

Structure and assembly of membrane proteins in native membranes by atomic force microscopy (AFM)

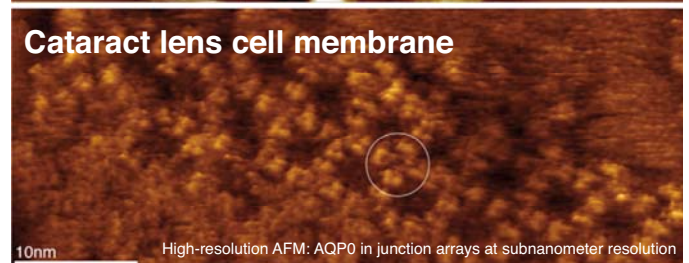
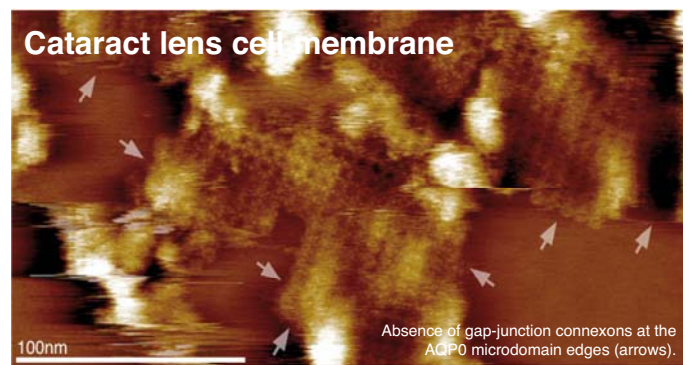
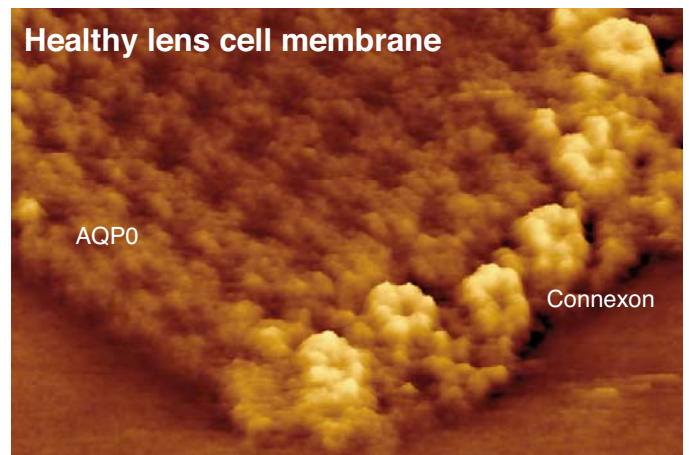
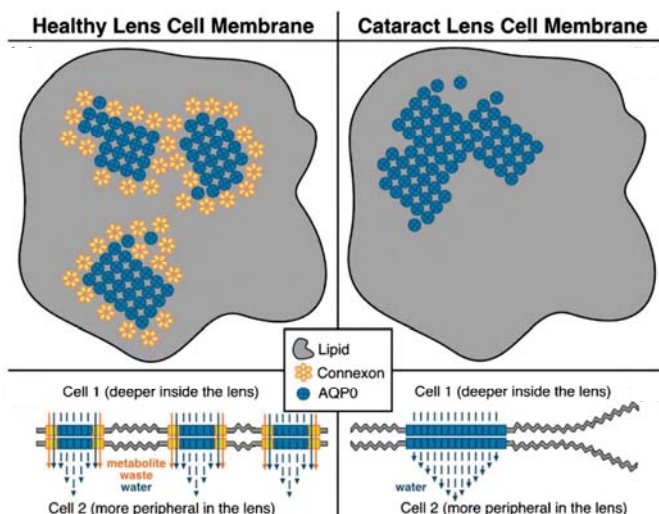
This first high-resolution view of membranes from a pathological human tissue provides insights into cataract development at the single membrane protein level and indicates the power of the atomic force microscopy (AFM) as a future medical nano-imaging tool.

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Human cataract lens membrane at subnanometer resolution

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Human pathologies often originate from molecular disorders. Therefore imaging technology as one of the bases for identification and understanding of pathologies must provide views of single molecules at subnanometer resolution. Membrane proteins mediate many of life's most important processes. Their malfunction is often lethal or leads to severe disease. Nowadays, atomic force microscopy (AFM) is a recognized technique able to reveal the structure of supramolecular assemblies of membrane proteins ¹. Using AFM as a medical nano-imaging tool, we imaged healthy ² and cataract affected ³ eye lens membranes at unprecedented resolution. Crucial differences in organization of the two membrane proteins, aquaporin-0 and connexin, are distinguished between healthy and pathological cases. Aquaporin-0 (AQP0) and connexons form together junctional microdomains between healthy lens core cells in which AQP0 form square arrays surrounded by connexons. In the pathological case connexons are lacking and AQP0 arrays are malformed. This first high-resolution view of the membrane of a pathological human tissue provides insights into cataract pathology at single membrane protein molecule level, and indicates the power of the AFM as a future tool in medical imaging at subnanometer resolution.



Healthy state: AQP0 form square arrays edged by connexons. Water and metabolite transport, and cell adhesion are provided.

Pathological state - senile cataract: Absence of connexons, AQP0 assemble in larger malformed domains leading to large non-adhering membrane areas. Breakdown of the lens microcirculation system.

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2) The supramolecular architecture of junctional microdomains in native lens membranes. EMBO R., 2007, 8, 1, 51-55, Nikolay Buzhynskyy, Richard Hite, Thomas Walz & Simon Scheuring*

3) Human cataract lens membrane at subnanometer resolution. J. Mol. Biol., 374 (1): 162-169, Nikolay Buzhynskyy, Jean-Francois Girmens, Wolfgang Faigle, & Simon Scheuring*