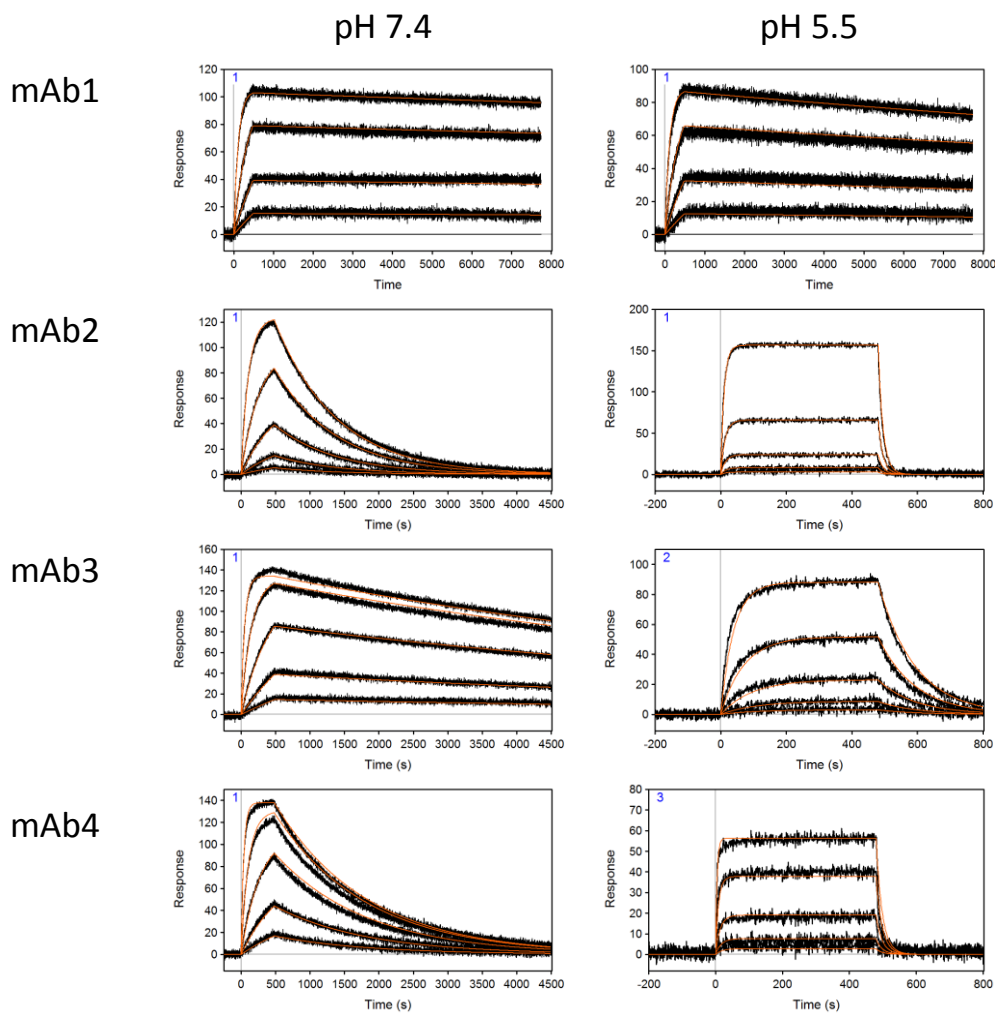


Supplemental Data.



Supplemental Figure 1. Representative SPR sensorgrams characterizing mAb1, mAb2, mAb3, and mAb4 Fab fragment binding to cynomolgus monkey PCSK9 surfaces at pH 7.4 and 5.5. Raw data (black lines) and the results from non-linear least squares regression analysis of the data fit to a 1:1 binding model (red lines) are shown.

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Supplemental Table 1. Study 1 Pairwise Comparison p-Values for CL/F (upper, red) and $t_{1/2,z}$ (lower, blue).

| | mAb1 | mAb2 | mAb3 | mAb4 | Control |
|---------|------------------|------------------|------------------|------------------|------------------|
| mAb1 | | <0.001 | <0.001 | <0.001 | <0.001 |
| mAb2 | <0.001 | | <0.001 | 0.088 | 0.927 |
| mAb3 | 0.193 | 0.009 | | 0.012 | <0.001 |
| mAb4 | 0.006 | 0.102 | 0.138 | | 0.072 |
| Control | <0.001 | 0.138 | <0.001 | 0.005 | |

Bold text indicates statistical significance ($p < 0.05$).

Supplemental Table 2. Study 1 Adjusted p-Values for LDL-C Difference from Baseline by Time Point.

| Time (d) | Adjusted p-Value | | | |
|----------|------------------|------------------|------------------|------------------|
| | mAb1 | mAb2 | mAb3 | mAb4 |
| 1 | <.0001 | 0.0002 | <.0001 | <.0001 |
| 2 | <.0001 | <.0001 | <.0001 | <.0001 |
| 3 | <.0001 | <.0001 | <.0001 | <.0001 |
| 4 | <.0001 | <.0001 | <.0001 | <.0001 |
| 6 | <.0001 | <.0001 | <.0001 | <.0001 |
| 9 | 0.5857 | <.0001 | <.0001 | <.0001 |
| 12 | 0.5843 | <.0001 | <.0001 | <.0001 |
| 15 | 0.2238 | <.0001 | <.0001 | <.0001 |
| 18 | 0.6714 | <.0001 | 0.0032 | <.0001 |
| 21 | 1 | <.0001 | 0.0918 | <.0001 |
| 24 | 1 | <.0001 | 0.4552 | <.0001 |
| 27 | 1 | <.0001 | 1 | <.0001 |
| 30 | 1 | 0.0001 | 0.1655 | <.0001 |
| 33 | 1 | 0.0009 | 0.1787 | 0.0003 |
| 36 | 0.7912 | 0.008 | 1 | 0.0104 |
| 39 | 1 | 0.0016 | 1 | 0.0105 |
| 42 | 0.5254 | 0.0022 | 0.3671 | 0.0548 |
| 45 | 1 | 0.0078 | 1 | 0.0826 |
| 48 | 0.8843 | 0.0509 | 0.5419 | 0.2091 |
| 51 | 0.5623 | 0.019 | 0.8267 | 0.211 |

Bold text indicates statistical significance ($p < 0.05$).

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Supplemental Table 3. Study 2 Pairwise Comparison p-Values for CL/F (upper, red) and $t_{1/2,z}$ (lower, blue).

| | mAb1 | mAb1_YTE | mAb1_LS | mAb2 | mAb2_YTE | mAb2_LS |
|----------|-------|----------|---------|-------|----------|---------|
| mAb1 | | 0.985 | 0.992 | | | |
| mAb1_YTE | 0.999 | | 0.994 | | | |
| mAb1_LS | 0.991 | 0.992 | | | | |
| mAb2 | | | | | 0.971 | 0.991 |
| mAb2_YTE | | | | 0.119 | | 0.959 |
| mAb2_LS | | | | 0.317 | 0.952 | |

Supplemental Table 4. Study 2 Adjusted p-Values for LDL-C Difference from Baseline by Time Point.

| Time (d) | Adjusted p-Value | | | | | |
|----------|------------------|------------------|------------------|------------------|------------------|------------------|
| | mAb1 | mAb1_YTE | mAb1_LS | mAb2 | mAb2_YTE | mAb2_LS |
| 0.04 | 0.0013 | 0.1145 | 0.0206 | 1 | 0.0796 | 0.6943 |
| 0.34 | 0.0003 | 0.0004 | 0.0038 | 0.0978 | 0.0003 | 0.0702 |
| 1 | <.0001 | <.0001 | 0.0004 | 0.0332 | <.0001 | 0.0053 |
| 3 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 |
| 7 | <.0001 | <.0001 | <.0001 | 0.0023 | 0.0006 | 0.0021 |
| 10 | 0.0037 | 0.0027 | 0.0007 | 0.0505 | 0.0395 | 0.0168 |
| 14 | 1 | 0.1625 | 0.8593 | <.0001 | <.0001 | <.0001 |
| 17 | 1 | 0.0379 | 1 | 0.0005 | <.0001 | <.0001 |
| 21 | 1 | 0.2957 | 1 | 0.0001 | <.0001 | <.0001 |
| 24 | 1 | 0.0768 | 1 | <.0001 | <.0001 | <.0001 |
| 28 | 1 | 1 | 1 | <.0001 | <.0001 | <.0001 |
| 31 | 1 | 1 | 1 | 0.0001 | <.0001 | <.0001 |
| 35 | 1 | 1 | 1 | 0.0223 | <.0001 | <.0001 |
| 42 | 1 | 1 | 1 | 0.1544 | <.0001 | <.0001 |
| 49 | 1 | 1 | 1 | 1 | 0.0562 | 0.0023 |
| 56 | 1 | 0.382 | 1 | 0.1337 | 0.0031 | <.0001 |
| 63 | -- | -- | -- | 1 | 0.4476 | 0.139 |
| 70 | -- | -- | -- | 1 | 0.6933 | 0.1125 |

Bold text indicates statistical significance ($p < 0.05$).

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Supplemental Table 5. Study 3 Pairwise Comparison p-Values for CL/F (upper, red) and $t_{1/2,z}$ (lower, blue).

| | mAb2 | mAb2_8 | mAb2_119 | mAb3 | mAb3_8 | mAb3_119 |
|----------|--------------|--------------|--------------|--------------|------------------|------------------|
| mAb2 | | 0.282 | 0.903 | | | |
| mAb2_8 | 0.525 | | 0.270 | | | |
| mAb2_119 | 0.989 | 0.234 | | | | |
| mAb3 | | | | | <0.001 | <0.001 |
| mAb3_8 | | | | 0.914 | | 0.541 |
| mAb3_119 | | | | 0.984 | 0.971 | |

Bold text indicates statistical significance ($p < 0.05$).

Supplemental Table 6. Study 3 Adjusted p-Values for LDL-C Difference from Baseline by Time Point.

| Time (d) | Adjusted p-Value | | | | | |
|----------|------------------|------------------|------------------|------------------|------------------|------------------|
| | mAb2 | mAb2_8 | mAb2_119 | mAb3 | mAb3_8 | mAb3_119 |
| 0.01 | 0.7962 | 0.9195 | 0.5829 | 0.1034 | 0.7042 | 1 |
| 0.04 | 1 | 1 | 1 | 0.0248 | 1 | 1 |
| 0.17 | 0.1536 | 0.8056 | 1 | 1 | 0.6843 | 1 |
| 2 | <.0001 | 0.0023 | 0.0007 | 0.0011 | <.0001 | 0.0012 |
| 4 | <.0001 | 0.0013 | <.0001 | <.0001 | <.0001 | <.0001 |
| 8 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 | <.0001 |
| 11 | <.0001 | 0.0003 | <.0001 | <.0001 | <.0001 | <.0001 |
| 15 | <.0001 | <.0001 | <.0001 | 0.3822 | <.0001 | <.0001 |
| 18 | <.0001 | <.0001 | <.0001 | 0.5377 | <.0001 | <.0001 |
| 22 | <.0001 | <.0001 | <.0001 | 1 | 0.2541 | 1 |
| 25 | 0.0001 | <.0001 | <.0001 | 1 | 1 | 1 |
| 29 | <.0001 | <.0001 | 0.0001 | 1 | 1 | 1 |
| 32 | <.0001 | <.0001 | 0.0007 | 1 | 1 | 1 |
| 36 | 0.0004 | 0.0001 | <.0001 | 1 | 1 | 1 |
| 43 | 0.1756 | 0.023 | 0.0033 | 1 | 1 | 1 |
| 50 | 1 | 0.6494 | 0.5103 | 1 | 1 | 0.6423 |
| 57 | 1 | 0.0384 | 0.2487 | 1 | 1 | 0.3707 |
| 64 | 1 | 0.014 | 0.0062 | 0.1845 | 1 | 1 |

Bold text indicates statistical significance ($p < 0.05$).