

Figure 1. Cryo-EM analysis of the Pendrin in NaCl. **a.** Representative electron micrograph of cryo-EM particle images. **b.** 2D class averages of Pendrin particles. **c.** Local resolution map for the 3D reconstruction of the Pendrin in NaCl. **d.** Representative densities of Pendrin map.

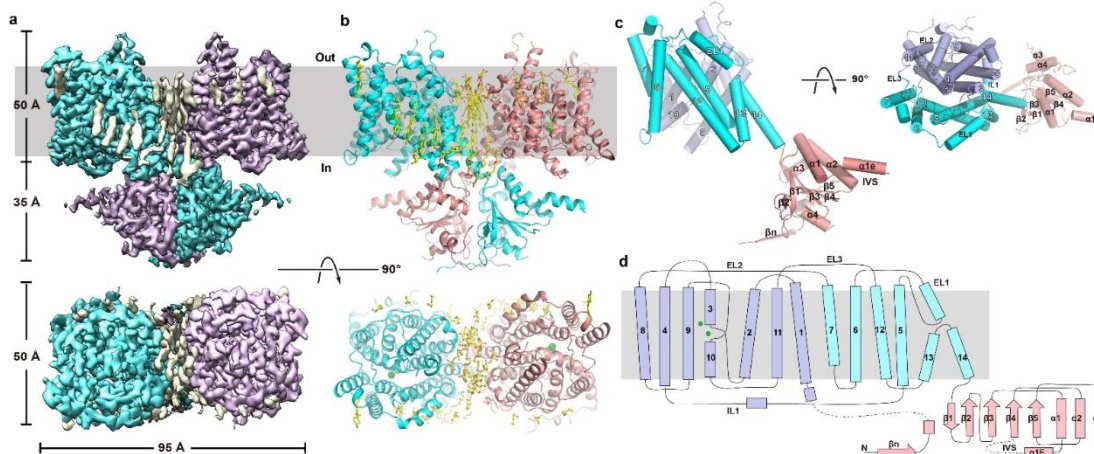


Figure 2. Overall structure of Pendrin in NaCl. **a, b** Cryo-EM density map (left) and cartoon representation (right) of the pendrin dimer as viewed from within the plane of the membrane (upper row), or the extracellular side of the membrane (bottom row). The two

protomers are colored as cyan and magenta, with lipids in yellow. **c.** Cartoon representation of a pendrin monomer in two orientations. The transport domain, scaffold domain, and STAS domain are colored violet, cyan, and salmon; respectively. **d.** Topology of pendrin. Bound Cl⁻ is shown as green spheres.

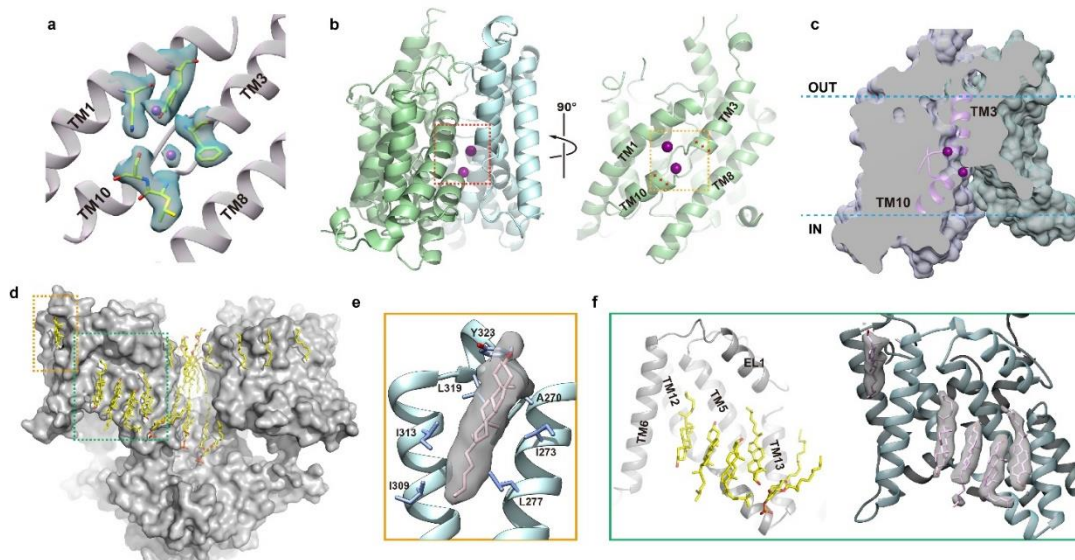


Figure 3. Structure of Pendrin in complex with iodide and bound lipids.

a. Anion binding sites of ssPendrin in the presence of I⁻. Residues are shown as sticks, anions as spheres, and densities as cyan surface. **b.** Left panel, two anion binding sites (violet spheres) in a pendrin monomer with the transport and scaffold domains colored in green and cyan, respectively. Right panel, anion binding sites and the transport

domain. **c.** Cutaway surface representation of pendrin. **d.** The structure of ssPendrin shown as surface with tightly bound lipids shown in sticks. **e.** Zoom-in view of yellow box in **a**. **f.** Zoom-in views of the green box in **a**. Density maps are shown for bound lipids.