

## SUPPLEMENTAL MATERIALS

**Table S1. Binding of LDLR fragments to RAP**<sup>1,2</sup>

LDLR fragment	$k_a$ (1/M × s)	$k_d$ (1/s)	$K_D$ (nM)	$\text{Chi}^2$	$R_{\text{max}}$ (RU)
LDLR-exodomain	$7.56 \times 10^6$	$6.47 \times 10^{-3}$	0.87	32.0	193
LDLR cluster	$3.62 \times 10^6$	$3.45 \times 10^{-3}$	0.95	21.4	135
CR.2-3	$1.01 \times 10^5$	$2.93 \times 10^{-3}$	28.9	24.9	412
CR.3-4	$1.42 \times 10^6$	$4.95 \times 10^{-3}$	3.48	26.4	248
CR.4-5	$7.26 \times 10^5$	$4.68 \times 10^{-3}$	6.44	24.8	173

<sup>1</sup> Corresponds to experiment shown in Fig. 3

<sup>2</sup> Association and dissociation signals were fitted with a 1:1 (Langmuir) model

**Table S2. Binding of LDLR fragments to FVIII**<sup>1,2</sup>

LDLR fragment	$k_a$ (1/M × s)	$k_d$ (1/s)	$K_D$ (nM)	$\text{Chi}^2$	$R_{\text{max}}$ (RU)
LDLR-exodomain	$1.83 \times 10^4$	$1.24 \times 10^{-3}$	67.9	9.56	139
LDLR cluster	$4.41 \times 10^4$	$1.43 \times 10^{-3}$	32.5	13.4	122
CR.2-3	$5.16 \times 10^4$	$2.10 \times 10^{-3}$	40.7	15.6	79.9
CR.3-4	$2.71 \times 10^4$	$2.36 \times 10^{-3}$	87.2	12.6	112
CR.4-5	$3.59 \times 10^4$	$2.66 \times 10^{-3}$	74.0	26.4	153

<sup>1</sup> Corresponds to experiment shown in Fig. 4

<sup>2</sup> Association and dissociation signals were fitted with a 1:1 (Langmuir) model

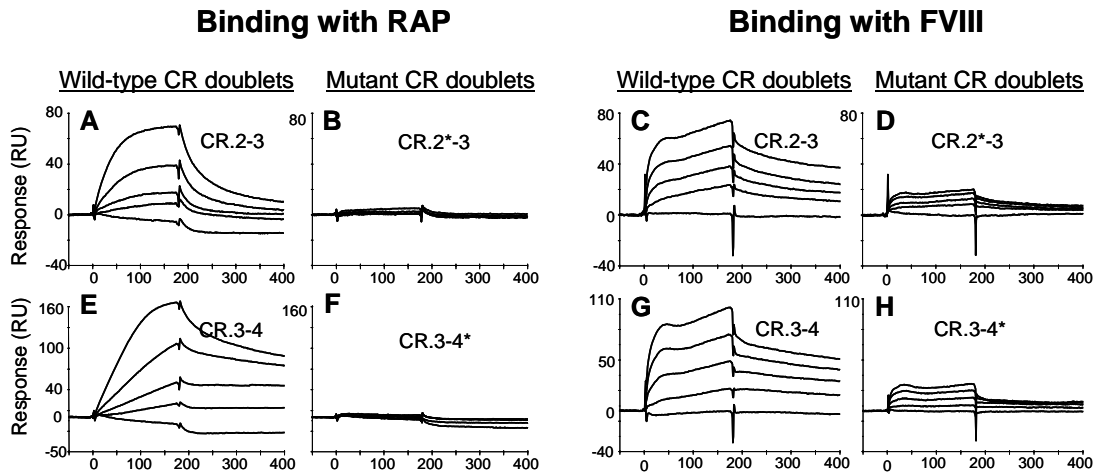


FIGURE S1. **Binding of RAP and FVIII to the mutants of CR.2-3 and CR.3-4.** In SPR, CR.2-3 (A and C), CR.2-3 W66S (B and D), CR.3-4 (E and G) and CR.3-4 W144S (F and H) were immobilized and tested for the binding with RAP (0.6 nM, 1.3 nM, 2.5 nM, and 5 nM) (A, B, E and F) and FVIII (full-size recombinant FVIII, 50 nM, 100 nM, 150 nM and 200 nM) (C, D, G and H); injections of the buffer only were used as controls. For each pair of a particular LDLR fragment and its mutant tested versus a given ligand, the signals are shown in the same scale. (\*) CR domains affected by mutagenesis.

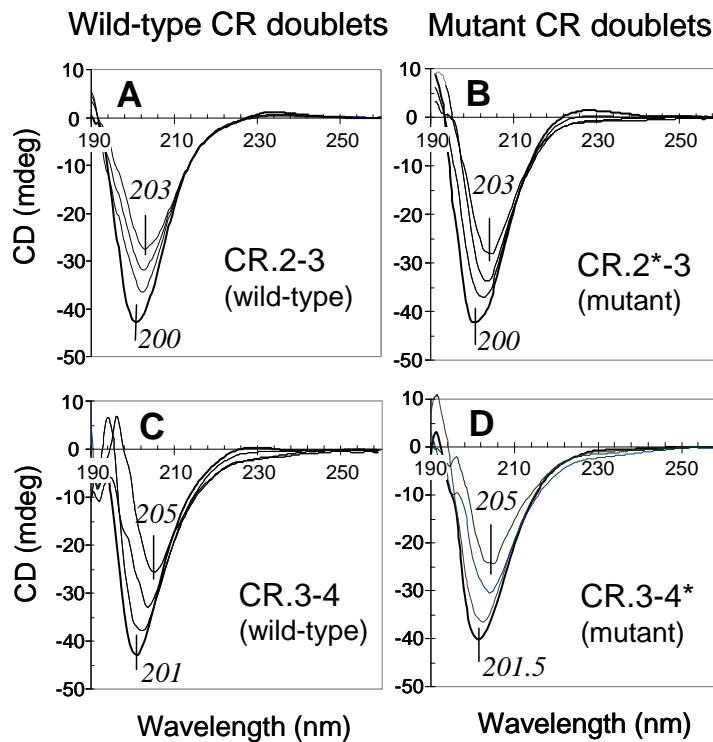


FIGURE S2. **Far-UV CD spectra of CR.2-3 and CR.3-4 and their mutants upon the titration by EDTA.** The CR doublets, CR.2-3 (A) and CR.3-4 (C) and their mutants, CR.2-3 W66S (B) and CR.3-4 W144S (D) were at concentrations of 30  $\mu$ M. The spectra correspond to the absence of EDTA (bottom curves in bold) and its increase as 1x, 2x and 3x over molar equivalent of  $\text{Ca}^{2+}$  in the solutions, shown as respective increase in the signals (upper curves).