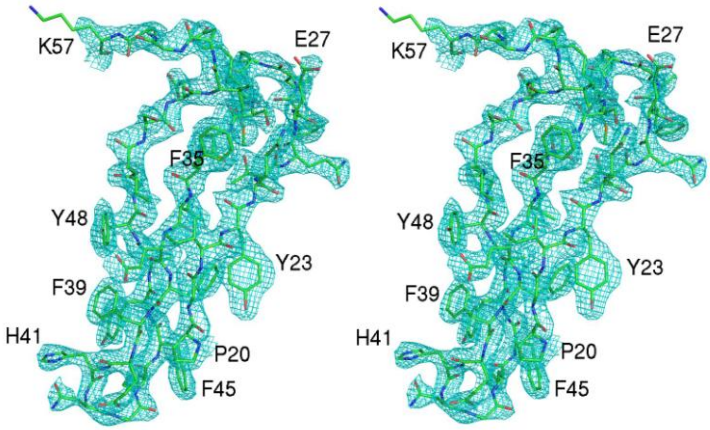
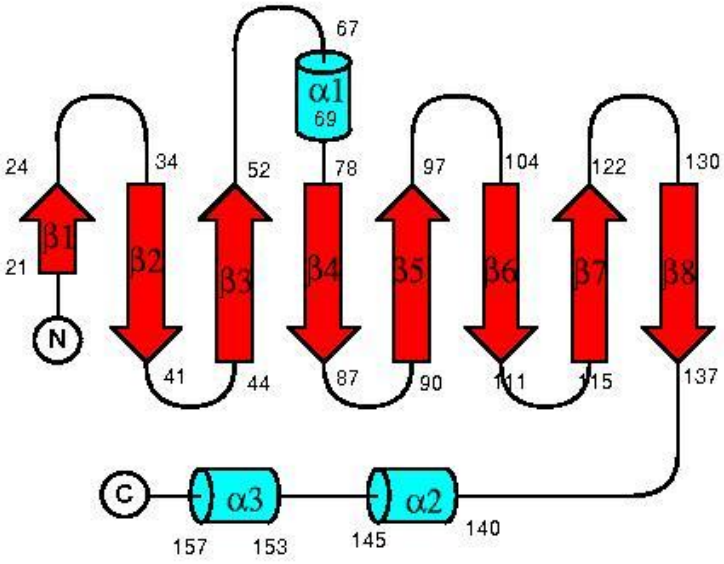
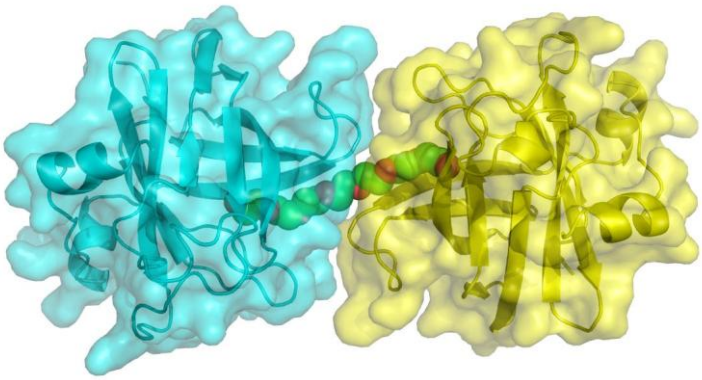
SUPPLEMENTARY MATERIAL



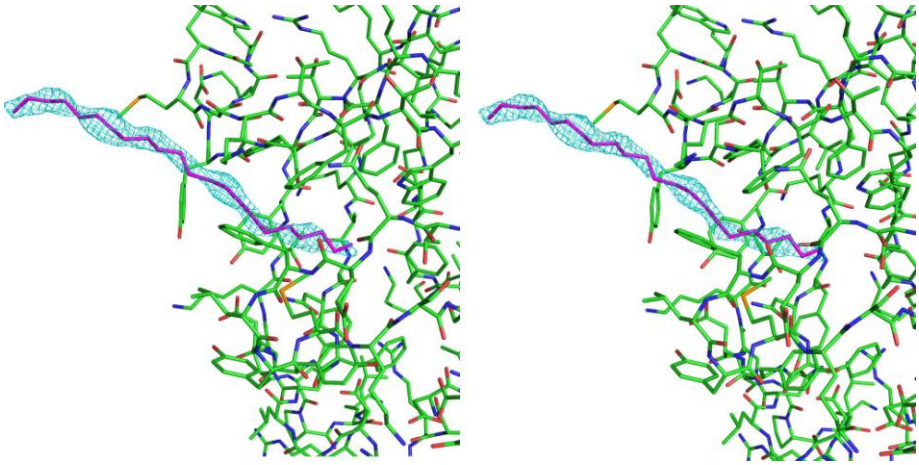
Supplementary Fig. S1. Electron density map calculated with coefficients $|2F_{obs}-F_{calc}|$. Contour level at 1.5 σ. Only β-strands from residues 20 to 137 are shown.



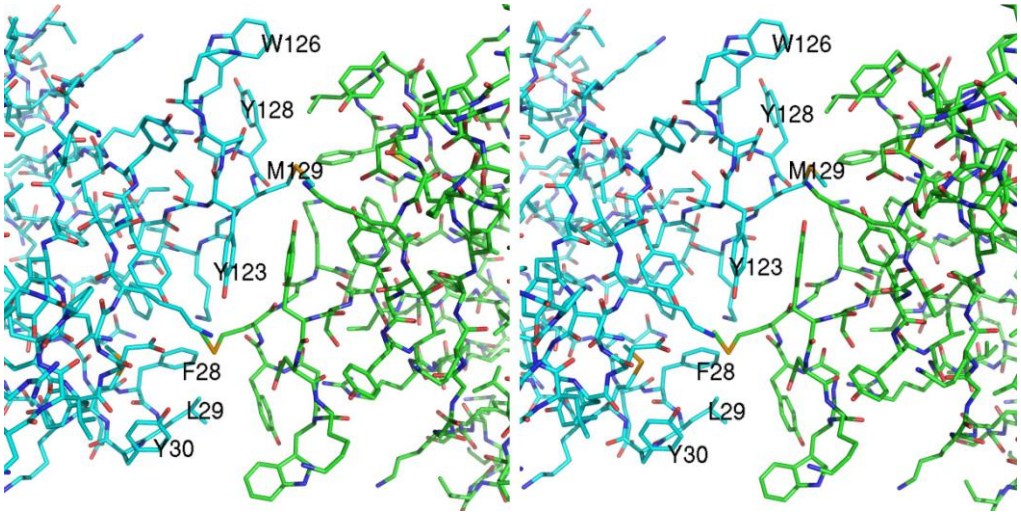
Supplementary Fig. S2. Schematic representation of HP1028 topology. B-strands are represented as red arrows, α-helices as cyan cylinders. N and C indicates the N- and C-terminus, respectively.



Supplementary Fig. S3. Overall view of the surface of the two monomers in the asymmetric unit, with a PEG chain fitted inside the cavity. The electron density of the ligand extends from one monomer to the other, but does not fill in the entire cavity till the bottom.



Supplementary Fig. S4. Stereo view of the electron density of the ligand present in HP1028 cavity. The electron density is calculated as in Fig. S1. The ligand extends inside a second HP1028 molecue, not shown for clarity of the drawing.



Supplementary Fig. S5. Stereo view of the residues present in the loops at the opening of the protein cavity and forming the interaction surface between the two monomers in the crystal. The C atoms of the two different monomers are shown in green and cyan.

SupplementaryTable. S1. List of protein structures that, according to DALI server {{1050 Holm,L. 2010;}}, bear a structural similarity to HP1028. Only one representative structure is reported for each protein. Proteins are listed according to the Z score. Columns 4 and 5 gives the total number and the number of residues aligned, respectively. Column 6 the percentage of identity, column 6 the PDB ID code, followed by the label of the chain considered. Only one member for each protein is reported in the Table.

Protein name	R.m.s.d. (Å)	Z score	N. Res.	Aligned	% identity	PDB ID
Avidin	2.8	7.7	124	93	12	2a5b-A
Avidin-related protein 4/5	3.5	7.5	120	92	12	1Y53-Y
Amine dehydrogenase	3.2	7.4	493	96	14	1jmx-A
Streptavidin	2.9	7.3	123	92	9	1vwj-B
Biotin binding protein A	3.6	7.2	123	93	12	2clq-A
Xenavidin	3.8	7.1	119	94	12	2uyw-D
Quinohemoprotein amine dehydrogenase 60kDa	4.2	7.0	489	100	8	1pby-A
Rhizavidin	3.1	7.0	114	89	9	3ew2-A
FABP liver	3.2	6.8	129	85	15	3vg4-A
D-aminopeptidase	3.1	6.5	518	84	8	1ei5-A
Cellular retinoic acid binding protein 2	2.8	6.4	117	87	13	2fs6-B
Tamavidin2	3.2	6.3	123	89	10	2zsc-B
CRCA protein	3.3	6.2	170	94	5	1mm5-A
Protein PAGP	2.8	6.2	155	84	2	3gp6-A
Nitrophorin 1	3.9	5.9	184	113	7	4np1-B
BLR5658	3.6	5.8	138	93	13	2y32-C
Lipoprotein putative	2.7	5.8	89	76	7	3ge2-A
Sodium-calcium exchanger	2.9	5.8	133	87	10	3ppt-A
Glycoside hydrolase YXIA	2.5	5.8	441	77	13	3lv4-A
BABP	2.9	5.8	127	82	13	2lba-A
Outer membrane proteinW	3.4	5.6	183	90	6	2flt-A
Complement protein C8γ	3.7	5.6	164	101	6	1lf7-A
Der F 13	3.2	5.5	131	83	18	2a0a-A
P-coumaric acid decarboxylase	3.5	5.4	161	88	10	2qc9-B
Odorant binding protein	3.8	5.4	148	100	9	1dzk-A
Ferulate decraboxylase	3.2	5.3	161	88	10	3nad-A
α-1-acid glycoprotein	3.1	5.3	172	95	6	3bx6-A
Endo-α-1,5-arabinanase	2.6	5.3	443	75	11	2x8t-A
Gastrotropin	2.6	5.2	127	77	13	1o1v-A
Crustacyanin A1 subunit	3.9	5.1	180	100	7	1s44-B
Allergene EQU C 1	3.9	5.1	159	100	8	1ew3-A
Retinol-binding protein	4.2	5.0	176	95	11	1fem-A
Von Ebner's gland protein	3.3	5.0	128	87	10	1xk1-A
YCF58	3.1	4.4	156	81	14	3bdr-A