Supporting Information

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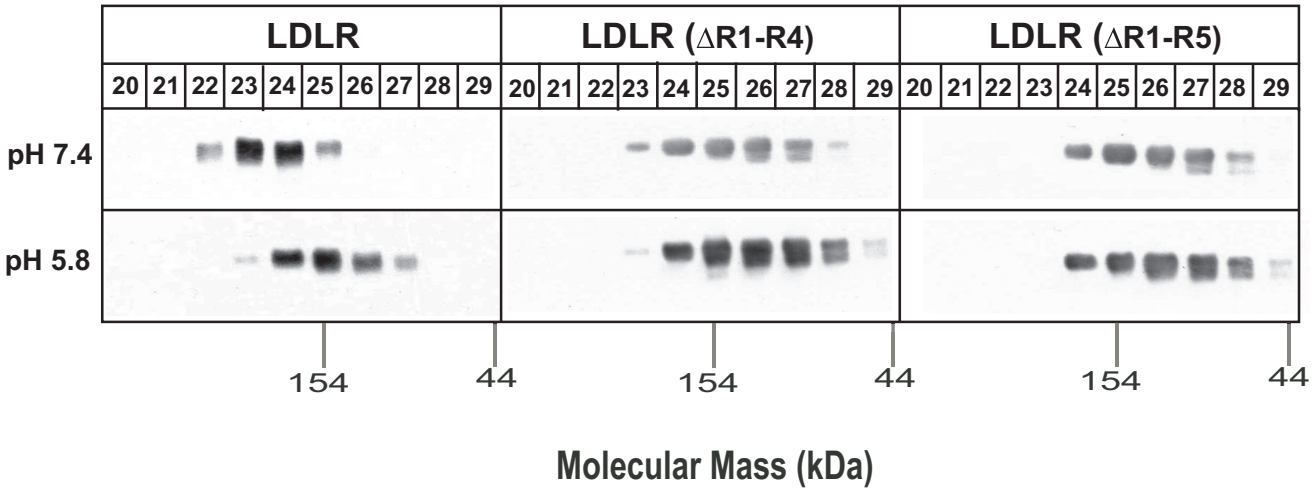

Fig. S1. No acid-dependent conformational change in the LDLR lacking four (R1–R4) or five (R1–R5) ligand binding repeats. Purified recombinant extracellular domain of the LDLR was incubated in 500 μl of buffer A (pH 7.4 or 6.0) for 2 h at room temperature. The samples were subjected to centrifugation and the supernatants were loaded on a Superdex 200 10/300 GL column equilibrated with Buffer A. The elution patterns of LDLR were determined by SDS/PAGE and immunoblotting of the collected fractions as described in Fig. 1. Interference with the pH-dependent change in the LDLR is not sufficient to cause degradation of the LDLR by PCSK9. No conformational change was seen in LDLR (ΔR1-R5), which fails to be degraded by PCSK9.