



Figure S1: Detailed surface view of UBA domain of Dsk2p protein complexed with ubiquitin (PDB ID: 1WR1). Residues M342, G343, and F344 are well conserved in the UBA domains and form the hydrophobic core of the large surface patch for interacting with ubiquitin.

	BeAtMuSiC	mCSM-PPI2		BeAtMuSiC	mCSM-PPI2
	$\Delta\Delta G$	$\Delta\Delta G$		$\Delta\Delta G$	$\Delta\Delta G$
SARS-CoV	(kcal/mol)	(kcal/mol)	SARS-CoV-2	(kcal/mol)	(kcal/mol)
N479E	0.86	0.805	Q493E	1.37	0.092
N479K	0.66	1.448	Q493K	1.06	0.808
N479Q	0.57	0.743	Q493N	1.36	-0.497
N479R	0.29	0.797	Q493R	0.76	0.552
N479S	0.91	-0.610	Q493S	1.86	-0.509
G482A	0.67	0.858	G496A	0.84	0.829
G482D	1.15	-1.466	G496D	0.65	-0.910
G482V	0.40	0.838	G496V	0.70	1.174
Y484F	0.45	0.872	Q498F	-0.42	0.466
Y484H	1.17	1.670	Q498H	0.13	0.415
Y484N	1.94	-0.333	Q498N	0.69	-1.103
Y484Q	1.65	1.605	Q498Y	-0.14	-1.961
Y484T	1.64	1.581	Q498T	0.39	1.363

Table S1: Changes in binding affinity of human SARS-CoV and human SARS-CoV-2 spike RBD complexed with hACE2 upon mutation as predicted by BeAtMuSiC and mCSM-PPI2.

Name	Spike Glycoprotein GenBank	Name	Spike Glycoprotein GenBank	Name	Spike Glycoprotein GenBank
SARS-CoV-Tor2	AAP41037.1	SARS-CoV PC4-115	AAV49719.1	Rhinolophus affinis CoV LYRa3 (SARS-like)	AHX37569.1
SARS-CoV BJ01	AAP30030.1	SARS-CoV PC4-145	AAV49721.1	Rhinolophus affinis CoV LYRa11 (SARS-like)	AHX37558.1
SARS-CoV CUHK-W1	AAP13567.1	SARS-CoV PC4-241	AAV49723.1	Bat SARS-like CoV Rs3367	AGZ48818.1
SARS-CoV Urbani	AAP13441.1	SARS-CoV civet014	AAU04661.1	Bat SARS-like CoV Rs4874	ATO98205.1
SARS-CoV Frankfurt-1	AAP33697.1	SARS-CoV PC4-137	AAV49720.1	Bat SARS-like CoV WIV1	AGZ48828.1
SARS-CoV CUHK-AG01	AAP94737.1	SARS-CoV civet020	AAU04664.1	SARS-like CoV WIV16	ALK02457.1
SARS-CoV TW6	AAR87567.1	SARS-CoV PC4-127	AAU93318.1	Bat SARS CoV RaTG13	QHR63300.2
SARS-CoV TW11	AAR87512.1	SARS-CoV B039	AAV97993.1	Bat SARS-like CoV Rs7327	ATO98218.1
SARS-CoV HKU-39849	ADC35483.1	SARS-CoV PC4-205	AAU93319.1	Bat SARS-like CoV Rs9401	ATO98231.1
SARS-CoV-2 Wuhan-Hu-1	QHD43416.1	SARS-CoV PC4-199	AAV49722.1	CoV BtRs-BetaCoV/YN2018B	QDF43825.1
SARS-CoV-2 CA-CDC-0139	QJV58828.1	SARS-CoV civet010	AAU04649.1	Bat SARS-like CoV RsSHC014	AGZ48806.1
SARS-CoV-2 France	QJT72590.1	SARS-CoV civet019	AAU04662.1	Bat SARS-like CoV Rs4084	ATO98132.1
SARS-CoV-2 WHUHuCoV011	QIU82034.1	SARS-CoV A022	AAV91631.1	Bat SARS-like CoV Rs4231	ATO98157.1
SARS-CoV-2 CA-CZB-1248	QKE49268.1	Civet SARS-CoV 007/2004	AAU04646.1	SARS-CoV strain BtKY72	APO40579.1
SARS-CoV-2 CA-CZB-1033	QJQ38756.1	SARS-CoV A001	AAV97984.1	SARS-like CoV BatCoV/BB9904/BGR/2008	ALJ94036.1
SARS-CoV-2 France/10070SK	QJT73010.1	PCoV GX-P2V	QIQ54048.1	Bat CoV BM48-31/BGR/2008 (SARS-like)	ADK66841.1
SARS-CoV-2 CA-CZB0103	QJE38330.1	PCoV GX-P4L	QIA48614.1	CoV BtRI-BetaCoV/SC2018	QDF43815.1
SARS-CoV-2 BetaCoV/Wuhan/IPBCAMS-WH-05	QHU36864.1	PCoV GX-P5L	QIA48632.1	BtRs-BetaCoV/HuB2013	AIA62310.1
SARS-CoV-2 CruiseA-18	QII57278.1			Bat SARS-CoV HKU3-1	AAY88866.1
SARS-CoV-2 CA-CZB-1105	QJS54754.1			Bat SARS-like CoV bat-SL-CoVZC45	AVP78031.1
				Bat SARS-like CoV bat-SL-CoVZXC21	AVP78042.1
				Bat SARS-CoV Rf1/2004	ABD75323.1
				Bat SARS-like CoV Rf4092	ATO98145.1
				Bat CoV Anlong-103	ARI44799.1
				Bat CoV Anlong-112	ARI44804.1
				Bat SARS-CoV Rp3/2004	AAZ67052.1
				CoV BtRs-BetaCoV/YN2018C	QDF43830.1
				Bat CoV Rp/Shaanxi2011	AGC74165.1
				Bat SARS-CoV Rm1	ABD75332.1

Table S2: GenBank accession numbers for the coronavirus sequences analysed in this study.