Mechanistics insights of hydrogen peroxide transport through PIP aquaporins pore

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Hydrogen peroxide (H_2O_2) is transported through membranes by aquaporins (AQP). In particular, some plant PIP aquaporins isoforms are efficient H_2O_2 channels. As water and H_2O_2 share physicochemical features, it was first supposed that all AQP that transport water could act as an H_2O_2 channel. However, experimental evidence showed that not all PIP that transport water can transport H_2O_2. So, the mechanism of H_2O_2 transport is still an unsolved issue for AQP channels.
*Mt*PIP2,3 is a plasma membrane AQP from the legume *Medicago truncatula* that permeates H_2O_2. To understand the structural and chemical selectivity mechanisms leading to H_2O_2 permeability in PIPs, we characterized the particularities of H_2O_2 passing through *Mt*PIP2,3 pore by 1 µs atomistic molecular dynamic simulations. As PIPs are tetrameric pH gated channels we constructed homology *Mt*PIP2,3 models in open and closed states, and with or without H_2O_2. All models were conformationally stable along the simulation and H2O2 permeation events were found in the simulations in the presence of this molecule. We find that: i- H_2O_2 molecules can cross the pore in a single file, ii- dihedral angles adopted by H_2O_2 along the pore Z axis present a different distribution compared to the angles visited in the solution; in the selectivity-determining NPA region, H_2O_2 adopts the wider range of dihedral angles, iii- higher residence times are located around the selectivity filter zone in the open channel and moves to the cytoplasmic filter area in the closed channel; and iv- the constriction in the cytoplasmic filter area seems to be more stringent for H_2O_2 passage than for water.

Our results shed light onto the molecular mechanism of H_2O_2 passage through *Mt*PIP2,3 and represent the first steps to understand the structural determinants of AQP differential selectivity for these molecules and water.

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