Supplementary Material
Mutations strengthened SARS-CoV-2 infectivity

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S1 TopNetTree model for protein-protein interaction (PPI) binding affinity changes upon mutation

The topology-based network tree (TopNetTree) was constructed by an innovative integration between the topological representation and NetTree for predicting protein-protein interaction binding affinity changes following mutation $\Delta\Delta G$ [7]. In this work, TopNetTree is applied to predict the binding affinity changes of mutations that happened on the RBD with ACE2 of SARS-CoV-2 after January 5, 2020. As shown in Figure S1, topology-based feature generation is the first step followed by a convolutional neural network (CNN)-assisted model. The topological representation uses element- and site-specific persistent homology to simplify the structural complexity of protein-protein complexes and encode vital biological information into topological invariants. NetTree is a recently developed deep learning algorithm that integrates the advantages of convolutional neural networks and gradient-boosting trees (GBT) [7]. In this section, we briefly describe the topology representation for machine learning training and prediction. Details can be found in the literature [7].

S1.1 Topology-based feature generation of PPIs

The topology-based feature generation is built upon from persistence homology starting with simplicial complex and filtration [2]. As a type of algebraic topology, persistence homology studies simplicial complex on discrete datasets under various settings. Among the many constructions, two that are widely used for point clouds are the Vietoris-Rips (VR) complex and alpha complex [3] which are applied in our approach. Built upon a simplicial complex, the topological invariants of a point-cloud dataset can be identified, such as the set of atoms in protein-protein interactions. Meanwhile, topological invariants (separated components, rings, and cavities) can be enumerated by counting the numbers referred to as Betti-0, Betti-1, and Betti-2, respectively. Thus taxing and uninformative features or calculations are fully abandoned, whereas geometric and topological characteristics persevere as data representation. Moreover, using persistent homology, the original 3D point-cloud data are characterized by topological barcodes that record the "birth" and "death" of each topological invariants and simplifying complicated structural representations of a PPI-complex. Although topology data presentation much simplifies the problem in many directions, better construction is required for it to extract patterns of different biological or chemical aspects. Before describing about more detailed feature generations, we first preset the constructions for a PPI complex into various subsets.

1. $\mathcal{A}_{\mathrm{m}}$: atoms of the mutation sites.
2. $\mathcal{A}_{\mathrm{mn}}(r)$: atoms in the neighbourhood of the mutation site within a cut-off distance r.
3. $\mathcal{A}_{\mathrm{Ab}}(r)$: antibody atoms within r of the binding site.

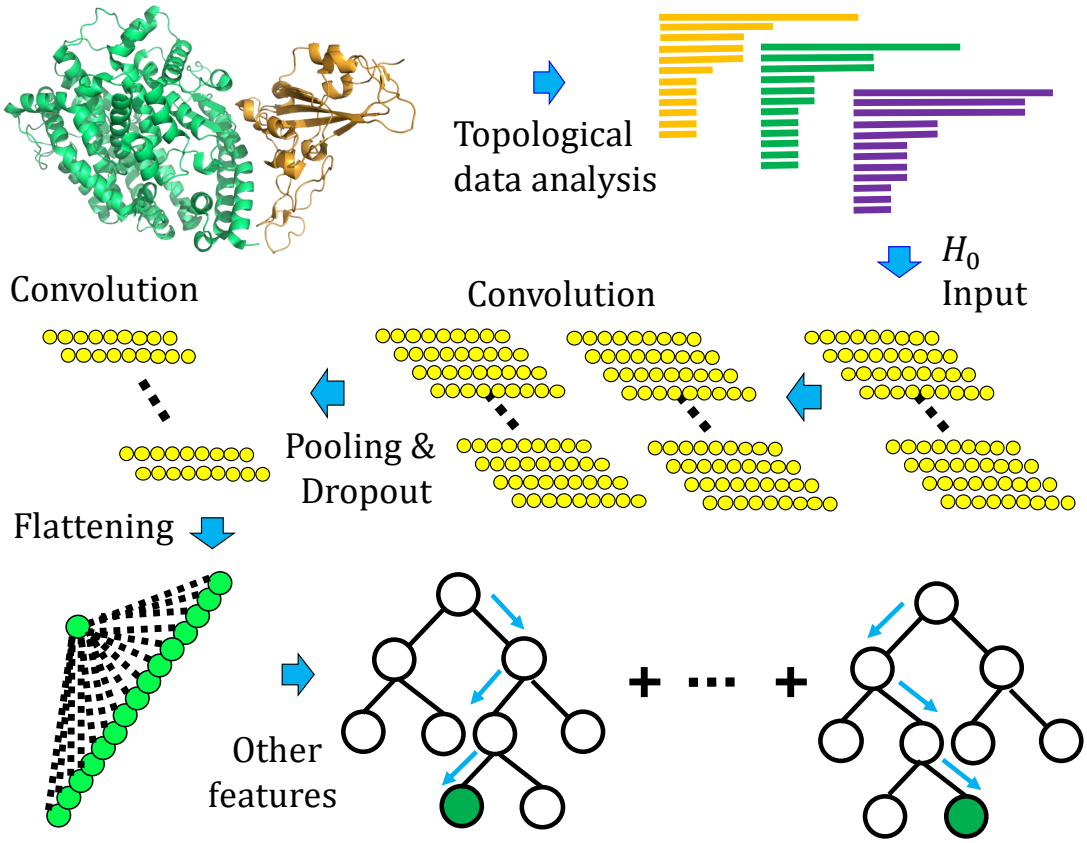

Figure S1: An illustration of the TopNetTree model. Protein structure shown in the plot is SARS-CoV-2 spike receptor-binding domain bound with ACE2 (PDB 6M0J). Here, H_0 are the 0-dimensional topological input features for machine learning model.

4. $\mathcal{A}_{\text{Ag}}(r)$: antigen atoms within r of the binding site.

5. $\mathcal{A}_{\text{ele}}(\text{E})$: atoms in the system that has atoms of element type E. The distance matrix is specially designed such that it excludes the interactions between the atoms form the same set. For interactions between atoms a_i and a_j in set $\mathcal{A}$ and/or set $\mathcal{B}$, the modified distance is defined as

$$D_{\text{mod}}(a_i, a_j) = \begin{cases} \infty, \text{ if } a_i, a_j \in \mathcal{A}, \text{ or } a_i, a_j \in \mathcal{B}, \\ D_e(a_i, a_j), \text{ if } a_i \in \mathcal{A} \text{ and } a_j \in \mathcal{B}, \end{cases} \tag{1}$$

where $D_e(a_i, a_j)$ is the Euclidian distance between a_i and a_j.

In algebraic topology, molecular atoms can be treated as points presented by v_0, v_1, v_2, ..., v_k as $k+1$ affinely independent points. Simplicial complex, the essential building blocks, is a finite collection of sets of points $K = \{\sigma_i\}$, and σ_i are called linear combinations of these points in $\mathbb{R}^n$ ($n \geq k$). For instance, a 0-, 1-, 2-, or 3-simplex in geometry representation is a vertex, an edge, a triangle, or a tetrahedron, respectively. A simplicial complex K is valid if a face τ of a k-simplex σ_i of K is also in K, such that $\tau \subseteq \sigma_i$ and $\sigma_i \in K$ imply $\tau \in K$ and the non-empty intersection of any two simplieces is a face for both. Given a simplicial complex K, a k-chain is a finite formal sum of k-simplices; that is, $\sum_i \alpha_i \sigma_i^k$. The set of all k-chains of the simplicial complex K equipped with an algebraic field (typically, $\mathbb{Z}_2$) forms an abelian group $C_k(K, \mathbb{Z}_2)$, which means the coefficients a_i are chosen from $\mathbb{Z}_2$. A boundary operator $\partial_k : C_k \to C_{k-1}$ for a k-simplex $\sigma^k = \{v_0, v_1, v_2, \cdots, v_k\}$ are homomorphisms defined as $\partial_k \sigma^k = \sum_{i=0}^{k} (-1)^i \{v_0, v_1, \cdots, \hat{v_i}, \cdots, v_k\}$, where $\{v_0, v_1, \cdots, \hat{v_i}, \cdots, v_k\}$ is a $(k-1)$-simplex excluding v_i from the vertex set. Consequently, a important property of boundary operator, $\partial_{k-1}\partial_k = \emptyset$, follows from that boundaries are boundaryless. Moreover the kth cycle group $Z_k = \ker \partial_k = \{c \in C_k \mid \partial_k c = \emptyset\}$ is defined to be the kernel of ∂_k, whose elements are called k-cycles; and the kth boundary group is the image of ∂_{k+1} denoted as $B_k = \text{im } \partial_{k+1} = \{\partial_{k+1} c \mid c \in C_{k+1}\}$. The algebraic construction to connect a sequence of complexes by boundary maps is called a chain complex

$$\cdots \xrightarrow{\partial_{i+1}} C_i(X) \xrightarrow{\partial_i} C_{i-1}(X) \xrightarrow{\partial_{i-1}} \cdots \xrightarrow{\partial_2} C_1(X) \xrightarrow{\partial_1} C_0(X) \xrightarrow{\partial_0} 0$$

and the kth homology group is the quotient group defined by

$$H_k = Z_k / B_k. \tag{2}$$

The key property of boundary operators implies $B_k \subseteq Z_k \subseteq C_k$. The Betti numbers are defined by the ranks of kth homology group H_k which counts k-dimensional holes, especially, $\beta_0 = \text{rank}(H_0)$ reflects the number of connected components, $\beta_1 = \text{rank}(H_1)$ reflects the number of loops, and $\beta_2 = \text{rank}(H_2)$ reveals the number of voids or cavities. Together, the set of Betti numbers $\{\beta_0, \beta_1, \beta_2, \cdots\}$ indicates the intrinsic topological property of a system.

Persistent homology is devised to track the multiscale topological information over different scales along a filtration [3]. A filtration of a topology space K is a nested sequence of subspaces $\{K^t\}_{t=0,\ldots,m}$ of K such that $\emptyset = K^0 \subseteq K^1 \subseteq K^2 \subseteq \cdots \subseteq K^m = K$. Moreover, on this complex sequence, we obtain a sequence of chain complexes by homomorphisms: $C_*(K^0) \to C_*(K^1) \to \cdots \to C_*(K^m)$ and a homology sequence: $H_*(K^0) \to H_*(K^1) \to \cdots \to H_*(K^m)$, correspondingly. The p-persistent kth homology group of K^t is defined as $H_k^{t,p} = Z_k^t / (B_k^{t+p} \bigcap Z_k^t)$, where $B_k^{t+p} = \text{im}\partial_{k+1}(K^{t+p})$. Intuitively, this homology group records the homology classes of K^t that are persistent at least until K^{t+p}. Under the filtration process, the persistent homology barcodes can be generated. Then the feature vectors can be constructed from these sets of intervals for machine learning models.

In a variety of vectorization methods, one discretizes the filtration parameter interval into bins and model the behavior of the barcodes in each bin [1]. To make use of advanced machine learning algorithms, we subdivide a filtration interval into bins of length. Then the numbers of persistence intervals are counted for each bin, such that birth events and death events can be represented. This approach gives us three feature

vectors for each topological barcode for the machine learning method. Note for different discretizations, the characterization of birth and death might not be stable so that only Betti-0 (H_0) barcodes obtained from the VR filtration are applied in this approach. Intuitively, features generated by binned barcode vectorization can reflect the strength of atom bonds, van der Waals interactions, and can be easily incorporated into a CNN, which captures and discriminates local patterns. Another method of vectorization is to get the statistics of bar lengths, birth values, and death values, such as sum, maximum, minimum, mean, and standard derivation. This method is applied to vectorize Betti-1 (H_1) and Betti-2 (H_2) barcodes obtained from alpha complex filtration based on the facts that higher-dimensional barcodes are sparser than H_0 barcodes.

S1.2 Machine learning models

Accurate prediction of binding affinity changes following mutation for PPIs is very challenging due to the complex dataset and 3D structures. A hybrid machine learning algorithm that integrates a CNN and GBT is designed to overcome difficulties. Briefly speaking, partial topologically simplified descriptions, specifically vectorized H_0 barcode feature, are converted into concise features by the CNN module. Then a GBT module is trained on the whole feature set for a robust predictor with effective control of overfitting.

TopGBT model. The gradient boosting tree (GBT) method produces a prediction model as an ensemble method which is a class of machine learning algorithms. It builds a popular module for regression and classification problems from weak learners. By the assumption that the individual learners are likely to make different mistakes, the method using a summation of the weak learners to eliminate the overall error. Furthermore, a decision tree is added to the ensemble depending on the current prediction error on the training dataset. Therefore, this method (a topology-based GBT or TopGBT) is relatively robust against hyperparameter tuning and overfitting, especially for a moderate number of features. The GBT is shown for its robustness against overfitting, good performance for moderately small data sizes, and model interpretability. The current work uses the package provided by scikit-learn (v 0.23.0) [5].

TopCNN model. CNN is a class of deep neural networks and is considered as some of the most successful architectures. CNN is a regularized case of a multilayer connected neural network, such that each neuron is connected locally to neurons in the next convolution layers and the weights are shared across different locations. To prepare the integration of CNN and GBT, CNN is treated as an intermediate model that converts vectorized H_0 topological features into a higher-level abstract feature for the downstream GBT model.

TopNetTree model. A supervised CNN model with the PPI $\Delta\Delta G$ as labels is trained for extracting high-level features from H_0 barcodes. Once the model is set up, the flatten layer neural outputs of CNN are feed into a GBT model to rank their importance. Based on the importance, and ordered subset of CNN-trained features is combined with features constructed from high-dimensional topological barcodes, H_1 and H_2 into the final GBT model as shown in Fig. S1. As for the parameters of the GBT model, 10 times 10-fold experiments are done for searching the optimal parameter setting.

S1.3 Cross-validation of TopNetTree

The proposed TopNetTree method is trained on the SKEMPI 2.0 dataset [4], which has 4,169 variants in 319 different complexes. A set "S8338" with 8,338 variants was derived from SKEMPI 2.0 dataset by setting the reverse mutation energy changes to the negative values of its original energy changes. To address the reliability of the TopNetTree method, we did the tenfold cross-validation on the SKEMPI 2.0 dataset with the averaged training accuracy, Pearson correlation coefficients R_{p}, Kendall's τ, and the root mean square error (RMSE), being 0.98, 0.89, and 0.37 kcal/mol. As shown in Table S1, these metrics are based on the average of ten random splittings of the ten-fold cross-validations which indicate TopNetTree is well trained. The performance test of tenfold cross-validation on dataset gives as $R_{\mathrm{p}} = 0.84$, $\tau = 0.60$, and RMSE = 1.06

Table S1: Ten-fold cross-validation of the TopNetTree on the SKEMPI 2.0 dataset.

	R_p	τ	RMSE (kcal/mol)		R_p	τ	RMSE (kcal/mol)
Fold 1 (Train)	0.981	0.884	0.366	Fold 6 (Train)	0.983	0.904	0.353
Fold 1 (Test)	0.835	0.595	1.065	Fold 6 (Test)	0.836	0.594	1.064
Fold 2 (Train)	0.982	0.902	0.360	Fold 7 (Train)	0.983	0.904	0.356
Fold 2 (Test)	0.839	0.600	1.061	Fold 7 (Test)	0.838	0.594	1.060
Fold 3 (Train)	0.982	0.887	0.366	Fold 8 (Train)	0.979	0.878	0.392
Fold 3 (Test)	0.837	0.595	1.068	Fold 8 (Test)	0.840	0.596	1.061
Fold 4 (Train)	0.981	0.880	0.369	Fold 9 (Train)	0.982	0.902	0.362
Fold 4 (Test)	0.841	0.596	1.059	Fold 9 (Test)	0.838	0.596	1.069
Fold 5 (Train)	0.982	0.906	0.365	Fold 10 (Train)	0.982	0.886	0.367
Fold 5 (Test)	0.839	0.594	1.062	Fold 10 (Test)	0.835	0.596	1.064
Average (Train)	0.982	0.893	0.366				
Average (Test)	0.838	0.596	1.063				

Table S2: Comparison of different methods' performance on S8338

Cross validation type	Method	R_p	RMSE (kcal/mol)
Leave one complex and its mutations out	TopNetTree	0.80	1.15
	MutaBind2 [8]	0.74	1.37
	mCSM-PPI2 [6]	0.75	1.30
Leave one interface type and its mutations out	TopNetTree	0.72	1.36
	MutaBind2 [8]	0.66	1.53
	mCSM-PPI2 [6]	0.67	1.39

kcal/mol, which is of the same level of accuracy as the best in the literature [7].

Finally, Table S2 illustrates the performance on the bench set S8338. Other methods in the comparison, namely MutaBind2 [8] and mCSM-PPI2 [6], are the-state-of-the-art in the field. There are 319 complexes and 5 types of interfaces in dataset S8338. Two different cross-validation strategies were designed in early work [6, 8]. The first cross validation strategy uses 318 complexes and their mutations as the training set to predict the left complex and its mutations. The second cross validation strategy collects four of five types of complexes and their mutations as the training set. The testing set is the rest type of complexes and mutations. As shown in Table S2, TopNetTree has the best performance among three methods.

S2 Supplementary Tables

S2.1 Six clusters of SARS-CoV-2 mutations on the RBD and predicted BA changes

Table S3: Six cluster binding affinity change prediction. Residue ID is according to SARS-CoV-2.

Cluster	Mutation	Frequency	Binding affinity change (kcal/mol)
I	G339D	1	0.038037932371751
I	E340K	1	-0.13915060303798316
I	A344S	1	-0.09148279588881875
I	T345S	1	0.037173505187905534

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Table S3 – continued from previous page

Cluster	Mutation	Frequency	Binding affinity change (kcal/mol)
I	R346K	2	0.609545129905911
I	A348S	2	-0.09604388978281342
I	N354K	3	0.35806448022647774
I	N354S	2	1.0806328048122054
I	D364Y	1	0.036473001468085235
I	V367F	3	1.155442051834433
I	V382L	1	-0.4911188069529559
I	P384L	1	-0.16402580528226846
I	P384S	1	-0.16736687642169268
I	T393P	1	-0.047913343538074846
I	R403K	8	0.0248089685344706
I	D405V	1	0.11496697449663433
I	Q414E	3	-0.07626851449790645
I	Q414P	1	0.12135308997471861
I	T415S	1	0.04852054861421278
I	I418V	1	0.1416451396868426
I	N439K	11	1.4272485828790165
I	N440K	1	0.36314255681801116
I	L441I	1	-0.06747155525566285
I	K444R	1	0.6864210980708181
I	V445I	1	0.13248603393474248
I	G446V	4	-0.4012543263543365
I	D467V	1	-0.33737906195422496
I	I468F	1	-0.08992045572938752
I	E471Q	1	0.496588369182639
I	A475V	1	-1.0578345095256103
I	S477I	2	0.26875869860161683
I	S477N	18	0.13667010071316804
I	T478I	3	-2.1527245830789186
I	P479S	12	-1.1671696465218049
I	E484K	2	0.8488387065159884
I	E484Q	1	-1.2015335893061114
I	F490S	1	0.5637651510270204
I	P491R	2	-0.9932790113649753
I	Q493L	2	-0.8654926033978836
I	S494P	3	-0.17593616566096387
I	L518I	2	0.19175847380447125
I	H519Q	1	-0.046046709226659814
I	A520S	6	0.03167236771877934
I	A520V	1	0.03974669900670044
I	P521R	3	-0.32702169487318955
I	P521S	2	-0.025743348681811433
I	A522S	5	0.0736485654015457
II	P337S	1	-0.057788809702088315
II	F338L	3	0.36052969791469974
II	W353R	1	-0.3918016236672974
II	N354D	2	0.21033658718881246
II	N354K	2	0.35806448022647774
II	D364Y	2	0.036473001468085235
II	V367F	11	1.155442051834433

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Table S3 – continued from previous page

Cluster	Mutation	Frequency	Binding affinity change (kcal/mol)
II	V382L	1	-0.4911188069529559
II	P384L	1	-0.16402580528226846
II	V395I	1	-0.3446213859997917
II	R408I	1	0.856911217217483
II	Q414E	1	-0.07626851449790645
II	V445A	1	0.5060805370683044
II	G446V	1	-0.4012543263543365
II	G446S	1	-0.14332357257299147
II	L455F	1	-0.6679875181636354
II	K458N	1	0.4945628365122759
II	I468T	3	-0.18186774146569967
II	I468V	4	0.01123955278800625
II	E471Q	1	0.496588369182639
II	A475V	2	-1.0578345095256103
II	S477G	1	0.3495445252588135
II	T478I	1	-2.1527245830789186
II	N481D	1	-0.05782995510366806
II	N481H	1	-0.4289756801167375
II	V483F	1	-0.1423809411877248
II	F490L	2	0.43675979855389196
II	F490S	1	0.5637651510270204
II	P491R	1	-0.9932790113649753
II	S494P	1	-0.17593616566096387
II	Y508H	1	-0.086199490516408
II	R509K	1	0.9500465207010513
II	V510L	1	-0.27304440255055507
II	A520S	3	0.03167236771877934
II	A522S	1	0.0736485654015457
III	A344S	2	-0.09148279588881875
III	N354S	1	1.0806328048122054
III	S359N	1	0.366390266794583
III	V367F	1	1.155442051834433
III	S373L	1	-0.3254958273948853
III	P384L	4	-0.16402580528226846
III	P384S	1	-0.16736687642169268
III	R408I	1	0.856911217217483
III	Q414K	1	0.2979791184958904
III	Q414R	1	0.09033073898683257
III	K417R	1	-0.1766171087241206
III	D427Y	1	-0.0780911400620959
III	G446V	6	-0.4012543263543365
III	G476S	3	-0.37562039340158543
III	S477N	34	0.13667010071316804
III	S477R	2	0.2589101045993276
III	T478I	11	-2.1527245830789186
III	V483F	1	-0.1423809411877248
III	E484D	3	2.5377213028701293
III	E484K	2	0.8488387065159884
III	Q493L	1	-0.8654926033978836
III	S494P	1	-0.17593616566096387

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Table S3 – continued from previous page

Cluster	Mutation	Frequency	Binding affinity change (kcal/mol)
III	L518I	1	0.19175847380447125
III	P521S	1	-0.025743348681811433
III	A522P	1	0.012553352056879272
IV	N354K	5	0.35806448022647774
IV	S359N	1	0.366390266794583
IV	P384L	1	-0.16402580528226846
IV	P384S	3	-0.16736687642169268
IV	Q414E	4	-0.07626851449790645
IV	Q414K	1	0.2979791184958904
IV	K417N	1	1.8393464219112645
IV	G446V	1	-0.4012543263543365
IV	L452R	2	2.506045056281037
IV	I472V	1	0.13755553567167822
IV	G476S	1	-0.37562039340158543
IV	S477R	3	0.2589101045993276
IV	P479L	1	-0.025670101732213135
IV	F490L	1	0.43675979855389196
IV	S494P	1	-0.17593616566096387
IV	L518I	3	0.19175847380447125
IV	A520S	1	0.03167236771877934
IV	A522S	1	0.0736485654015457
V	P337S	1	-0.057788809702088315
V	V341I	10	-0.6840279672104417
V	A344S	1	-0.09148279588881875
V	V367F	3	1.155442051834433
V	T385A	1	0.30752735295981476
V	R403S	1	1.0159224763603825
V	Q414K	1	0.2979791184958904
V	Q414R	1	0.09033073898683257
V	S438F	2	0.4669774102303501
V	N439K	40	1.4272485828790165
V	G446V	1	-0.4012543263543365
V	N450K	1	-0.1289154953463872
V	G485S	1	-0.46991910769565354
V	Q493L	1	-0.8654926033978836
V	Y508H	1	-0.086199490516408
V	A520V	1	0.03974669900670044
VI	A344S	1	-0.09148279588881875
VI	A348T	1	0.5659671045565193
VI	N354K	1	0.35806448022647774
VI	V367F	1	1.155442051834433
VI	G476S	6	-0.37562039340158543
VI	V483A	30	0.07757513964237478
VI	A520S	5	0.03167236771877934
VI	A522S	2	0.0736485654015457

S2.2 Predicted BA changes for most likely, likely, and unlikely future mutations

Table S4, Table S5, and Table S6 predicted BA changes for most likely, likely, and unlikely future mutations, respectively.

Table S4: Most likely mutation binding affinity change prediction. Residue ID is according to SARS-CoV-2.

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
T333S	0.24913391236864485	T333P	0.4948450195626233
T333A	0.29643295322361884	T333K	0.24620078919692548
T333I	0.4492306933718574	T333R	0.1850244150885822
N334Y	0.012101605495477376	N334H	0.01873899635169411
N334D	0.90664742343163	N334I	-1.4998660225663956
N334T	0.21676557979348612	N334S	0.16403075990607197
N334K	0.2964534357367737	L335M	0.04529483584560694
L335V	0.1933082001870466	L335S	-0.03863994891012686
L335W	0.013660413714865727	L335F	0.06928648414955062
C336S	0.3389031732622413	C336R	-0.26035352195914585
C336G	0.5522520010453154	C336Y	0.14365397266408633
C336F	0.15363147106748784	C336W	0.37738254464411264
P337T	-0.007713270032751285	P337S	0.04432167144462246
P337A	0.29087550949069935	P337H	0.2807148520459687
P337L	0.2205250410348804	P337R	0.3929714513126442
F338I	0.8655540034033651	F338L	0.4663890476735936
F338V	0.9276461736291889	F338Y	0.02803607787959067
F338S	1.6610890038152504	F338C	2.6318584493855646
G339S	0.18509093279916838	G339C	0.24732078620489778
G339R	0.3173055015233107	G339D	0.18067056501052392
G339V	0.41185478121553	G339A	0.3281601229440679
E340K	-0.06991657581872732	E340Q	0.04872937130261334
E340V	-0.1761046051860954	E340A	0.21468823120010366
E340G	0.014256306619225407	E340D	0.024657318990608572
V341I	-0.3211503967541004	V341F	-0.09746318875188693
V341L	-0.03358242733110293	V341D	0.5932199944987488
V341A	0.5613690277328757	V341G	0.6029333734376439
F342I	1.2113921068873323	F342L	0.9237039948652737
F342V	1.2135847993354798	F342Y	1.4872086687296062
F342S	1.1148676549647631	F342C	1.5104419288859887
N343Y	0.03271457644396167	N343H	-0.24046773387026305
N343D	-0.07888703233719371	N343I	0.12313161905096096
N343T	-0.24375880860442667	N343S	0.00864342072808808
N343K	0.10760297467057281	A344T	-0.007049228223977383
A344S	-0.04125198258324198	A344P	-1.2742964505287293
A344D	-0.008789848601416166	A344V	-0.11437960158527141
A344G	0.17428569739920588	T345S	0.12576057214093883
T345P	0.24980595488927998	T345A	0.1853882956812602
T345N	0.16281247902635754	T345I	0.22413429251094935
R346G	0.13249084224177277	R346K	0.6113937933023611
R346I	0.2370591325334817	R346T	0.4607626695711703
R346S	0.5734018850782477	F347I	1.6124256772769112
F347L	-1.5591498142694724	F347V	0.1409745319048388
F347Y	-0.642952278656219	F347S	-0.8635148204711409
F347C	0.9415192577610763	A348T	0.4032798999039886
A348S	-0.011716079731933764	A348P	-0.18598365599130073

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
A348E	0.4516308237180057	A348V	0.12136804727956174
A348G	0.011490780819049513	S349T	0.12877221060745808
S349P	0.23672124917735604	S349A	0.3929734880693034
S349Y	0.3452287648403499	S349F	0.28207506769031887
S349C	0.4650705624882298	V350I	0.021581481691081948
V350F	-0.1902935396529904	V350L	-0.3960556226201801
V350D	1.1231347007388703	V350A	0.3793293736563982
V350G	0.9577734170189803	Y351N	1.1053760563745418
Y351H	-0.06460547264795223	Y351D	-0.3080558774584835
Y351F	1.0225577918673907	Y351S	1.3551176285940587
Y351C	1.586399116760241	A352T	-0.2230434123896357
A352S	-0.20085406636820496	A352P	-0.11218219876239152
A352D	-0.23714037897566692	A352V	-0.009653812605597074
A352G	-0.041969250598363726	W353R	-0.24341517171511334
W353G	0.5172124515511507	W353L	-0.8201659179799492
W353S	-0.15600346107590768	W353C	0.33619294201984296
N354Y	0.03878260602178178	N354H	0.35220179134011037
N354D	0.26141794315673145	N354I	0.46021554118267555
N354T	0.5903630768907759	N354S	0.9428101661334573
N354K	0.3757453952423922	R355W	-0.016051723946579128
R355G	0.38767673181753504	R355K	0.3713112142946372
R355M	-0.7439990038120337	R355T	0.47345028303616254
R355S	0.6751859143084539	K356Q	0.2509070528907299
K356E	0.15832333351359815	K356M	0.11650832060605343
K356T	-0.06939424320841683	K356R	0.11143680877733034
K356N	0.1265735783626832	R357G	0.1338347348024357
R357K	-0.17391128364842828	R357I	-0.14843615110798314
R357T	0.10220787113357355	R357S	0.28425698265191035
I358F	0.002925421892911681	I358L	-0.057688353473168884
I358V	0.2086360593742474	I358N	0.10279875890107408
I358T	0.23328533860481895	I358S	-1.3441081822776157
I358M	0.08394334766305026	S359C	0.5777236355256218
S359R	0.5887407355315373	S359G	0.4700168587190453
S359N	0.20661801749345393	S359I	0.6414125035450409
S359T	0.6713327079295475	N360Y	0.1266004579395466
N360H	0.19724314966628895	N360D	0.08325735519144452
N360I	0.2343105749173675	N360T	0.036945176952569866
N360S	0.12972416453303576	N360K	0.07942225993308014
C361S	0.2568848165363412	C361R	0.261297626257119
C361G	0.32125428801463624	C361Y	0.35235346139222173
C361F	0.5694415592116309	C361W	0.32924551469213814
V362I	0.1563934258071795	V362F	0.08835007249191264
V362L	0.15494780881891695	V362D	-0.34412619120599913
V362A	0.2628488243984194	V362G	0.19710671813841138
A363T	0.07951828164544741	A363S	0.058553496194755826
A363P	0.11973934402695019	A363D	-0.29681249039227287
A363V	1.9440144433663051	A363G	2.108947217680433
D364N	0.3047344418940573	D364Y	0.10347150378416836
D364H	0.269749210791841	D364V	0.06208207818277717
D364A	0.35933030204299526	D364G	0.19526855692711026

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
D364E	0.44661069159913713	Y365N	0.1325377601379911
Y365H	-0.05798150751242165	Y365D	0.45911015238238295
Y365F	1.8303467550853239	Y365S	1.2143022550142324
Y365C	0.629862479956575	S366T	-1.2755898198238425
S366P	-0.11193067904000979	S366A	0.09277272574687871
S366Y	0.05516937651434815	S366F	0.0522302090835763
S366C	0.07640235176529288	V367I	-0.09965983280453664
V367F	0.8357106189680511	V367L	0.46253698405069155
V367D	0.5546610985945162	V367A	0.6944872228751848
V367G	0.45832743364029627	L368I	0.10664773629572892
L368V	0.3666610186292523	L368Q	-1.8151831713737052
L368P	0.7255393229724192	L368R	0.008990635555027266
Y369N	-1.4727011814925246	Y369H	-1.3487423396015434
Y369D	-0.01911792858384651	Y369F	0.125066954371854
Y369S	0.6203837980404984	Y369C	-0.11014317243587139
N370Y	-0.8337992345089716	N370H	-0.14185666287409884
N370D	0.07606209223365797	N370I	0.26793632223451963
N370T	0.22320660599308764	N370S	0.18426571378467177
N370K	0.023851509758524053	S371T	-0.7244153578164689
S371P	0.2200931640273362	S371A	-0.2412900065519258
S371Y	-2.0840308059246886	S371F	-0.5882262830160941
S371C	-0.2922865221794804	A372T	0.11466710059611844
A372S	0.03613190962953393	A372P	0.22576789141400347
A372E	0.18417383612394758	A372V	0.19328441257250478
A372G	0.16513528072965544	S373T	-0.029163415076847787
S373P	0.27794468166360714	S373A	-0.3462189279495859
S373L	-0.4397830055999882	F374I	0.15990307910411006
F374L	0.20307149060772098	F374V	0.22563685109975426
F374Y	-0.129342508232773	F374S	0.13418494381770435
F374C	0.3546236329046702	S375T	-0.5060385543288999
S375P	0.3070648736640623	S375A	0.4326059683380419
S375Y	-0.3375955110705636	S375F	-0.5316744989240492
S375C	0.4405635562417041	T376S	0.0718146559745398
T376P	0.05919265993715504	T376A	0.3624931894389257
T376N	-0.5906725478857087	T376I	0.024598157775892426
F377I	0.3141751810966202	F377L	0.27952673971917136
F377V	0.6562454301611154	F377Y	-0.39774828545547136
F377S	0.3206345173841759	F377C	0.5231008401097254
K378Q	0.32705711689961353	K378E	0.24883658036110448
K378M	0.4523417202939453	K378T	0.13061324848240835
K378R	-0.15902452750926768	K378N	0.4142852481376374
C379S	0.1778139782336757	C379R	0.05765032951688944
C379G	0.35257802580179975	C379Y	0.3316685356352388
C379F	0.22857860616784645	C379W	0.025659924009120687
Y380N	0.09133626650378264	Y380H	-2.3276170188469316
Y380D	0.22073311712403312	Y380F	-1.1627187739374185
Y380S	0.4209740415613513	Y380C	0.5393426508552451
G381R	0.08945722642526073	G381E	-1.0925755200732723
G381V	0.43252222313873945	G381A	0.334874229430187
V382M	0.1780464548599529	V382L	-0.4288208969463881

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
V382E	0.032243580147796144	V382A	0.24485410662669524
V382G	0.2106174081543135	S383T	0.22755446312971928
S383P	0.38566279682859156	S383A	0.3548776472606493
S383Y	0.30056010531080596	S383F	0.34144347905092415
S383C	0.21935292266440812	P384T	-0.28852260587365736
P384S	-0.08772259168302372	P384A	0.2205376728977571
P384H	-0.04463099868489974	P384L	-0.0981901800391797
P384R	-0.24505324398617684	T385S	0.12955399863136277
T385P	0.3670779020985816	T385A	0.2331104551774414
T385N	0.15390850110324683	T385I	0.2273591133643742
K386Q	0.10680580246705618	K386E	0.13077332597653296
K386I	0.09478580023388018	K386T	0.22019740195961837
K386R	0.14710112443956633	K386N	0.017022570170579378
L387I	-0.10583642472021784	L387V	0.21114198630111547
L387S	0.17587248245262513	L387F	-0.09221112665096451
N388Y	-0.7857832341546318	N388H	0.6158159763512802
N388D	-0.6135633963531206	N388I	0.28866952151548775
N388T	0.1443114582475875	N388S	0.1683248626108456
N388K	0.553648170180494	D389N	0.18513629116128424
D389Y	0.06637410398009147	D389H	-0.21394110711289618
D389V	0.059138973862084374	D389A	-0.337577246585835
D389G	-0.4902119125927527	D389E	0.29352122566186123
L390I	0.15930610337493398	L390F	0.036925049729395074
L390V	0.2584943674685412	L390H	-0.18339121240624376
L390P	-0.1645605794277048	L390R	0.0984795105324792
C391S	0.5772808430184776	C391R	0.5401557036700838
C391G	0.6115377395951113	C391Y	0.5300637163530482
C391F	0.44949811772619475	C391W	0.5884743913670197
F392I	0.035374183687838956	F392L	0.20140339909449884
F392V	0.21632957178350892	F392Y	0.006359916036343558
F392S	-1.1809039727104298	F392C	0.4698665327385106
T393S	0.3292814375651362	T393P	0.13429738001163277
T393A	0.414616695963079	T393N	0.27492658248633034
T393I	0.2881433465466534	N394Y	0.264495444487595
N394H	0.264826188064102	N394D	-0.29441928677136625
N394I	0.254838578687291	N394T	-0.36605374895158865
N394S	-0.0220835765530737	N394K	0.3336423977299207
V395I	-0.22839404731608548	V395F	-0.33519290108600375
V395L	-0.121952833195517	V395D	-0.12338889217624423
V395A	-0.004151718046287715	V395G	0.0009771860708210761
Y396N	0.21532967561631677	Y396H	-1.5684581318900213
Y396D	0.004873953130532212	Y396F	0.27264829591886375
Y396S	0.1304348694340659	Y396C	0.4172680064190146
A397T	-0.40837169429003206	A397S	-0.2815186022991424
A397P	-0.16227202002810442	A397E	-0.1873477118097272
A397V	-0.15631680954281063	A397G	-0.04853078811786507
D398N	-0.08479992255783457	D398Y	1.486713816155063
D398H	0.21148299103726792	D398V	-0.2735299498022382
D398A	0.4287607807915805	D398G	0.8526580139431525
D398E	1.1097593769090877	S399T	-0.12384162028931327

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
S399P	0.16644626977542498	S399A	0.5160785681789303
S399L	0.3315484181653289	F400I	0.5624892537921723
F400L	0.48434106945179706	F400V	2.644092470304538
F400Y	-0.8901678369338406	F400S	1.1945694987817062
F400C	3.451682681938329	V401I	-0.021154563716588536
V401L	-0.45958522696902826	V401E	1.3923671215021902
V401A	0.07763754173552899	V401G	-0.12602217066906035
I402F	-0.5252064012760208	I402L	-0.7042674394953443
I402V	0.2172987445030746	I402N	-0.042533199051799066
I402T	-0.19254666354298014	I402S	0.2669057363437908
I402M	0.9094373436111486	R403G	0.24927845306619326
R403K	-0.1540014483229981	R403I	-3.3642539977774257
R403T	0.743129927202145	R403S	1.5372714651165202
G404S	-0.2781582647713932	G404C	-0.3156706651840403
G404R	1.2801678757472632	G404D	-2.5070696867934488
G404V	-0.7511410694944046	G404A	1.0608956281422686
D405N	0.3233007184794145	D405Y	-0.4253565386814139
D405H	2.275054773721481	D405V	0.09462640917076834
D405A	0.6732732684321031	D405G	1.6526500834751623
D405E	0.8804340274741567	E406K	1.3527116589995234
E406Q	-0.5797458043970181	E406V	-0.08351739666869787
E406A	-1.3890266192823824	E406G	1.6947619062794346
E406D	-0.07774894454469768	V407I	0.1961745599540688
V407F	0.1776740017219499	V407L	0.4242521718741109
V407D	-0.4199253741675938	V407A	0.5633764682459477
V407G	0.5515388069100433	R408G	0.525137323276756
R408K	0.15551380141748639	R408I	0.7185229732219426
R408T	-0.13776833168085173	R408S	0.40457294209047967
Q409K	-0.11441906152653065	Q409E	0.17618982355936624
Q409L	0.4525461777057395	Q409P	0.923368938785474
Q409R	0.053605078126428604	Q409H	0.208567241035503
I410F	0.07510816621228911	I410L	0.08662183972562806
I410V	1.775842962360041	I410N	-1.2753178333262647
I410T	0.04456183975801921	I410S	0.08339975014957558
I410M	0.8433003289392225	A411T	-0.05064235892989225
A411S	0.1022560363053419	A411P	0.924340535366993
A411D	0.39819129331837744	A411V	0.4781565178582413
A411G	-0.11336103623893032	P412T	0.049381369787584437
P412S	1.5148005318044584	P412A	0.0942161218364969
P412Q	0.6306068663342914	P412L	-0.16042093877106295
P412R	-0.15501234206073894	G413R	0.10524007427218703
G413W	0.3941851240751258	G413E	0.2815702331976316
G413V	0.3146613237639368	G413A	0.2656546683262053
Q414K	0.3142601222028851	Q414E	0.013471069748342751
Q414L	0.0869188738717254	Q414P	0.18669390624215132
Q414R	0.16202354109424297	Q414H	0.2186848690664772
T415S	0.19609141221460719	T415P	0.3440606463959551
T415A	0.31131280969290426	T415N	0.05914039721018408
T415I	0.21295684964547848	G416R	-0.23181046473918662
G416E	-0.7671563768241201	G416V	-0.334256354881596

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
G416A	0.05759965944640836	K417Q	0.7289986555705803
K417E	2.2588807839231175	K417M	0.42630365062194775
K417T	1.1213620774655302	K417R	-0.6318493868181239
K417N	1.624001401293493	I418F	0.3290550732515197
I418L	0.5132705933061522	I418V	0.3302798600140032
I418N	0.3211171712807716	I418T	0.5150068497932977
I418S	0.6329868604250599	I418M	0.1383790717683886
A419T	-0.24862589304634067	A419S	-0.20941374076150182
A419P	0.059952008001694514	A419D	-0.46566224778160015
A419V	0.12366232822677066	A419G	0.1632768811911982
D420N	0.09138004295415995	D420Y	-2.0208215320592275
D420H	-2.194496207205497	D420V	-0.25462864637382576
D420A	0.3392721822667723	D420G	-1.1756188707733155
D420E	0.08324130457079953	Y421N	1.480409938666254
Y421H	2.198062933549146	Y421D	0.9529022252884483
Y421F	-1.4558124521904225	Y421S	3.2777806006492733
Y421C	2.342762029425388	N422Y	-0.23427006767341077
N422H	-0.7821514543640347	N422D	1.1944264057857295
N422I	1.7944083950864644	N422T	0.12337691134769908
N422S	0.5132231752931145	N422K	1.081515928131789
Y423N	0.3294633862934705	Y423H	2.410859599402351
Y423D	0.6906496509736977	Y423F	2.993016039259897
Y423S	2.7200706254543365	Y423C	4.123301561003104
K424Q	-0.14203887214705135	K424E	-2.951883716302306
K424I	0.5574081079151687	K424T	-0.4387999807983746
K424R	-0.148088126357111	K424N	-0.5573864029090279
L425I	0.1169792325032821	L425V	0.104287323241625
L425S	-0.13346610066638237	L425F	-0.25258304580683455
P426T	0.029968957578821526	P426S	0.07086988619890666
P426A	0.36332393860460893	P426Q	-1.0534607658983988
P426L	0.21553808747549094	P426R	-0.8571390693635053
D427N	-0.5116975923576057	D427Y	0.042660830965629455
D427H	-1.6557859954113439	D427V	-1.5438530525696772
D427A	-1.3168996248518137	D427G	-1.4602862260359717
D427E	0.26078039951428944	D428N	0.15523465924996288
D428Y	0.22116660883306163	D428H	0.19046449896005044
D428V	0.09114992197098779	D428A	0.2032667470049528
D428G	0.10979108314385486	D428E	0.39905438947904404
F429I	0.5666759538606381	F429L	0.41770485592769935
F429V	0.7521433967119527	F429Y	-0.5826400139098615
F429S	0.3627064520960252	F429C	0.9577695972637637
T430S	0.11265285337756062	T430P	0.045351924823145096
T430A	0.23973959336915715	T430K	0.1202123112351768
T430I	-0.045213658138019086	T430R	0.08138621912904008
G431S	-0.5808840517103666	G431C	0.8826458305138705
G431R	-1.3647423032480752	G431D	-0.5496934779391942
G431V	1.2005952491167458	G431A	0.9539525457756601
C432S	0.41470807234679474	C432R	-1.2109021923174397
C432G	0.5330499107503103	C432Y	-1.0332313498964818
C432F	0.22543764490686763	C432W	-1.1908631190467514

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Table S4 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
V433I	0.01799703077221899	V433F	-0.21600502409453975
V433L	0.07886221145124853	V433D	0.5849996778014136
V433A	1.1214008899104644	V433G	2.1499434278973277
I434L	2.028915216128472	I434V	0.17521781481652982
I434K	1.2095539957369579	I434T	0.7596976149377997
I434R	-0.6514806836435769	I434M	0.9148790521737103
A435T	-0.7841949353787718	A435S	-0.5098448530507129
A435P	-0.1599593498748767	A435D	-0.7849945152109113
A435V	-0.4457231953154565	A435G	-0.08149129214492341
W436R	0.10641740902084809	W436G	-0.4156442186409201
W436L	0.037191147948873085	W436S	0.4176544599542121
W436C	0.28870321816995087	N437Y	-0.008799824688542485
N437H	0.20625688614546514	N437D	-0.3161040827949376
N437I	-0.11856385438817867	N437T	0.24107701193460707
N437S	0.49845666891100315	N437K	-0.42438425302908883
S438T	0.21848620597966928	S438P	0.2117594481756032
S438A	0.2531340781481068	S438Y	0.1557844398113804
S438F	0.47717653012743844	S438C	0.5247244654834946
N439Y	-0.009540820636208685	N439H	0.31301399517655476
N439D	0.07006643780839132	N439I	-0.08249445169763271
N439T	0.3568026836933999	N439S	0.375686184032336
N439K	0.8626084497824443	N440Y	-1.8247756018753905
N440H	0.5891599359082569	N440D	-1.3840589837979942
N440I	-0.028328699845948824	N440T	-0.020075192117766573
N440S	0.12281112251352373	N440K	0.11029036211884999
L441I	0.030443897642331512	L441F	-0.0012812190088082396
L441V	0.19826829375530824	L441H	0.14015934005758668
L441P	-0.019971657620791793	L441R	-0.25373056129000326
D442N	-0.11877187944181274	D442Y	-0.1295048653055501
D442H	-0.44500299713543867	D442V	-0.573721522334031
D442A	0.34413082173378856	D442G	0.24470082146987057
D442E	0.38147094088094013	S443T	0.07063796450729777
S443P	0.2784689949984909	S443A	0.2062793912192055
S443Y	-0.16931955802569204	S443F	-2.6481477874052515
S443C	0.08952776179204079	K444Q	-0.18732041630599447
K444E	0.8604902792616667	K444M	0.23812652369406498
K444T	1.9965506900073156	K444R	0.2504666058531847
K444N	0.718715074337289	V445I	0.06435087193221263
V445F	-1.2659852736055262	V445L	-0.1280475228647033
V445D	0.13295748821566344	V445A	0.4216034932967716
V445G	0.31996898207718794	G446S	-0.17387687141232702
G446C	-0.19094948151993182	G446R	-0.687836948599875
G446D	-0.1367938110150647	G446V	0.05442393087119697
G446A	-0.2007756352951245	G447S	0.04744051497484867
G447C	0.3480424293921826	G447R	-1.0280616803279075
G447D	-0.2588628337157757	G447V	-0.04652175938582986
G447A	0.24610308414924648	N448Y	0.12922003670402643
N448H	1.171104344440943	N448D	-0.16122217332601868
N448I	-0.35983590264618015	N448T	-0.9335467278865688
N448S	-0.22073942113902442	N448K	-0.24914995931274259

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
Y449N	0.7062699391206391	Y449H	0.49493966180292226
Y449D	1.0654150585561701	Y449F	0.5234238937362738
Y449S	1.3364421584633317	Y449C	1.331492393710499
N450Y	0.5877105715683469	N450H	0.012968994057574656
N450D	-0.12657818943358637	N450I	0.5679072851169998
N450T	0.015643578967986776	N450S	1.2281977272189715
N450K	-0.10831459576993932	Y451N	-0.09026682554477479
Y451H	-0.0012062349276773152	Y451D	-0.04095067800308942
Y451F	0.2325209046823503	Y451S	1.015896672388902
Y451C	0.8823129010436954	L452M	2.349587964412996
L452V	0.29354317612440584	L452Q	2.1887790195889543
L452P	2.4632243701044003	L452R	1.8653280920071815
Y453N	-0.09423622578022275	Y453H	-0.44727911888055216
Y453D	0.6322687821615927	Y453F	0.5575955265164342
Y453S	1.1109809598875846	Y453C	1.339659466380781
R454G	0.42245879283728793	R454K	-0.36623438248348716
R454I	-0.4440403032554836	R454T	-2.5251335039262863
R454S	-0.15555359452543893	L455M	-0.26220942530639973
L455V	-0.07356810476614975	L455S	-0.14918947527779067
L455W	-1.3434850319410683	L455F	-0.8112384716968842
F456I	0.7216267103680749	F456L	0.5779845797312917
F456V	0.9618559482357053	F456Y	-0.3925375342775286
F456S	0.6502816701948945	F456C	1.0548365219804094
R457W	0.13001776717859437	R457G	0.17237171012974178
R457K	-0.0895233401203911	R457M	0.3033133890549317
R457T	-0.04153156513853915	R457S	0.12813055384655103
K458Q	0.07716316863544176	K458E	0.7964354630121215
K458M	0.23699119672349314	K458T	0.27428365401145827
K458R	0.3209332112205051	K458N	0.34269851584990924
S459T	0.10276386488532221	S459P	0.05804425949371565
S459A	0.18718570151743666	S459Y	-0.13607176722715364
S459F	-0.08434222004666371	S459C	0.22033931329455275
N460Y	-0.02543756614274269	N460H	1.3323631789661496
N460D	1.6765764464624282	N460I	1.8935796792141821
N460T	2.459084930681346	N460S	0.5813146900947588
N460K	0.92714207093615	L461I	0.06027602594098157
L461F	0.012507969704434763	L461V	0.21284415760183467
L461H	1.7395607511439402	L461P	0.6343202045036624
L461R	-0.7169704550433786	K462Q	0.017469717724478997
K462E	0.07438584193134455	K462I	-0.06937559188500307
K462T	-0.054311750986405574	K462R	0.0044011392738165485
K462N	0.07871123421299729	P463T	-0.15655582606833002
P463S	-0.049676568054920274	P463A	-0.06555794209778806
P463H	0.23754907849067322	P463L	-0.24719989067499065
P463R	-0.29636947574889777	F464I	0.09245662873990079
F464L	0.019243984042158647	F464V	0.14816546646730597
F464Y	-0.35072913772064135	F464S	-0.05445059403208905
F464C	-0.8944157401458165	E465K	-0.3459607249076006
E465Q	-0.020047811083925924	E465V	-0.15078178533127512
E465A	0.1490120863290807	E465G	0.12115353825474587

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
E465D	-0.09367125537823659	R466G	0.3956486561513509
R466K	0.18241439017072397	R466I	0.25996889292824676
R466T	-1.0908445503280082	R466S	0.17315716398091324
D467N	-0.14279158460847602	D467Y	-0.16145019273428096
D467H	-0.3085751999161742	D467V	-0.38525107070168235
D467A	0.3492308461076162	D467G	0.37398851896838675
D467E	-0.07275863483602714	I468F	0.009024957617629892
I468L	0.07041429366230838	I468V	-0.04886220947746198
I468N	-0.01716925693626502	I468T	-0.13394971345113826
I468S	-0.12306215025787057	I468M	-0.10578080497517292
S469T	0.052422840427469905	S469P	0.2814272122661719
S469A	0.1347887992870976	S469L	0.1663104899573289
T470S	-1.2293807599318005	T470P	0.15365984771643743
T470A	0.1360916690076706	T470N	0.023023570880600724
T470I	0.16197924674591885	E471K	-0.05874277145438141
E471Q	0.06304851211107892	E471V	-0.04138692630037956
E471A	0.23627514973835345	E471G	0.006622058578229367
E471D	0.0652969684950794	I472F	0.01778145839059516
I472L	0.1301357774893857	I472V	0.09109909722214632
I472N	0.6892965618747763	I472T	0.05356791957294922
I472S	0.24251291449441686	I472M	0.2843851319345797
Y473N	0.6113315435659658	Y473H	-2.9732918487460522
Y473D	0.6386868732975338	Y473F	0.2928621285405816
Y473S	1.3895325641231766	Y473C	0.6556485838291759
Q474K	-0.4387787647259482	Q474E	0.004007791650379204
Q474L	0.06361305227746093	Q474P	0.5098965259009725
Q474R	-0.3204586284758477	Q474H	1.402351822801425
A475T	-0.6875878850362699	A475S	-0.4825148455485497
A475P	-0.32512525412735716	A475D	-0.7856586539931625
A475V	-0.6193027554947864	A475G	0.10082524074859771
G476S	0.047926575826977694	G476C	-0.04926105400324925
G476R	0.049971483614199654	G476D	-0.15056898099173044
G476V	0.0963320671302791	G476A	0.22939633463302575
S477C	0.0445152201005128	S477R	0.04069117804303392
S477G	0.32808744945097706	S477N	0.16282071917992852
S477I	0.3495416683554832	S477T	0.20082813629022364
T478S	0.2857294749927698	T478P	-1.047292499672844
T478A	0.4618211916444747	T478K	0.16890741585464394
T478I	-1.1721065113832618	T478R	-0.06008539792854124
P479T	0.03240812104995058	P479S	-1.3207445854417705
P479A	0.13734689954303678	P479H	0.11550682261605427
P479L	0.12917370097840078	P479R	0.2398194220251273
C480S	0.20824234924435006	C480R	-0.07651322557362124
C480G	0.4291165889847104	C480Y	0.10834422259147578
C480F	0.09610258363342504	C480W	-0.16284742088076148
N481Y	-0.3750152289389536	N481H	-0.345385267051758
N481D	0.013569647123549803	N481I	-0.0861503346958373
N481T	-0.1673955356453527	N481S	-0.02430566422405578
N481K	-0.07576559483883363	G482S	0.15603048600019215
G482C	0.0009635067538956647	G482R	0.07647921777173014

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
G482D	0.16936509498042585	G482V	0.22577873886182367
G482A	0.14169890205947194	V483I	0.09401562862078862
V483F	-0.1318144196907681	V483L	0.11588962218678231
V483D	0.031894684430140076	V483A	0.07090948635698724
V483G	0.0266395905566901	E484K	0.3889980712601367
E484Q	-1.4424535273020045	E484V	0.775796004839009
E484A	1.0600757233168725	E484G	1.8009725848469558
E484D	1.9263429758355088	G485S	-0.43379093498879645
G485C	0.35304518796643525	G485R	0.1507643971466069
G485D	0.2169335439650923	G485V	0.28238040397044073
G485A	0.2517964058117856	F486I	0.7943534233601064
F486L	0.6860432734092584	F486V	1.0304461706367014
F486Y	-0.26036361230492183	F486S	0.9581795680047074
F486C	0.609926036625938	N487Y	0.2774858912764635
N487H	0.6296070158022531	N487D	0.4987990888782819
N487I	0.5042486194820142	N487T	0.38714371714547685
N487S	0.6391572809945342	N487K	0.26262907031354493
C488S	0.6226370074170549	C488R	0.17495175251210976
C488G	0.3610472490805131	C488Y	-0.3962077749547831
C488F	-0.08413639190044582	C488W	-0.17520777190153936
Y489N	2.4692833591816017	Y489H	4.158511542648542
Y489D	3.9495188935545045	Y489F	3.160693058550614
Y489S	1.6654071272995847	Y489C	2.731243720265536
F490I	0.7164682794904339	F490L	0.4710684580090536
F490V	0.8009104298504651	F490Y	0.0291879840276975
F490S	0.45897874018982315	F490C	0.7325504366615461
P491T	-0.2649128858731087	P491S	-0.24026394511633162
P491A	0.4395763144501575	P491H	0.047378986202032
P491L	-0.0005777757613911333	P491R	-0.6860253986169476
L492I	-0.18665716467344717	L492V	-0.04971307375752051
L492S	0.22976046200300954	L492F	-0.4080845089601123
Q493K	-0.97484240695699	Q493E	-0.24334580754560667
Q493L	-0.9725222079360467	Q493P	-0.27323149929707297
Q493R	0.3518296643914156	Q493H	1.6631979526213911
S494T	-0.26806911311902015	S494P	-0.07361595624320341
S494A	0.2627102190875382	S494L	-0.19940692726541423
Y495N	4.453774987734683	Y495H	2.4466347795920735
Y495D	1.8786153780192993	Y495F	0.6919540235247663
Y495S	1.0034240822960778	Y495C	1.33552728808187
G496S	0.2019433793738568	G496C	0.2274037817532474
G496R	-1.170174391274189	G496D	-0.01708362189732279
G496V	-0.23410778989332331	G496A	0.5573101024172533
F497I	0.6540312025806432	F497L	0.4451156099963752
F497V	0.7984510604395286	F497Y	-0.4183692917105818
F497S	0.5768452217856271	F497C	0.9860015608722377
Q498K	0.20046963535114556	Q498E	0.2880893730187563
Q498L	0.6068647733763773	Q498P	0.7080502809816315
Q498R	0.31213176861698605	Q498H	0.3075009308129441
P499T	-0.9779182460094088	P499S	-1.3202466447329324
P499A	0.2494956167034609	P499H	0.556968909254117

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
P499L	-0.3244921208380976	P499R	-0.34422969636317385
T500S	0.3805817480249617	T500P	0.36518516870729967
T500A	0.6583809018853561	T500N	2.944501459773469
T500I	0.28571380033589666	N501Y	0.008176664020130066
N501H	-0.08542359330421585	N501D	0.42096141744659227
N501I	1.7229311882198899	N501T	1.3722144407101737
N501S	2.966011817655139	N501K	-0.6360853190180881
G502S	-1.2346813284959972	G502C	-0.11554750486742946
G502R	-0.4051550086645717	G502D	-0.667464583711077
G502V	-0.27848124775250716	G502A	-0.0523513087093224
V503I	-0.09670433755131967	V503F	0.4270666688682674
V503L	-0.010733078231622511	V503D	0.11093319161472484
V503A	0.6467291793922666	V503G	0.8600898722876078
G504S	-0.4739125146741219	G504C	-0.41129994777452705
G504R	-0.5929758801964633	G504D	-0.08696046206079011
G504V	-0.5081452199197457	G504A	-0.4117025858597221
Y505N	0.7916739870207682	Y505H	3.6221381612801915
Y505D	0.3971302979283701	Y505F	-0.7968505426032857
Y505S	0.4079157485460091	Y505C	1.7841209418873683
Q506K	1.1214773786190542	Q506E	0.3656442594434449
Q506L	0.2769013502198106	Q506P	1.04285168560247
Q506R	1.775941871399624	Q506H	0.4251664383407815
P507T	-0.16318024273519066	P507S	2.2922949551460583
P507A	0.31282764485386705	P507Q	-0.3025257103400314
P507L	-0.1120364991739683	P507R	0.14145169831415755
Y508N	0.437306184594462	Y508H	-0.023952181216801642
Y508D	0.4796602611426787	Y508F	0.23230748215884156
Y508S	-0.006673176371398153	Y508C	0.4990722062528734
R509G	0.10188541497646948	R509K	0.9256289235639065
R509I	0.20305156748554304	R509T	0.3240056651772013
R509S	-0.01831547844723258	V510I	-0.13593064079091863
V510L	-0.14634863230862322	V510E	-0.7387751800925344
V510A	0.16452053119807175	V510G	0.32172573663639403
V511I	-2.2510920118212363	V511L	-2.0950787589315065
V511E	2.831479191867628	V511A	-1.1925507333641474
V511G	-1.5911580742780629	V512I	1.036511677907285
V512L	2.472822627526483	V512E	0.024318311192341072
V512A	1.139630359275301	V512G	0.09242621943949597
L513I	-0.10092677159047522	L513F	-0.12602728050855594
L513V	0.03463468441791892	L513H	-0.713508435951803
L513P	0.25765920190299707	L513R	-1.2326833403330606
S514T	0.08766446124826124	S514P	0.05220743935332478
S514A	0.32856333210394384	S514Y	0.3591133039019021
S514F	0.26519152016202746	S514C	0.19735529194960516
F515I	1.2666219832174044	F515L	1.1198179948395992
F515V	0.2770992309395645	F515Y	-0.11263854527731199
F515S	0.34375238622982485	F515C	1.0371844608564067
E516K	-0.32755279541191096	E516Q	-0.21610566306031723
E516V	0.5926736063480301	E516A	0.04849950124257807
E516G	-1.1706930572590755	E516D	-0.4274415365895237

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
L517I	-0.1282350314195009	L517F	-0.30684147771872816
L517V	0.12704886077841826	L517H	0.12040000162369732
L517P	0.0440364520758754	L517R	-0.28366872341894295
L518I	0.35440129898514744	L518V	0.2805610839464838
L518Q	0.03716100506441392	L518P	0.24504939332275555
L518R	-0.08059421627099501	H519N	0.1269627398055571
H519Y	0.15046252528638093	H519D	-0.09072981539589503
H519L	0.25509585379189137	H519P	0.2686150578693283
H519R	0.10425945034599789	H519Q	0.18831800846532457
A520T	0.08731837064404224	A520S	0.07095201002836367
A520P	0.4041100589290541	A520E	0.10247910835890303
A520V	0.1992627874631823	A520G	0.34537344632494915
P521T	0.03808988518735238	P521S	0.04880487875248997
P521A	0.20961511697987714	P521Q	0.17842919736990703
P521L	0.2308306213205773	P521R	-0.0065610031087648514
A522T	0.030669113099624352	A522S	0.1404360895874541
A522P	0.17596900810252228	A522E	0.045908464072034416
A522V	0.17323086302755886	A522G	0.28043749784783417
T523S	0.2955248243124004	T523P	0.5907045155284703
T523A	0.6332250314527801	T523N	0.6962472281778261
T523I	0.7491367607812094	V524I	-0.26808077480250875
V524F	-0.13643569796174218	V524L	0.8830277962856353
V524D	1.0003694379810084	V524A	1.3857184060847776
V524G	1.3389330525980532	C525S	0.6864321828805163
C525R	0.5410401888358585	C525G	0.6016343181815996
C525Y	0.3709288086712334	C525F	0.403863269097925
C525W	0.2197903008792516	G526R	-1.1884795266533699
G526E	-0.3816521392053786	G526V	-2.945790087503917
G526A	0.188441869182812		

Table S5: Likely mutation binding affinity change prediction. Residue ID is according to SARS-CoV-2.

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
T333L	0.36711414198162123	T333Q	0.2944171016528851
T333E	0.28351593033661665	T333V	0.34837438687921685
T333G	0.4200215149946123	T333N	0.20992592285458667
T333M	0.2047272635752992	N334F	0.08471263263309878
N334C	-0.3744686921975172	N334L	-0.25743991480502126
N334P	0.5870933293317209	N334R	-0.019984080717318824
N334V	0.4606882935368657	N334A	-0.22205901791083096
N334G	0.04978463996692858	N334Q	-0.15264867556794223
N334E	1.0032145233553824	N334M	0.6470893703083734
L335K	-0.21409984794776654	L335T	-0.4280108273635263
L335R	-2.631891479662934	L335Q	0.5502134889673533
L335P	0.3873026733750947	L335E	-0.13217396543541343
L335A	0.2320214165841903	L335G	0.18315829086127428
L335I	0.2501163595268764	L335Y	-0.4605089193686703
L335C	0.10340261769853434	C336N	0.35858070811654985
C336I	0.2878398970645796	C336T	-0.09713307826975079

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
C336H	-0.016387495510664256	C336L	0.001790501926396615
C336P	0.3921826367800033	C336D	-0.34909778761533894
C336V	0.24715082243452438	C336A	0.41770720684747686
P337N	0.18638306097231022	P337I	-0.006678173981198654
P337Y	0.07623953301123451	P337F	0.19922467342170974
P337C	0.14177558536959894	P337D	0.14090285993209145
P337V	0.2528880124442296	P337G	0.3126738024368957
P337Q	0.2006123221089957	F338N	0.27159958939300044
F338T	0.3284332902084772	F338H	1.0090342180442964
F338P	1.4808660776302902	F338R	0.22845080279336835
F338D	0.8620473427019798	F338A	2.7142282011047842
F338G	1.4811459408348466	F338M	0.9029404872897693
F338W	1.0052043818251883	G339N	0.3512248326079045
G339I	0.3818760655998165	G339T	0.2024571534332734
G339Y	0.31277736027454955	G339F	-0.30451281142007336
G339H	0.4369420944664961	G339L	0.32339624004836953
G339P	0.20783078761973434	G339W	0.2513234110088286
G339E	0.3252278488226295	E340I	-0.26708364745659086
E340T	0.0552334017490184	E340R	-0.010451199409254115
E340L	0.004955078249118843	E340S	0.1259073032881047
E340P	0.22364344602241698	E340N	-0.0212562442944646
E340Y	-0.032255356259882295	E340H	0.05169659224259826
V341N	-1.762240554169106	V341T	-0.10105597956043533
V341S	0.47590787259905837	V341Y	-0.32051725428702715
V341C	0.637745043517461	V341H	-0.41868727177360665
V341P	0.4039030950889	V341R	-0.03581812496550252
V341M	0.3286853435552745	V341E	-0.24018586584771823
F342N	0.07999343083076557	F342T	1.18760555702351
F342H	2.3292436191051413	F342P	1.6263873472878327
F342R	1.1171950413236038	F342D	1.1305604733681414
F342A	1.5547464037859968	F342G	1.218270347851369
F342M	1.387407400094697	F342W	1.2375068398441043
N343F	-1.5440348565494904	N343C	-0.2808647919427268
N343L	-0.007702556100912364	N343P	0.09452918391061718
N343R	-1.7642367649485837	N343V	0.08653837992920141
N343A	-0.14653928282582443	N343G	-0.1655326425378049
N343Q	-0.0007961745475319401	N343E	0.07384303883519008
N343M	-1.4134982200046702	A344N	0.10493544637706109
A344I	-0.16131085695362932	A344Y	-0.0017085347946742032
A344F	-0.013750711534165983	A344C	0.06975247176684352
A344H	-0.15908765792247065	A344L	0.008370849804871551
A344R	-1.3545105738596175	A344E	-0.13847045262457083
T345Y	0.045312075817320815	T345F	0.20421585439426168
T345C	0.03429697659932192	T345H	-1.1481157510756002
T345L	0.19486303862323665	T345R	0.18142634750141753
T345D	-0.005191711175726464	T345V	0.1838564083652279
T345G	0.12842052884802702	T345K	0.08401192592745524
T345M	0.06345609921634535	R346L	0.11821028096106408
R346Q	0.23057827727717645	R346P	0.5895698207658844
R346E	0.5028308480186643	R346V	0.4229749393322442

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
R346A	0.5633235286579769	R346C	0.4048595206495622
R346W	-0.11462741832232785	R346N	0.08125550136025614
R346M	0.525245398006787	F347N	3.3659591398651374
F347T	2.3126586286148942	F347H	0.7568208114383773
F347P	0.7288790200039444	F347R	1.9260333989966152
F347D	-0.2412981889808834	F347A	0.805163099568303
F347G	0.6935799311290428	F347M	0.36330410094485577
F347W	1.079343262329541	A348K	-0.2768866919242218
A348I	-0.1420690866206204	A348R	-0.2833959247465061
A348L	-0.04503022152499691	A348Q	-0.06261955359362867
A348D	0.4288603005397379	S349N	-0.12517905506730445
S349I	0.024756537141285107	S349H	0.06535686953607892
S349L	-0.10336593821467358	S349R	1.915859791157807
S349D	0.23877093964721804	S349V	0.3387902565246805
S349G	0.3167224532588867	S349W	0.2514751363613729
V350N	0.7198773327234307	V350T	0.13067390125499145
V350S	-0.007410970940766222	V350Y	-0.894519764298274
V350C	0.45250068048615455	V350H	-0.20477890514960878
V350P	0.42736664831097143	V350R	0.0010065105681489079
V350M	-0.06806747585364817	V350E	0.8152818338624384
Y351I	-0.07728400426328888	Y351T	-0.6451325204814776
Y351L	0.6124206314367939	Y351P	0.7149403204301136
Y351R	0.5226585459688343	Y351V	1.3954029373722203
Y351A	1.467384477596199	Y351G	2.398114458122118
Y351K	0.868199933610153	Y351Q	-0.9066264093551112
Y351E	0.8951935821794359	Y351W	0.3046234713642753
A352N	-0.26137514247455435	A352I	-0.11699884734452407
A352Y	-0.08544094538991999	A352F	-0.042987815366750996
A352C	-0.030498358045014946	A352H	-0.12235030690459588
A352L	-0.1585805971586019	A352R	-0.3663617917754086
A352E	-0.30872632139307593	W353K	-0.27869601862125126
W353M	0.2610964202645987	W353T	-0.18136857474669751
W353Q	-0.6924449491453935	W353P	-0.009966331762967257
W353E	-0.5181433036289946	W353V	-0.4989760892354373
W353A	0.2629626505080159	W353Y	0.2602646822642389
W353F	0.33967832602971104	N354F	0.5668450059138468
N354C	0.7127403702938417	N354L	0.5543526394141532
N354P	0.5094752172655629	N354R	-0.3184471829082041
N354V	0.30974559649156247	N354A	0.8315892569874566
N354G	0.42021723483780227	N354Q	0.3798271739036113
N354E	0.27658423840802626	N354M	0.5483120352358831
R355L	0.2937271622494081	R355Q	0.6052446548834985
R355P	1.104998752538954	R355E	0.20950715933054748
R355V	-0.9344901675362364	R355A	0.321457401654143
R355C	0.11984944123123609	R355N	0.31454074731720827
R355I	0.4814205470436443	K356L	0.048319187762920414
K356S	0.05219484552291052	K356W	-0.24519358348250836
K356P	-0.5594395000881911	K356V	-1.8854985378763824
K356A	0.23647942213205328	K356G	0.1627771375511085
K356Y	1.1674597969066502	K356H	0.654842973900289

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
K356D	-1.0544765246909726	K356I	-0.0628644202124165
R357L	2.063566026379174	R357Q	1.6238627643773296
R357P	0.4913206103268283	R357E	0.19430390942422224
R357V	0.18745386091721655	R357A	0.4163270261966048
R357C	0.43142767278227756	R357W	0.3507749452761727
R357N	0.7196512596754386	R357M	0.38257961788424677
I358Y	-0.12744534484049427	I358C	0.40937438765814027
I358H	-0.37307415003233413	I358P	0.38156930141887824
I358R	-1.6266718104886688	I358D	0.20812395760329205
I358A	0.46451435831352417	I358G	0.35184671400192397
I358K	-0.10067979984982647	S359Y	0.22521652000795997
S359F	0.4454893292825813	S359H	0.4754579276249077
S359L	0.6523853610767139	S359P	0.37840937502204375
S359D	0.127135726495169	S359V	0.8315761887986384
S359A	0.6001893930486933	S359W	0.7222216310569651
S359K	0.11009060527968731	S359M	0.657230660236167
N360F	0.24650612948776568	N360C	0.13891629196399394
N360L	0.30310358183415176	N360P	0.17030895405383709
N360R	0.15324912449981548	N360V	0.17429722146033977
N360A	0.235531589300487	N360G	0.13748643891431053
N360Q	0.17689077533067088	N360E	0.20573841627079106
N360M	0.12365214437123953	C361N	0.3451692465332896
C361I	0.08739991032141944	C361T	0.4038713708874105
C361H	0.252574619759458	C361L	0.390864832419348
C361P	0.31684416842683477	C361D	0.2273942728424409
C361V	0.42097317661245165	C361A	0.5073071964087812
V362N	0.04792689107690225	V362T	0.24210019238230923
V362S	0.2477500197529751	V362Y	-0.016920542631958878
V362C	0.19260135731562095	V362H	0.10561397394764638
V362P	0.29524634736216465	V362R	0.2142038847746086
V362M	0.23904148086599575	V362E	0.1794905832805453
A363N	0.0023582561752718803	A363I	1.5128967355404839
A363Y	-0.8441517938941686	A363F	1.579958094830846
A363C	-0.005753210198915401	A363H	-2.1290953318644252
A363L	0.19217149279145115	A363R	-1.1421856841672997
A363E	0.1676420675220488	D364I	0.04560848359805036
D364T	0.11282656905428763	D364S	0.24261822895221888
D364F	0.03449843379832905	D364C	0.26809229570194343
D364L	0.17438506444471852	D364P	0.20005691248717722
D364R	0.2529588012200351	D364K	0.20537273776639703
D364Q	0.22483180318374316	Y365I	3.2906441389630197
Y365T	1.238153334343976	Y365L	0.14557991138089715
Y365P	0.2820539996149506	Y365R	0.16412504258395605
Y365V	3.5381084956531574	Y365A	0.7157301803486937
Y365G	1.49187266192086	Y365K	0.04175873611292048
Y365Q	0.12093597839500995	Y365E	0.4258973068411137
Y365W	-1.1308332909116077	S366N	-1.614318883368572
S366I	-0.11185755349496769	S366H	-0.10897746489970939
S366L	0.10826519458738755	S366R	0.07319710734438589
S366D	-1.8351416373449023	S366V	0.06405130288196767

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
S366G	0.08170544756353378	S366W	0.26840064056217283
V367N	-0.20035631137103477	V367T	-0.056539335499473174
V367S	-0.6375746846307413	V367Y	0.4328293690480646
V367C	0.6149771518213828	V367H	1.187711785712945
V367P	0.6840540613142467	V367R	-0.26397196317196847
V367M	0.5667510569079531	V367E	0.01827309630949744
L368K	1.2259728977315638	L368T	0.7465482394622804
L368S	1.928870752067938	L368E	2.422665322962998
L368A	2.041267027039175	L368G	0.8894732803981503
L368M	0.36152239549792203	L368F	0.33939002097710463
L368H	1.978737480597228	Y369I	-1.5794177500806952
Y369T	-0.07243948959704012	Y369L	-1.3688494779776623
Y369P	-1.2846539506231591	Y369R	-1.5193214710564762
Y369V	-1.3842162268630052	Y369A	0.05373785436355424
Y369G	-1.0788739144796842	Y369K	-1.7564382262713074
Y369Q	-0.25663218280014377	Y369E	-0.09957193588429683
Y369W	0.3038512028714467	N370F	-2.9377948556343747
N370C	0.003612554766990844	N370L	0.2618965874639211
N370P	0.4393211918473335	N370R	-0.35381471754400184
N370V	0.2230687310263328	N370A	0.18106294814004947
N370G	-0.09312546532263884	N370Q	-2.9629449775376195
N370E	0.23051889894389282	N370M	0.07902576526789752
S371N	-0.9343050091030746	S371I	-1.6022680226392239
S371H	-2.858379060454566	S371L	-2.329377596782451
S371R	-1.2171158702951403	S371D	-1.492107218935479
S371V	-2.245868541805055	S371G	-2.279953315203346
S371W	-0.04061130054973855	A372K	0.10705247229093966
A372I	0.2169170650570252	A372R	-0.13970131906334013
A372L	0.16455524867689614	A372Q	0.13286375649567672
A372D	-0.06955371713617137	S373K	-0.42980197925189667
S373I	-0.5019702029578088	S373R	-1.0123111805889797
S373Q	0.34791187036362264	S373E	0.3389620001361424
S373V	-0.10150728830920148	S373G	-0.37930219405877436
S373Y	-0.4743020716664169	S373F	0.2437893845371919
S373C	-0.4394473826993325	S373W	0.19784726665159313
F374N	0.16255413937956475	F374T	-0.19609681374786644
F374H	0.17518555529507315	F374P	0.556559880323588
F374R	-0.13470417320861852	F374D	0.11701899796193241
F374A	0.3901347671112269	F374G	0.10539132378805446
F374M	0.17965950417952625	F374W	0.12421747745237022
S375N	0.0905319837257881	S375I	0.08003754463318445
S375H	0.010714323227297743	S375L	-0.050998752103090336
S375R	-0.5653792633470671	S375D	-0.18201590400066978
S375V	0.25161770245145954	S375G	0.10079457201543078
S375W	-0.8078741565551079	T376Y	-0.1382730915311325
T376F	0.1091628623588163	T376C	0.4168619677447419
T376H	-0.09290789852360903	T376L	-0.03764069131861294
T376R	-1.4843507371762332	T376D	-1.879984502599011
T376V	0.41284397187841576	T376G	1.1942837672143607
T376K	-0.704289073305508	T376M	-0.11370086153235288

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
F377N	0.5363113768259671	F377T	0.18266038724904632
F377H	0.18351147894661293	F377P	0.7707575319448396
F377R	-0.7093971982385915	F377D	-1.342485057005301
F377A	0.7731298739362428	F377G	0.4977609823788218
F377M	0.316477706682566	F377W	-0.41138701181959964
K378L	0.2775431717302423	K378S	0.37076695017618644
K378W	0.3262691912467635	K378P	0.1575365271522551
K378V	0.6142796170320284	K378A	0.6067990364981375
K378G	0.21955949784566603	K378Y	0.18617762335365404
K378H	0.5556674763191841	K378D	0.32531612497554574
K378I	0.39095664112502526	C379N	0.26203488670597597
C379I	0.28540659131236124	C379T	0.03411912668418713
C379H	0.2532045111227837	C379L	0.0791019050621764
C379P	0.3242688650047029	C379D	0.08501288281543591
C379V	0.12073705752272335	C379A	0.39213241754872064
Y380I	0.42453280743339306	Y380T	0.5964018355588967
Y380L	0.4438200332412956	Y380P	0.5742820683101126
Y380R	0.26588322724819347	Y380V	0.40523111202577045
Y380A	0.5242989088298531	Y380G	0.24552725381814247
Y380K	-1.293737214309824	Y380Q	0.34416982323274165
Y380E	0.6158052984271805	Y380W	0.16877334473617783
G381K	-1.603327217040905	G381I	-1.1941568481071239
G381T	0.048026332217306525	G381L	0.20801372993943165
G381S	0.4335696208027544	G381Q	-1.3524537069405813
G381P	0.30112669262485514	G381C	0.4079474522058254
G381W	-3.3836696099724124	G381D	-3.0418201551252335
V382K	1.4128627814879342	V382T	-0.04647164063699464
V382R	1.0942130014420548	V382S	-0.3310844023799896
V382W	0.04398783211826964	V382Q	-0.22168078161448257
V382P	0.15599957157037098	V382I	0.16607479448652313
V382F	0.19244766627531235	V382D	-0.1325257653237396
S383N	0.23340723437903707	S383I	0.42931039008897687
S383H	0.3295039029482738	S383L	0.38912806769789016
S383R	0.2796307387628073	S383D	0.046609328942757315
S383V	0.4006471203566436	S383G	0.2590632182890112
S383W	0.43236683491968986	P384N	1.0468671275077823
P384I	-0.04322799740848164	P384Y	0.047530603833653866
P384F	0.34749703208104277	P384C	0.1660545925472359
P384D	-0.3688922918801786	P384V	0.08384833306671362
P384G	0.09689552417675648	P384Q	-0.1450143640858802
T385Y	0.03258417388726313	T385F	-0.07166427601316541
T385C	0.16753305783204422	T385H	0.10786022289470656
T385L	0.2220367811733658	T385R	0.24990324352100712
T385D	0.09166821514646209	T385V	0.23615107792427223
T385G	0.055270300676494945	T385K	0.13621124990978578
T385M	0.24999595084520276	K386L	0.05933355101853387
K386S	0.16424412334784716	K386P	0.33954919829447056
K386V	0.0991633865508944	K386A	0.1734919498981415
K386G	0.09676479053715134	K386Y	-0.013545069219757708
K386H	0.09245373405899901	K386D	-0.08060142469500406

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
K386M	0.05241577650599825	L387K	-0.21566013283485566
L387T	0.14711311633997778	L387R	-0.3954138722747453
L387Q	-0.4318732903677759	L387P	0.6349905817293126
L387E	-0.0359902917517348	L387A	0.666340553197047
L387G	0.3601300362699994	L387M	-0.013129214865123634
L387Y	-0.47670849797807335	L387C	0.526541101009095
L387W	-0.5661921080465366	N388F	0.25297606685106666
N388C	0.5134625181245619	N388L	0.3564982774342179
N388P	0.5724372525686129	N388R	-0.07831466579523666
N388V	0.2439705569905458	N388A	0.5100123923797002
N388G	0.10359090224149643	N388Q	0.008054367209907192
N388E	0.0073448742643349215	N388M	0.4915127453142455
D389I	0.10378599037057981	D389T	-0.01954165411051952
D389S	1.076498177726712	D389F	-0.06256576148145011
D389C	-0.5009123199307111	D389L	0.028244989988776455
D389P	0.1517932456622885	D389R	0.0911521316426411
D389K	0.003581327447950258	D389Q	0.15420527556418379
L390N	0.04748868030337227	L390T	0.1303675903683367
L390S	0.2710854015489026	L390Y	0.09492618590974496
L390C	0.35966755529686323	L390D	0.16253239353843568
L390A	0.3577712513249426	L390G	0.2758142419923063
L390M	0.24001630123801404	L390Q	0.17969487199865022
C391N	0.4807214819223919	C391I	0.5246545765977824
C391T	0.5370674235488887	C391H	0.515671848016521
C391L	0.5399853009796496	C391P	0.7033035184023753
C391D	0.38723810154019983	C391V	0.5791830683922817
C391A	0.6716721490757671	F392N	-0.03274042201887174
F392T	-1.3487832189356703	F392H	-0.2038243964373423
F392P	0.2740360207554921	F392R	-0.16011323189521615
F392D	-1.237495802944048	F392A	0.4005315995971001
F392G	0.24375112619262493	F392M	0.2575505583150949
F392W	-0.3010403839023437	T393Y	0.3316587981425056
T393F	0.26896096244236256	T393C	0.26014118140747283
T393H	0.14068484598313793	T393L	0.2861317585412183
T393R	0.184552213178305	T393D	0.18271120809328206
T393V	0.2457116864128103	T393G	0.1938437647400993
T393K	0.00044598605949665684	T393M	0.31050962743624033
N394F	0.3246936398477954	N394C	0.18842143785062282
N394L	0.2307211072132782	N394P	0.3708516930088857
N394R	0.24838255419122518	N394V	0.08895686612481304
N394A	0.15227157065999036	N394G	-0.03336859584521647
N394Q	0.13972500856122988	N394E	-0.02318075938663813
N394M	0.497519578550611	V395N	-0.546593125595327
V395T	-0.3010429326472537	V395S	-0.06704173475405308
V395Y	-0.35061604703584404	V395C	0.027721561735848783
V395H	-0.4052687859903587	V395P	0.056415762294375005
V395R	-0.7016374478447218	V395M	-0.6320836909832158
V395E	-0.1830500395364248	Y396I	0.22888310462050043
Y396T	-0.02070472935614384	Y396L	0.21813399388409732
Y396P	0.3019625865624341	Y396R	0.02549940799243743

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
Y396V	0.2739871091371279	Y396A	0.33223064334965546
Y396G	0.2066469897702424	Y396K	0.08379458772790205
Y396Q	-0.042728170339307966	Y396E	0.25796086929868334
Y396W	-0.1406297396568322	A397K	-0.2142978766624423
A397I	-0.2005475219434813	A397R	-0.8094328682995954
A397L	0.005304654435396482	A397Q	0.33967299248906735
A397D	-0.1318943389719577	D398I	0.2821957184318705
D398T	0.7082060237308619	D398S	0.8533383762396172
D398F	0.04799193353080398	D398C	0.7507143620654653
D398L	-0.47308136365007936	D398P	0.5492751123360909
D398R	-1.115139921847215	D398K	1.4717080148523634
D398Q	-0.743963950033501	S399K	0.2532052027649542
S399I	0.2516578851907669	S399R	-0.4565155731364288
S399Q	-0.07437091565631876	S399E	-0.09408612361942384
S399V	0.1325205850880716	S399G	-2.871424376547335
S399Y	0.38894986579443563	S399F	0.38271440215885455
S399C	0.48817881482477044	S399W	0.057210490540511125
F400N	-0.04939502049637009	F400T	0.6617110772380672
F400H	0.6622249795672912	F400P	0.6129458750611678
F400R	0.5956437864327319	F400D	-0.15205100477678513
F400A	3.6191692973208482	F400G	3.0476062266887287
F400M	0.18184042604949396	F400W	2.067491857548174
V401K	-1.2511462305162322	V401T	3.144388863919312
V401R	-1.4825399676449025	V401S	2.459818561397605
V401Q	-0.9818525239084727	V401P	0.05759446172693694
V401M	-0.6400340452304389	V401F	0.7339736200537483
V401D	1.0196847698745455	I402Y	-0.8520088868903498
I402C	0.05616806642303944	I402H	2.6410462229974216
I402P	0.2502190910811251	I402R	-1.2697003617815903
I402D	-0.008894851260239377	I402A	-0.0001637674057261805
I402G	0.6632078355821877	I402K	-0.7126556646958366
R403L	-0.6917311096656378	R403Q	0.46518123185190347
R403P	-2.0803238688545633	R403E	0.1702922339097655
R403V	0.6190862144527081	R403A	0.8691513530797105
R403C	0.635035720555665	R403W	-3.6351771021026296
R403N	0.7594105797082162	R403M	0.20358841026659982
G404N	0.6801921887243768	G404I	-0.32788482492972565
G404T	-0.4794249080170082	G404Y	-2.2558272495526146
G404F	-1.0763419741728002	G404H	-0.5066970971991213
G404L	-0.5382449353583101	G404P	0.49707882436018413
G404W	-1.231239926850856	G404E	-0.6528987886086559
D405I	-0.10124515031112466	D405T	0.06829908231465184
D405S	0.3685584813814407	D405F	-0.5841092823720216
D405C	0.6263735917404539	D405L	0.08030724094695142
D405P	0.9273600687243052	D405R	0.06282519746473539
D405K	2.1044031164586223	D405Q	2.056157101292315
E406I	-2.871146110373879	E406T	-1.7709061724440265
E406R	-0.2093971129452279	E406L	-2.0802967802652486
E406S	0.29876677866557755	E406P	-0.4417757780514372
E406N	0.01244914377416088	E406Y	-3.4581507055668133

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
E406H	1.101899992558512	V407N	-0.9326793819209843
V407T	-0.19510493479079888	V407S	-0.15953522869953832
V407Y	0.20469432779947067	V407C	0.6224618612016871
V407H	0.1564088785593663	V407P	0.3708677777988083
V407R	0.09416341966425026	V407M	0.3863822149776886
V407E	0.2298906118513957	R408L	1.4696735416498994
R408Q	0.7849054048285239	R408P	0.7939893217449854
R408E	0.7236194083117512	R408V	0.7855563483199162
R408A	0.7282456390777868	R408C	0.6587637088173424
R408W	0.5761068251134869	R408N	1.993950933864261
R408M	0.3789366796365958	Q409I	0.42515396031292185
Q409T	0.6026036292008043	Q409S	0.5352149373164716
Q409V	0.5637825989848647	Q409A	0.7744141503180748
Q409G	0.521821347933815	Q409N	0.9439512844681064
Q409Y	-0.08809370765442001	Q409D	0.6182431909403584
I410Y	-1.153118937018789	I410C	1.375822163591144
I410H	-0.9616957211683831	I410P	2.005492776925252
I410R	-0.7643389916399055	I410D	1.3955663093607573
I410A	1.3600583753262312	I410G	2.4301332610499355
I410K	-0.13846878976687585	A411N	-0.025646106602062034
A411I	0.0076124898795057435	A411Y	-1.6517258422061467
A411F	-0.640508486588075	A411C	-0.297097003572724
A411H	0.10436741812492609	A411L	-0.2835242488072584
A411R	-0.7463357816817018	A411E	0.9268074333633181
P412K	0.08535445251560311	P412I	0.04400363911516468
P412E	0.6687032415764695	P412V	0.1827072511015025
P412G	-0.12081964396864353	P412H	-0.06984887888197668
G413K	0.4113969171737234	G413M	0.18478008405349017
G413T	-0.4007435950146269	G413L	0.4039071442987203
G413S	0.26540599018757643	G413Q	0.2909147638539128
G413P	-0.07797772093833316	G413C	0.18055091820010535
G413D	0.23551165368487426	Q414I	-0.06106622100760965
Q414T	-0.2564405645598039	Q414S	-0.1562304757415291
Q414V	0.17911926876860554	Q414A	0.4060645344128986
Q414G	0.3932915847698727	Q414N	-0.15736706708543852
Q414Y	0.20656023207088275	Q414D	-0.1635659064218214
T415Y	-0.14311119049685206	T415F	-0.07376004007650941
T415C	0.0515001060580213	T415H	-0.2270760022375403
T415L	0.053310642140792175	T415R	0.3041812145577413
T415D	0.016962572527459897	T415V	0.2190117812610206
T415G	0.2946142121961084	T415K	0.096217400659141
T415M	0.032095657775701836	G416K	-0.7975084128147943
G416I	-0.529994456129114	G416T	-0.33353068051518386
G416L	-0.358102680916746	G416S	0.06730629904802218
G416Q	-0.43550404968194323	G416P	0.46810322174757835
G416C	0.09842776409459424	G416W	-1.2186915822490894
G416D	-0.6599579030294662	K417L	0.928840673700148
K417S	1.3875895365485067	K417W	-1.3688737066601422
K417P	1.5514295553584994	K417V	1.0466360242250543
K417A	2.1707783218129943	K417G	1.954204446852041

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
K417Y	-0.12559968291688503	K417H	-0.44952388201283683
K417D	1.0731315252826332	K417I	-0.2656272352616868
I418Y	-2.6561565079735496	I418C	1.1585727794030978
I418H	-0.9127375486679137	I418P	0.4759780648670625
I418R	1.2461302540623551	I418D	-0.07034403699196513
I418A	1.2037730039081527	I418G	1.2140177400146683
I418K	-0.7523134540865432	A419N	-0.6867767500199702
A419I	-0.3131317541888791	A419Y	-0.4921132222992074
A419F	-0.41245942789894696	A419C	0.25941869487612546
A419H	-1.3680368351653531	A419L	-0.30249773541529085
A419R	-0.6991026937645316	A419E	-0.37470301451045707
D420I	-1.313064025854916	D420T	0.12147656421859573
D420S	0.3036587558169427	D420F	-2.234751323646837
D420C	0.2787723988502672	D420L	-0.5200918298276871
D420P	-0.03405856051521754	D420R	-1.1683411622541573
D420K	-0.5096889108795489	D420Q	-0.11286532003676866
Y421I	0.9075361401978075	Y421T	1.4418973766043472
Y421L	1.122377932506724	Y421P	1.8158260530487838
Y421R	-0.3052966631912549	Y421V	2.1020985992592984
Y421A	2.4271383957170536	Y421G	2.252816476347309
Y421K	-1.4074107653672299	Y421Q	0.22704644954624204
Y421E	0.6464171014262197	Y421W	2.28066199415082
N422F	0.986504217914922	N422C	2.93547219576798
N422L	1.6530546963633328	N422P	4.602272538460145
N422R	1.090840116352359	N422V	2.561661114682687
N422A	2.710696669196033	N422G	4.123951419159619
N422Q	-0.5446720189309348	N422E	1.7251887708637448
N422M	2.119643378280686	Y423I	3.591273932180303
Y423T	1.1468235281498478	Y423L	2.3550221069041446
Y423P	3.9272181513469646	Y423R	2.217037239553325
Y423V	3.815097484269162	Y423A	4.308483397360085
Y423G	1.8419796411529403	Y423K	2.253401988461181
Y423Q	0.2273696519410196	Y423E	-1.9884866795059977
Y423W	2.4674469069219014	K424L	0.01996124768461904
K424S	-0.17652681708283832	K424P	0.5521282497717477
K424V	0.49556261424815196	K424A	0.18308526926827334
K424G	0.11654090368838739	K424Y	0.043690112576660896
K424H	-0.06295066853359867	K424D	0.16134154840956516
K424M	0.23220845483232297	L425K	-0.4593938263507136
L425T	-0.336796770944888	L425R	-1.695172715796544
L425Q	-0.6130221587039906	L425P	0.3003625197629127
L425E	-0.9212459571199668	L425A	0.31984123912911266
L425G	0.4148331886279714	L425M	-0.0182806953617612
L425Y	-1.1639064398298768	L425C	0.45843086508398
L425W	-0.5490358028492779	P426K	-0.8989804321045314
P426I	0.183686983809215	P426E	0.07632824739209379
P426V	-0.20977395549349045	P426G	0.24814121132267575
P426H	-0.07298381692516284	D427I	-1.8243252965279055
D427T	-1.5940032102550235	D427S	-1.4720239253341016
D427F	-1.8211500336467594	D427C	-1.6398095020865977

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
D427L	-0.4073395889019847	D427P	-1.1942696874371785
D427R	-1.6259187035595168	D427K	-1.6439279410264702
D427Q	-1.5147068273660629	D428I	0.03827092830733503
D428T	0.08010439720144677	D428S	0.10499862100847195
D428F	0.15539941112253947	D428C	0.004890891663219981
D428L	0.1068669919772883	D428P	0.282975843615496
D428R	0.38311162125802223	D428K	0.17908686218623843
D428Q	0.2282020885279759	F429N	0.6845682364518699
F429T	0.6793605906818356	F429H	1.9576691014844023
F429P	0.9601171734268344	F429R	1.9389489506867783
F429D	-1.4736923278771437	F429A	0.9257442214638051
F429G	0.9758718822388557	F429M	-0.7408155553512608
F429W	0.3504949089555767	T430L	0.09980003611873525
T430Q	0.4322739514681241	T430E	0.3476310561727059
T430V	0.04760571610718504	T430G	0.18271235097910452
T430N	-0.28150130309965704	T430M	0.19003064725570434
G431N	-2.539783477558341	G431I	-0.7432039360375738
G431T	-0.6930348284793799	G431Y	-0.5677646957039626
G431F	-0.9070702387261325	G431H	-0.6304272152110985
G431L	0.36303892505467805	G431P	0.6932216005021752
G431W	-1.3830603938565238	G431E	0.031789012693079335
C432N	1.3242275176259208	C432I	-1.8407951746210074
C432T	-0.6110962076196281	C432H	-0.87076186735739
C432L	-0.523487766344736	C432P	0.1489790974503254
C432D	0.24366001827237688	C432V	0.4555736312161917
C432A	0.5200682296255925	V433N	-0.008509162203217329
V433T	0.41665398679432775	V433S	0.6918585928501516
V433Y	-0.349233030766125	V433C	1.2251492745228894
V433H	-0.8190955355583089	V433P	0.32234369604631985
V433R	-0.0031749352658920647	V433M	0.8791908356835378
V433E	0.4429577983442787	I434S	2.470423322891207
I434Q	0.8047929665004323	I434P	2.042676488830017
I434E	-0.1061542650545821	I434A	2.621295554308351
I434G	0.26759412912103925	I434F	-0.07118334959774184
I434N	-1.2361391324276947	A435N	-0.7943542826233643
A435I	-0.6371571773365976	A435Y	-0.190524839727734
A435F	-0.9295955494018241	A435C	0.03609415702599271
A435H	-0.9929421175737261	A435L	-0.400832671030708
A435R	-0.3835980909671004	A435E	-2.641449804551379
W436K	0.21306330792443257	W436M	-0.554667109386062
W436T	-2.703827123343816	W436Q	-1.6432201430349014
W436P	-0.6864500365667373	W436E	0.4485146698485748
W436V	0.4953370691724911	W436A	0.4354315723656884
W436Y	0.09264755449124674	W436F	0.37238186153794695
N437F	0.15216818833135665	N437C	0.44335583729415234
N437L	-0.14775491871483304	N437P	0.37674204599787686
N437R	-0.5269749391528716	N437V	0.04166330822484487
N437A	0.5234949157251895	N437G	0.23663483681669523
N437Q	-0.012802201159387289	N437E	-0.13098334338390868
N437M	0.22666088397032716	S438N	0.13965692157531073

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
S438I	0.094915485606009	S438H	-0.11686797317720858
S438L	-0.04360750961310132	S438R	-0.044152640415388966
S438D	-0.27330661543410445	S438V	0.47804051062847497
S438G	2.307705014062354	S438W	0.020598745395904235
N439F	0.08329191713981865	N439C	0.6180654023953902
N439L	2.045025927907209	N439P	0.6394607480808374
N439R	0.008940743742822978	N439V	0.3019477256629612
N439A	0.6527614634134988	N439G	0.4239223902044046
N439Q	-0.03475691905652167	N439E	0.5006368035751948
N439M	0.42733302346100277	N440F	-0.4676765138079448
N440C	0.21478658126952369	N440L	-0.34829943424644527
N440P	0.17838068989879835	N440R	-0.2433085256398801
N440V	0.017664201764625673	N440A	0.32591826990972994
N440G	0.030978380409861013	N440Q	0.5004257177521648
N440E	1.0619144245654266	N440M	-0.46492250716125527
L441N	0.007241924324132567	L441T	0.29118253861279375
L441S	0.10521016757048078	L441Y	0.003459090292642118
L441C	0.11514495951813646	L441D	-0.39459254823466744
L441A	0.29620874705533307	L441G	0.08653785572830375
L441M	-0.13406472097755004	L441Q	-0.03856600247663292
D442I	-0.9047989336925589	D442T	0.007843672459906376
D442S	0.02661634927364535	D442F	-0.47104215038360586
D442C	0.34597943637926043	D442L	-0.7355682140438555
D442P	0.022975927438759224	D442R	-0.6774964666340739
D442K	-0.45378860372149765	D442Q	-0.17072416179992772
S443N	0.3872242849118611	S443I	-2.0044402732355384
S443H	-2.706417212837728	S443L	-2.8356062002939444
S443R	-2.4189796571149964	S443D	0.012863926491140936
S443V	0.20011022122593936	S443G	-0.7753375897057939
S443W	-2.588906040953984	K444L	2.2202268823949907
K444S	0.9749691264184591	K444W	1.4619707778541686
K444P	3.2707266360158798	K444V	2.221654954684536
K444A	1.7345707427500596	K444G	1.2434145012364446
K444Y	1.593635246095515	K444H	2.674146975262097
K444D	-0.029579224396264425	K444I	1.8329163541237818
V445N	-0.11560316483248734	V445T	0.25011665174134434
V445S	0.33096427010594176	V445Y	-1.6210865360094608
V445C	0.16345481120066557	V445H	-0.48873877877090066
V445P	0.40157491238392284	V445R	0.1591827442423664
V445M	-0.47902498457030146	V445E	-0.18877227419038003
G446N	-0.23249014571524512	G446I	0.003412518914075785
G446T	-0.23428359510970784	G446Y	-2.120883420773848
G446F	-1.1032094844887503	G446H	0.4638352334320536
G446L	-0.2771762060696231	G446P	-0.0179254363995969
G446W	-1.384395541173311	G446E	-0.9036665881284373
G447N	-0.7085087766726812	G447I	-0.07739203370044101
G447T	-0.14671936561360652	G447Y	-0.8093947932443353
G447F	-0.3963222411990709	G447H	-1.1866720119383705
G447L	-0.3584835170739525	G447P	0.2661561613375667
G447W	-1.130125150828017	G447E	-0.5761576595757207

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
N448F	0.08841906943497085	N448C	-0.1125083340889979
N448L	-1.2742450773574014	N448P	-0.11551145818930746
N448R	-1.5541964464635014	N448V	0.6540083933272057
N448A	0.030830625032351955	N448G	-0.41923486051659464
N448Q	1.2432879985293188	N448E	-0.9143443907867995
N448M	-0.048478588427680505	Y449I	0.959191122571645
Y449T	0.9129311640401745	Y449L	0.8958248520447565
Y449P	1.5045608574362705	Y449R	0.5487813711258746
Y449V	1.0260459536610103	Y449A	1.5006740431821264
Y449G	1.3479271339127281	Y449K	-1.1675279557719378
Y449Q	0.6652141760332494	Y449E	0.8581600554294807
Y449W	-1.4208648522749217	N450F	0.6893910641130462
N450C	0.8118479476047173	N450L	0.5516813921959278
N450P	0.11940529985230934	N450R	-0.5088357725609419
N450V	0.760887586719978	N450A	0.7587318188689643
N450G	0.49907384988373493	N450Q	2.0583072609971307
N450E	0.3950511493377623	N450M	0.7112480458682404
Y451I	0.5583307564804837	Y451T	-2.9538370386418316
Y451L	-0.15476528936084266	Y451P	0.6883562705725893
Y451R	-0.19134388518378043	Y451V	0.45001670098566643
Y451A	0.7944720794858686	Y451G	1.0570815196891037
Y451K	0.06810211913297452	Y451Q	0.1656355592297779
Y451E	-0.22650600572717905	Y451W	0.47671492829669626
L452K	-0.6906175699346959	L452T	2.0355147250561574
L452S	1.4559591562304863	L452W	0.8776071743577486
L452E	-0.9731778249316904	L452A	1.9619089870665234
L452G	1.2505522458245844	L452I	-1.4863913832805324
L452F	-0.5202240146117277	L452H	3.1179328384421305
Y453I	0.6264632171508121	Y453T	0.9018352178591942
Y453L	1.4696182868477812	Y453P	1.4800418200951495
Y453R	-0.5449547526411362	Y453V	1.102049546919883
Y453A	1.4273017451504038	Y453G	1.2853811270855189
Y453K	-0.36997780475547903	Y453Q	0.3108939788277939
Y453E	0.4399288736778514	Y453W	-0.34088805000354255
R454L	-0.37089881995687896	R454Q	-0.9084917076852248
R454P	-1.2915636994500472	R454E	2.6848411315566336
R454V	-1.907806318319985	R454A	0.397022744265861
R454C	0.2954572874123712	R454W	-0.27037840214020487
R454N	0.8029969737482672	R454M	-2.107236720803126
L455K	1.353695543626061	L455T	-0.27086479771847094
L455R	-2.266270674494373	L455Q	-0.3882201616333587
L455P	-0.4180495765162937	L455E	-0.5309871870445565
L455A	0.6326752551822747	L455G	0.4855781017912955
L455I	-0.229817050671162	L455Y	-0.6843613119566184
L455C	0.3496483510271277	F456N	-2.604355212490244
F456T	0.791558060530448	F456H	-1.6646862309364365
F456P	1.1042114340601956	F456R	-0.045057188862784904
F456D	0.6782819741547559	F456A	1.2794170017924484
F456G	0.9482973938002222	F456M	0.7156223678279992
F456W	-3.526118781159672	R457L	-0.16996681191875893

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
R457Q	-0.49149040279783823	R457P	0.39988639189879915
R457E	-0.06408199808737694	R457V	-0.15934934471425294
R457A	0.4492786466715265	R457C	0.40539094403348563
R457N	-0.5628962605407221	R457I	-0.16816031487477912
K458L	0.03536414512261203	K458S	0.33823915297930646
K458W	-0.6762182832204818	K458P	0.36996268797691056
K458V	0.9763417438917446	K458A	0.844075239654946
K458G	1.1487447954575594	K458Y	-0.35089144628978286
K458H	0.08667732752144007	K458D	0.20701908744294797
K458I	0.5583910054278836	S459N	0.08672373822822055
S459I	0.22217414453447146	S459H	0.14831050017773598
S459L	0.15658131672809114	S459R	-0.0632793265814269
S459D	-0.0988043293390459	S459V	0.20684588502692383
S459G	0.10733450017921557	S459W	-0.16271310749178663
N460F	1.6948162940703029	N460C	2.3554478453513
N460L	1.73730747327538	N460P	1.0488084760353829
N460R	-1.6665514983797707	N460V	1.1638148583273096
N460A	2.49478785642845	N460G	1.2454869269223656
N460Q	0.666229274363213	N460E	0.5064154080244465
N460M	1.311827670786648	L461N	-0.3950286305319911
L461T	-0.11302762028607209	L461S	0.10784177279558065
L461Y	-0.10104324389037107	L461C	0.6288282286753593
L461D	0.15834972049707247	L461A	0.5729585557234548
L461G	0.6190779516895212	L461M	0.2481733767341369
L461Q	-0.16208396210907278	K462L	-0.017250783158793154
K462S	0.15466810104331188	K462P	0.27578750105034044
K462V	0.003933262265301761	K462A	0.16682632894730046
K462G	0.10230534161432617	K462Y	-0.10752760037689155
K462H	0.036807284523651784	K462D	0.039418702659017014
K462M	0.033410287289026674	P463N	-0.426038627110534
P463I	-0.09518274659656548	P463Y	-0.36395068473370384
P463F	-0.4534796998006464	P463C	-0.1609386073665659
P463D	-0.1005532060552335	P463V	-0.07349143960365626
P463G	-0.06380116031102792	P463Q	-0.06574100201276487
F464N	-0.5849053713952281	F464T	-1.5841561815446468
F464H	1.2532511562996367	F464P	0.45401458273449447
F464R	-0.9039556248439873	F464D	-1.6032041991851784
F464A	-0.9070814771315117	F464G	0.16427475571117384
F464M	-0.018301738491006175	F464W	-0.15742102160587612
E465M	-0.15794865784890785	E465T	-0.08698816727582086
E465R	-0.5457498047019868	E465L	-0.5103978696338073
E465S	0.04073405715994855	E465W	-0.04938050521475533
E465P	-0.171782005533399	E465N	-0.010101317078734014
E465Y	-0.402557949790087	E465H	-0.18926910666635735
R466L	0.1274100737232281	R466Q	-0.09979380392492558
R466P	0.7247337010041415	R466E	0.42576627266087064
R466V	0.40132138730862543	R466A	0.6864785603307391
R466C	0.684580414176885	R466W	0.4572231359327197
R466N	0.12380737105087725	R466M	0.6062175544996725
D467I	-0.6585588292995302	D467T	0.02387587042386186

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
D467S	0.11350470378125917	D467F	-0.5307318014029111
D467C	0.3791724299296542	D467L	-0.5811754946800062
D467P	-0.13019309882383504	D467R	-0.45441153161604547
D467K	-0.4212684735179078	D467Q	0.05249584395634773
I468Y	-0.11406587675002958	I468C	0.03042343674103623
I468H	0.22660553157597932	I468P	0.23008060427635982
I468R	-0.3561969765664775	I468D	-0.07128381222501853
I468A	0.19256889920530462	I468G	0.05868422388612345
I468K	-0.02248934087731922	S469K	0.11458287709045131
S469I	-0.3269394250973685	S469R	-0.2916134334655807
S469Q	0.19938816954762134	S469E	-0.9481755384905199
S469V	0.19215141512208767	S469G	0.11957749812911636
S469Y	0.061154277571174843	S469F	0.1543792060111817
S469C	-0.05980293765582299	S469W	0.12465338182947328
T470Y	-0.207177936217608	T470F	-0.157718345980476
T470C	0.07917529676770842	T470H	-0.28151824300670225
T470L	0.00034072077103690574	T470R	-1.1074387599209308
T470D	0.012675164366301528	T470V	0.15411046229264674
T470G	-0.037835864983559536	T470K	-1.4249422902793136
T470M	-0.09636784736850898	E471I	-0.11592606127282297
E471T	0.2848893809942154	E471R	-0.11468579784585957
E471L	-0.047413693764019584	E471S	0.3503155377443127
E471P	0.03798097858447401	E471N	0.22356550917510756
E471Y	-0.19822991158624156	E471H	-4.2508028695613405
I472Y	0.08124702915538748	I472C	0.4136899415958002
I472H	-2.6263278140891577	I472P	0.49495589661742007
I472R	0.4477279899991844	I472D	0.42897892738201016
I472A	0.5435901437375119	I472G	0.3538151035290403
I472K	0.6271053108208653	Y473I	0.5016435292750795
Y473T	0.3894415686336056	Y473L	0.4744691326533449
Y473P	0.9490268228345997	Y473R	0.22589906095567666
Y473V	-0.8607358972544918	Y473A	0.7451770710335103
Y473G	0.5277275133933005	Y473K	0.32063257335616613
Y473Q	0.08381165797681639	Y473E	-0.4584140677462333
Y473W	0.23683915358194865	Q474M	0.25388748516722176
Q474T	-0.17389805753532767	Q474S	1.2593146869906577
Q474W	-0.49555880464928637	Q474V	0.04321635393839789
Q474A	0.5357661523776348	Q474G	0.30435326677011376
Q474N	-0.7427677758800151	Q474Y	-0.17083751021056168
Q474D	0.1664315550599919	A475N	-0.4730374726198997
A475I	-0.6263656665361911	A475Y	-1.8584286011615756
A475F	-0.8308277352890661	A475C	-0.259174273960272
A475H	-1.0823688861877048	A475L	-0.5713568715400064
A475R	-1.084118909416938	A475E	-0.9357473104829968
G476N	-0.1431833133977813	G476I	-1.5569860039146195
G476T	0.7080442358912629	G476Y	-0.3717369836715786
G476F	-0.9035264670604753	G476H	-0.09450182479868294
G476L	-0.7768152290501069	G476P	-1.1956782483258606
G476W	-0.7164327704491906	G476E	-0.17794105246788927
S477Y	-0.03686733863917966	S477F	0.08954653853480722

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
S477H	0.16276375511536084	S477L	0.4429810731256496
S477P	0.36409996464007527	S477D	-0.029090122965994697
S477V	0.43527331233102473	S477A	0.3089622225959847
S477W	-0.17949355283271515	S477K	0.23973644503656694
S477M	0.2290437881229231	T478L	0.07916796992157353
T478Q	0.10986469712554195	T478E	0.17138313477790726
T478V	0.09442355985935161	T478G	0.24985165996664366
T478N	0.08857098423953107	T478M	-1.1989712921500992
P479N	-0.012838553718728926	P479I	0.22668995258026364
P479Y	0.08209595496899832	P479F	0.11929485482999273
P479C	-0.07515218396158038	P479D	-1.1501381754547182
P479V	0.15166913013107322	P479G	0.10197211007258862
P479Q	0.11616995412728333	C480N	-0.9508115437970872
C480I	-0.002970326970688476	C480T	0.27108669769540283
C480H	-0.1874470256583936	C480L	0.07355191805576795
C480P	0.34195011548325016	C480D	-0.5573724903477237
C480V	0.08973951561531875	C480A	0.41156144318280824
N481F	-0.47433905389314424	N481C	-0.3911224887564305
N481L	-0.026361925781032795	N481P	0.16648383987293972
N481R	-0.23568912001805625	N481V	-0.23214539439387205
N481A	-0.18035302389736985	N481G	-0.15153602989973608
N481Q	-0.09700053895158187	N481E	-0.23879256650951816
N481M	-0.17169077025537183	G482N	0.16907850891320947
G482I	0.28712640009717993	G482T	0.20520093855767976
G482Y	0.12851563143082184	G482F	0.16243516941170683
G482H	0.20913969807415578	G482L	0.21953331696129902
G482P	0.3992868766124523	G482W	0.05524569695305076
G482E	0.21509834013734458	V483N	0.030469004042414927
V483T	-0.11316559161545672	V483S	-0.012095054218635947
V483Y	-0.13474929458853727	V483C	-0.05875437825627035
V483H	0.10530537244884178	V483P	0.15778867815759917
V483R	0.04281186042208447	V483M	-0.0531552528210545
V483E	0.10199374141612913	E484I	0.1393919505483133
E484T	-1.4557616040076824	E484R	-1.1404130822258998
E484L	0.6078093743504895	E484S	1.5656724407551494
E484P	1.7264912621270607	E484N	1.3451283382162846
E484Y	0.26543552586327185	E484H	0.5593734751588715
G485N	0.12375068675743857	G485I	0.2794593089455816
G485T	0.16411392669778516	G485Y	-0.23865540578206373
G485F	-0.0918994419261973	G485H	0.09254783323636116
G485L	0.1979669821013185	G485P	0.19521946688575798
G485W	-0.18565201119060273	G485E	0.20324346566530535
F486N	0.8141581273836647	F486T	0.7159194656679458
F486H	1.1499283127358606	F486P	1.1258621495317027
F486R	0.8861029616104374	F486D	-0.6667983846012092
F486A	0.9200986782693775	F486G	0.7459659431517613
F486M	0.6452947941396829	F486W	0.2852502621233624
N487F	0.3162840332795067	N487C	0.8950500759947154
N487L	0.5413067981066152	N487P	1.0193884652728182
N487R	0.7119526868588544	N487V	1.2419473671134111

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Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
N487A	1.0085304745673187	N487G	0.7196138861581399
N487Q	-0.9062386322451961	N487E	0.5850747304976713
N487M	1.2189019505002168	C488N	0.05257970128485534
C488I	0.09232493025939167	C488T	0.19825572253337412
C488H	-0.0745400764733611	C488L	0.05773198983650248
C488P	0.10911850804222187	C488D	0.12337178465316503
C488V	0.22026230362077753	C488A	0.509355159457225
Y489I	2.0687086225280242	Y489T	2.8595065823112185
Y489L	3.328997783244252	Y489P	3.4878761266218894
Y489R	2.6018139784678866	Y489V	2.3306804459530936
Y489A	2.8303576884259467	Y489G	3.8767062820568925
Y489K	3.554488194923087	Y489Q	3.5245898135934146
Y489E	3.0224267539524563	Y489W	2.095495328306142
F490N	0.5216076814700503	F490T	0.17850245699387363
F490H	0.9579819582935649	F490P	0.9229947568304404
F490R	0.10427857104047651	F490D	0.5559528055917398
F490A	0.7771263248755629	F490G	0.7291569476548918
F490M	0.5487079230386612	F490W	0.3343071674847178
P491N	0.8923917733460227	P491I	-0.28878008263704674
P491Y	0.09288871209861951	P491F	-0.2565319995561
P491C	0.4394460616183614	P491D	0.0775626282477545
P491V	0.020660836390701435	P491G	0.4109238908796266
P491Q	-0.41806375347885866	L492K	0.31501028535961273
L492T	0.16089145750259168	L492R	-0.034736153232858266
L492Q	0.008451826122055762	L492P	1.0291279511068692
L492E	0.2668673549356261	L492A	1.0052355537765734
L492G	0.48342427555160983	L492M	-0.5529239015440983
L492Y	-0.22084076732315397	L492C	1.1424949255154897
L492W	1.1375960874240865	Q493I	1.8698680204370075
Q493T	-0.12966178780807872	Q493S	0.42892975508810005
Q493V	-0.5633552253131799	Q493A	2.226113922876471
Q493G	1.2700962920884344	Q493N	-1.1856350499090245
Q493Y	0.9209849410469555	Q493D	-0.32641223210199644
S494K	-0.31660097360225464	S494I	-0.1997536565003554
S494R	-0.26605985125467924	S494Q	-1.8016760375265761
S494E	-0.5091905688774663	S494V	-0.4676196007396671
S494G	0.2870840314591076	S494Y	-0.9259060326714051
S494F	-0.5617263419275469	S494C	0.1338891862897647
S494W	-0.9643426825787017	Y495I	0.788571269172388
Y495T	0.8585420422185617	Y495L	-0.3710257822779591
Y495P	-0.42605972149898375	Y495R	3.7037900148678915
Y495V	-2.6481252497719963	Y495A	1.3406535527648087
Y495G	-1.7574293142613537	Y495K	1.8365733010781564
Y495Q	3.4943050977205936	Y495E	0.5536919633452965
Y495W	1.0134498810558092	G496N	-0.07292074497741804
G496I	-0.5371494934225638	G496T	-0.24440884831514453
G496Y	-1.2595556051925316	G496F	-1.254879795580654
G496H	2.383008622803003	G496L	-0.7302099534919916
G496P	-0.5433945647999086	G496W	2.37173789905886
G496E	-0.9567835611496658	F497N	-0.5810539809186916

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
F497T	0.5339433566400469	F497H	-0.4763974478211835
F497P	0.8816524401333646	F497R	-0.32571064650455145
F497D	0.22656166096624658	F497A	1.122501329637979
F497G	1.0289140604755698	F497M	0.7179387658333563
F497W	-0.30313290656514036	Q498I	0.34547274072986084
Q498T	0.2747060289054572	Q498S	0.6308876452519263
Q498V	0.6364204492566058	Q498A	0.8558870164492784
Q498G	0.9894633836701724	Q498N	0.4430631320358224
Q498Y	-0.41271257393316485	Q498D	0.05858330158520567
P499N	-0.24760089750812772	P499I	0.40345797682667506
P499Y	-1.7495719305312574	P499F	-0.3963975873360791
P499C	0.18483906954948517	P499D	-0.46586046985918034
P499V	-0.015695644269561427	P499G	0.007194744825854096
P499Q	-0.1609778349445597	T500Y	-2.0859449459796644
T500F	0.06502253090993926	T500C	0.430635516016884
T500H	-1.7392904541056466	T500L	0.021255830061814193
T500R	0.043354998387680685	T500D	-0.7658521184154594
T500V	0.9613207853553403	T500G	2.399206799257318
T500K	-0.31728831536669616	T500M	0.19822969783981337
N501F	-0.04385977247764152	N501C	1.0439369512335408
N501L	0.18341469720698914	N501P	1.1609463991960838
N501R	-0.7441464154535433	N501V	3.965497877149798
N501A	1.1852260420841207	N501G	0.38130741094221754
N501Q	-0.40521444437824233	N501E	-0.47102212719029657
N501M	1.382764667958684	G502N	-0.1049075533287536
G502I	-0.6926329920064511	G502T	-0.285344394100541
G502Y	-0.921811520303691	G502F	-0.576493263354875
G502H	-0.20559029965274994	G502L	-0.5671088229101959
G502P	-0.10139439929755241	G502W	-0.8767128631282775
G502E	-0.37910317570040536	V503N	1.0967388249672534
V503T	-0.04569451812155616	V503S	0.5844626128165492
V503Y	-0.02384079012367129	V503C	0.4509271759068342
V503H	0.28082778448573625	V503P	0.11756147082026469
V503R	-0.21616903988720484	V503M	-0.009731243983262394
V503E	-0.027539387202509664	G504N	-0.20331123859110534
G504I	-0.06370358570189512	G504T	-0.15617241391762424
G504Y	-1.4263632739486383	G504F	-0.5003645249655616
G504H	-1.6964188204959219	G504L	-0.5045378548940749
G504P	-0.13589613963574762	G504W	-1.7176558290068844
G504E	-0.02947514167831017	Y505I	-3.467147511981561
Y505T	0.7785040665354467	Y505L	0.2958366346393961
Y505P	1.5915037169810309	Y505R	2.52662820267434
Y505V	-0.9092522194726437	Y505A	1.907615764828416
Y505G	4.768169533634241	Y505K	2.911848681970258
Y505Q	1.8789389514342922	Y505E	1.3532547380461049
Y505W	-1.8072251009011002	Q506I	-0.33059365388009765
Q506T	0.2598174570020193	Q506S	1.5240796861263903
Q506V	0.5797347329269933	Q506A	1.1697961799344203
Q506G	0.37302499129504063	Q506N	0.5810940509309088
Q506Y	-0.4469687925419093	Q506D	-0.289210659246448

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
P507K	-0.4114804642960072	P507I	0.03571326545060595
P507E	0.10148492827838544	P507V	-0.1458046036347433
P507G	0.054115878130992875	P507H	0.014675406072253549
Y508I	0.5784949044830723	Y508T	1.2342474504324068
Y508L	0.419395837623682	Y508P	1.1757926039992443
Y508R	0.12365877341819036	Y508V	0.6766562136533377
Y508A	0.42740616097241285	Y508G	0.3568508435882431
Y508K	0.6614148998900773	Y508Q	0.20702703829055932
Y508E	-0.19147818447719123	Y508W	0.27038476046435067
R509L	0.4180190377749927	R509Q	0.4688403523426993
R509P	0.7023611054384744	R509E	0.3481358378982541
R509V	0.12633475900477426	R509A	0.3621914382018112
R509C	0.4037149437047788	R509W	0.3608264633584104
R509N	1.200598770930513	R509M	0.4273970164495964
V510K	-0.4818586377736228	V510T	-0.29171626715335297
V510R	-0.5752634268775207	V510S	-0.506409333203224
V510Q	-0.7753363647935946	V510P	-0.010412517278919842
V510M	0.024950603713397346	V510F	-0.21633560435112614
V510D	-0.6810368536201123	V511K	-2.572126205954558
V511T	1.0656264295619846	V511R	-3.0569506362909937
V511S	-1.9367099380925321	V511Q	3.513213294731527
V511P	-1.8840216048560907	V511M	-2.2415404264587586
V511F	-1.630475399487398	V511D	-1.4705066057986802
V512K	-1.2529820855928369	V512T	0.7758144366419877
V512R	0.7507992656671869	V512S	0.14653727145204912
V512Q	-0.02862537588314193	V512P	0.4016552595249828
V512M	0.3266475247266181	V512F	1.2966284789154074
V512D	1.2732678737619492	L513N	0.3263585783246893
L513T	0.2044945343405317	L513S	0.240075365438216
L513Y	-0.45025133317421384	L513C	0.4046997298149261
L513D	-0.11800024479221179	L513A	0.4332801693992187
L513G	0.36445347807120243	L513M	-0.21475431740595496
L513Q	-0.04706119931115208	S514N	0.11253819497321796
S514I	0.0697152801450835	S514H	0.6834461710970589
S514L	0.31838385119005463	S514R	0.06170166622411431
S514D	-0.019612994313028397	S514V	0.13916366502279032
S514G	-0.005999564234634944	S514W	0.4614271756678666
F515N	1.7391426613751921	F515T	1.4059268469844515
F515H	-0.5867102638541396	F515P	0.0825244834417588
F515R	-0.02798682853691018	F515D	0.6019666645152028
F515A	1.3066996459181985	F515G	1.3184779077776052
F515M	1.687318561382129	F515W	1.8989919207835846
E516I	0.33434982440468175	E516T	-0.07114549763358052
E516R	-0.5739477438052276	E516L	-0.2451664912330393
E516S	0.1883679930848659	E516P	-0.03251400587771075
E516N	-0.5168454823042706	E516Y	-0.7410776900577012
E516H	-0.27768247613840796	L517N	0.03725614305790226
L517T	-0.0658318099980003	L517S	0.037379220697849366
L517Y	-0.04992565146987564	L517C	0.06579994933352533
L517D	-1.8405131167293671	L517A	0.2618793059821508

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Table S5 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
L517G	0.00726076304289465	L517M	0.15918026005586072
L517Q	-1.773652453091889	L518K	0.036736264682740646
L518T	0.055156531685865415	L518S	-0.01901648991827292
L518E	0.19755642142809998	L518A	0.3681229182613314
L518G	0.27466041869769303	L518M	0.18012407903819103
L518F	0.33161318793651207	L518H	0.32071311333695385
H519I	0.19550960252101332	H519T	0.10829071581286479
H519S	0.12536228301640415	H519F	0.22542804239144226
H519C	-0.04095977029425426	H519V	0.2161806745604705
H519A	0.2741018034253032	H519G	0.24100116045220682
H519K	0.17465590929378358	H519E	0.3302499626009706
A520K	0.18815257451734463	A520I	0.14750254370499757
A520R	-0.20701126643177403	A520L	0.2936273444728296
A520Q	-0.020121526259257	A520D	0.23674805512236627
P521K	0.142642005822125	P521I	0.19116706361527908
P521E	0.17155849372934995	P521V	0.18530866759402792
P521G	0.22449309283513624	P521H	0.10797148365079064
A522K	-0.07811806221872608	A522I	0.045237343415504845
A522R	0.010082253892655222	A522L	-0.046668011903408774
A522Q	-0.16911887747369186	A522D	0.04544407638273804
T523Y	0.2574102045301572	T523F	0.5814201950203837
T523C	0.5629995114666447	T523H	0.6756646673111713
T523L	0.4774490184247681	T523R	0.4953454249607522
T523D	0.26197201405569437	T523V	0.4273969305616685
T523G	0.2986339441279401	T523K	0.41978240259171695
T523M	0.5006656529482786	V524N	1.8923163489217558
V524T	0.996020426627967	V524S	2.131985576890781
V524Y	-0.36583593788500657	V524C	1.3735292020874623
V524H	-0.18948706103497398	V524P	0.6612827682236818
V524R	-0.563434616625101	V524M	1.3776899767974111
V524E	0.6332136709875742	C525N	-0.7812551410544439
C525I	0.37770578220002093	C525T	0.6354308523644421
C525H	0.4057453924765685	C525L	0.5597910254431415
C525P	0.5886193287791198	C525D	-0.7851323423560228
C525V	0.47187589318198064	C525A	0.607870889268009
G526K	-0.16636624162594643	G526I	-1.302820004435949
G526T	-1.0633939960273977	G526L	0.13840453988560703
G526S	-0.06652132249728182	G526Q	-0.13987945121516715
G526P	0.21967057587224295	G526C	0.3556635229172211
G526W	0.11176410635794995	G526D	-0.1450505804358385

Table S6: Unlikely mutation binding affinity change prediction. Residue ID is according to SARS-CoV-2.

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
T333Y	0.24207507093715092	T333F	0.29634814042280905
T333C	0.030545913887769605	T333W	0.3380257088853784
T333H	0.3017683627962638	T333D	0.29901602918999254
N334W	0.21865334474229145	L335N	-0.29723300906792643
L335H	0.4202664927798433	L335D	-0.2506871042346782

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
C336K	-0.21135472415672724	C336M	0.4439400191790419
C336Q	-0.40512638908694704	C336E	0.2938299322425579
P337K	0.21662573834688587	P337M	0.16046260933681114
P337W	0.06569878428692157	P337E	0.32398654958829837
F338K	1.6318666057301372	F338Q	-0.28561167788120234
F338E	1.0397023043064877	G339K	0.33120475427556445
G339M	0.3197075588950395	G339Q	0.3198570745228727
E340M	-0.07251237800049302	E340F	-0.002504242307229357
E340C	0.3153990715147169	E340W	0.07962545350800865
V341K	-0.00043742341144481224	V341W	-0.21878390871573422
V341Q	-0.14767817035555747	F342K	3.1158001772756716
F342Q	2.301482828016689	F342E	1.7607243016951248
N343W	0.1123560161181831	A344K	-0.0694101462313823
A344M	0.014360881318925161	A344W	-0.17629647411984956
A344Q	0.1975648223563149	T345W	0.1762140139909577
T345Q	0.21824404192929658	T345E	0.23905583556634608
R346Y	0.20630900206660238	R346F	0.1916181522809627
R346H	0.8360669536226307	R346D	0.438923461861072
F347K	1.298207619914493	F347Q	0.8400625317862286
F347E	-0.02876532886695022	A348N	-0.1400862335155758
A348M	0.08750497165210987	A348Y	-0.035518122240894956
A348F	0.11403793169418011	A348C	0.21501206935491904
A348W	0.40697303163033405	A348H	-0.04848679995183082
S349K	0.0038340977504157546	S349M	0.25108832423296834
S349Q	0.17628323544758986	S349E	0.026155982265649552
V350K	-0.5751902929353583	V350W	-1.2366744959398632
V350Q	0.5618845015263113	Y351M	1.0431508537600183
A352K	-0.2863935375504048	A352M	-0.08645811555201148
A352W	-0.004997168005624239	A352Q	-0.13145626025349777
W353N	-0.14538378725989998	W353I	-0.03525942957933148
W353H	-0.4577604638101893	W353D	-0.25812219251112273
N354W	0.3775881634820072	R355Y	-0.8902931298204833
R355F	0.5518232015737332	R355H	0.10022289932500154
R355D	-1.0077979655938605	K356F	0.48229266859393116
K356C	0.3206594382161754	R357Y	0.2906016179842271
R357F	0.25956034032687186	R357H	0.42824676785821864
R357D	0.13346587124996137	I358W	-0.1830424842222454
I358Q	-0.36489912551325665	I358E	0.14538583295001253
S359Q	0.3122845033276875	S359E	0.16879863775328055
N360W	0.13060730963149875	C361K	0.3867335585886608
C361M	0.6214452847414231	C361Q	0.2562180477728113
C361E	0.17035502136255526	V362K	0.9991545900279177
V362W	0.06858189473708089	V362Q	0.13240683032531814
A363K	0.11239212852950922	A363M	0.672567442255831
A363W	-1.473215698658069	A363Q	-0.22963764644599527
D364M	0.20375645291200745	D364W	0.29129657676807047
Y365M	2.7066634520895283	S366K	-1.3181949812591665
S366M	0.07747077301760458	S366Q	0.09686696898208265
S366E	-0.05145393857076869	V367K	0.005226960223673406
V367W	2.581421710720353	V367Q	0.02393461503634065

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
L368N	0.3443397746166931	L368Y	0.6107188018138878
L368C	2.1174708865170566	L368W	2.102855756871054
L368D	0.6811373715464464	Y369M	-1.2776338490904036
N370W	-0.681028825221538	S371K	-0.7201140143279854
S371M	-0.7694665031288215	S371Q	-0.15567538416856677
S371E	-0.3511460754505119	A372N	0.002349594782218159
A372M	0.10579431043422724	A372Y	0.027933933914040532
A372F	0.0347458818647869	A372C	-0.026835654269857113
A372W	0.041755765026709434	A372H	0.10207757568827311
S373N	-0.0011554669299099318	S373M	-1.1189754621047763
S373H	-0.2945234012979018	S373D	0.22145311673743912
F374K	-0.11841108481156774	F374Q	0.30946293724577023
F374E	0.26044423064874433	S375K	-0.41343206030418783
S375M	0.12783139905418875	S375Q	0.19377180329470753
S375E	0.03665519312644801	T376W	0.16981841838246647
T376Q	-1.4216574343082047	T376E	-0.07040857945923785
F377K	-2.0846215708987503	F377Q	-0.5511805677960031
F377E	0.4512813031473562	K378F	0.41381586379878554
K378C	0.5047492378486751	C379K	0.11491526683117967
C379M	0.2914596117803444	C379Q	0.06933920822671875
C379E	0.1831623432972993	Y380M	0.5354168768480405
G381N	-2.9148885386889605	G381M	0.5292234543708774
G381Y	0.42449415653527156	G381F	0.20130307886963528
G381H	-1.648143137624976	V382N	0.16088574312585957
V382Y	-3.091709526776927	V382C	0.3778392061475063
V382H	1.0736005323094684	S383K	0.32338886062898187
S383M	0.3459403039492712	S383Q	0.3710812401346672
S383E	0.22125419784218212	P384K	-0.10083589092545062
P384M	0.17327724030772126	P384W	0.30281732077468715
P384E	0.012398692239318516	T385W	0.17908731999766897
T385Q	0.28212972958769145	T385E	0.21889308890053258
K386F	0.03732104138170026	K386C	0.057060367781029145
K386W	0.08316262096275852	L387N	-0.048683153098090605
L387H	-0.1962728608301724	L387D	0.27803070369952476
N388W	0.4734425327996097	D389M	-0.029196803712912018
D389W	0.020750402589802618	L390K	0.22321019890509858
L390W	0.0934311272444029	L390E	0.013684139611596063
C391K	0.5993537576342104	C391M	0.5491500181528629
C391Q	0.4472242644098852	C391E	0.44952700608536855
F392K	-1.718073185456733	F392Q	-0.23925202335611964
F392E	0.33916083256427754	T393W	0.38602137594352987
T393Q	0.25447484817557364	T393E	0.09102925982646592
N394W	-0.578788585392207	V395K	-0.8392053764716583
V395W	-0.4874999062029869	V395Q	-0.5503967356155103
Y396M	0.36170200900771937	A397N	-0.6486004247553037
A397M	-0.045996453135712156	A397Y	-1.0043539657438878
A397F	-0.44426997711345156	A397C	0.16598889365892458
A397W	-0.24644754316747108	A397H	-3.718487564037563
D398M	-0.07649690331695785	D398W	-1.4568151761233261
S399N	-0.8079321888357283	S399M	0.18697554389553883

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
S399H	-0.15611853346032248	S399D	-0.14513677517914475
F400K	-0.05959352495865624	F400Q	0.26098425948111187
F400E	0.25387258806475743	V401N	1.768556625452015
V401Y	2.199939372982614	V401C	0.1951442755584068
V401W	0.3336469621884698	V401H	-5.042137051565744
I402W	1.5711650012142482	I402Q	-0.4523591971240003
I402E	-0.034473887330676974	R403Y	-2.823195818772567
R403F	-3.7418363007154865	R403H	0.26648794568980494
R403D	0.8012123688001023	G404K	-0.7949999822060961
G404M	-0.1522308168135505	G404Q	-0.8849638164540204
D405M	-0.11387547305172363	D405W	2.0695382564353144
E406M	-2.3340907741774726	E406F	-3.191958257456072
E406C	-1.4540917829863647	E406W	0.6290700844936282
V407K	0.19184378089061593	V407W	0.2854860928133522
V407Q	-0.3546637179730154	R408Y	0.40449547791516416
R408F	0.16364206734468714	R408H	0.48510163176798066
R408D	0.7470033426617957	Q409M	0.6037577433075352
Q409F	0.17804286292218618	Q409C	0.8360986768697284
Q409W	-1.51562562911253	I410W	1.1518169197306456
I410Q	-1.0113367198153778	I410E	0.46419781940556437
A411K	-0.6685235656394444	A411M	0.2944297229906322
A411W	0.551492071811934	A411Q	0.1498988841877601
P412N	2.095245060506571	P412M	0.258861001224826
P412Y	-0.16246950977197938	P412F	0.03989156351997471
P412C	0.03509682006033844	P412W	0.14835711732262843
P412D	1.0771722249663758	G413N	0.2709521610197464
G413I	0.34350779373971907	G413Y	0.25385614154126446
G413F	0.2685078630958308	G413H	0.40160073351002595
Q414M	0.2631357738819827	Q414F	0.1784320844236394
Q414C	0.2954781786185815	Q414W	0.2251009983672949
T415W	0.016672945569760282	T415Q	0.4987121314198902
T415E	0.25638519043049035	G416N	-0.33706531911336485
G416M	-0.31819222053249785	G416Y	-1.2855190455754433
G416F	-1.2723496296786603	G416H	-0.5728769334919663
K417F	-0.5408881950538802	K417C	2.120132479571659
I418W	3.215994098093014	I418Q	-1.8071548750095652
I418E	-0.6229716345061209	A419K	1.007420338798919
A419M	-0.1772828809449888	A419W	-1.300527181364991
A419Q	-0.973138390619158	D420M	-2.0120986088604407
D420W	-1.3016077748636488	Y421M	1.249752832872942
N422W	0.8922630270239766	Y423M	3.395932946357507
K424F	0.1012641333705591	K424C	0.16003561282296336
K424W	-0.33144126002139707	L425N	1.0231247310555203
L425H	-0.7288648369193514	L425D	-0.4798132983622908
P426N	-0.369204913543011	P426M	-0.0009256988454088525
P426Y	-0.04021432620081504	P426F	0.16362463471805377
P426C	0.3167031658090848	P426W	-0.17852902729051895
P426D	-0.16041877199235383	D427M	-0.6572888793082845
D427W	-1.6662453661327106	D428M	0.12904632475332933
D428W	0.3526763011960877	F429K	-2.140562210898895

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
F429Q	-0.2522323118513622	F429E	-0.28012482295314395
T430Y	0.06585934178081121	T430F	-0.0023039597434025227
T430C	0.13737679001561215	T430W	0.16306321905005955
T430H	0.12755142524198945	T430D	-0.21182641996122978
G431K	-0.7451217307049399	G431M	1.1686106107969958
G431Q	0.40303223963708523	C432K	-0.9245793371458035
C432M	-0.009717122791781817	C432Q	-0.46842626547124755
C432E	0.3915720030649029	V433K	-0.32969796943843405
V433W	-2.4064199817369074	V433Q	-0.34587879979117486
I434Y	0.34314491842311357	I434C	2.6549373726027374
I434W	-1.8136731460909161	I434H	-0.5625575254825991
I434D	0.8578003177067641	A435K	-0.11941504594271952
A435M	-0.05633270010327772	A435W	-2.898899518894752
A435Q	-1.9065054034659101	W436N	0.3973466736579986
W436I	-1.3742048632314403	W436H	0.042306081479278806
W436D	0.3915223714363889	N437W	-0.04550000193971064
S438K	0.1449155826586989	S438M	0.18977155503429982
S438Q	0.04450806206034016	S438E	-0.07333554866005366
N439W	-0.04291182896859453	N440W	-1.465660949613466
L441K	-0.1542478561100039	L441W	0.011952475047604365
L441E	0.1409884901324948	D442M	-0.003063243141086876
D442W	-0.5193392000222161	S443K	-0.7945372408890906
S443M	-2.0677055978357624	S443Q	-0.4586181180626743
S443E	-0.04226086081611559	K444F	1.3058234286797346
K444C	1.7112725972048577	V445K	-0.354148279767807
V445W	-1.3578920948690985	V445Q	0.11333478359718643
G446K	0.7407444570455642	G446M	-0.6070017155724519
G446Q	-1.2999051037825993	G447K	-1.118365330736824
G447M	-0.14669806718563874	G447Q	-0.5319300613334905
N448W	0.5606963235973238	Y449M	0.5206613189344319
N450W	0.9258528024036948	Y451M	0.5545277658647274
L452N	0.8672180998965514	L452Y	0.5793478303935762
L452C	1.7447191707770586	L452D	1.4685149809290368
Y453M	1.4072974652468875	R454Y	-1.4493356063199676
R454F	-0.3534385146437125	R454H	-2.0619397129637607
R454D	-2.124875366363889	L455N	-0.4540899088760951
L455H	-0.5876689271769696	L455D	-0.555754281694056
F456K	0.06618674402869576	F456Q	0.5074489249214893
F456E	0.584824010614921	R457Y	-0.0024188611074833417
R457F	0.23067781869270704	R457H	-0.0009201855931538931
R457D	0.01030193510801925	K458F	0.740645031935683
K458C	0.7183975736078261	S459K	0.008833388750074719
S459M	0.06482150991293753	S459Q	-0.1011913574651282
S459E	0.12945949235958226	N460W	1.5684332106195555
L461K	-0.2642345949933306	L461W	-1.3254577506276457
L461E	-0.22714478837614954	K462F	-0.03624938657511821
K462C	0.06203607784658856	K462W	0.0017024615229722928
P463K	-0.17472876233128565	P463M	-0.6120223006801093
P463W	-0.1356076261018299	P463E	-0.0861078422962825
F464K	-2.352936426194467	F464Q	-4.0187890361828655

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
F464E	-0.04075405721396566	E465I	-0.3026183723863488
E465F	-0.4274090937352278	E465C	0.19715006930746226
R466Y	0.4266868838554445	R466F	0.4635660867191572
R466H	0.7558857829146377	R466D	0.20110386852715986
D467M	-0.1357849152325862	D467W	-1.6814272655674884
I468W	-0.09266281317216996	I468Q	-0.13426758481804085
I468E	0.15002350788025046	S469N	0.17984055832298043
S469M	0.05241214623613184	S469H	0.14766979159393118
S469D	-0.2971685254994074	T470W	-0.06122965235630294
T470Q	0.270181532689938	T470E	0.08949888710170506
E471M	-0.028829117556518034	E471F	-0.037293461971902295
E471C	0.26272661138845077	E471W	-0.15316024521953076
I472W	0.3103352766180671	I472Q	0.5111473950595167
I472E	0.4122634245564071	Y473M	0.6086286389292285
Q474I	0.018557972589238685	Q474F	-0.5987792141249517
Q474C	0.49934316268622503	A475K	-0.9279018393646968
A475M	-2.16206381898927	A475W	-1.019685387800203
A475Q	-0.8911061783819667	G476K	-0.07687614541617224
G476M	-0.032558112773395056	G476Q	-0.2944884196822526
S477Q	0.2614472299192538	S477E	0.10257821186794377
T478Y	-0.19769486688965646	T478F	-0.7538846244428853
T478C	0.312071105872698	T478W	-0.16936895769986343
T478H	-1.3061614890710582	T478D	-0.0281241085339912
P479K	0.10771996402796913	P479M	-0.022103404897591064
P479W	0.25429659886503375	P479E	0.06923953942434599
C480K	0.05828259183136162	C480M	0.2207100418288571
C480Q	0.8870505976877652	C480E	0.20998117023157561
N481W	-0.34229458476786423	G482K	0.15296926370504896
G482M	0.09858967865895407	G482Q	0.14412500187234226
V483K	0.01768838818821852	V483W	-0.01565639460611414
V483Q	0.06513932586760349	E484M	0.8155791234574297
E484F	1.285714967004722	E484C	1.0516754423560861
E484W	0.05128974661474325	G485K	0.12637181056164298
G485M	0.19308008160247317	G485Q	0.2189887426113269
F486K	0.6507039915589268	F486Q	0.6155350161311833
F486E	-0.46884410399225257	N487W	-1.6000913458930377
C488K	0.13909718958381306	C488M	0.40281166733388546
C488Q	0.11370127822407858	C488E	0.26708695185602876
Y489M	3.3004062293339964	F490K	0.2579564577908684
F490Q	2.0338635459056866	F490E	0.5324832650870002
P491K	-0.25154508451639074	P491M	0.004408409466631897
P491W	-0.31042714281125455	P491E	0.32284156973505984
L492N	3.3616003181289456	L492H	0.04090738322017429
L492D	0.9467783716866485	Q493M	0.7811201070175381
Q493F	0.2831238839475347	Q493C	2.053140678866535
Q493W	0.7311622631457801	S494N	-0.3816703638276617
S494M	-0.13730053768164388	S494H	1.0467656008211839
S494D	-1.4423320135694575	Y495M	0.20831850216973483
G496K	-0.6096176327770747	G496M	-0.7540319647774985
G496Q	-0.6140597931088385	F497K	0.37580660918216263

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
F497Q	-0.8732056051831719	F497E	1.1547500675563707
Q498M	0.08150204542742172	Q498F	-0.21904572321591176
Q498C	0.7489095437669969	Q498W	0.11631277733256506
P499K	-0.8694701583228355	P499M	-0.33500718678542096
P499W	-0.1384794367948713	P499E	0.16284984549729625
T500W	-0.7246710186700434	T500Q	1.1425353496163428
T500E	1.075852098342644	N501W	-0.31454939945041993
G502K	-0.8408206392363077	G502M	-0.42402056063435517
G502Q	0.10304133158838631	V503K	0.5481848537694747
V503W	-0.5996209955785896	V503Q	1.1919699483897959
G504K	0.611201928425668	G504M	-0.2394992939865618
G504Q	1.1313894319519153	Y505M	0.17331897920030664
Q506M	0.5914563968709594	Q506F	1.388550842602894
Q506C	1.0935566733466522	Q506W	-0.46427216007386896
P507N	0.31449283606622036	P507M	0.5696266764436271
P507Y	-0.4563733509266242	P507F	-0.6330467163043908
P507C	0.4244122627491029	P507W	-1.0814541332656937
P507D	0.13254673484305224	Y508M	0.9050830510980564
R509Y	1.5816262112323218	R509F	0.17116175324431412
R509H	0.0623346248031457	R509D	-2.0198262821923856
V510N	-0.6427645065341381	V510Y	-0.8554819539396187
V510C	0.22763786251992232	V510W	-0.5334666964127239
V510H	-0.6495928713526932	V511N	-0.7086302639406159
V511Y	-2.716477570665056	V511C	-1.1356583574983445
V511W	-3.6837446779025207	V511H	-2.009195599076541
V512N	-0.592742738150965	V512Y	-1.50881138417807
V512C	1.1799477534866059	V512W	-0.07217208041885595
V512H	-0.3309716784869912	L513K	-0.1547011716492395
L513W	-0.561287052591257	L513E	0.16369945258970903
S514K	0.09044293914215532	S514M	0.3544249208279361
S514Q	-0.04657134211510431	S514E	0.05649932454381871
F515K	0.35024643808833483	F515Q	0.017644588943358276
F515E	2.1531101465397846	E516M	1.036404405147896
E516F	-0.5427142655154131	E516C	0.04224730575879035
E516W	-0.39934841058343934	L517K	0.06928065216791865
L517W	-0.13785979655013209	L517E	0.04102218362040223
L518N	0.026910437209509593	L518Y	0.10637568972686924
L518C	0.22650370914524215	L518W	0.11664177508341862
L518D	0.08919882242899499	H519M	0.09915282026899312
H519W	0.2863948598999872	A520N	0.18495503273730718
A520M	0.05065719823240546	A520Y	0.15921486032667398
A520F	0.24819171233699314	A520C	0.27574999359145685
A520W	0.19873522169670538	A520H	0.2548467049815884
P521N	-0.22909261968122854	P521M	0.04425752947635832
P521Y	-0.03325881571341416	P521F	0.10163317887858055
P521C	-0.019792645975685884	P521W	-0.2153759354532915
P521D	0.05618657811915619	A522N	0.13193285395800058
A522M	0.16808919863603297	A522Y	0.06161960782774599
A522F	0.12224999150958962	A522C	-0.005613281483158757
A522W	0.1755552589876184	A522H	-0.10147421756897938

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Table S6 – continued from previous page

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
T523W	0.6883493833454931	T523Q	0.5171701632837328
T523E	0.3967537692508082	V524K	-0.194263147687278
V524W	1.7778879695520378	V524Q	2.1571939321157294
C525K	0.5660980277107361	C525M	0.5484441215930687
C525Q	0.20979048088137295	C525E	-0.8606766422395253
G526N	-0.3795088904034186	G526M	0.26280584146539504
G526Y	-0.46570857018616	G526F	-0.5720850563953427
G526H	-0.0606342823660725		

S2.3 Predicted BA changes for all mutations from SARS-CoV to SARS-CoV-2.

Table S7: Binding affinity prediction from SARS-CoV to SARS-CoV-2. Residue ID is according to SARS-CoV.

Mutations	Binding affinity change (kcal/mol)	Mutations	Binding affinity change (kcal/mol)
K333R	-0.10359754921303413	P335A	0.3212151191179889
E341N	0.8368514240314354	K344R	0.11465686826831675
T359A	0.20748319448197822	F360S	0.3562795571703173
A371P	0.32441540521635565	V389I	-0.2031424443319469
K390R	-1.7441591796657139	D393E	-0.9896440375025348
V404K	-0.20714869387450055	M417T	-0.10962104369517127
L421I	-0.20029693545802285	T425S	0.7664401607840219
R426N	0.01476290825847672	I428L	-0.15641518978554975
A430S	-0.20596618588966087	T431K	0.022688505030826214
S432V	-0.09515241606390148	T433G	0.4853718082937637
K439L	-0.28177774792466864	Y442L	1.1037522663565902
L443F	-0.5273288533377353	H445K	-0.32283081058973695
G446S	0.21609722530913525	K447N	0.1937550325988337
R449K	0.2864687750191611	N457T	0.17052040315666897
V458E	0.3860490583680413	P459I	0.03158425269684419
F460Y	0.2651433886946123	S461Q	-0.0432150026616928
P462A	0.3716844862211602	D463G	0.5908664315789177
G464S	0.21082880440230464	K465T	0.3194566314728193
T468N	0.2206752545345611	P469G	0.2553950194573119
P471E	0.32119888251323336	A472G	0.5768583617503635
L473F	0.43415144307791714	W477F	0.11116224994963846
N480Q	0.23735507010135506	D481S	1.6343732194606992
Y485Q	0.0738761940317186	T486P	-1.467504027152281
T488N	-1.0281989412820935	I490V	0.026002567283284355

References

[1] Z. Cang, L. Mu, and G.-W. Wei. Representability of algebraic topology for biomolecules in machine learning based scoring and virtual screening. *PLoS computational biology*, 14(1):e1005929, 2018.

[2] G. Carlsson. Topology and data. *Bulletin of the American Mathematical Society*, 46(2):255–308, 2009.

[3] H. Edelsbrunner, D. Letscher, and A. Zomorodian. Topological persistence and simplification. In *Proceedings 41st annual symposium on foundations of computer science*, pages 454–463. IEEE, 2000.

[4] J. Jankauskaitė, B. Jiménez-García, J. Dapkūnas, J. Fernández-Recio, and I. H. Moal. Skempi 2.0: an updated benchmark of changes in protein–protein binding energy, kinetics and thermodynamics upon mutation. *Bioinformatics*, 35(3):462–469, 2019.

[5] F. Pedregosa, G. Varoquaux, A. Gramfort, V. Michel, B. Thirion, O. Grisel, M. Blondel, P. Prettenhofer, R. Weiss, V. Dubourg, et al. Scikit-learn: Machine learning in python. *the Journal of machine Learning research*, 12:2825–2830, 2011.

[6] C. H. Rodrigues, Y. Myung, D. E. Pires, and D. B. Ascher. mcsm-ppi2: predicting the effects of mutations on protein–protein interactions. *Nucleic acids research*, 47(W1):W338–W344, 2019.

[7] M. Wang, Z. Cang, and G.-W. Wei. A topology-based network tree for the prediction of protein–protein binding affinity changes following mutation. *Nature Machine Intelligence*, 2(2):116–123, 2020.

[8] N. Zhang, Y. Chen, H. Lu, F. Zhao, R. V. Alvarez, A. Goncearenco, A. R. Panchenko, and M. Li. Mutabind2: predicting the impacts of single and multiple mutations on protein-protein interactions. *Iscience*, page 100939, 2020.