

Preventing The Interaction between Coronaviruses Spike Protein and Angiotensin I Converting Enzyme 2: An *In Silico* Mechanistic Case Study on Emodin as a Potential Model Compound

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The accession codes of proteins under analysis are reported in Table S1.

Table S1. Accession code of protein sequences under analysis.

Protein	PDB code	GeneBank accession code
Human ACE2	6ACG (chain A, B, C); 6M0J (chain A)	BAB40370.1
SARS-CoV-1 S protein	6ACG (chain D)	ABD72970.1
SARS-CoV-2 S protein	6M0J (chain E)	QJE37811.1

The results of computational alanine scanning of SARS-CoV-1 S protein-ACE2 are reported in Table S2.

Table S2. Computational alanine scanning results of SARS-CoV-1 S protein-ACE2.

	Residue Position	$\Delta\Delta G$
S protein	426	0.41
	436	0.98
	440	0.33
	442	1.42
	443	0.47
	463	-0.06
	472	0.53
	473	0.33
	475	2.23
	479	0.03
	480	-0.09
	484	1.76
	486	0.46
	487	0.33
	489	0.52
	491	2.04
ACE2	492	0.27
	24	0.09
	27	0.57
	28	0.32
	30	-0.19
	31	0.27
	34	0.36
	35	-0.03
	37	0.04
	38	-0.15
	41	2.74
	42	1.54
	45	0.58
	79	0.46
	82	0.34
	83	0.25
	324	0.02
	325	1.42
	329	-0.06
	330	0.62
	353	1.33
	355	0.94

Note: most important amino acid position in PPI (i.e. $\Delta\Delta G > 1$) are colored in red and highlighted in bold

The results of computational alanine scanning of SARS-CoV-2 S protein-ACE2 are reported in Table S3

Table S3. Computational alanine scanning results of SARS-CoV-2 S protein-ACE2.

	Residue position	$\Delta\Delta G$
S protein	417	0.62
	449	1.61
	453	0.20
	455	1.21
	456	1.64
	486	2.06
	487	4.38
	489	2.27
	493	0.51
	494	0.00
	495	0.00
	498	1.15
	500	0.69
	501	1.18
	503	0.07
	505	2.47
ACE2	24	2.20
	27	0.66
	28	0.25
	30	0.52
	31	0.50
	34	0.70
	35	-0.13
	37	1.07
	38	0.68
	41	4.69
	42	2.26
	45	0.45
	79	0.54
	82	0.21
	83	2.90
	330	0.19
	351	0.03
	353	0.26
	355	3.63
	357	2.12
	393	0.00

Note: most important amino acid position in PPI (i.e. $\Delta\Delta G > 1$) are colored in red and highlighted in bold

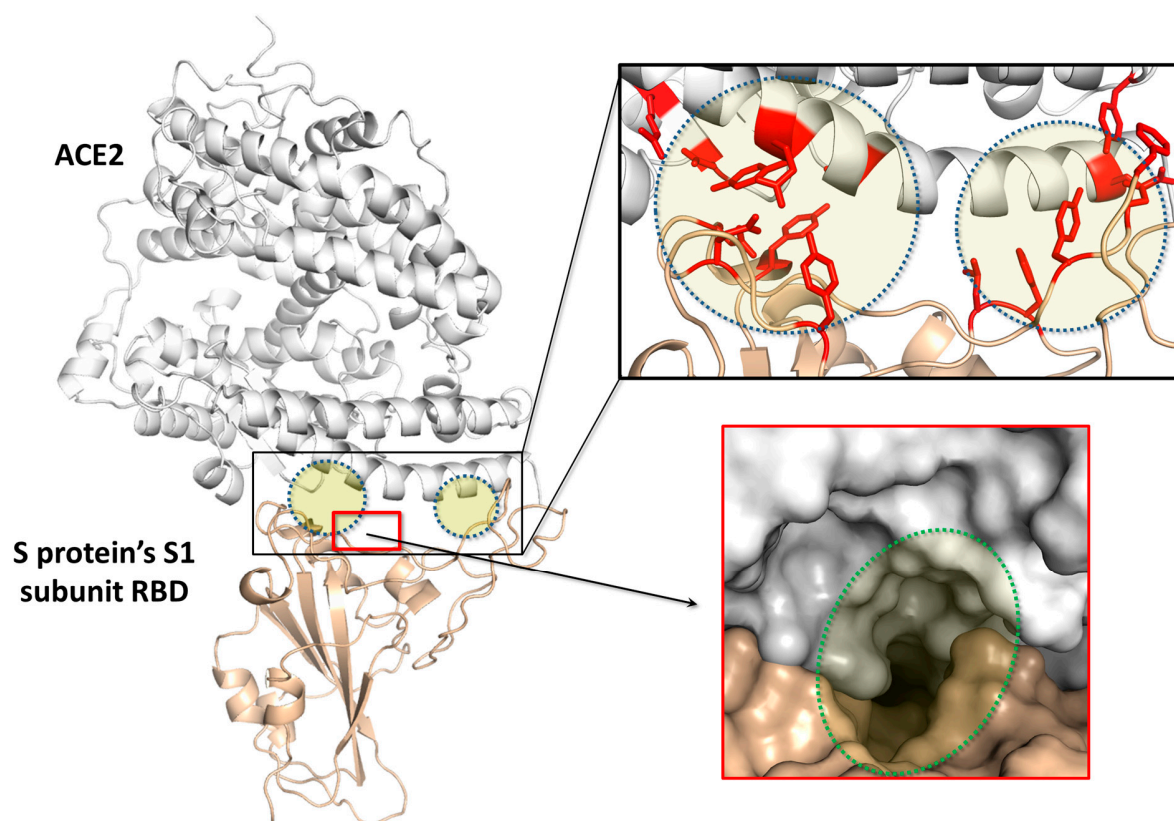


Figure S1. Graphical representation of SARS-CoV-2 S protein-ACE2 complex derived from the crystallographic structure having PDB code 6M0J. SARS-CoV-2 S protein is colored in yellow, ACE2 is colored in white. The black box on the left figure indicates the protein-protein contact surface, while the yellow dotted circles indicate the protein-protein interaction hotspots (which are highlighted in red sticks in the close-up on the top right). The red box on the left figure indicates the position of the surface pocket identified at the protein-protein contact surface, which is detailed in a surface representation on the bottom-right close-up and highlighted with a dotted ring.