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Aquaporin 7 (AQP7): what's old and new?

Content

In contrast to orthodox aquaporins as water channels, AQP7 is a glycerol channel abundantly expressed in human adipose tissue facilitating the glycerol efflux upon lipolytic signal. Structural information of AQP7 has been raveled by X-ray crystallography, suggesting that AQP7 forms tetramers as others AQPs and each monomer is a glycerol channel, however the role of central pore formed by four monomers is still unclear yet. Additionally, the inhibitor of AQPs is rarely studied although AQPs are physiologically important and relevant with cancers development.

Here we report an AQP7 cryo-EM structure at 2.55 Å resolution in the formation of dimer of tetramers. And two tetramers adhere each other in a twisted way by extracellular loop C. Well-defined densities are identified in the central pore and restricted by the leucine filters. GC/MS analysis suggests glycerol-3-phosphate (Gro3P) presents in the protein sample and is compatible with densities in the central cavity. Thus, we propose rationally that AQP7, in addition to function as a glycerol channel, may serve as a junction protein. Furthermore, glycerol presents in all eight monomers in the cryo-EM structure, but to a varied degree, implying a dynamic glycerol channel. The channel is blocked structurally by AQP7 inhibitor, presented from the complex structure of AQP7 and inhibitor determined by cryo-EM. Interestingly, the inhibitor is coordinated by A91 and H92 in the glycerol channel, considerably conserved in the AQP family, thus providing the possibility for the application of the inhibitor into the other AQPs.

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