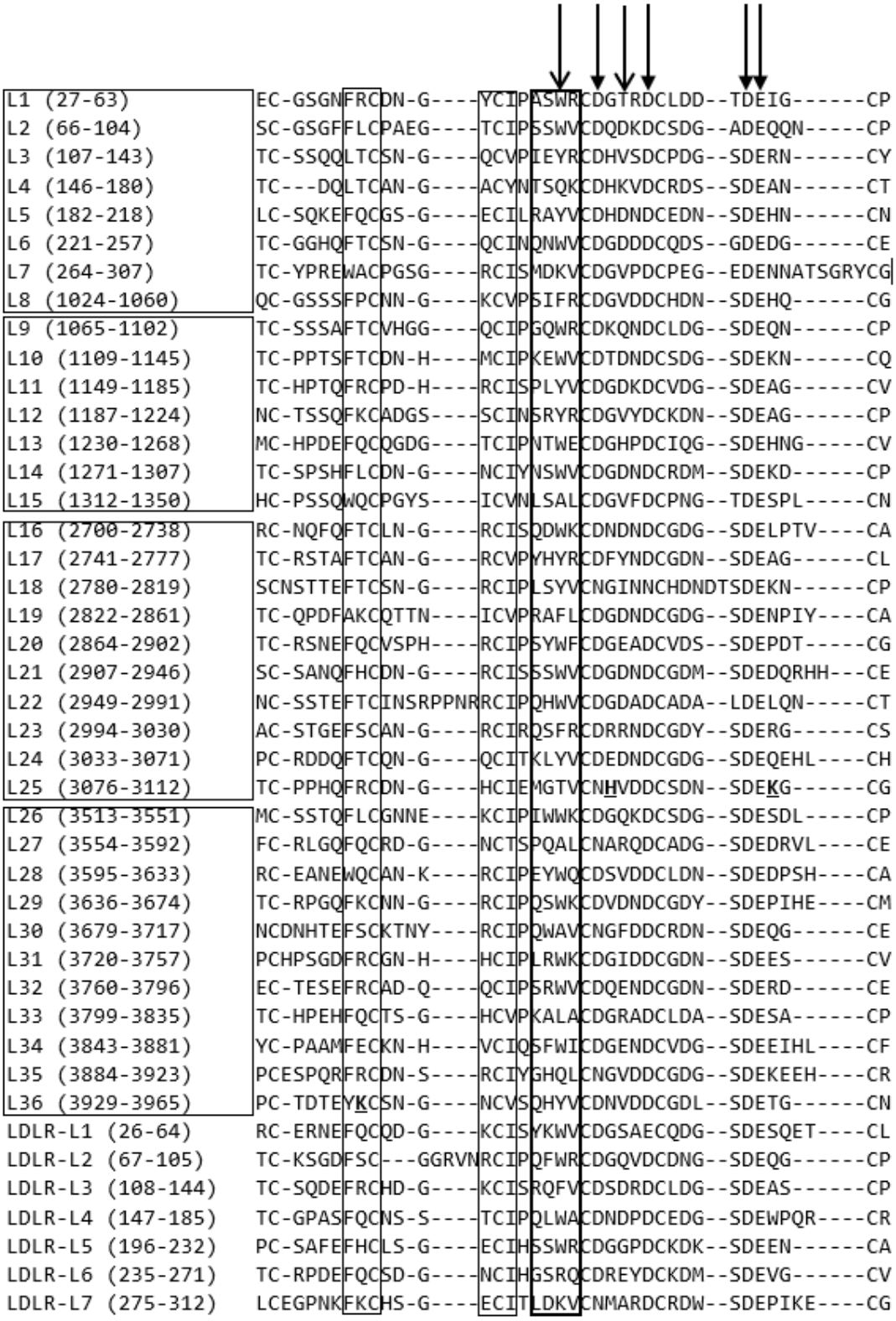

Table S1. Related to **Figure 1, Figure 2, Figure S1; Alignment of ligand-binding repeats (L) in LRP2 and LDLR**
The four groups of L repeats in LRP2 are boxed at left. Regions of beta-sheet are boxed at 0.75 pt weight, and regions of alpha-helix are boxed at 1.5 pt weight. Arrows above the alignment identify Ca^{2+} coordinating residues: solid arrows indicating involvement of the residue's side chain, and open arrows indicating involvement of the residue's main chain carbonyl. Intramolecular ligands in L25 and L36 are in bold and underlined.

Table S2. Related to **Figure 1, Figure 2, Figure S1**; **Alignment of EGF-like domains (E) in LRP2 and LDLR**
EGF-like pairs are boxed at left. Regions of beta-sheet are boxed in the alignment. Residues from calcium-binding (cb) EGF-like domains whose side chain coordinates a Ca^{2+} ion are underlined and italicized. Intramolecular ligands from the EGF-like pairs are in bold and underlined.

Protein	MW (kD)	Exclusive Spectrum Count	Exclusive Peptide Count	Percent Coverage	Quantitative Value (emPAI)
LRP2	519	2627	244	40	24.8
CUBN	399	83	38	14	0.5
ATP5o	23	9	6	36	1.6
ACTB	42	7	7	23	0.7
LRPAP1	42	6	5	17	0.5
ATP5a1	60	5	4	7	0.2
ABCG2	73	4	4	7	0.2
SLC25a4	33	4	3	9	0.3
SLC23a1	66	3	3	7	0.2
MEP1b	80	3	3	5	0.1
EZR	69	3	3	6	0.1
SLC6a18	69	3	2	4	0.1
SLC22a12	60	2	2	3	0.1

Table S3. Related to **Figure 1; Mass spectrometry of endogenously purified LRP2 from mouse kidney**
Proteins identified in SDS-PAGE purified protein with apparent molecular weight 600kDa: tandem mass spectrometry (MS/MS) based protein and peptide identifications are expressed as exclusive spectrum count of the peptide spectral matches. Exclusive peptide count, identified protein percent sequence coverage, and the protein abundance index (emPAI factor that defines the ratio of the observed to observable peptides) are also listed.

Structure		LRP2 pH 5.2	LRP2 pH 7.5
Composition (#)			
Chains		2	2
Atoms		67552 (Hydrogens: 0)	59410 (Hydrogens: 0)
Residues		8756 (Nucleotide: 0)	7636 (Nucleotide:0)
Water		0	0
Ligands	Ca	88	84
	NAG	82	62
	NGA	44	32
Bonds (RMSD)			
Length (Å) (# > 5σ)		0.007 (0)	0.005 (0)
Angles (°) (# > 5σ)		1.274 (0)	0.987 (0)
MolProbity Score		1.49	1.13
Clash Score		3.17	1.10
Ramachandran Plot (%)			
Outliers		0.00	0.00
Allowed		5.51	4.55
Favored		94.49	95.45
Rotamer outliers (%)		0.43	0.13
Cβ outliers (%)		0.00	0.00
Peptide plane (%)			
Cis-proline/general		2.3/0.0	2.1/0.0
Twisted proline/general		0.0/0.0	0.0/0.0
CaBLAM outliers (%)		2.77	2.35
CC (mask)		0.69	0.80
CC (box)		0.82	0.84
CC (peaks)		0.69	0.76
CC (volume)		0.70	0.80
Mean CC for ligands		0.62	0.68
FSC Map-Model = 0.5 (Å)		3.32	3.17

Table S4. Related to **Figure 2; Validations of the cryo-EM 3D reconstructions of LRP2 at pH 5.2 and pH 7.5** Validations were conducted in Phenix of the molecular models of LRP2 against a composite of the unsharpened locally refined maps.