Electronic Supplementary Material (ESI) for Molecular BioSystems.

Design of gliadin peptide analogues with low affinity for the celiac disease associated HLA-DQ2 protein

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Electronic Supplementary Information

Table S1 – Docking results, expressed as Prime MM-GBSA ΔG_{bind}, for the selected five conformers of α-gliadin epitopes and their diHyp containing analogues.[a]

Name	ID conf.	ΔG (kcal mol^{-1})	backbone RMSD (Å)[b]				P9 sidechain[c]
			P1-P9	P1-P3	P4-P7	P8-P9	
DQ2.5-glia-α1a	**4**	**-193.45**	**0.93**	**1.17**	**0.44**	**1.18**	**OUT**
	2	-191.64	1.25	1.11	0.51	2.14	IN
	3	-190.79	1.69	2.55	0.73	1.32	OUT
	5	-186.89	1.18	1.34	0.52	1.72	OUT
	1	-185.79	0.89	0.46	0.39	1.69	OUT
DQ2.5-glia-α1a-3,4-diHyp	**4**	**-168.60**	**1.80**	**2.08**	**1.60**	**1.68**	**OUT**
	1	-138.75	1.75	2.09	0.88	2.36	OUT
	5	-136.55	1.97	1.23	2.04	2.62	OUT
	2	-134.37	2.85	2.51	2.50	3.79	--
	3	-131.41	4.53	5.37	4.80	1.85	--
DQ2.5-glia-α1b	**2**	**-195.48**	**1.24**	**1.39**	**0.49**	**1.86**	**IN**
	3	-191.68	0.98	1.15	0.51	1.32	OUT
	1	-190.25	1.53	1.29	0.62	2.67	IN
	4	-170.45	1.55	0.48	0.74	3.04	IN
	5	-159.68	1.76	0.95	2.14	1.89	OUT
DQ2.5-glia-α1b-3,4-diHyp	**1**	**-165.62**	**0.94**	**0.60**	**1.12**	**1.00**	**OUT**
	2	-156.32	1.33	1.16	1.15	1.79	OUT
	5	-137.42	3.36	5.41	1.19	1.79	--
	3	-116.46	16.25	18.09	9.55	22.37	--
	4	-96.78	15.74	22.59	11.42	8.88	--
DQ2.5-glia-α2	**3**	**-182.78**	**2.64**	**0.65**	**2.38**	**1.21**	**IN**
	1	-178.98	2.60	0.52	2.37	1.05	IN
	4	-171.79	2.73	0.95	2.55	0.96	IN
	5	-167.62	2.69	0.95	2.37	1.87	OUT
	2	-156.43	2.68	0.58	2.38	1.80	OUT
DQ2.5-glia-α2-3,4-diHyp	**3**	**-148.43**	**3.04**	**2.65**	**2.57**	**1.15**	**IN**
	2	-143.58	17.15	24.22	8.45	17.18	--
	1	-140.12	17.51	25.16	8.34	16.91	--
	4	-122.27	6.89	6.90	6.80	5.87	--
	5	-120.26	4.24	4.18	4.14	1.86	--

[a] bold: the best docking pose; red: incorrect assignment of peptide residues to the P1-P9 receptor registers.
[b] with respect to DQ2.5-glia-α1a crystal structure (PDB ID: 1S9V).[9]
[c] IN and OUT refer to the position of the residue side-chain with respect to the P9 receptor binding cavity.

Table S2 – Docking results, expressed as Prime MM-GBSA ΔG_{bind}, for DQ2.5-glia-α2 and 15 Hyp and diHyp containing analogues

Name	ΔG_{bind} (kcal mol^{-1})	$\Delta\Delta G_{bind}$[a] (kcal mol^{-1})	backbone RMSD (Å)[b]
3-Hyp-8	-187.96	-5.18	0.91
3,4-diHyp-6	-187.32	-4.54	1.79
3,4-diHyp-8	-184.58	-1.81	1.64
DQ2.5-glia-α2	-182.78	--	0.00
3-Hyp-6	-182.72	0.06	1.33
4-Hyp-8	-181.77	1.01	1.71
3-Hyp-3	-181.17	1.61	0.92
4-Hyp-6	-178.98	3.80	0.78
4-Hyp-1	-178.86	3.92	0.75
3-Hyp-1	-177.03	5.75	0.81
3,4-diHyp-1	-171.35	11.43	1.33
4-Hyp-3	-171.33	11.44	1.03
4-Hyp-1-3-6-8	-167.80	14.97	1.04
3-Hyp-1-3-6-8	-164.70	18.07	0.99
3,4-diHyp-3	-157.75	25.03	1.00
3,4-diHyp-1-3-6-8	-148.43	34.34	1.96

[a] with respect to the DQ2.5-glia-α2 docking pose
[b] with respect to the DQ2.5-glia-α2 crystal structure

Table S3 – H-bond networks [a] in the best docking pose of each nonamer[b]

Name	DONOR		ACCEPTOR		Distance Acceptor – H (Å)	Type [d]
	Atom [c]	Residue	Atom [c]	Residue		
DQ2.5-glia-α1a	N	Phe (P2)	OD1	Asn E82	1.67	bb/sc
	ND2	Asn E82	O	Phe (P2)	1.79	sc/bb
	N	Gln (P4)	O	Tyr D9	2.14	bb/bb
	NZ	Lys E71	OE1	Gln (P4)	2.26	sc/sc
	N	Glu (P6)	OD1	Asn D62	1.86	bb/sc
	OH	Tyr E9	OE1	Glu (P6)	2.10	sc/sc
	ND2	Asn D69	O	Leu (P7)	1.92	sc/bb
	N	Tyr (P9)	OD1	Asn D69	2.28	bb/sc
	NH2	Arg D76	OXT	Tyr (P9)	1.95	sc/bb
DQ2.5-glia-α1a-3,4-diHyp	OH4	diHyp (P1)	OD1	Asn E82	2.36	sc/sc
	OH3	diHyp (P3)	O	Tyr D9	1.76	sc/bb
	OH4	diHyp (P3)	O	Tyr D9	1.69	sc/bb
	NZ	Lys E71	OE1	Gln (P4)	2.06	sc/sc
	NZ	Lys E71	O	diHyp (P5)	2.41	sc/bb
	ND2	Asn D69	O	Leu (P7)	2.07	sc/bb
DQ2.5-glia-α1b	N	Tyr (P2)	OD1	Asn E82	1.69	bb/sc
	ND2	Asn E82	O	Tyr (P2)	1.72	sc/bb
	N	Gln (P4)	O	Tyr D9	1.96	bb/bb
	NZ	Lys E71	OE1	Gln (P4)	2.28	sc/sc
	N	Glu (P6)	OD1	Asn D62	1.77	bb/sc
	OH	Tyr E9	OE1	Glu (P6)	2.40	sc/sc
	ND2	Asn D69	O	Leu (P7)	2.08	sc/bb
	NE1	Trp E61	O	Pro (P8)	2.43	sc/bb
	OH	Tyr (P9)	OH	Tyr E9	2.40	sc/sc
DQ2.5-glia-α1b-3,4-diHyp	N	Tyr (P2)	OD1	Asn E82	1.94	bb/sc
	ND2	Asn E82	O	Tyr (P2)	2.07	sc/bb
	OH4	diHyp (P3)	O	Tyr D9	2.09	sc/bb
	OH3	diHyp (P5)	OD1	Asn D62	2.41	sc/sc
	NZ	Lys E71	OE1	Gln (P4)	2.38	sc/sc
	ND2	Asn D69	O	Leu (P7)	1.86	sc/bb
	N	Tyr (P9)	OD1	Asn D69	2.06	bb/sc
DQ2.5-glia-α2	N	Gln (P2)	OD1	Asn E82	2.19	bb/sc
	ND2	Asn E82	O	Gln (P2)	1.95	sc/bb
	N	Glu (P4)	O	Tyr D9	2.37	bb/bb
	NZ	Lys E71	OE1	Glu (P4)	1.78	sc/sc
	NZ	Lys E71	OE2	Glu (P4)	2.32	sc/sc
	NZ	Lys E71	O	Leu (P5)	2.06	sc/bb
	ND2	Asn D69	O	Tyr (P7)	1.96	sc/bb
	NE1	Trp E61	O	Pro (P8)	2.39	sc/bb
	NH2	Arg D76	OXT	Gln (P9)	2.49	sc/bb
DQ2.5-glia-α2-3,4-diHyp	ND2	Asn E82	O	diHyp (P1)	1.98	sc/bb
	N	Gln (P2)	OD1	Asn E82	2.38	bb/sc
	OH3	diHyp (P3)	OH	Tyr D22	2.03	sc/sc
	OH4	diHyp (P3)	O	Tyr D9	1.93	sc/bb
	N	Gln (P9)	OD1	Asn D69	2.33	bb/sc
	NH2	Arg D76	OE1	Gln (P9)	2.33	sc/sc

[a] Computed by Glide XP[28] (max. distance = 2.5 Å, donor angle = 120°, acceptor angle = 90°).
[b] The peptide residues are highlighted in blue and the corresponding register position is in quotes
[c] PDB atom type, with exception of OH3 and OH4 to indicate the Oxygen of the hydroxyl group in position 3 or 4 of the Hyp residues.
[d] bb = backbone, sc = sidechain.