A multimethodological approach uncovers previously undetected conformational change in CLC transporters

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CLC secondary active transporters exchange Cl- for H+. Crystal structures have suggested that the conformational change from occluded to outward-facing states is unusually simple, involving only the rotation of a conserved glutamate (Gluex) upon its protonation. We used F-19 NMR, crystallography, crosslinking, and molecular dynamics simulations to investigate the hypothesis that rotation of Gluex alone is sufficient to effect the outward opening. The crystallographic data were collected at BL12-2. The large variations in the diffraction quality of the crystals necessitated screening of 100s of crystals using the SAM robot. The multimethodological approach in this study reveals the formation of a previously uncharacterized “outward-facing open” state, thus providing a new framework for understanding CLC transporter mechanisms. Details of the work will be presented.