

Supplementary Material

Mechanism of the Blood-Brain Barrier Modulation by Cadherin Peptides

Table S1. Interacting EC1 residues for each HADDOCK cluster per peptide

ADT Peptide	Interacting EC1 Domain Residues
ADTC5	<u>Cluster#1</u> S8, S9, P10, T99, D100, Q101, N102, D103, K105
	<u>Cluster#2</u> P6, R68, T73, L95, T97, V98, T99, D100
	<u>Cluster#3</u> P5, P6, I7, S8, P10, L21, T99, K105
	<u>Cluster#4</u> I7, S8, S9, P10, T99, D100, Q101, N102, D103, N104, K105
	<u>Cluster#5</u> P6, S8, S9, P10, T97, T99, D100, Q101, D103, K105
	<u>Cluster#6*</u> Q23, K25, E56, G58, S26, N27, Y36, I24, D29, K30
	<u>Cluster#7</u> W2, V3, P5, P6, I7, S8, L21, V22, Q23, W59
	<u>Cluster#8</u> P6, S8, P10, T99, D103, K105
ADTC7	<u>Cluster#1</u> E13, K19, N20, L21, K105, P106, G124, S126, T125
	<u>Cluster#2</u> I7, P10, E13, K19, N20, L21, K105, P106, T125, S126
	<u>Cluster#3</u> G15, P18, K19, N20, L21, P106, Glu107, F108, T125, S126, A132
	<u>Cluster#4</u> I4, P5, P6, I7, S8, L21, K105, V122
	<u>Cluster#5</u> I7, S8, E13, K19, N20, L21, W59, K105, P106, T125
	<u>Cluster#6*</u> T109, F113, K114, G115, S116, M128, V130
	<u>Cluster#7</u> I4, P5, I7, S8, P10, N20, L21, V22, Q23, K105, W59
ADTC9	<u>Cluster#1</u> S9, P10, E13, K19, N20, L21, K105, P106, T125, G124, S126
	<u>Cluster#2</u> S9, P10, E13, P16, N20, L21, W59, T99, K105, F108, P106, T125, G124, S126
	<u>Cluster#3</u> E13, P16, K19, N20, L21, K105, P106, T125, G124, Ser126
	<u>Cluster#4</u> I4, P5, P6, I7, S8, P10, N20, L21, V22, W59, K105
	<u>Cluster#5</u> P16, K19, N20, K105, P106, E107, F108, T125, S126, A132
	<u>Cluster#6</u> P5, P6, I7, S8, P10, E13, N20, L21, D103, K105

* Represent models that were docked differently from the other models for ADTC7 or ADTC5 peptides.

Table S2. Protein-Ligand Interactions

ADT peptides	Cluster	Hydrogen bond		Non-bonded Interaction	
		EC1 residue	Peptide residue		
ADTC5	#5	Lys105	Asp2 sidechain	Asp103	
		Ser8	Pro5 carbonyl backbone	Pro6	
		Thr99	Amide nitrogen- C terminus	Gln101	
		Thr97	Amide nitrogen- C terminus	Pro10	
		Ser9	Amide nitrogen- C terminus	Asp100	
	ADTC7	#7			Val98
			Gln23	Pro5 carbonyl backbone	Pro5
			Ser8	Cys8 S sidechain	Val22
				Cys8 N terminus	Ile4
					Ile7
ADTC9	#1			Lys105	
				Pro10	
				Leu21	
				Trp59	
		Lys105	Asp3 sidechain	Glu13	
		Pro106	Cys1 N terminus	Ser9	
		Asn20	Pro6 carbonyl backbone	Pro10	
Ser126	Amide nitrogen- C terminus (2x)	Leu21			
		Thr125	Pro5 carbonyl backbone	Gly124	
				Lys19	