

Supplementary information

BLAST results

The best two hit comparison obtained from BLAST

The symbol '#' means the atoms in the pdb file were not successfully solved or missing.

for the standard stem region of CD44s

CD44s : 181 DVSSGSTIEKSTPEGYILHTDLPTS-QPTGDRDDAFFIGSTLAT 223

similarity

4XGU_A : 83 EN--DLTINPSNIHVYKLHKDGPLS#####SQLWQ 126

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11/43 = 25.58%

CD44s : 181 DVSSGSTIEKSTPEGYILHTDLPTSQPTGDRDDAFFIGSTLAT 223

2DK1_A : 3 SGSSGRWVEGITSEGYHYYYDLISGASQWEKPEGFQGDLLKTS 45

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11/43 = 25.58%

for the stem of CD44v6

CD44v6 : 181 DVSSGSTIEKSTP--

EGYILHTDLPTSQPTGDRDDAFFIGSTLATWADPNSTTEEAATQKEKWFENEWQGKNPPTPSED SHVT

EGTT 265

3DWL_A : 183 VVDSGDGVTHIIPVAEGYVIGSSIKT-

MPLAGRDVTYFVQSLLR#####LKTAERIKECCYVCPDIVKEFSRFDR#####LKYA 269

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similarity= 18/85 = 21.18%

CD44v6 : 181 DVSSGSTIEKSTPEGYILHTDLPTSQPTGD-----

RDDAFFIGSTLATWADPNSTTEEAATQKEKWFENEWQGKNPPTPSED SHVTEGTT 265

3LQ1_A : 276

FLKEAEIIDKLTPEVVIRFGSMPVSKPLKNWLEQLSDIRFYVVDPGAAWKDPIKAVTDMIHC DERFLL

DIMQ-QNMPDDAKDAAWLNGWT 364

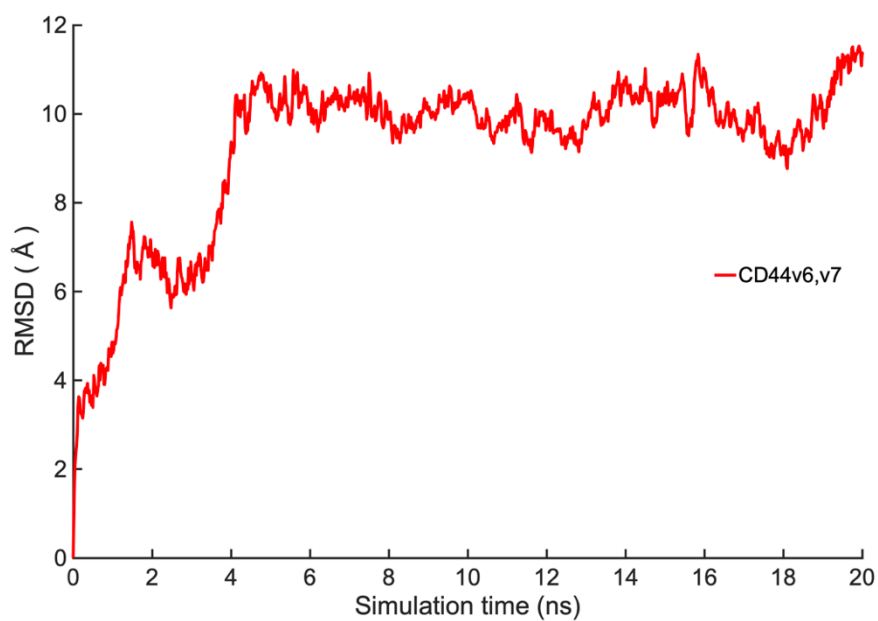
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similarity= 22/85 =25.88%

Figure S1 Representative sequence comparison results obtained from BLAST server. An * (asterisk) indicates positions which have a single, fully conserved residue.

(a)



(b)

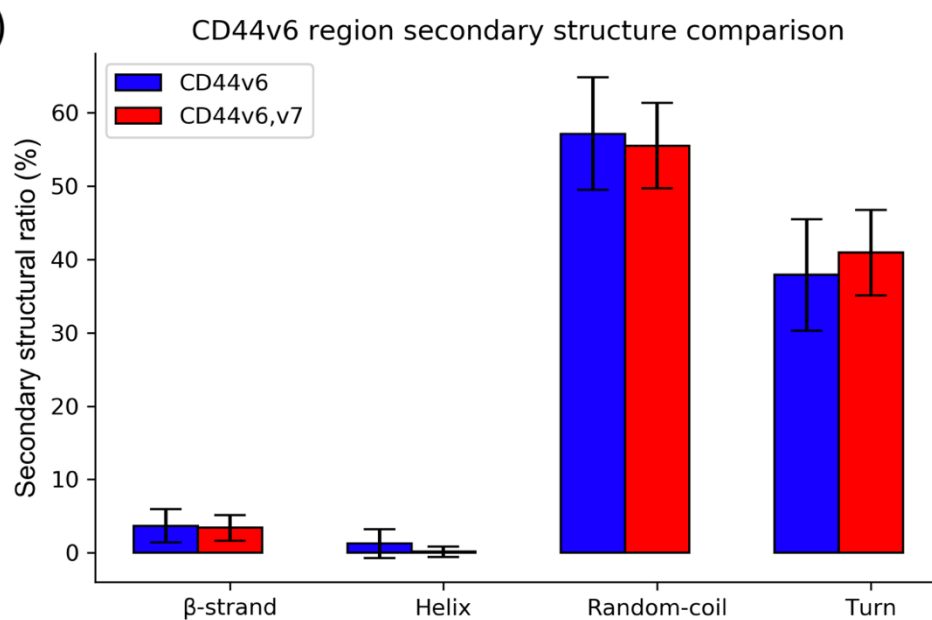


Figure S2 (a) The RMSD of CD44v6+v7 and (b) secondary structure comparison between CD44v6 and CD44v6+v7.

Table S1. Hydrogen bond occupancies for CD44s cluster 1. The hydrogen bonds involved in β -sheets were underlined. (Only occupancies above 35% are shown.)

Donor	Acceptor	Occupancy (%)
<u>HIS199-Main-N</u>	<u>PHE215-Main-O</u>	<u>88.60%</u>
<u>ILE217-Main-N</u>	<u>ILE197-Main-O</u>	<u>81.58%</u>
GLY195-Main-N	THR192-Main-O	64.04%
THR192-Main-N	TYR196-Main-O	50.88%
TYR196-Main-N	THR192-Side-O	50.00%
<u>THR187-Main-N</u>	<u>THR200-Main-O</u>	<u>43.86%</u>
<u>PHE215-Main-N</u>	<u>HIS199-Main-O</u>	<u>42.98%</u>
<u>THR200-Main-N</u>	<u>THR187-Main-O</u>	<u>40.35%</u>
LEU202-Main-N	GLY185-Main-O	39.47%
GLU194-Main-N	THR192-Side-OG1	35.96%
<u>GLU189-Main-N</u>	<u>LEU198-Main-O</u>	<u>35.09%</u>

Table S2. Hydrogen bond occupancies for CD44s cluster 2 The hydrogen bonds involved in β -sheets were underlined. (Only occupancies above 35% are shown.)

Donor	Acceptor	Occupancy (%)
<u>ILE217-Main-N</u>	<u>SER183-Main-O</u>	<u>66.67%</u>
<u>SER183-Main-N</u>	<u>PHE215-Main-O</u>	<u>65.71%</u>
LEU202-Main-N	THR200-Side-O	51.43%

Table S3. Hydrogen bond occupancies for CD44v6 cluster 1. The hydrogen bonds involved in β -sheets were underlined. (Only occupancies above 35% are shown.)

	Donor	Acceptor	Occupancy (%)
Within standard stem	GLU194-Main-N	SER191-Main-O	58.73%
	GLN206-Main-N	THR204-Side-O	45.63%
	GLY209-Main-N	GLN206-Main-O	42.46%
	LEU221-Main-N	GLY218-Main-O	40.08%
	GLY195-Main-N	SER191-Side-O	38.89%
	ALA214-Main-N	ARG211-Main-O	38.89%
Between standard stem and v6	<u>TRP224-Main-N</u>	<u>PHE215-Main-O</u>	<u>75.40%</u>
	<u>PHE215-Main-N</u>	<u>TRP224-Main-O</u>	<u>63.10%</u>
	TYR196-Main-N	ASP226-Main-O	55.16%
Within variant 6	GLU245-Main-N	PHE242-Main-O	38.89%
	LYS238-Main-N	THR236-Side-O	35.71%

Table S4. Occupancies of hydrophobic and aromatic contacts with Phe215 (Only occupancies above 35% are shown.)

	Hydrophobic/aromatic residue	Occupancy (%)
CD44s, cluster 1	HIS199	63.2%
	ILE217	45.6%
CD44s, cluster 2	VAL182	70.5%
	ILE217	60.0%
	PRO203	37.1%
CD44v6, cluster 1	TYR196	68.7%
	TRP224	61.1%
	ILE197	40.1%
	ILE217	40.1%

Table S5 Hydrogen bond occupancies for CD44v6+v7 between standard stem and v6

Between standard stem and v6	Donor	Acceptor	Occurancy (%)
	TRP224-Main-N	PHE215-Main-O	96.71
	PHE215-Main-N	TRP224-Main-O	82.73
	TYR196-Main-N	ASP226-Main-O	98.3