Supporting information for article:

LAT1 (SLC7A5) and CD98hc (SLC3A2) complex dynamics revealed by single-particle cryo-EM

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**Table S1**  Residues used in crosslinking experiments for the validation of LAT2 and CD98hc ectodomain docking

Residues chosen for cross-linking experiments with LAT2, their equivalent residues in LAT1. The estimated distance between these residues and residues in CD98hc ectodomain are shown as reported by Rosell et al., 2014 for LAT2 and calculated from docking of the volume series of PCs 1 – 3 for LAT1 to the nearest Å.

| CD98hc | LAT2 | LAT1 | Distance from cross-linking (Å) | LAT2 Average distance from cryo-EM (Å) |
|--------|------|------|---------------------------------|---------------------------------|
| S151   | C210 | G220 | 13.4                            | 25 ± 2                          |
|        | A315 | S324 | 14.9                            | 32 ± 2                          |
| S195   | C210 | G220 | 17.5                            | 20 ± 2                          |
|        | A315 | S324 | 15.5                            | 31 ± 2                          |
| S412   | C210 | G220 | 11.5                            | 36 ± 2                          |
| S487   | G392 | S401 | 12.9                            | 34 ± 1                          |
| G505   | A235 | V244 | 8.4                             | 23 ± 1                          |
| S441   | S450 | 8.1  | 32 ± 1                          |
Table S2  Residues predicted to be at the dimer interface of LAT2 and CD98hc and their distances from cross-linking experiments by (Rosell et al., 2014).

Similarity between residues increases as similarity score goes from 1 – 9, with identical residues having no score. The Consurf score increases with decreasing variability at that position between orthologues, indicating degree of conservation.

|   |   |   | LAT1 Consurf Score | <10 Å in LAT1 EM structure |
|---|---|---|-------------------|---------------------------|
| K63 | T73 | 7 | 9 | No |
| G64 | G74 | | 9 | No |
| E67 | K77 | 7 | 1 | No |
| F155 | F161 | | 4 | No |
| P157 | P167 | 6 | 6 | Yes |
| N221 | F231 | 6 | 3 | Yes |
| F223 | F233 | 8 | 8 | Yes |
| L239 | Y248 | 7 | 8 | No |
| L297 | L306 | 5 | 5 | Yes |
| N300 | E309 | 7 | 1 | Yes |
| A301 | A310 | 9 | 9 | Yes |
| A303 | A312 | 9 | 9 | No |
| M384 | I393 | 9 | 6 | No |
| Y385 | F394 | 9 | 2 | No |
| Y390 | F399 | 9 | 5 | No |
| F393 | F402 | 7 | 7 | No |
| F440 | V449 | 7 | 5 | No |
| L442 | F451 | 8 | 5 | No |
| W443 | W452 | 2 | 2 | No |
Figure S1  Distance restraints provided to Cluspro for docking of CD98hc ectodomain and LAT1 in json used for ClusPro. LAT1 was submitted as receptor and CD98hc ectodomain as ligand to the server. Residues same as those given in Supplementary Table S2.

Supplementary Movie S1. Visualization of conformational dynamics of CD98hc ectodomain (tan) and LAT1 (pink), along PC1. The two subunits can be seen moving in a ratchet like motion relative to each other. The cryo-EM volumes along the principle component are shown as a mesh.

Supplementary Movie S2. Visualization of conformational dynamics of CD98hc ectodomain (tan) and LAT1 (pink), along PC2. CD98hc ectodomain and the LAT1/micelle density can be seen in a rocking motion with respect to each other. Cryo-EM volumes along the principle component are shown as a mesh.

Supplementary Movie S3. Visualization of conformational dynamics of CD98hc ectodomain (tan) and LAT1 (pink), along PC3. In this volume series, the two densities can be seen moving up and downward in opposite directions along the normal to the long axis of the larger density. Cryo-EM volumes along the principle component are shown as a mesh.