POREDESIGNER: A COMPUTATIONAL TOOL FOR THE DESIGN OF MEMBRANE PORES FOR SEPARATIONS

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Monodispersed angstrom-size pores embedded in a suitable matrix are promising for highly selective membrane-based separations. They can provide substantial energy savings in water treatment and small molecule bioseparations. Such membrane proteins (primarily aquaporins) are commonplace in biological membranes but difficult to implement in synthetic industrial membranes due to their modest and non-tunable selectivity. Here we describe PoreDesigner, a computational design workflow for the redesign of the robust beta-barrel Outer Membrane Protein F as a scaffold targeting of any specified pore diameter (spanning 3–10 Å), internal geometry and chemistry. PoreDesigner uses a mixed-integer linear program to optimally place long side -chain hydrophobic amino acids at the pore constriction region that yield a smaller and more hydrophobic pore by maximizing the interaction energy between the pore wall and the permeating water wire. We appended a design assessment step in each iteration by accepting only those designs that fit the user-fed pore dimensions. We first ran PoreDesigner to obtain pore sizes lesser than 4 Å that would exhibit aquaporin-like single file water transport yet maintaining high water permeation rates. 40 accepted OmpF redesigns were obtained and were classified as off-center (OCD), uniform closure (UCD), and cork-screw designs (CSD) dictated by their internal pore architecture. The narrowest pore design from each category was chosen and set in a membrane-patch and an all-atom 200ns molecular dynamics forward-osmosis simulation was performed to corroborate the PoreDesigner-predicted pore sizes. Subsequently, stopped-flow light scattering experiments on these three designs revealed complete salt rejection by the UCD mutant and an order of magnitude higher single-channel water permeabilities than any reported aquaporin till date (for all three designs). Follow-up efforts are being made to tune the membrane-pore interactions for various biomimetic membrane materials, by systematic alteration of the hydrophobicity of the membrane-facing residues without altering their pore size. This would enable easier incorporation of these redesigned proteins in 2D planar membrane sheets and serve as viable filtration assemblies for performing precise angstrom-scale separations. PoreDesigner has been made freely downloadable from http://www.maranasgroup.com/software.htm.

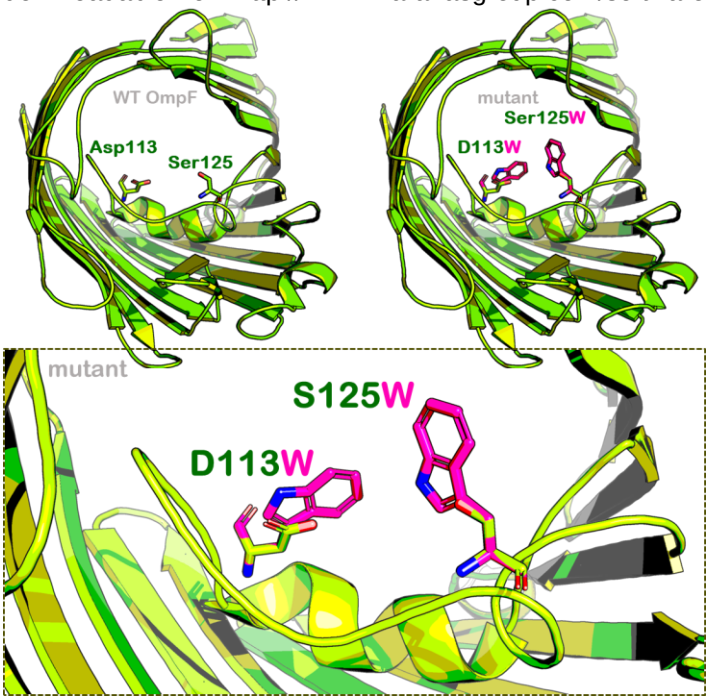

Figure 1. Two mutations from PoreDesigner predicted in silico redesign of OmpF. The D113W and S125W mutations resulted in a smaller pore lumen and a more hydrophobic inner pore wall. The wild type residues have been shown in green and the altered residues have been shown as pink sticks.