Supplementary Material

*Original Research*

**In Silico Optimization of SARS-CoV-2 Spike Specific Nanobodies**

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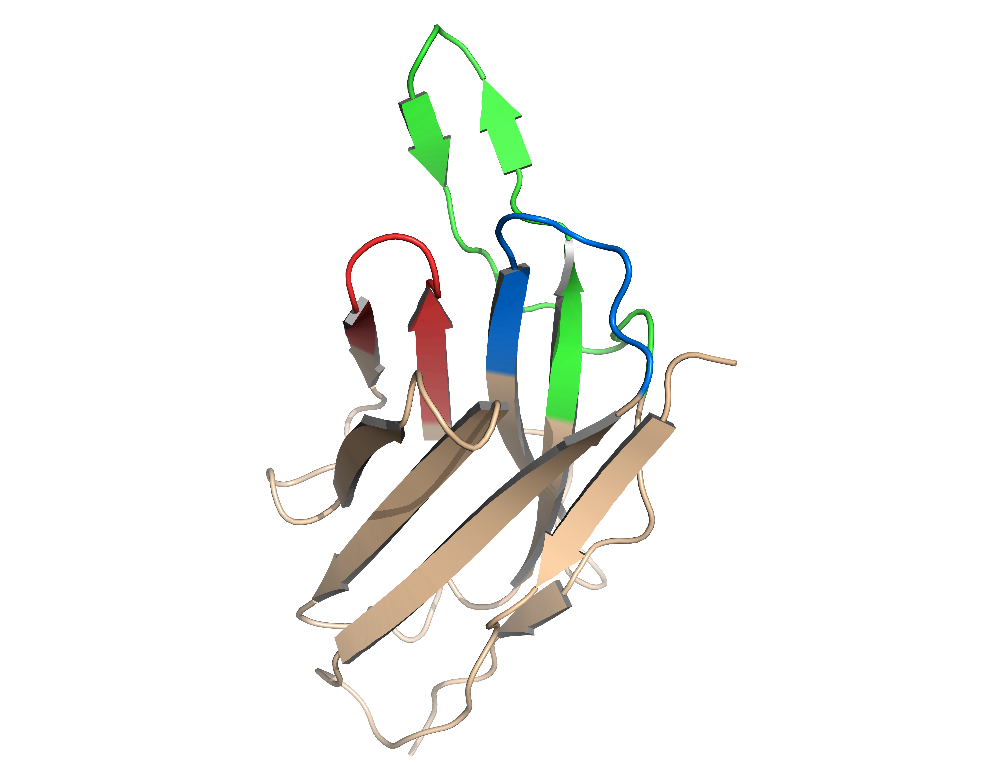
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**Supplementary Fig. 1.** Cartoon representation of a nanobody (PDB ID: 7KSG). CDR1, CDR2, and CDR3 are colored in blue, red, and green respectively.

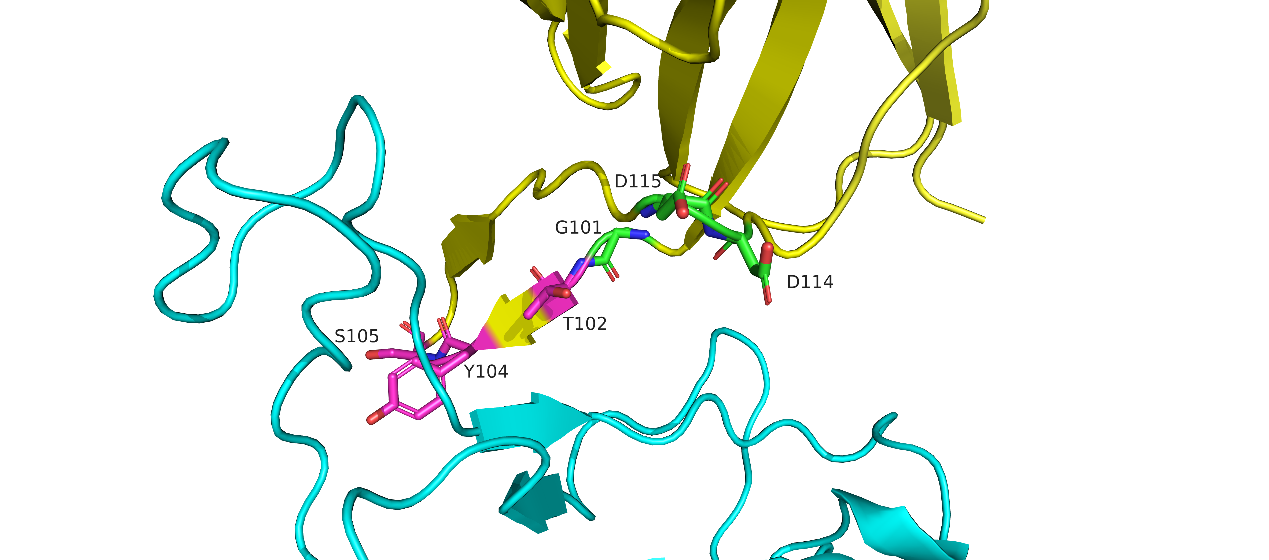
**Supplementary Table 1.** The binding free energy () of the novel four nanobodies.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| No. | Nanobody-spike complex | Spike protein | Nanobody |  |
| 7KSG\_ALL | -597.41 | -560.87 | 3.5 | -40.04 |
| 7KSG\_CDR1 | -583.22 | -560.87 | 4.54 | -26.89 |
| 7KSG\_CDR2 | -589.53 | -560.87 | -1.55 | -27.11 |
| 7KSG\_CDR3 | -594.22 | -560.87 | 2.8 | -36.15 |
| 7KSG | -584.41 | -560.87 | 1.53 | -25.07 |

图表, 条形图

描述已自动生成

**Supplementary Fig. 2.** Comparison of the energy barriers during the activation process between the wild-type and the other variants.



**Supplementary Fig. 3.** The interaction between the spike protein and the nanobody (PDB ID: 7KSG). The spike protein and nanobody are colored in blue and yellow, respectively. Residue positions that lead to the increasing of the binding energy after mutation are indicated in purple, while residue positions that lead to the decreasing of the binding energy after mutation are colored by green.