Aquaporins

Aquaporins in Human Body

<table>
<thead>
<tr>
<th>Aquaporin</th>
<th>Location</th>
<th>Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>AQP0</td>
<td>Lens fiber cells</td>
<td>Fluid balance of the eye</td>
</tr>
<tr>
<td>AQP1</td>
<td>Red blood cells, kidney proximal tubules, eye, corneal epithelium, bronchial glands, lung alveolar epithelium</td>
<td>Osmotic protection, Donor-recipient,Aquaporin number, Production of CBF, Alveolar hydration</td>
</tr>
<tr>
<td>AQP2</td>
<td>Kidney, collecting ducts, Tuba anti-salt cells</td>
<td>Anti-hormone activity</td>
</tr>
<tr>
<td>AQP3</td>
<td>Kidney, collecting ducts, Trachea epithelial cells</td>
<td>Reabsorption of water, Secretion of water</td>
</tr>
<tr>
<td>AQP4</td>
<td>Kidney, collecting ducts, Brain, ameloblasts, brain, hypophysis, lung bronchial</td>
<td>Reabsorption of water, CBF fluid balance,</td>
</tr>
<tr>
<td>AQP5</td>
<td>Kidney, collecting ducts, Lung bronchial</td>
<td>Very low water permeability</td>
</tr>
<tr>
<td>AQP6</td>
<td>Kidney, collecting ducts, Lung bronchial, bone</td>
<td>Osmo-regulating function?</td>
</tr>
<tr>
<td>AQP7</td>
<td>Testis, androgens</td>
<td>Osmo-regulating function?</td>
</tr>
<tr>
<td>AQP8</td>
<td>Testis, pancreas, liver</td>
<td>Osmo-regulating function?</td>
</tr>
<tr>
<td>AQP9</td>
<td>Leukocytes</td>
<td>Osmo-regulating function?</td>
</tr>
</tbody>
</table>

More are suspected to exist. Congenital cataracts, Diabetes insipidus, ...

VMD Developers:
- Fatemeh Khalili
- John Stone
- Elizabeth Villa
- Dan Wright
- Emad Tajkhorsid
- John Eargle
- Brijeeet Dhaliwal
- Zan Luthey-Schulten
Physical Bioinformatics - A Case Study

Sequence and structure information are the bedrock on which an understanding of cellular functions and the underlying physical mechanisms can be built. This lecture illustrates how the two sources of information are combined to investigate by means of the program VMD function and mechanism of the aquaporin family of membrane channels that transport water and certain small solutes across cell walls. Introducing first the key architectural features of a single aquaporin, structures and sequences of four aquaporins are aligned and common features recognized. The shared and distinct features are examined closely and used as guideposts leading quickly to key questions regarding the mechanism underlying aquaporin's efficient conduction and selection. The questions are addressed by means of molecular dynamics simulations using the program NAMD that reveal the physical principles behind water transport and highly selective solute co-transport in aquaporins. Sequence-structure information is viewed again to elucidate tetramer binding and pathologies connected with certain aquaporin mutants. The lecture introduces the concepts behind the programs employed and emphasizes those aspects of the case study that can be applied for investigations of other protein families.
Physical Bioinformatics - A Case Study
Aquaporin Family of Membrane Channels
Klaus Schulten, U. Illinois at Urbana-Champaign

AQP cluster

GLP cluster

AQP0  HUMAN  LNTLHPAHSVGCATTVEIFLTLQVLCIFATYDE-RRNGQLGQVALAVGFSLALGHLFMYTTYGAM  183
AQP1  HUMAN  RNDLADGVNSGCGLGIEIIGTQLVLVCVGATTDR-RRRLDGGAPAHLGVALGHLLAIDYTCCGI  191
AQP2  HUMAN  VNALSNSTTAGAVFVELPLTLQVLCIFASTDB-RRGENPTAPLTSIGFSLVALGHLLGIHYTGCSM  183
AQP3  HUMAN  GIFTYPSCHLDMINGFDFOITGASTIVPDLPNVPGRLEAFTVGLVVLIGTSMGFSNVGAV  214
AQP4  HUMAN  VTMVHGNLTAQGGHGLVLGIEITFTQLVFFTPASCDS-XRTDVTGSAIAIGFSVAIGHLFAINYTCA  212
AQP5  HUMAN  VNALNNTIQGCMVVELLIFQGALICIFASTDS-RRTSPVSAPLGSLIGVTLHGLViTFCGSM  184
AQP6  HUMAN  IVNVRNSVTGCAVQELLIITLQLVLVCIFQSTDS-RQTS--GSPATMIGISWALGHLLICIGLFTGCSM  195
AQP7  HUMAN  GIFTYTPDHLTTLRWFGLNEAWLTFGLQLCFAITDQQENNPALPGTEALVIGLVVIIIGSLSMTGYAI  225
AQP8  HUMAN  AAFVTVQEQQVQCSSALVEEIIILITTILALAVCMCAIN--EKTXGPLAPFSIGFAVTHVdalecggC  209
AQP9  HUMAN  HAFATYPAPYLLSLANAFADQQCATMLIIVFVAIFDSRLGAAPRGLPITAIAGLLITVIASSGLNSCCAM  215
GLPF_ECOLI  GTSSTYPNPHINFVCFAVEEMVTAIIMLLILALTDGNCVPRGPLPLLIGLIAVIGASMGPLTGFAAM  202

ruler ...180......190......200......210......220......230......240....
The Aquaporin Superfamily

GLP cluster
- GLP2
- GLPY1
- GLPB1
- GLPA
- (Bacterial)
- (Yeast)
- (Animal)

Glycerol transport

(AQPA)
- AQPA
- AQFarc
- AQPsco
- AQPS
- (Bacterial)

(AQP cluster)
- AQP0
- AQP1
- AQP2
- AQP3
- AQP4
- AQP5
- AQP6
- AQP7
- AQP9
- (Animal)
- (Plant)

Water transport

### Water and Glycerol Channels in the Human Body

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<th>Aquaporin</th>
<th>Location/Function</th>
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<tr>
<td>Aquaporin-0</td>
<td>Eye: lens fiber cells, Fluid balance of the lens</td>
</tr>
<tr>
<td>Aquaporin-1</td>
<td>Red blood cells, Kidney: proximal tubules, Eye: ciliary epithelium, Brain: choroid plexus, Lung: alveolar epithelial cells, Osmotic protection, Concentration of urine, Aqueous humor, Production of CSF, Alveolar hydration</td>
</tr>
<tr>
<td>Aquaporin-2</td>
<td>Kidney: collecting ducts, ADH hormone activity</td>
</tr>
<tr>
<td>Aquaporin-3</td>
<td>Kidney: collecting ducts, Trachea: epithelial cells, Reabsorption of water, Secretion of water</td>
</tr>
<tr>
<td>Aquaporin-5</td>
<td>Salivary glands, Lacrimal glands, Production of saliva, Production of tears</td>
</tr>
<tr>
<td>Aquaporin-6</td>
<td>Kidney, Very low water permeability!</td>
</tr>
<tr>
<td>Aquaporin-7</td>
<td>Testis and sperm</td>
</tr>
<tr>
<td>Aquaporin-8</td>
<td>Testis, pancreas, liver</td>
</tr>
<tr>
<td>Aquaporin-9</td>
<td>Leukocytes</td>
</tr>
<tr>
<td>Aquaporin-10</td>
<td></td>
</tr>
</tbody>
</table>

Additional members are suspected to exist.
Functionally Important Features of Aquaporins

- Water and glycerol transport
- Exclusion of ions and protons
- Tetrameric arrangement in membrane

Aquaporins of known structure:
- GlpF – E. coli glycerol channel (aquaglyceroporin)
- AQP1 – Mammalian aquaporin-1 (pure water channel) -Sui et al, Nature (2001)

~100% conserved -NPA- signature sequence
Load Aquaporin 1J4N into VMD
VMD Permits Different Rendering Styles

movie

cartoon
Comparing Sequences of Aquaporins
Highlighting Key Conserved Residues
Load Aquaporins 1j4n, 1fqy, 1lda, 1rc2 into VMD
Aligning Structures and Sequences
Comparing Structures by Similarity - Q Value
Comparing Structures by Similarity - Q Value
Exhibiting Sequence Identity - Side View
Exhibiting Sequence Identity - Top View
Showing Conserved Residues - Monomer
Showing Conserved Residues - Tetramer
Dynamics of Protein, Lipid, Water System

Equilibrated Structure after 1 ns

note the curved adjustment between lipids-protein

Morten Jensen, Emad Tajkhorshid
Glycerol Conduction

• Spontaneous glycerol conduction on ns time scale;
• Conduction occurs independently in each monomer;
• Exposed backbone carbonyl oxygen atoms dictates glycerol and water pathway; this explains the non-helical secondary structure in the aquaporin family;
• Glycerol resides at the positions of conserved motif for the longest time during simulation = minimum energy sites;
• Water molecules are essential for the glycerol transport.