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A Tale of Two Aquaporins: Structural Mechanisms of Gating and Inhibition in Aqp3 and Aqp7

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Aquaglyceroporins (AQPs) facilitate the transport of small solutes like glycerol and hydrogen peroxide (H2O2) across cellular membranes, with emerging roles in redox regulation and cancer. Using single-particle cryo-EM and molecular dynamics simulations, we reveal the structural basis for pH-dependent gating and H2O2-mediated autoregulation of AQP3, as well as ligand-induced inhibition of AQP7 via cytoplasmic binding. These findings uncover distinct (auto)regulatory mechanisms of AQPs and offer a molecular framework for therapeutic targeting in diseases such as cancer.