Supplementary Information

Hemolytic actinoporins interact with carbohydrates using their lipid-binding module.

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Footnote.

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PDB ID	Protein	Class	Z score	RMSD	No. res. ^[a]	No. ali. ^[b]	%id ^[c]
3vwi	Fragaceatoxin C	PFT	38.2	0.2	177	177	100
1iaz	Equinatoxin II	PFT	35.4	0.4	175	174	90
1gwy	Sticholysin II	PFT	34.6	0.7	175	175	63
2ks4	Sticholysin I	PFT	22.5	2.0	176	172	61
4jox	Insecticidal protein cry34Ab1	PFT	14.3	1.5	118	112	18
40eb	Pleurotolysin A	PFT	11.4	2.4	135	116	14
3qdx ^[d]	Boletus edulis lectin	Lectin	11.2	2.5	142	123	11
1x99	Xerocomus chrysenteron lectin	Lectin	11	2.7	143	125	13
2ofd ^[d]	Sclerotium rolfsii lectin	Lectin	10.9	2.7	141	124	11
3a57	Thermostable direct hemolysin	PFT	10.5	3.3	154	131	4
$1y2v^{[d]}$	Agaricus bisporus lectin	Lectin	10.5	2.6	143	122	12

Table S1. Structural homology of FraC (http://ekhidna.biocenter.helsinki.fi/dali_server/start).

[a] Number of residues.

[b] Number of structurally equivalent residues.

[c] Percentage of identical amino acids among structurally equivalent residues.

[d] Structures with sugars found.



Figure S1. Kinetics of hemolysis by FraC in the presence of saccharides. (a) Inhibitory effect of various monosaccharides. The hemolytic toxin was added at a final concentration of 25 nM. The concentration of PEG200 (gray) and monosaccharides glucose (magenta), galactose (orange), mannose (blue), fructose (green), or GlcNAc (light brown) was 400 mM. **(b)** Influence of the number of hexoses of the saccharide on the kinetics of hemolysis. Data for glucose (one unit, magenta), sucrose (two units, brown), raffinose (three units, red) and maltopentaose (five units, olive) are shown.



Figure S2. Depiction of the lipid/carbohydrate binding region of FraC. (**a**, **b**) The cluster of aromatic residues of FraC are colored in red. (**c-e**) Electrostatic potential of FraC. The color gradient set from red to blue represents negative (-3 kT/e) to positive (+3 kT/e) electrostatic potentials. (**f**, **g**) Location of residues W112 and W116 with respect to the sugar GlcNAc(6S).



Figure S3. Comparison of FraC with a fungal lectin. (a, b) Side view of FraC (a) and a fungal lectin from *Boletus edulis* (b). Helices and β -strands are shown as cylinders and arrows, respectively. The β strands are colored in rainbow from blue (near N-terminus) to red (near C-terminus). (c, d) Topology map of actinoporins (c) and the fungal lectin from *Boletus edulis* (d). Circles and cylinders represent helices. β strands are shown as triangles that are numbered sequentially. Triangles drawn with opposite orientation indicate antiparallel strands.