Supplementary figures

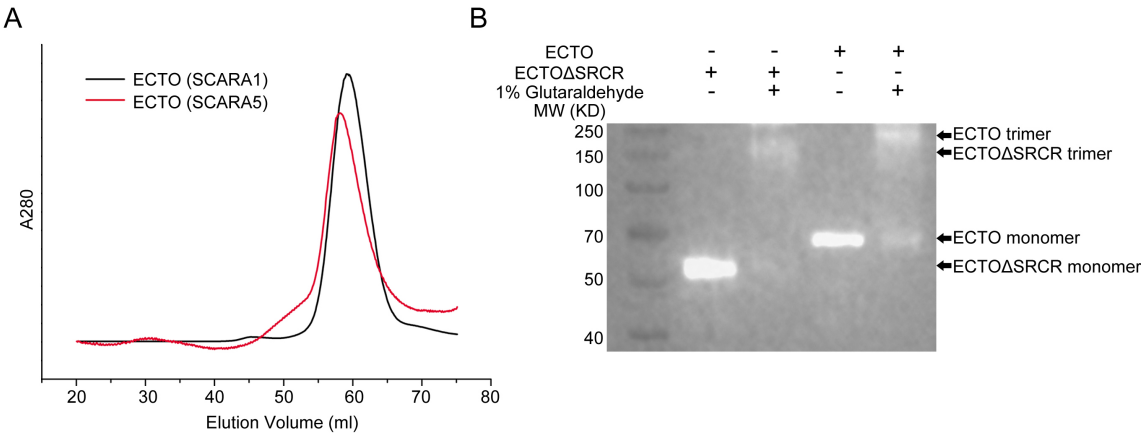


Figure S1. The ectodomain of SCARA5 forms homotrimers.

(A) The SEC profiles of the ectodomains (ECTO) of SCARA5 and SCARA1 had similar elution volumes.

(B) The cross-linked intact ectodomain (ECTO) as well as the ectodomain without the SRCR domain (ECTOΔSRCR) of SCARA5 run as trimers on SDS-PAGE.

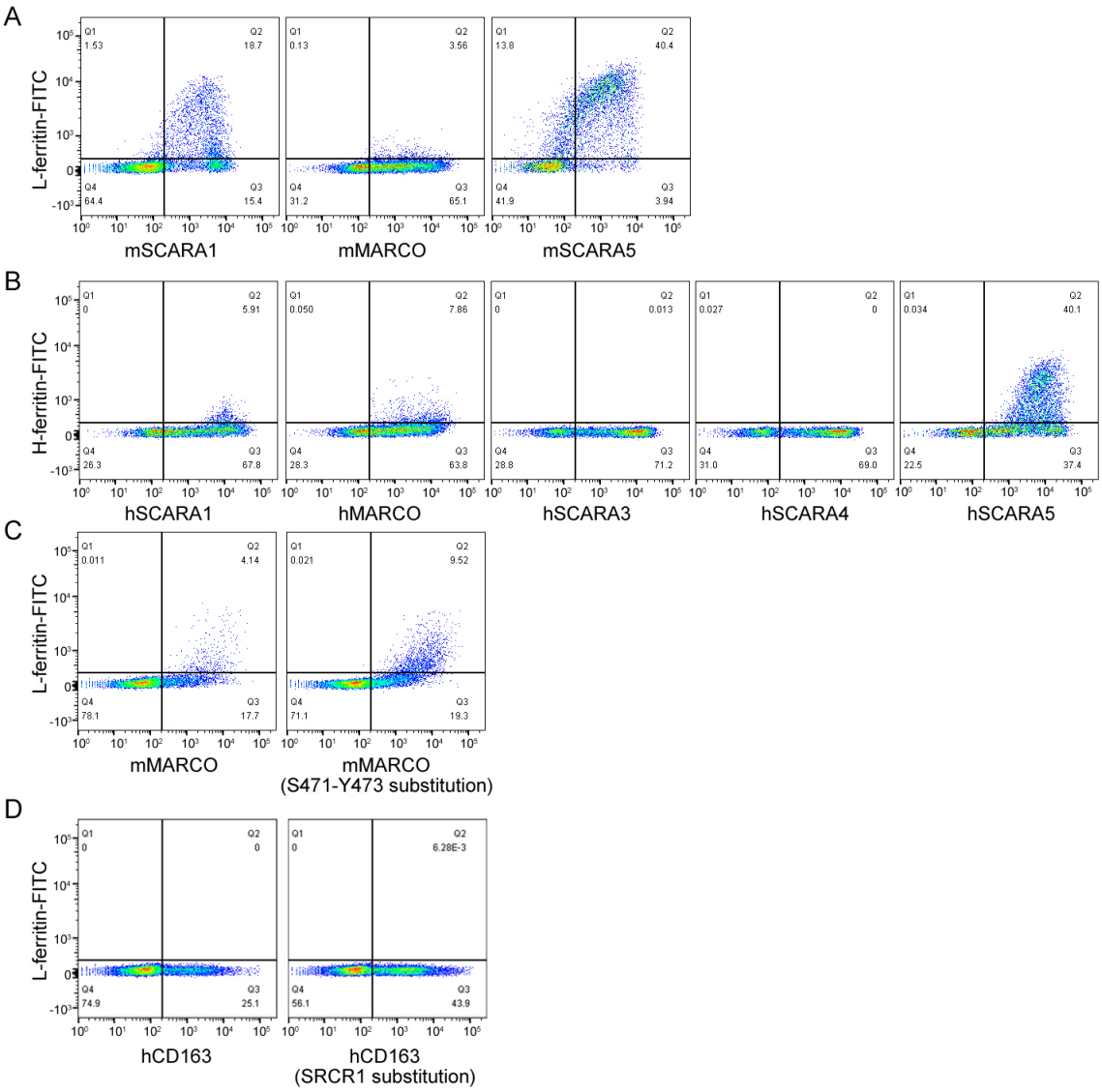

A
L-ferritin-FITC
Q1 1.53
Q2 18.7
Q4 64.4
Q3 15.4
mSCARA1
Q1 0.13
Q2 3.56
Q4 31.2
Q3 65.1
mMARCO
Q1 13.8
Q2 40.4
Q4 41.9
Q3 3.94
mSCARA5
B
H-ferritin-FITC
Q1 0
Q2 5.91
Q4 26.3
Q3 67.8
hSCARA1
Q1 0.050
Q2 7.86
Q4 28.3
Q3 63.8
hMARCO
Q1 0
Q2 0.013
Q4 28.8
Q3 71.2
hSCARA3
Q1 0.027
Q2 0
Q4 31.0
Q3 69.0
hSCARA4
Q1 0.034
Q2 40.1
Q4 22.5
Q3 37.4
hSCARA5
C
L-ferritin-FITC
Q1 0.011
Q2 4.14
Q4 78.1
Q3 17.7
mMARCO
Q1 0.021
Q2 9.52
Q4 71.1
Q3 19.3
mMARCO
(S471-Y473 substitution)
D
L-ferritin-FITC
Q1 0
Q2 0
Q4 74.9
Q3 25.1
hCD163
Q1 0
Q2 6.28E-3
Q4 56.1
Q3 43.9
hCD163
(SRCR1 substitution)

Figure S2. Interactions of the SR-A members with ferritin.

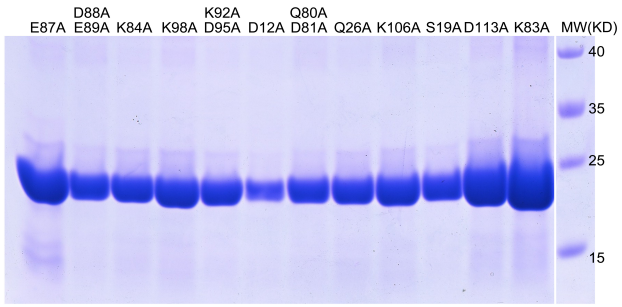
(A) FACS data showed that L-ferritin could bind to the cells transfected with mSCARA5, mSCARA1 or mMARCO, but the binding with mMARCO is much weaker than that of mSCARA5 or mSCARA1.

(B) FACS data showed that H-ferritin could bind to the cells transfected with hSCARA5, hSCARA1 or hMARCO with different affinities, but no binding for the hSCARA3 or hSCARA4 transfected cells.

(C) FACS data showed that when the loop region (S471-Y473) of mMARCO was replaced by the loop (R444-F448) of hSCARA5, it had enhanced interaction with L-ferritin.

(D) FACS data showed that when the N-terminal SRCR domain (SRCR1) of human CD163 was replaced by the SRCR domain of hSCARA5, the chimeric molecule did not show any detectable binding with L-ferritin.

A



B

	Ferritin	Binding affinity
hFTL	WT	+++
	K84A, E87A, D88A/E89A K92A/D95A, K98A	+++
	S19A, Q26A, Q80A/D81A K106A, D113A	++
	K83A	+
hFTH	WT	++
	K87A	+

Figure S3. Expression of the ferritin mutants and their binding with SCARA5.

(A) The SDS-PAGE of the L-ferritin mutants after purification.

(B) Binding of the ferritin mutants with SCARA5.

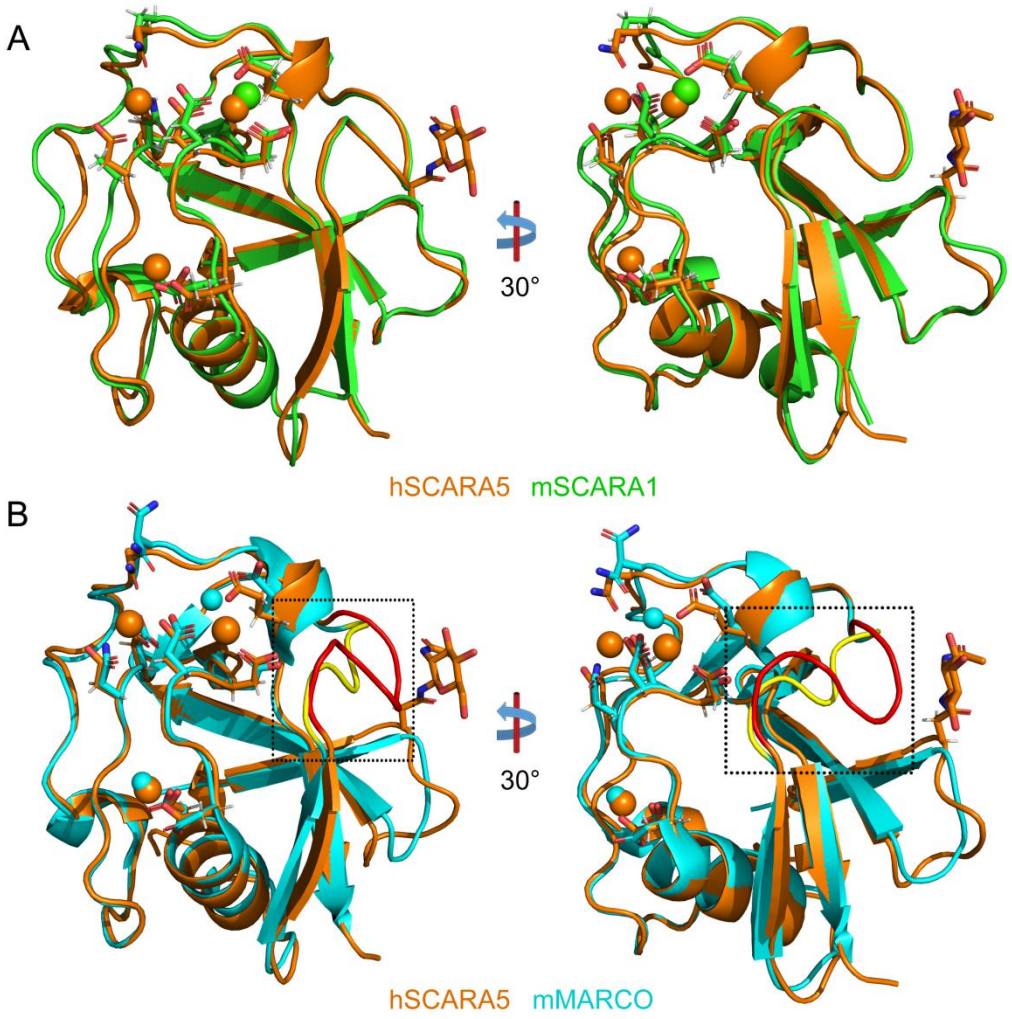


Figure S4. Structural comparison of the SRCR domains of SCARA5, SCARA1 and MARCO.

(A) Superposition of the crystal structures of the SRCR domain of hSCARA5 (orange) and mSCARA1 (green; PDB entry 6J02).

(B) Superposition of the crystal structures of the SRCR domain of hSCARA5 (orange) and mMARCO (cyan; PDB entry 2OY3). The loop regions of SCARA5 (R444-F448, red) and mMARCO (S471-Y473, yellow) are indicated by the dashed black rectangles. Divalent cations (Ca^{2+} or Mg^{2+}) are shown as spheres.

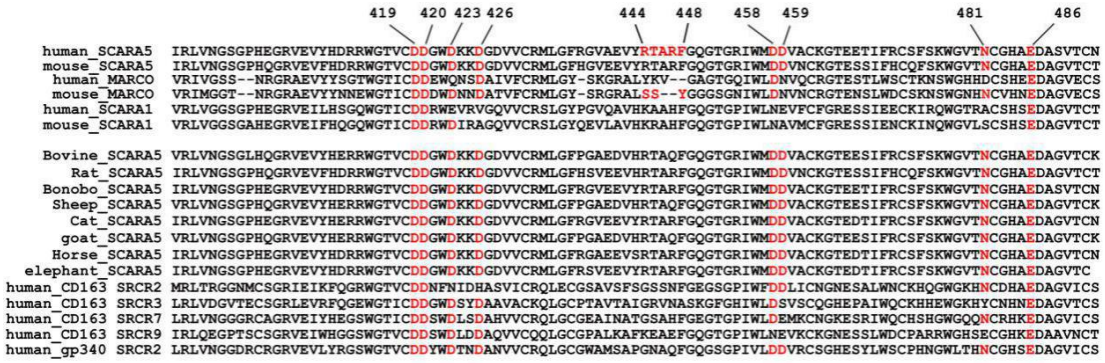


Figure S5. Sequence alignments of the SRCR domains within the SR-A family among mammalians and human CD163. The residues at the Ca^{2+} binding sites and a loop region (444-448 for hSCARA5) are colored in red.