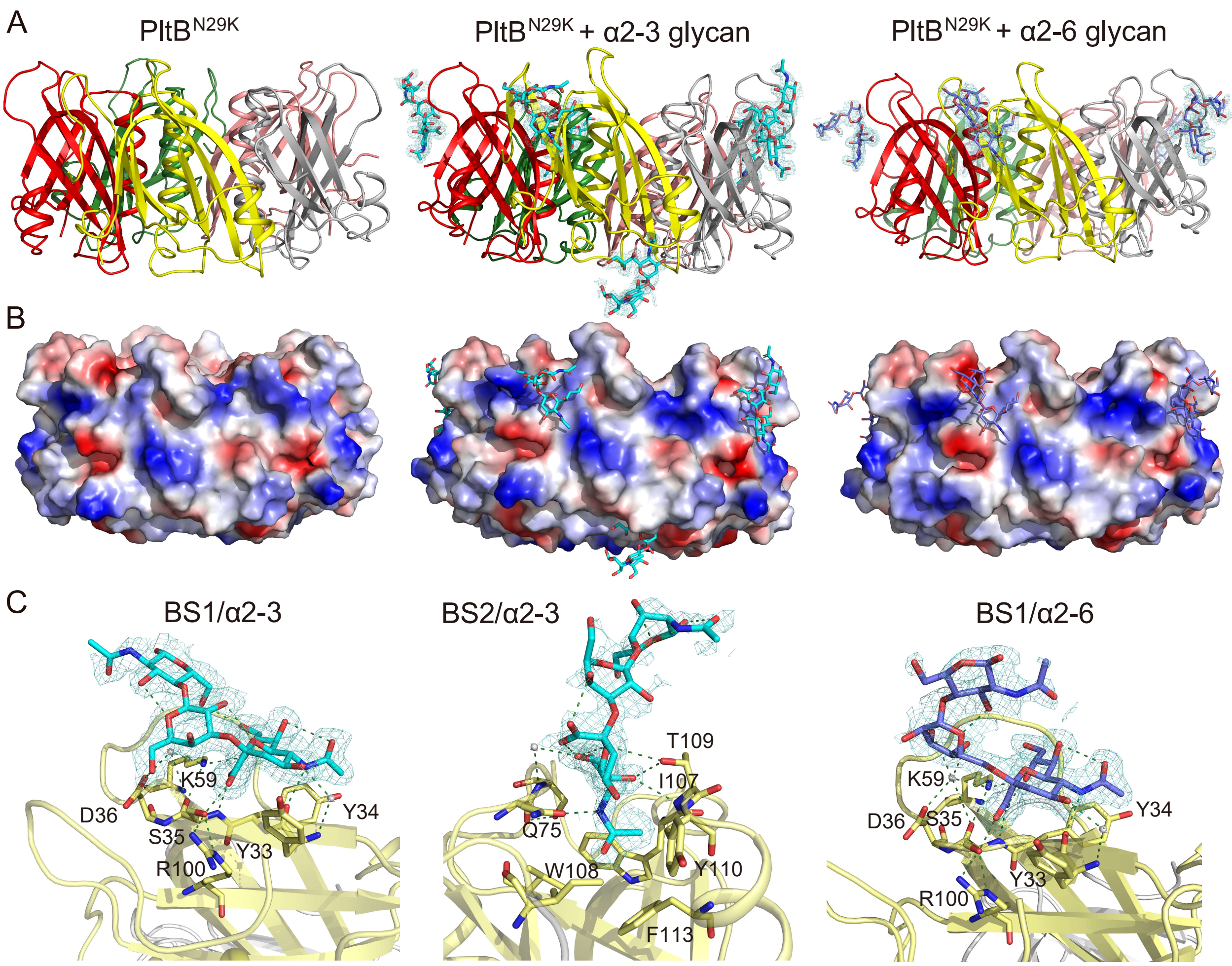

Figure S5. Crystal structures of PltB^{N29K} native and PltB^{N29K} bound to specific glycan moieties, related to Fig. 6A. A, Crystal structures of PltB^{N29K} pentamer (left), PltB^{N29K} in complex with Neu5Ac-α2-3-Gal-β1-4-GlcNAc (middle) or Neu5Ac-α2-6-Gal-β1-4-GlcNAc (right) are shown as ribbon cartoons with each protomer depicted in a different color. **B**, Surface charge distributions of corresponding crystal structures shown in A. **C**, Close-up views of the binding sites (BS) 1 and 2 of PltB^{N29K} in complex with Neu5Ac-α2-3-Gal-β1-4-GlcNAc or Neu5Ac-α2-6-Gal-β1-4-GlcNAc.

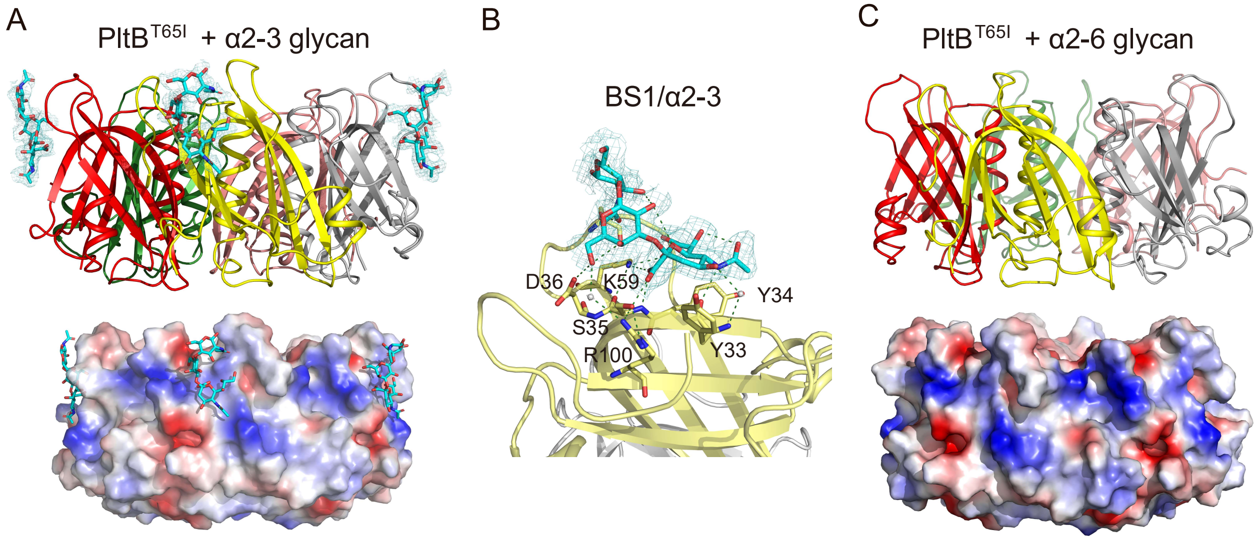

Figure S6. Crystal structures of PltB^{T65I} native and PltB^{T65I} bound to specific glycan moieties, related to Fig. 6C. A, Crystal structures of PltB^{T65I} in complex with Neu5Ac-α2-3-Gal-β1-4-GlcNAc (ribbon cartoon, top; surface charge distribution, bottom). **B**, Close-up view of the binding sites (BS) 1 of PltB^{T65I} in complex with Neu5Ac-α2-3-Gal-β1-4-GlcNAc. In the PltB^{T65I} crystal that we solved its structure, we observed symmetry mates that hindered the binding of the α2-3 glycan to the BS2 and 3, which is consistent with data shown in Figures 4C and 5 indicating that there is no reason for not having α2-3 glycan on the BP2 and 3 of PltB^{T65I}. **C**. Ribbon cartoon and surface charge distribution of the crystal structure of PltB^{T65I} soaked for 20 hrs in a crystallization condition buffer containing Neu5Ac-α2-6-Gal-β1-4-GlcNAc.

Table S2. *S.* Typhi *pltB* sequences used in this study, related to Figs. 4A-C. Shown are the first 100 hits from the BLAST search using *S.* Typhi CT18 *pltB*.

Serovar	Strain	Sequence ID	Start	End	Length	Identity (%)
Typhi	CT18	Sty1891	1788687	1788274	414	100
Typhi	R19_2839	CP046429.1	2684230	2683817	414	100
Typhi	2018K-0756	CP044007.1	2313144	2312731	414	100
Typhi	WGS1146	CP040575.1	2684661	2684248	414	100
Typhi	Ty2 4316STDY6559669	LR590081.1	2568088	2567675	414	100
Typhi	311189_217186	CP029646.1	1787549	1787136	414	100
Typhi	311189_201186	CP029958.1	1787568	1787155	414	100
Typhi	311189_218186	CP029925.1	1788480	1788067	414	100
Typhi	343078_273110	CP029846.1	1787719	1787306	414	100
Typhi	343078_256191	CP029959.1	1726503	1726090	414	100
Typhi	343078_251131	CP029960.1	1788099	1787686	414	100
Typhi	343078_228140	CP029962.1	1787808	1787395	414	100
Typhi	343078_223175	CP029964.1	1787907	1787494	414	100
Typhi	343078_211126	CP029848.1	1787796	1787383	414	100
Typhi	343078_203125	CP029850.1	1787691	1787278	414	100
Typhi	343078_201101	CP029852.1	1788012	1787599	414	100
Typhi	343077_292148	CP029855.1	1787884	1787471	414	100
Typhi	343077_286126	CP029856.1	1787067	1786654	414	100
Typhi	343077_285138	CP029858.1	1787839	1787426	414	100
Typhi	343077_281186	CP029853.1	1726037	1725624	414	100
Typhi	343077_278127	CP029863.1	1787499	1787086	414	100
Typhi	343077_267164	CP029906.1	1790717	1790304	414	100
Typhi	343077_260153	CP029861.1	1787799	1787386	414	100
Typhi	343077_255118	CP029907.1	1790401	1789988	414	100
Typhi	343077_228157	CP029864.1	1787663	1787250	414	100
Typhi	343077_228140	CP029866.1	1827555	1827142	414	100
Typhi	343077_215174	CP029868.1	1790707	1790294	414	100
Typhi	343077_214162	CP029862.1	1788094	1787681	414	100
Typhi	343077_214135	CP029872.1	1787901	1787488	414	100
Typhi	343077_213147	CP029897.1	1882683	1882270	414	100
Typhi	343077_212159	CP029870.1	1726862	1726449	414	100
Typhi	343077_212138	CP029919.1	1790394	1789981	414	100
Typhi	343077_211171	CP029873.1	1787670	1787257	414	100
Typhi	343076_294172	CP029888.1	1788337	1787924	414	100
Typhi	343076_269157	CP029881.1	1827552	1827139	414	100
Typhi	343076_253155	CP029890.1	1827830	1827417	414	100
Typhi	343076_252143	CP029892.1	1787952	1787539	414	100
Typhi	343076_249107	CP029913.1	1787807	1787394	414	100
Typhi	343076_248190	CP029882.1	1789926	1789513	414	100
Typhi	343076_241106	CP029899.1	1790429	1790016	414	100
Typhi	343076_232188	CP029900.1	1787868	1787455	414	100

Typhi	343076_227128	CP029875.1	1787865	1787452	414	100
Typhi	311189_282186	CP029920.1	1787761	1787348	414	100
Typhi	343076_217103	CP029914.1	1790493	1790080	414	100
Typhi	343076_202113	CP029915.1	1787839	1787426	414	100
Typhi	311189_291186	CP029894.1	1787546	1787133	414	100
Typhi	311189_269186	CP029922.1	1787670	1787257	414	100
Typhi	311189_268186	CP029883.1	1787273	1786860	414	100
Typhi	311189_268103	CP029902.1	1832789	1832376	414	100
Typhi	311189_256186	CP029917.1	1787985	1787572	414	100
Typhi	311189_255186	CP029885.1	1787948	1787535	414	100
Typhi	311189_252186	CP029896.1	1787765	1787352	414	100
Typhi	311189_239103	CP029908.1	1789500	1789087	414	100
Typhi	311189_232103	CP029918.1	1789005	1788592	414	100
Typhi	311189_231186	CP029904.1	1787588	1787175	414	100
Typhi	311189_224186	CP029878.1	1787585	1787172	414	100
Typhi	311189_223186	CP029880.1	1788850	1788437	414	100
Typhi	311189_222186	CP029909.1	1828203	1827790	414	100
Typhi	311189_221186	CP029923.1	1787191	1786778	414	100
Typhi	311189_220186	CP029886.1	1787992	1787579	414	100
Typhi	311189_219186	CP029911.1	1787778	1787365	414	100
Typhi	311189_217103	CP029927.1	1789682	1789269	414	100
Typhi	311189_216103	CP029928.1	1828252	1827839	414	100
Typhi	311189_215186	CP029930.1	1787043	1786630	414	100
Typhi	311189_214186	CP029933.1	1787624	1787211	414	100
Typhi	311189_213186	CP029936.1	1787792	1787379	414	100
Typhi	311189_212186	CP029944.1	1788004	1787591	414	100
Typhi	311189_211186	CP029945.1	1790441	1790028	414	100
Typhi	311189_210186	CP029946.1	1787772	1787359	414	100
Typhi	311189_209186	CP029952.1	1787691	1787278	414	100
Typhi	311189_208186	CP029949.1	1787768	1787355	414	100
Typhi	311189_208103	CP029932.1	1788052	1787639	414	100
Typhi	311189_207186	CP029938.1	1726111	1725698	414	100
Typhi	311189_206186	CP029940.1	1789029	1788616	414	100
Typhi	311189_205186	CP029950.1	1787384	1786971	414	100
Typhi	311189_204186	CP029954.1	1787710	1787297	414	100
Typhi	311189_203186	CP029942.1	1787052	1786639	414	100
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Typhi	Ty21a	CP023975.1	2176424	2176837	414	100
Typhi	LXYSH	CP030936.1	4243329	4243742	414	100
Typhi	OVG_041	LT906560.1	516042	515629	414	100
Typhi	SGB90	LT904870.2	2806254	2805841	414	100
Typhi	ISP_03_07467_SGB110-sc-1979083	LT905060.2	2662091	2661678	414	100
Typhi	1036491	LT906495.1	2657594	2657181	414	100
Typhi	ERL024120	LT906494.1	509382	509795	414	100

Typhi	1554-sc-2165329	LT906493.1	2657605	2657192	414	100
Typhi	E98_3139-sc-1927833	LT905143.1	2366618	2367031	414	100
Typhi	H12ESR00755-001A	LT905142.1	369292	368879	414	100
Typhi	OVG_041	LT905141.1	1896510	1896923	414	100
Typhi	ERL082356	LT905140.1	2441262	2441675	414	100
Typhi	2010-007898	LT905139.1	2657610	2657197	414	100
Typhi	ty3-243	LT905090.1	4566056	4566469	414	100
Typhi	ERL024120	LT905088.1	1520236	1520649	414	100
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Typhi	lupe_GEN0059-sc-1979081	LT905063.1	2072707	2073120	414	100
Typhi	403Ty-sc-1979084	LT905062.1	4644368	4644781	414	100
Typhi	ERL12960	LT904894.1	2657509	2657096	414	100
Typhi	1016889	LT904893.1	2657582	2657169	414	100
Typhi	80-2002	LT904891.1	4585640	4586053	414	100
Typhi	H12ESR00394-001A	LT904890.1	2060046	2060459	414	100
Typhi	129-0238-M	LT904888.1	4564955	4565368	414	100

Table S3. ***Salmonella pltB*** **sequences used in the sequence comparison and phylogram study, related to Figs. 4A-C.**

Serovar	Strain	Sequence ID	Gene location	Identity (matched/total nt)
Typhi	CT18	Sty1891	1788274 - 1788687	414/414
ParatyphiA	ATCC 11511	CP019185.1	2124946 - 2125359	408/414
Javiana	CFSAN001992	CP004027	1038518 - 1038931	400/414
Minnesota	ATCC 49284	CP019184.1	2578989 - 2579402	401/414
Gaminara	CFSAN070644	CP024165.1	2739327 - 2739740	401/414
Give	CFSAN024229	CP019174.1	2732040 - 2732453	401/414
Oranienburg	CFSAN001285	CP019197.1	2655115 - 2655528	401/414
Salamae	N/A	LS483456.1	3180621 - 3181034	401/414
Bredeney	NCTC6026	LS483481.1	2600268 - 2600681	401/414
Rubislaw	ATCC 10717	CP019192.1	2608673 - 2609086	402/414
Antsalova	S01-0511	CP019116.1	1219075 - 1219488	402/414
Montevideo	CFSAN051296	CP029336.1	2722398 - 2722811	402/414
Pomona	ATCC 10729	CP019186.1	2519059 - 2519472	402/414
Poona	ATCC BAA-1673	CP019189.1	2675112 - 2675525	402/414
Waycross	RSE24	CP034707.1	2576749 - 2577162	402/414
Brandenburg	SA20113174	CP029999.1	2636161 - 2636574	403/414
Goldcoast	NCTC13175	LR134158.1	2227697 - 2228110	403/414
Saintpaul	SARA26	CP017727.1	1978960 - 1979373	404/414
Mbandaka	ATCC 51958	CP019183.1	2813181 - 2813594	404/414
Manchester	ST278	CP019414.1	1213378 - 1213791	404/414
Mikawasima	RSE13	CP034715.1	2637938 - 2638351	404/414
Stanleyville	RSE10	CP034716.1	1959439 - 1959852	404/414
Moero	RES29	CP034705.1	2614796 - 2615209	404/414
Bareilly	RSE03	CP034721.1	1965862 - 1966275	404/414
Indiana	D90	CP022450.1	2756648 - 2757061	405/414
Milwaukee	SA19950795	CP030175.1	1950681 - 1951094	406/414

Table S4. Crystallization and glycan soaking conditions for typhoid toxin PltB, related to Figs. 5 and 6.

PDB ID	Protein	Conc. (mg/ml)	Crystallization condition	Glycan	Soaking condition	Cryo-protection
*	PltB	5.1	26% PEG1500, Sodium actetate pH 4.4	No		No
6P4M	PltB	5.1		α2-3 glycan	5 mM, 2hr, RT	No
6P4N	PltB	5.1		α2-6 glycan	5 mM, 2hr, RT	No
6P4P	$PltB^{N29K}$	5.7	25% PEG1500, Sodium actetate pH 4.4	No		20% Ethylene glycol
6P4Q	$PltB^{N29K}$	5.7		α2-3 glycan	5 mM, 2hr, RT	20% Ethylene glycol
6P4R	$PltB^{N29K}$	5.7		α2-6 glycan	5 mM, 2hr, RT	20% Ethylene glycol
6P4S	$PltB^{T65I}$	8.3	0.2M Sodium Chloride 0.1M Sodium Acetate pH 4.5 1.26M Ammonium sulfate	No		20% Ethylene glycol
6P4T	$PltB^{T65I}$	8.3		α2-3 glycan	5 mM, 2hr, RT	20% Ethylene glycol
*	$PltB^{T65I}$	8.3		α2-6 glycan	5 mM, 2hr, RT	20% Ethylene glycol
*	$PltB^{T65I}$	8.3		α2-6 glycan	5 mM, overnight, RT	20% Ethylene glycol

* Structure not deposit due to similarity to the corresponding apo structures.

Table S5. X-ray data collection and refinement statistics for the *S.* Typhi PltB structures, related to Figs. 5 and 6.

	PltB WT with α2-3 glycan	PltB WT with α2-6 glycan	PltB^{N29K} apo	PltB^{N29K} with α2-3 glycan	PltB^{N29K} with α2-6 glycan	PltB^{T65I} apo	PltB^{T65I} with α2-3 glycan
PDB ID	**6P4M**	**6P4N**	**6P4P**	**6P4Q**	**6P4R**	**6P4S**	**6P4T**
Glycan bound	3 in BS1 3 in BS2 3 in BS3	3 in BS1	-	5 in BS1 1 in BS2	5 in BS1	-	3 in BS1
Date collected	11/11/2018	3/11/2019	4/25/2019	4/26/2019	4/26/2019	5/22/2019	5/24/2019
Data collection							
Space group	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
Cell dimensions							
a, *b*, *c* (Å)	68.706, 97.745, 105.209	68.736, 98.483, 105.307	60.5091, 96.3499, 118.368	61.0534, 96.8941, 119.006	60.9162, 96.8269, 118.928	61.0681, 97.4982, 118.437	61.2823, 97.7139, 119.076
α, β, γ (°)	90, 90, 90	90, 90, 90	90, 90, 90	90, 90, 90	90, 90, 90	90, 90, 90	90, 90, 90
Resolution (Å)	40.00-1.80 (1.83-1.80)	50.00-1.70 (1.73-1.70)	27.26 -2.00 (2.07-2.00)	27.42 - 1.77 (1.83-1.77)	27.40-1.87 (1.94-1.87)	28.30-2.00 (2.07-2.00)	28.40- 2.17 (2.25-2.17)
R_{sym} or R_{merge}	9.5% (51.1%)	6.1% (24.9%)	5.2% (15.3%)	7.0% (31.7%)	10.0% (38.8%)	12.5% (58.6%)	12.7% (33.1%)
I / σI	21.84 (3.38)	27.79 (4.83)	30.55 (5.97)	15.1 (3.1)	17.08 (2.71)	16.90 (1.95)	12.0 (3.0)
Completeness (%)	99.6% (94.0%)	99.3% (95.8%)	99.4% (99.5%)	99.5 (99.6)	99.8 (99.9)	99.3 (99.1)	99.2 (99.2)
Redundancy	4.6 (3.2)	6.5 (6.1)	3.9 (2.9)	4.0 (3.0)	3.8 (2.9)	4.3 (2.8)	4.1 (3.0)
Refinement							
Resolution (Å)	40.00-1.80 (1.83-1.80)	50.00-1.70 (1.73-1.70)	27.26 -2.00 (2.07-2.00)	27.42 - 1.77 (1.83-1.77)	27.40-1.87 (1.94-1.87)	28.30-2.00 (2.07-2.00)	28.40- 2.17 (2.25-2.17)
No. reflection	66141 (3078)	79595 (7234)	47226 (4666)	69147 (6872)	54382 (5882)	88483 (8849)	38256 (3738)
R_{work} / R_{free}	16.88% / 19.32% (19.52%/24.78%)	17.66% / 19.62% (19.62%/24.85%)	18.28% / 22.14% (19.82%/26.25%)	18.04% / 20.33% (20.63%/24.51%)	17.94% / 0.55% (22.72%/23.56%)	19.70% / 4.52% (22.93%/29.79%)	18.61% / 2.72% (19.25%/24.13%)
No. atoms							
Protein	4431	4562	4450	4450	4450	4438	4438
Ligand/ion	414	138	-	276	230	-	138
Water	359	295	265	371	429	404	342
B-factors							
Protein	20.32	20.11	12.11	11.49	12.57	17.98	20.82
Ligand/ion	51.96	50.82	-	43.33	43.43	-	55.65
Water	25.76	27.81	17.28	15.30	17.61	23.61	24.59
R.m.s. deviations							
Bond lengths (Å)	0.007	0.007	0.007	0.006	0.007	0.007	0.008
Bond angles (°)	1.2	0.9	0.9	1.1	1.1	0.9	1.0

* Each dataset was collected from a single crystal.
* Values in parentheses are for highest-resolution shell.
BS, binding site.

Table S6. List of plasmids and strains used in this study, related to Key Resource Table.

ID	Description	Reference
pSB5022	pET28a-pltB-pltA-cdtB-His_6	(Song et al., 2013)
pSB4987	pET28a-$pltB^{S35A}$-pltA-cdtB-His_6	(Song et al., 2013)
pSB5592	pET28a-pltB-His_6	(Deng et al., 2014)
pSB5055	pET28a-$pltB^{K59A}$-pltA-cdtB-His_6	(Deng et al., 2014)
pJS0008	pET28a-$pltB^{N29K}$-pltA-cdtB-His_6	This study
pJS0009	pET28a-$pltB^{S50G}$-pltA-cdtB-His_6	This study
pJS0010	pET28a-$pltB^{T65I}$-pltA-cdtB-His_6	This study
pJS0020	pET28a-pltB-JapltA-cdtB-His_6	This study
pJS0030	pET28a-JapltB-JapltA-cdtB-His_6	This study
pJS0031	pET28a-JapltB-pltA-cdtB-His_6	This study
pJS0032	pET28a-$pltB^{Q75A}$-pltA-cdtB-His_6	This study
pJS0033	pET28a-$pltB^{I107A}$-pltA-cdtB-His_6	This study
pJS0034	pET28a-$pltB^{W108A}$-pltA-cdtB-His_6	This study
pJS0035	pET28a-$pltB^{T109A}$-pltA-cdtB-His_6	This study
pJS0036	pET28a-$pltB^{Y110A}$-pltA-cdtB-His_6	This study
pJS0037	pET28a-$pltB^{F113A}$-pltA-cdtB-His_6	This study
pJS0038	pET28a-$pltB^{E24A}$-pltA-cdtB-His_6	This study
pJS0039	pET28a-$pltB^{D28A}$-pltA-cdtB-His_6	This study
pJS0040	pET28a-$pltB^{D48A}$-pltA-cdtB-His_6	This study
pJS0052	pET28a-$pltB^{N29K}$-His_6	This study
pJS0054	pET28a-$pltB^{T65I}$-His_6	This study
JS0001	Wild-type *S.* Javiana (isolate FSL S5-0395)	(den Bakker et al., 2011)
JS0004	ΔJaviana toxin islet	This study
JS0005	ΔJaviana toxin islet :: Javiana toxin islet	This study

Table S7. List of primers used in this study, related to Star Methods.

Oligomers used for Figure 2C	
Genes	Sequences (5'-3')
ST3GAL1	Forward TTGGAGGACGACACCTACCGAT Reverse CACCACTCTGAACAGCTCCTTG
ST3GAL2	Forward TCCGACTGGTTTGACAGCCACT Reverse CTTCTCCAGCACCTCATTGGTG
ST3GAL3	Forward CGAATCCTCAACCCATATTTCATCC Reverse CACTGCCACACTGCCAAG
ST3GAL4	Forward GGCTGGTGCCAGTATGAC Reverse CCACCCTGACTGGATCTCG
ST3GAL5	Forward AGAGCCTCAGTCAAGGTTCTGG Reverse GAGGTCATATCCAAAACCCGCC
ST3GAL6	Forward CTGACCTCAAGAGTCCTTTGCAC Reverse TCTTGAGTCAAGTTGATTACGAGG
ST6GAL1	Forward CTGAATGGGAGGGTTATCTGCC Reverse ACCTCAGGACTGCGTCATGATC
Oligomers used for Figure 2F	
ST3GAL3	Forward CGCAAGTGGGCTAGAATCC Reverse CATTGCCCACGATGATGCAG
ST3GAL4	Forward CATCCTGAGTGATAAGAAGCGG Reverse GGCAGGCTCAGCAGTTTG
β-actin	Forward AGAGCTACGAGCTGCCTGAC Reverse AGCACTGTGTTGGCGTACAG