

**Table S1: The resultant score provided by the computationally based interface scanning for alanine in ADK protein (binding with CP viral protein)**

| pdb# | chain | int_id | res# | aa | DDG(complex) | DDG(complex,obs) | DG(partner) |
|------|-------|--------|------|----|--------------|------------------|-------------|
| 85   | A     | 1      | 85   | 15 | 0.24         | 0                | 1.67        |
| 86   | A     | 1      | 86   | 3  | 0.38         | 0                | -0.9        |
| 88   | A     | 1      | 88   | 10 | 0.74         | 0                | 2.58        |
| 89   | A     | 1      | 89   | 9  | 1.21         | 0                | 0.02        |
| 91   | A     | 0      | 91   | 16 | -0.01        | 0                | -0.19       |
| 95   | A     | 1      | 95   | 16 | 0.69         | 0                | 0.66        |
| 96   | A     | 1      | 96   | 9  | 0.08         | 0                | -0.11       |
| 103  | A     | 1      | 103  | 12 | 0.25         | 0                | -0.27       |
| 168  | A     | 1      | 168  | 4  | 0.26         | 0                | -0.49       |
| 171  | A     | 1      | 171  | 10 | 2.06         | 0                | 0.22        |
| 174  | A     | 1      | 174  | 15 | 2.56         | 0                | 1.65        |
| 175  | A     | 0      | 175  | 8  | 0.13         | 0                | 1.55        |
| 176  | A     | 0      | 176  | 2  | 0            | 0                | 5.26        |
| 177  | A     | 1      | 177  | 16 | -0.21        | 0                | -0.55       |
| 178  | A     | 1      | 178  | 4  | 0.97         | 0                | -0.54       |
| 185  | A     | 1      | 185  | 18 | 0.24         | 0                | 0.6         |
| 211  | A     | 0      | 211  | 8  | 0.11         | 0                | 0.56        |
| 212  | A     | 0      | 212  | 16 | 0.11         | 0                | -0.39       |
| 213  | A     | 0      | 213  | 9  | 0.97         | 0                | 0.74        |
| 214  | A     | 1      | 214  | 10 | 0.12         | 0                | 2.96        |
| 215  | A     | 1      | 215  | 8  | 1.91         | 0                | 0.37        |
| 216  | A     | 1      | 216  | 17 | 0.99         | 0                | 0.75        |
| 217  | A     | 1      | 217  | 15 | 2.53         | 0                | 1.37        |
| 220  | A     | 0      | 220  | 3  | 2.13         | 0                | 0.93        |
| 221  | A     | 1      | 221  | 17 | 0.34         | 0                | 0.25        |
| 222  | A     | 0      | 222  | 4  | -0.05        | 0                | -0.29       |
| 22   | B     | 1      | 282  | 18 | 0.93         | 0                | 0.59        |
| 25   | B     | 0      | 285  | 10 | 0.12         | 0                | 2.03        |
| 26   | B     | 1      | 286  | 14 | 2.9          | 0                | -0.15       |
| 29   | B     | 1      | 289  | 4  | 0.47         | 0                | 0.03        |
| 30   | B     | 1      | 290  | 9  | 1.55         | 0                | -0.58       |
| 31   | B     | 0      | 291  | 17 | 0            | 0                | 0.6         |
| 32   | B     | 0      | 292  | 20 | 0.24         | 0                | -0.18       |
| 35   | B     | 1      | 295  | 3  | -0.17        | 0                | 0.52        |
| 39   | B     | 0      | 299  | 7  | -0.01        | 0                | 0.9         |
| 41   | B     | 1      | 301  | 10 | 0.84         | 0                | 1.77        |
| 43   | B     | 0      | 303  | 15 | 0.02         | 0                | 0.21        |
| 44   | B     | 1      | 304  | 3  | 0.58         | 0                | -0.92       |
| 45   | B     | 0      | 305  | 10 | 0.05         | 0                | 1.98        |
| 47   | B     | 0      | 307  | 16 | -0.04        | 0                | -0.09       |
| 48   | B     | 0      | 308  | 18 | 0.32         | 0                | 0.61        |
| 54   | B     | 1      | 314  | 20 | 1.68         | 0                | -0.56       |

|    |   |   |     |    |      |   |       |
|----|---|---|-----|----|------|---|-------|
| 58 | B | 1 | 318 | 17 | 0.01 | 0 | 0.4   |
| 60 | B | 1 | 320 | 15 | 1.68 | 0 | 0.05  |
| 61 | B | 1 | 321 | 20 | 2    | 0 | -0.03 |
| 63 | B | 0 | 323 | 7  | 0.15 | 0 | -0.92 |
| 64 | B | 1 | 324 | 5  | 2.89 | 0 | 0.62  |
| 65 | B | 1 | 325 | 7  | 0.99 | 0 | 0.39  |
| 67 | B | 1 | 327 | 15 | 2.02 | 0 | 0.46  |
| 68 | B | 1 | 328 | 10 | 0.83 | 0 | 1.8   |

**CHAIN A: ADK Host Protein ( blue colour indicates the domain residues)**

**CHAIN B : CP virus Protein**

### **DDG=ΔΔG**

# pdb#- Number of mutated residues in pdb file

# chain- pdb chain

identifier

# int-id- score '1' for interacting residue and '0' for indirect contact or buried upon binding

# res#- continuous numbering for each residue of all partners

# aa- amino acid type according to one-residue nomenclature in alphabetical order (1-A, 2-B 3-C, 4-E....)

# ΔΔG (bind)- predicted change in binding free energy upon alanine mutation

# ΔΔG (bind,obs)- observed changes in binding free energy (user input, otherwise set to zero)

# ΔG (partner)- predicted change in protein stability of the mutated complex partner (adk) upon alanine mutation

**Table S2: The resultant score was provided by the computationally based interface scanning for alanine in ADK protein ( binding with betaC1 viral protein).**

| pdb# | chain | int_id | res# | aa | DDG(complex) | DDG(complex,obs) | DG(partner) |
|------|-------|--------|------|----|--------------|------------------|-------------|
| 67   | A     | 0      | 67   | 16 | -0.06        | 0                | -0.39       |
| 70   | A     | 1      | 70   | 16 | 0.28         | 0                | -0.41       |
| 71   | A     | 1      | 71   | 17 | 0.95         | 0                | -0.07       |
| 77   | A     | 1      | 77   | 7  | 0.47         | 0                | 0.91        |
| 82   | A     | 1      | 82   | 3  | 0.73         | 0                | -0.54       |
| 83   | A     | 1      | 83   | 10 | 0.67         | 0                | 1.93        |
| 85   | A     | 0      | 85   | 15 | -0.11        | 0                | 0.95        |
| 86   | A     | 1      | 86   | 3  | 1.12         | 0                | -1.02       |
| 87   | A     | 1      | 87   | 4  | 1.12         | 0                | 0.2         |
| 88   | A     | 0      | 88   | 10 | 0.14         | 0                | 2.45        |
| 89   | A     | 1      | 89   | 9  | 1.09         | 0                | 0.14        |
| 90   | A     | 1      | 90   | 16 | 1.08         | 0                | 0.09        |
| 91   | A     | 1      | 91   | 16 | 0.3          | 0                | -0.35       |
| 93   | A     | 1      | 93   | 16 | 0.01         | 0                | -0.26       |
| 94   | A     | 0      | 94   | 10 | 0            | 0                | 1.6         |
| 95   | A     | 1      | 95   | 16 | -0.06        | 0                | 0.48        |
| 96   | A     | 1      | 96   | 9  | 1.02         | 0                | -0.16       |
| 103  | A     | 1      | 103  | 12 | 0.29         | 0                | -0.31       |
| 119  | A     | 1      | 119  | 9  | 0.82         | 0                | -0.01       |
| 120  | A     | 1      | 120  | 15 | 0.11         | 0                | 1.96        |
| 123  | A     | 1      | 123  | 12 | 0.5          | 0                | -0.9        |
| 127  | A     | 1      | 127  | 9  | -0.23        | 0                | -0.34       |
| 129  | A     | 1      | 129  | 4  | -0.07        | 0                | 0.43        |
| 175  | A     | 1      | 175  | 8  | 0.13         | 0                | 1.41        |
| 177  | A     | 0      | 177  | 16 | 0.24         | 0                | -0.78       |
| 178  | A     | 1      | 178  | 4  | 0.72         | 0                | -0.2        |
| 179  | A     | 1      | 179  | 2  | -0.08        | 0                | 5.79        |
| 181  | A     | 1      | 181  | 9  | 0.83         | 0                | -0.41       |
| 182  | A     | 1      | 182  | 12 | 0.11         | 0                | -0.53       |
| 215  | A     | 1      | 215  | 8  | 0.5          | 0                | 0.78        |
| 43   | B     | 1      | 285  | 9  | 0.31         | 0                | -0.4        |
| 44   | B     | 0      | 286  | 9  | 0            | 0                | -0.4        |
| 45   | B     | 1      | 287  | 17 | 0.92         | 0                | 0.13        |
| 46   | B     | 0      | 288  | 5  | 0.35         | 0                | 0.05        |
| 47   | B     | 1      | 289  | 11 | 0.16         | 0                | 0.19        |
| 48   | B     | 1      | 290  | 8  | 0.4          | 0                | 0.06        |
| 60   | B     | 1      | 302  | 3  | 0.4          | 0                | -1.58       |
| 64   | B     | 1      | 306  | 10 | 0.69         | 0                | 1.69        |
| 75   | B     | 1      | 317  | 11 | 0.51         | 0                | 0.55        |
| 76   | B     | 1      | 318  | 20 | 0.01         | 0                | 3.24        |
| 77   | B     | 1      | 319  | 9  | 1.66         | 0                | 0.48        |
| 78   | B     | 0      | 320  | 3  | -0.12        | 0                | 0.38        |
| 79   | B     | 1      | 321  | 16 | -0.11        | 0                | -0.03       |

|    |   |   |     |    |       |   |       |
|----|---|---|-----|----|-------|---|-------|
| 80 | B | 1 | 322 | 15 | 1.71  | 0 | -0.27 |
| 81 | B | 1 | 323 | 8  | 1.66  | 0 | 0.63  |
| 82 | B | 1 | 324 | 19 | 1.43  | 0 | -1.4  |
| 83 | B | 1 | 325 | 4  | -0.08 | 0 | -0.03 |
| 85 | B | 1 | 327 | 15 | 0.85  | 0 | -0.05 |
| 89 | B | 1 | 331 | 11 | 0.45  | 0 | 0.98  |
| 91 | B | 1 | 333 | 4  | 0.02  | 0 | -0.2  |
| 93 | B | 1 | 335 | 8  | 0.08  | 0 | 0.11  |
| 94 | B | 1 | 336 | 3  | 0.26  | 0 | -0.49 |
| 95 | B | 1 | 337 | 8  | 0.52  | 0 | 1.51  |

**CHAIN A: ADK Host Protein ( blue colour indicates the domain residues)**

**CHAIN B : betaC1 virus Protein**

**DDG=ΔΔG**

# pdb#- Number of mutated residues in pdb file

# chain- pdb chain identifier

# int-id- score '1' for interacting residue and '0' for indirect contact or buried upon binding

# res#- continuous numbering for each residue of all partners

# aa- amino acid type according to one-residue nomenclature in alphabetical order (1-A, 2-B 3-C, 4-E....)

# ΔΔG (bind)- predicted change in binding free energy upon alanine mutation

# ΔΔG (bind,obs)- observed changes in binding free energy (user input, otherwise set to zero)

# ΔG (partner)- predicted change in protein stability of the mutated complex partner (adk) upon alanine mutation

**Table S3: The resultant score provided by the computationally based interface scanning for alanine in GLO1 protein (binding with Rep viral protein)**

| pdb# | chain | int_id | res# | aa | DDG(complex) | DDG(complex,obs) | DG(partner) |
|------|-------|--------|------|----|--------------|------------------|-------------|
| 8    | A     | 1      | 6    | 11 | 0.42         | 0                | -0.04       |
| 11   | A     | 0      | 9    | 4  | 1.9          | 0                | 0.49        |
| 12   | A     | 1      | 10   | 4  | 0.34         | 0                | -0.37       |
| 15   | A     | 1      | 13   | 9  | 2.07         | 0                | -0.34       |
| 16   | A     | 1      | 14   | 9  | 0.63         | 0                | -0.53       |
| 17   | A     | 1      | 15   | 9  | 0.05         | 0                | 0.3         |
| 20   | A     | 1      | 18   | 9  | 2.39         | 0                | -0.64       |
| 21   | A     | 0      | 19   | 11 | 0.12         | 0                | 1.16        |
| 24   | A     | 1      | 22   | 3  | 4.16         | 0                | -0.99       |
| 28   | A     | 1      | 26   | 16 | 0.98         | 0                | 0.6         |
| 31   | A     | 1      | 29   | 4  | 0.18         | 0                | 0.62        |
| 32   | A     | 1      | 30   | 3  | 0.15         | 0                | -0.93       |
| 33   | A     | 1      | 31   | 14 | 0.78         | 0                | 0.88        |
| 34   | A     | 0      | 32   | 19 | -0.01        | 0                | 1.23        |
| 36   | A     | 1      | 34   | 10 | 0.08         | 0                | 1.68        |
| 38   | A     | 1      | 36   | 4  | 1.21         | 0                | 0.63        |
| 40   | A     | 1      | 38   | 15 | 3.55         | 0                | 1           |
| 41   | A     | 1      | 39   | 12 | 0.22         | 0                | 0.19        |
| 44   | A     | 1      | 42   | 16 | -0.08        | 0                | -0.33       |
| 164  | A     | 1      | 162  | 15 | 0.26         | 0                | 2.09        |
| 166  | A     | 1      | 164  | 4  | 0.82         | 0                | 1.04        |
| 169  | A     | 0      | 167  | 8  | 0.02         | 0                | 0.25        |
| 170  | A     | 1      | 168  | 9  | 2.91         | 0                | -0.33       |
| 171  | A     | 1      | 169  | 12 | 1.74         | 0                | 0.81        |
| 172  | A     | 1      | 170  | 15 | 1.47         | 0                | 0.1         |
| 290  | A     | 1      | 288  | 15 | 1.84         | 0                | 2.42        |
| 297  | A     | 1      | 295  | 9  | -0.08        | 0                | 2.07        |
| 7    | B     | 1      | 359  | 5  | 0.6          | 0                | 2.58        |
| 8    | B     | 0      | 360  | 14 | 0.33         | 0                | -0.1        |
| 9    | B     | 1      | 361  | 8  | 0.17         | 0                | 2.06        |
| 10   | B     | 0      | 362  | 20 | -0.02        | 0                | 1.18        |
| 15   | B     | 1      | 367  | 5  | 0.02         | 0                | 2.81        |
| 17   | B     | 1      | 369  | 17 | -0.07        | 0                | 0.66        |
| 20   | B     | 0      | 372  | 14 | 0.28         | 0                | 0.63        |
| 49   | B     | 1      | 401  | 4  | 2.69         | 0                | 2.83        |
| 51   | B     | 1      | 403  | 7  | 2.03         | 0                | 0.68        |
| 52   | B     | 1      | 404  | 4  | 0.04         | 0                | -0.42       |
| 53   | B     | 1      | 405  | 12 | 0.16         | 0                | 0.28        |
| 55   | B     | 1      | 407  | 4  | 0.16         | 0                | 1.26        |
| 57   | B     | 1      | 409  | 7  | 1.07         | 0                | 0.9         |
| 59   | B     | 1      | 411  | 7  | 3.06         | 0                | 2.71        |
| 73   | B     | 1      | 425  | 12 | 0.84         | 0                | -0.4        |
| 88   | B     | 1      | 440  | 7  | 0.57         | 0                | -1.26       |

|     |   |   |     |    |       |   |       |
|-----|---|---|-----|----|-------|---|-------|
| 90  | B | 1 | 442 | 12 | 4     | 0 | 0.03  |
| 91  | B | 0 | 443 | 8  | -0.08 | 0 | 2.83  |
| 92  | B | 1 | 444 | 14 | 1.15  | 0 | -0.58 |
| 95  | B | 1 | 447 | 9  | 0.58  | 0 | -0.46 |
| 99  | B | 0 | 451 | 3  | -0.05 | 0 | -1.19 |
| 103 | B | 1 | 455 | 20 | 2.91  | 0 | 1.01  |
| 106 | B | 1 | 458 | 9  | 0.04  | 0 | 0.03  |
| 107 | B | 1 | 459 | 3  | 0.33  | 0 | 0.11  |
| 124 | B | 1 | 476 | 15 | 1.66  | 0 | 0.12  |
| 127 | B | 1 | 479 | 14 | 0.33  | 0 | -0.88 |

**CHAIN A: GLO1 Host Protein ( blue colour indicates the domain residues)**

**CHAIN B : Rep virus Protein**

**DDG=ΔΔG**

# pdb#- Number of mutated residues in pdb file

# chain- pdb chain

identifier

# int-id- score '1' for interacting residue and '0' for indirect contact or buried upon binding

# res#- continuous numbering for each residue of all partners

# aa- amino acid type according to one-residue nomenclature in alphabetical order (1-A, 2-B 3-C, 4-E....)

# ΔΔG (bind)- predicted change in binding free energy upon alanine mutation

# ΔΔG (bind,obs)- observed changes in binding free energy (user input, otherwise set to zero)

# ΔG (partner)- predicted change in protein stability of the mutated complex partner (Rep) upon alanine mutation

**Table S4: Prediction of effect of mutation in ADK host protein using PROVEAN tool**

| Mutation postion | Score         | Effect of mutation |
|------------------|---------------|--------------------|
| <b>71,T,A</b>    | <b>-0.467</b> | <b>Neutral</b>     |
| 77,H,A           | -8.667        | Deleterious        |
| 82,D,A           | -6.933        | Deleterious        |
| 83,L,A           | -4.833        | Deleterious        |
| 85,R,A           | -5.8          | Deleterious        |
| <b>86,D,A</b>    | <b>-1.966</b> | <b>Neutral</b>     |
| 87,E,A           | -4.867        | Deleterious        |
| 88,L,A           | -4.011        | Deleterious        |
| <b>89,K,A</b>    | <b>-1.206</b> | <b>Neutral</b>     |
| <b>96,K,A</b>    | <b>-1.33</b>  | <b>Neutral</b>     |
| 103,N,A          | -4.1          | Deleterious        |
| 119,K,A          | -3.765        | Deleterious        |
| 120,R,A          | -5.733        | Deleterious        |
| <b>123,N,A</b>   | <b>0.568</b>  | <b>Neutral</b>     |
| 129,E,A          | -4.9          | Deleterious        |
| <b>168,E,A</b>   | <b>-1.26</b>  | <b>Neutral</b>     |
| 171,L,A          | -3.196        | Deleterious        |
| 174,R,A          | -5.68         | Deleterious        |
| 175,I,A          | -2.867        | Deleterious        |
| 176,C,A          | -8.667        | Deleterious        |
| 178,E,A          | -4            | Deleterious        |
| <b>181,K,A</b>   | <b>-1.767</b> | <b>Neutral</b>     |
| 182,N,A          | -5.253        | Deleterious        |
| 185,V,A          | -3.44         | Deleterious        |
| <b>211,I,A</b>   | <b>0.21</b>   | <b>Neutral</b>     |
| 213,K,A          | -3.467        | Deleterious        |
| 214,L,A          | -3.607        | Deleterious        |
| <b>215,I,A</b>   | <b>-1.426</b> | <b>Neutral</b>     |
| <b>216,T,A</b>   | <b>-1.808</b> | <b>Neutral</b>     |
| 217,R,A          | -4.661        | Deleterious        |
| 220,D,A          | -6.939        | Deleterious        |
| 221,T,A          | -3.498        | Deleterious        |

Score thresholds for prediction

(1) Default threshold is -2.5, that is:

**-Variants with a score equal to or below -2.5 are considered "deleterious,"**

**-Variants with a score above -2.5 are considered "neutral."**

(2) How to use a more stringent threshold

number of clusters: 30

number of supporting sequences used: 65

**Table S5: Prediction of effect of mutation in GLO1 host protein using PROVEAN tool**

| Mutation postion | Score  | Type of muation |
|------------------|--------|-----------------|
| 8,M,A            | 0.679  | Neutral         |
| 11,E,A           | -4.47  | Deleterious     |
| 12,E,A           | -2.373 | Neutral         |
| 15,K,A           | -2.945 | Deleterious     |
| 16,K,A           | -1.223 | Neutral         |
| 17,K,A           | -1.076 | Neutral         |
| 20,K,A           | -4.644 | Deleterious     |
| 21,M,A           | -2.125 | Neutral         |
| 24,D,A           | -6.896 | Deleterious     |
| 31,E,A           | -3.02  | Deleterious     |
| 32,D,A           | -5.408 | Deleterious     |
| 33,Q,A           | -4.274 | Deleterious     |
| 36,L,A           | -4.615 | Deleterious     |
| 38,E,A           | -4.214 | Deleterious     |
| 40,R,A           | -0.811 | Neutral         |
| 41,N,A           | -1.066 | Neutral         |
| 164,R,A          | -4.274 | Deleterious     |
| 166,E,A          | -2.925 | Deleterious     |
| 169,I,A          | -3.34  | Deleterious     |
| 170,K,A          | -3.846 | Deleterious     |
| 171,N,A          | -7.826 | Deleterious     |
| 172,R,A          | -3.458 | Deleterious     |
| 290,R,A          | -5.385 | Deleterious     |
| 297,K,A          | -5.675 | Deleterious     |

Score thresholds for prediction

(1) Default threshold is -2.5, that is:

**-Variants with a score equal to or below -2.5 are considered "deleterious,"**

**-Variants with a score above -2.5 are considered "neutral."**

(2) How to use a more stringent threshold

number of clusters: 30

number of supporting sequences 21

used: 0

**Table S6: Prediction of stability of individual and multiple mutation in ADK host protein using DDMut tool**

| Individual $\Delta\Delta G$ stability Mutation | $\Delta\Delta G$ |
|------------------------------------------------|------------------|
| A T71A                                         | 0.01             |
| A D86A                                         | 0.01             |
| A K89A                                         | 0.04             |
| A K96A                                         | 0.06             |
| A N123A                                        | 0.09             |
| A E168A                                        | 0.25             |
| A K181A                                        | -0.08            |
| A I211A                                        | -0.9             |
| A I215A                                        | -1.65            |
| A T216A                                        | -0.64            |

Multiple Prediction  $\Delta\Delta G^{\text{stability}}$  1.07

**T71A; D86A; K89A; K96A; N123A; A E168A**

**Table S7: Prediction of stability of individual and multiple mutation in GLO1 host protein using DDMut tool**

| Individual $\Delta\Delta G$ stability Mutation | $\Delta\Delta G$ |
|------------------------------------------------|------------------|
| A M8A                                          | -1.12            |
| A E12A                                         | 0.04             |
| A K16A                                         | 0.1              |
| A K17A                                         | 0.05             |
| A M21A                                         | -1.18            |
| A R40A                                         | -1.11            |
| A N41A                                         | 0.08             |

multiple Prediction  $\Delta\Delta G^{\text{stability}}$  0.74

**E12A; A K16A; K17A; N41A**