

SUPPLEMENTARY MATERIAL

Supplementary Table S1. Diffraction data collection and refinement statistics. ^aHighest resolution shell is shown in parenthesis; ^bR_{free} was calculated with a randomly selected test set consisting of 5% reflections.

Supplementary Table S2. Plasma PCSK9 concentrations in different mouse strains. Plasma PCSK9 levels were measured by the mouse total PCSK9 DELFIA assay. In most studies, samples were diluted 4 fold in the assay buffer before measurement.

Supplementary Figure S1. Structural comparison of 1D05/PCSK9ΔC and EGF(A)/PCSK9ΔC complexes. PCSK9 (magenta) bound to 1D05-Fab (yellow) as ribbon representation. B Ribbon representation of the PCSK9/EGF(A) complex in ribbon representation (dark gray). C Superposition of the PCSK9/1D05-Fab complex on the PCSK9/EGF(A) complex. The PCSK9 molecules were used for the superposition.

Supplementary Figure S2. CETP/LDLr-hemi mice with a human-like lipoprotein profile. Plasma samples were collected from both adult male and female mice. LDLc, HDLc, total cholesterol and TG were measured as described in the Experimental Procedures. Results are mean ± SEM, n=14.

Supplementary Figure S3. Duration of the effect of 1D05-IgG2 on LDLc, total cholesterol and HDLc in CETP/LDLr-hemi mice. Mice were injected with a single dose of 1D05-IgG2 (3 mpk, i.v.). % of inhibition relative to PBS (vehicle control) in plasma LDLc (A), total cholesterol (B) and HDLc (C) were measured at post-treatment time as indicated. Results are mean ± SEM, n=8.

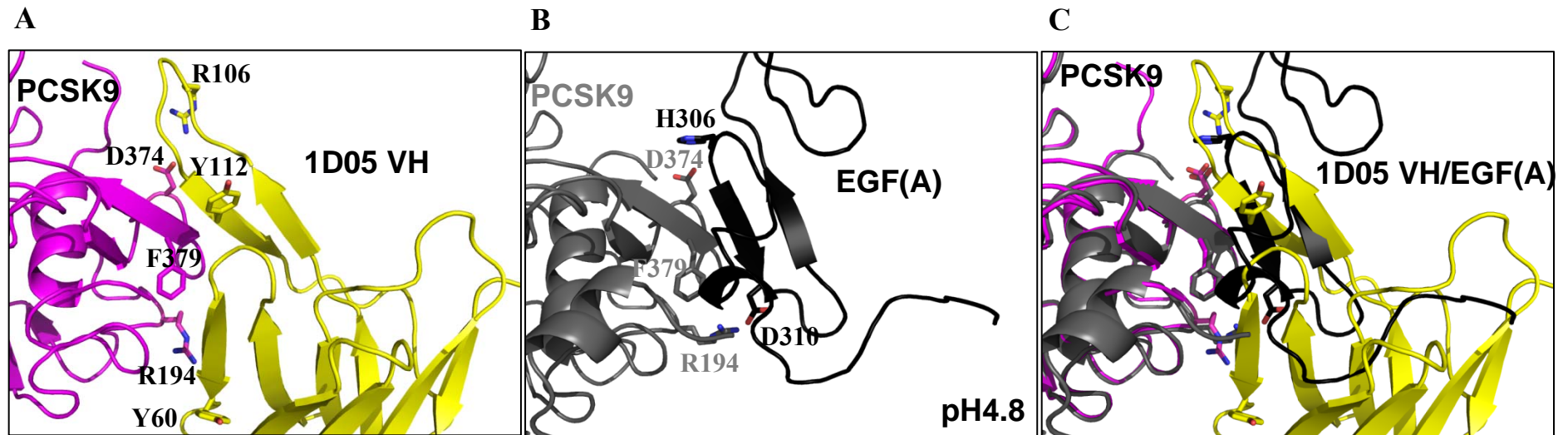
Supplementary Table S1: Diffraction data collection and refinement statistics

| Data collection | | Refinement | |
|--|---|---|-------------|
| Space group | P2 ₁ 2 ₁ 2 ₁ | No. reflections | 30,522 |
| Cell dimension: <i>a</i> , <i>b</i> , <i>c</i> (Å) | 66.59, 67.83, 250.86 | R _{work} /R _{free} ^b | 0.202/0.259 |
| Cell dimensions α , β , γ (°) | 90.00, 90.00, 90.00 | No. atoms | 6,096 |
| Resolution (Å) | 40-2.70 (2.85-2.70) ^a | Mean <i>B</i> -value (Å ²) | 34.08 |
| R _{sym} | 0.13 (0.51) | R.m.s deviations | |
| <I / σ I> | 10.5 (2.6) | Bond lengths (Å) | 0.010 |
| No. observations | 163,731 (21,781) | Bond angles (°) | 1.413 |
| No. unique | 32,238 (4,605) | | |
| Completeness (%) | 100 (99.9) | | |
| Redundancy | 5.1 (4.7) | | |

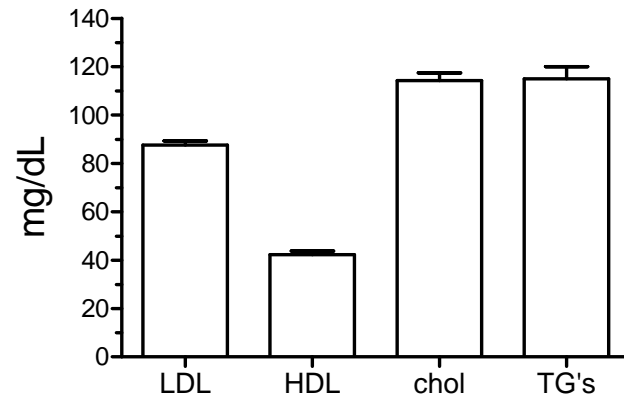
Supplementary Table S2. Plasma PCSK9 concentrations in different mouse strains

| Strain | Ave, nM | SD, nM | N | CV% |
|----------------|------------|-----------|----|-------|
| C57BL/6J | 3.1 | 1.5 | 31 | 48.2 |
| ApoE -/- | 4.1 | 4.4 | 6 | 108.2 |
| CETPtg/LDLR+/- | 15.7 | 4.6 | 9 | 29.0 |

Supplementary Figure S1. Structural comparison of 1D05/PCSK9 Δ C and EGF(A)/PCSK9 Δ C complexes



Supplementary Figure S2. CETP/LDLr-hemi mice with a human-like lipoprotein profile



Supplementary Figure S3. Duration of the effect of 1D05-IgG2 on LDLc, total cholesterol and HDLc in CETP/LDLr-hemi mice

