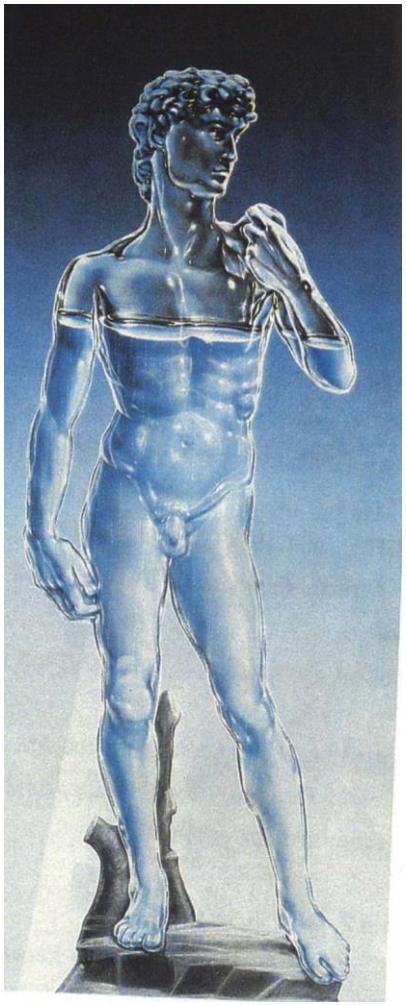
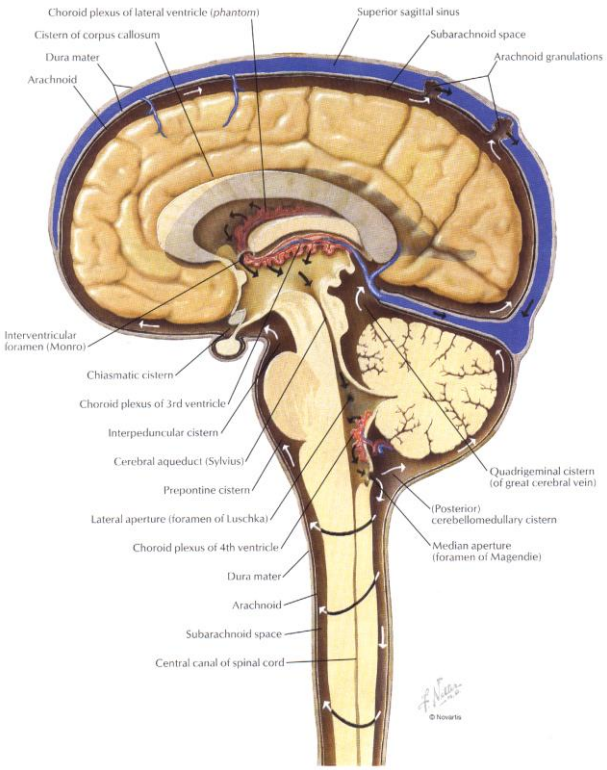
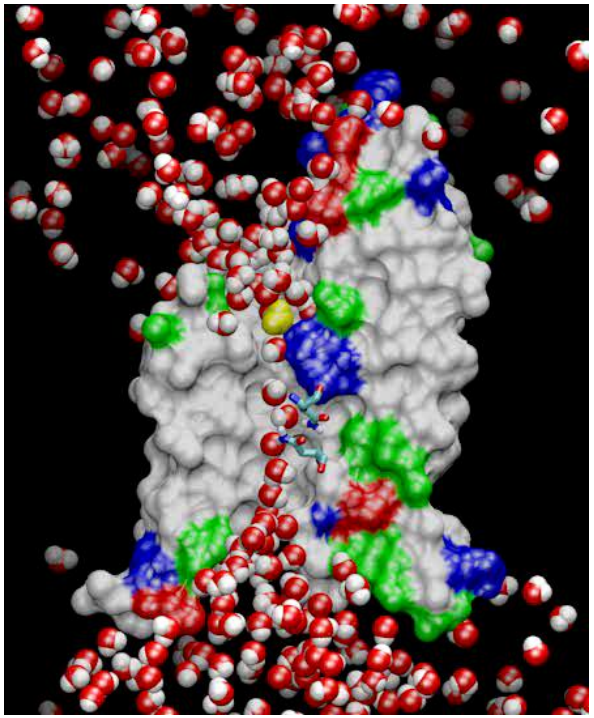
Water Biology: Roles of aquaporins







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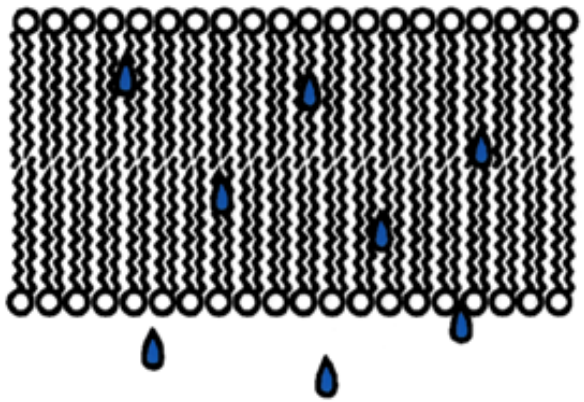
Dept. of Pharmacology
Keio School of Medicine

KEIO 150
Design the Future
150th Anniversary in 2008

Transmembrane water permeability

Bilayer Diffusion



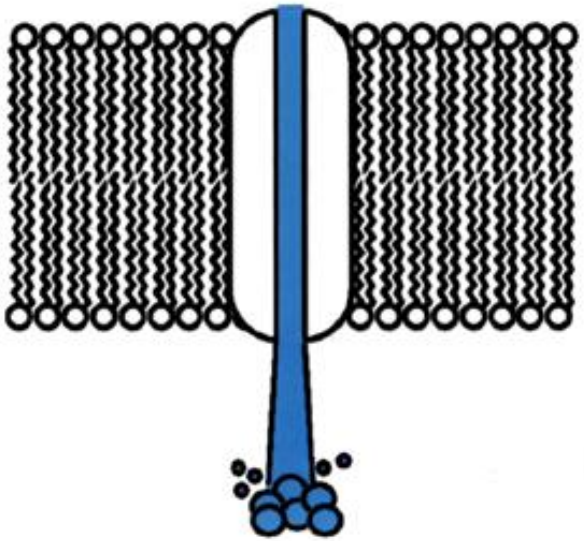
All biological membranes

Low capacity

No known inhibitors

E_a 10 kcal/mol

Water Channels



Renal tubules, secretory glands, red cells

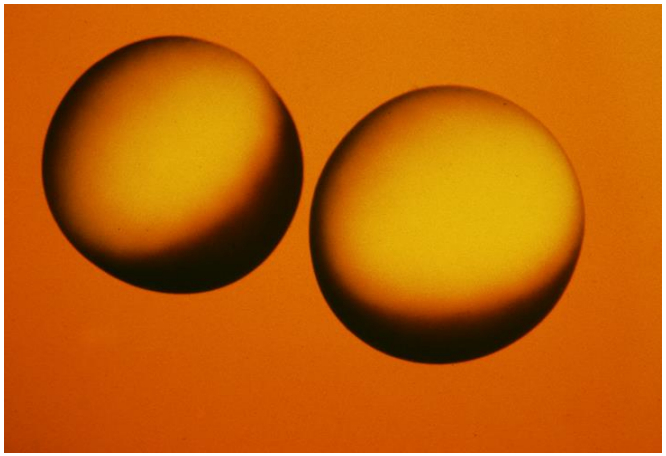
High capacity for H_2O, not H_3O^+

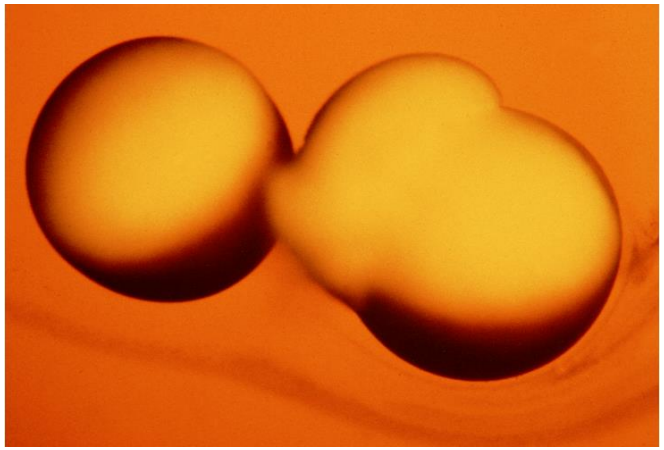
Reversibly inhibited by Hg^{++}

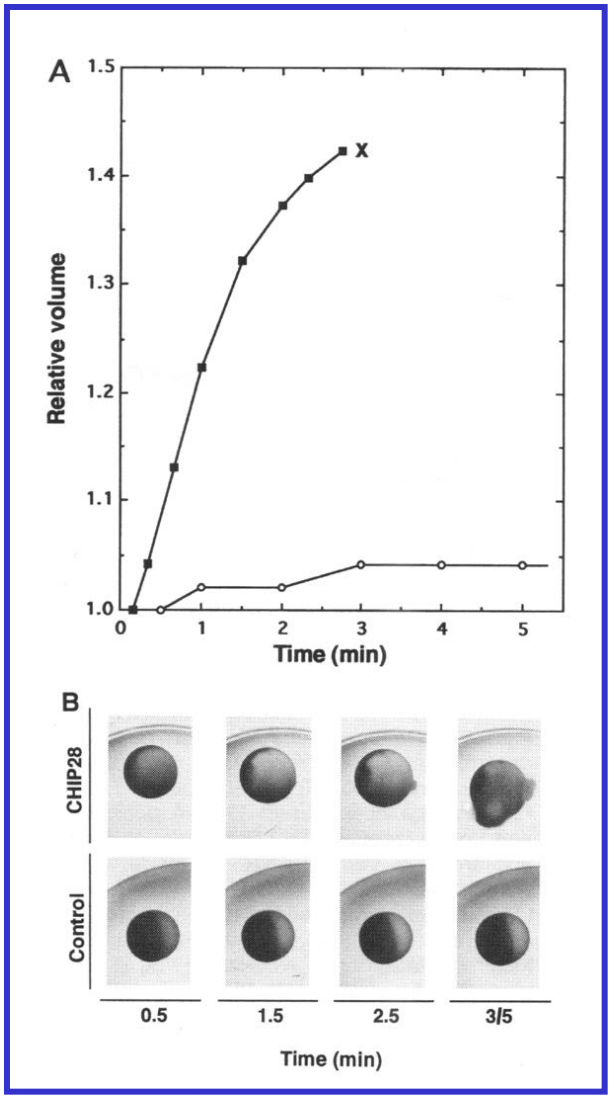
E_a 5 kcal/mol

Discovery of Aquaporin-1

Functional expression



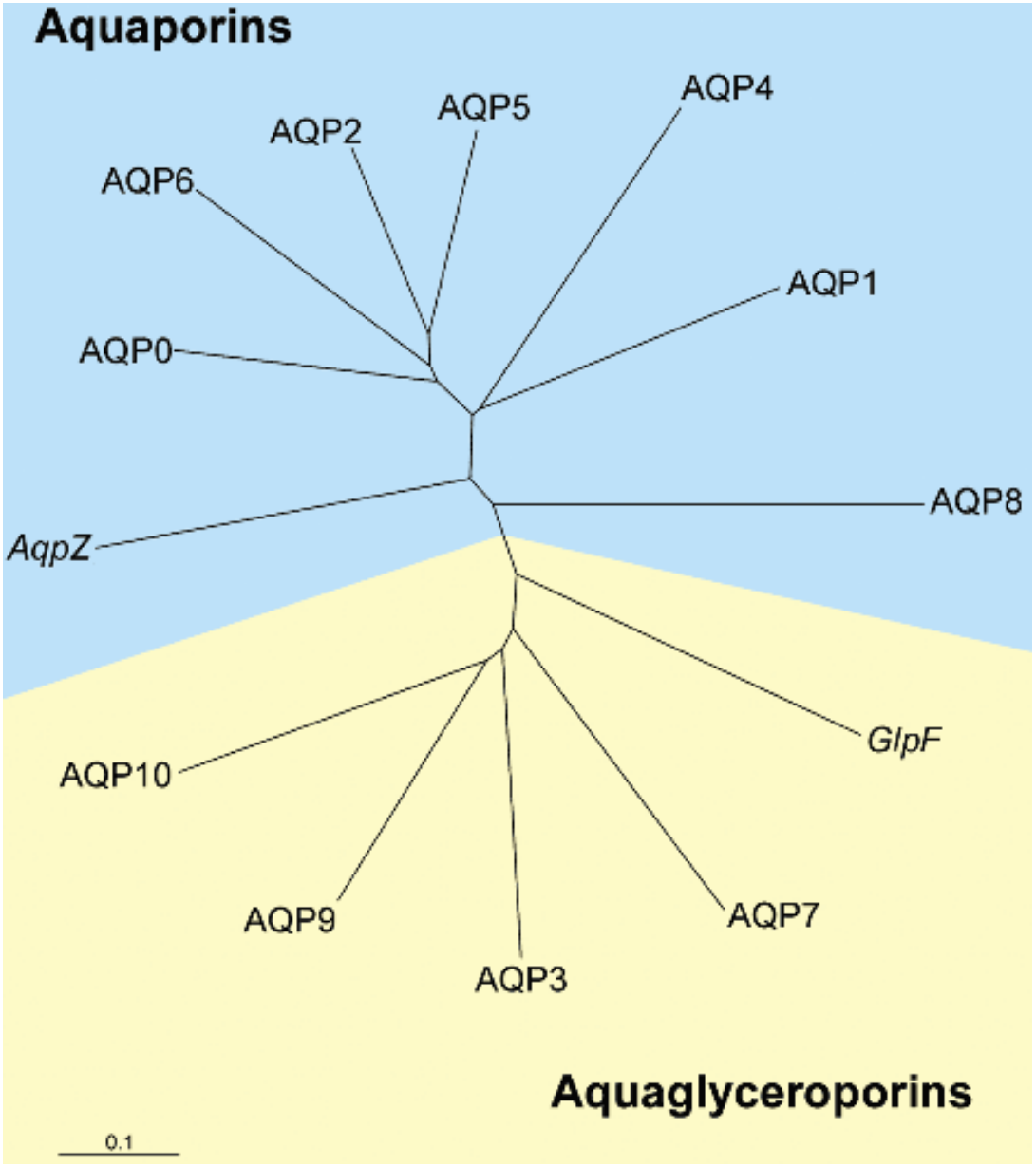




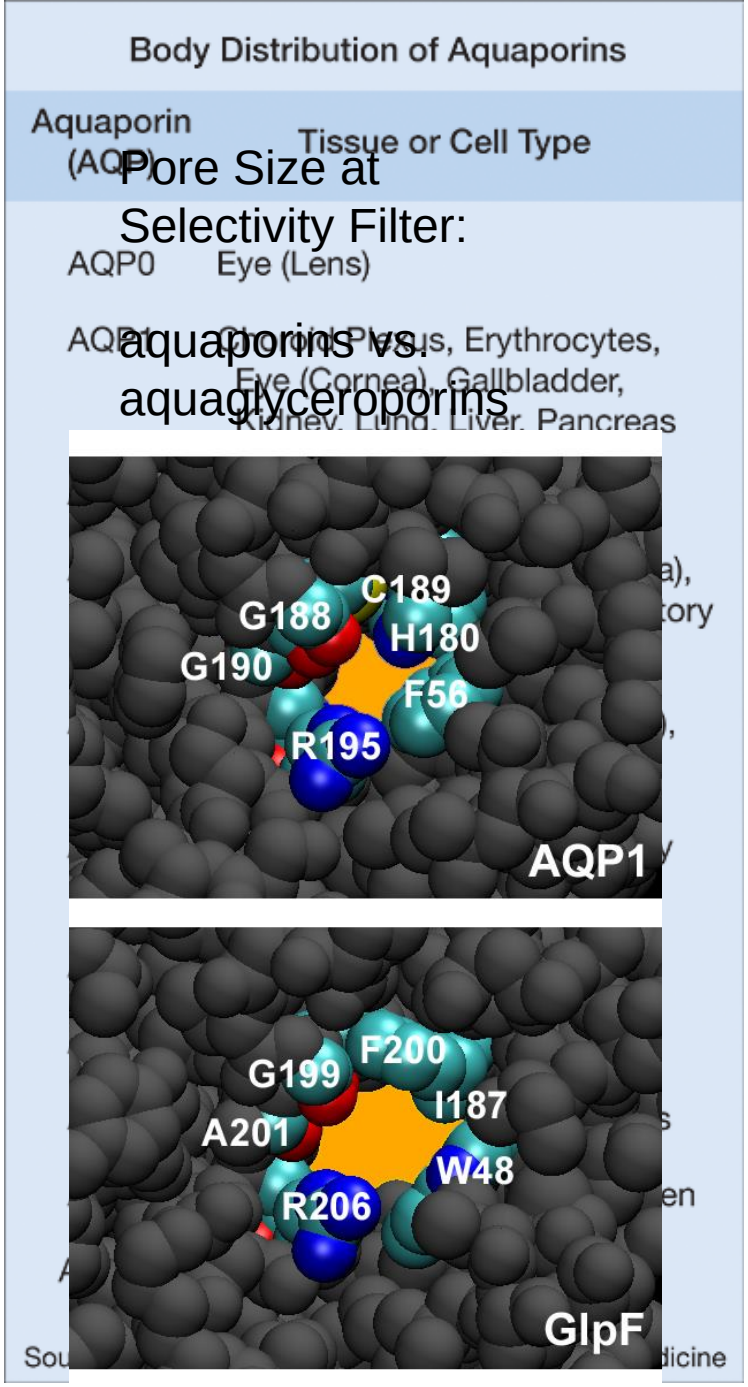
Hypo-osmolar swelling
Hg^{++} inhibited, no currents

Preston *et al., Science* 1992

Human Aquaporin Repertoire



Pore Size at Selectivity Filter: aquaporins vs. aquaglyceroporins



(M. Yasui, *JAMA*, 2004)

Clinical relevance of Aquaporin

schizophrenia

Brain edema

Cataract

Mood disorders

Malaria infection

Dry eye

glaucoma

Obesity

DM

Dry mouth

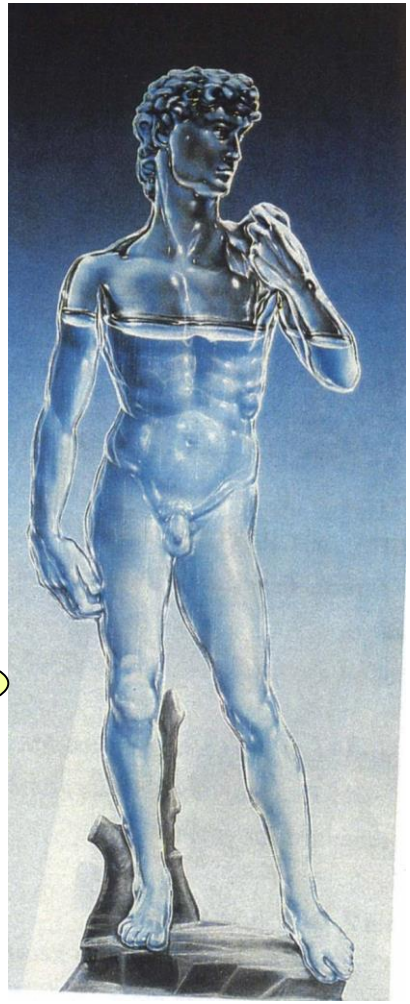
Lung edema

DI

Dry skin

Polycystic kidney

Skin regeneration



Cell Biology:

Secretion/absorption
Epithelial regeneration
Tumor Growth
Vascular regeneration
Cell cycle

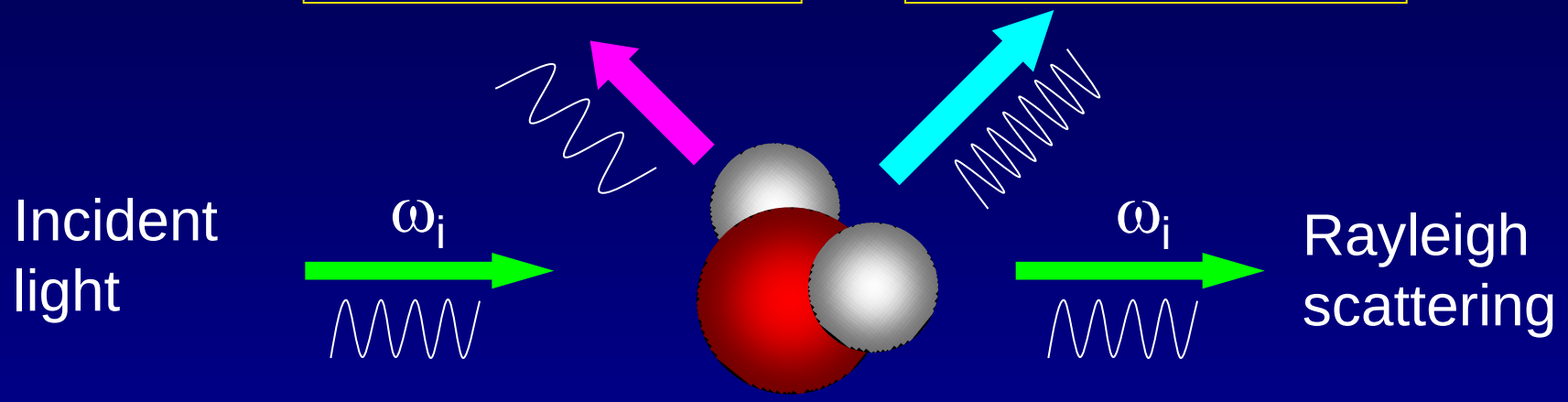
Toxemia of pregnancy

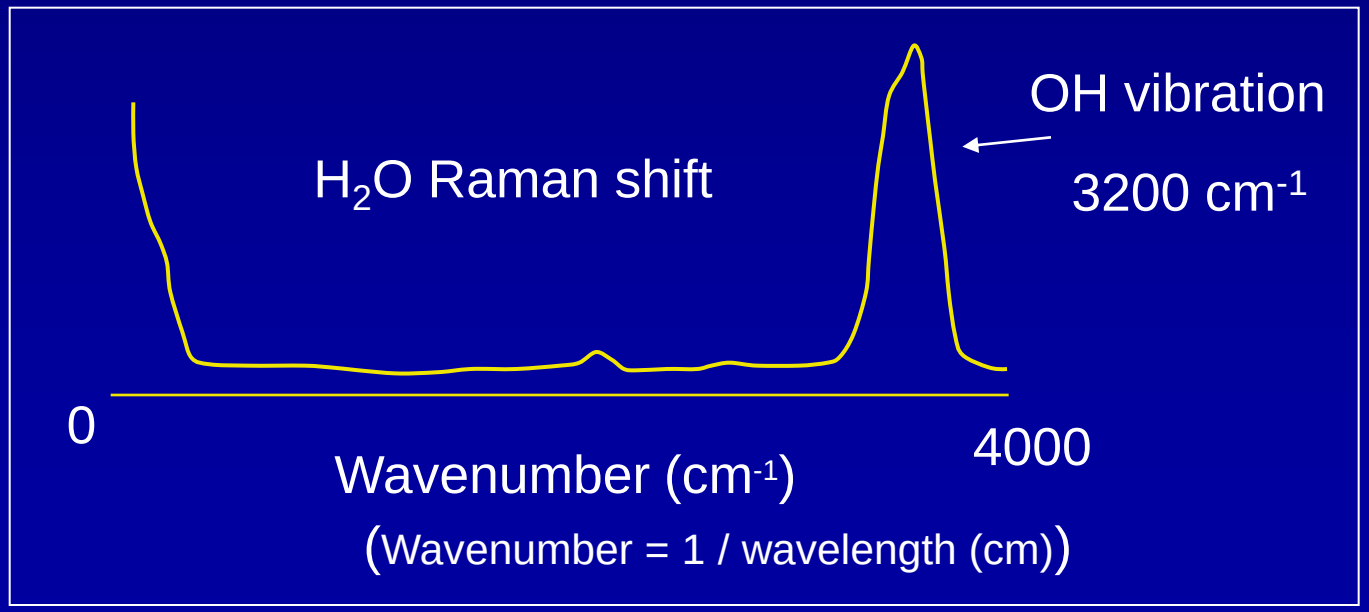
Raman scattering

Incident light interacts with molecular vibration

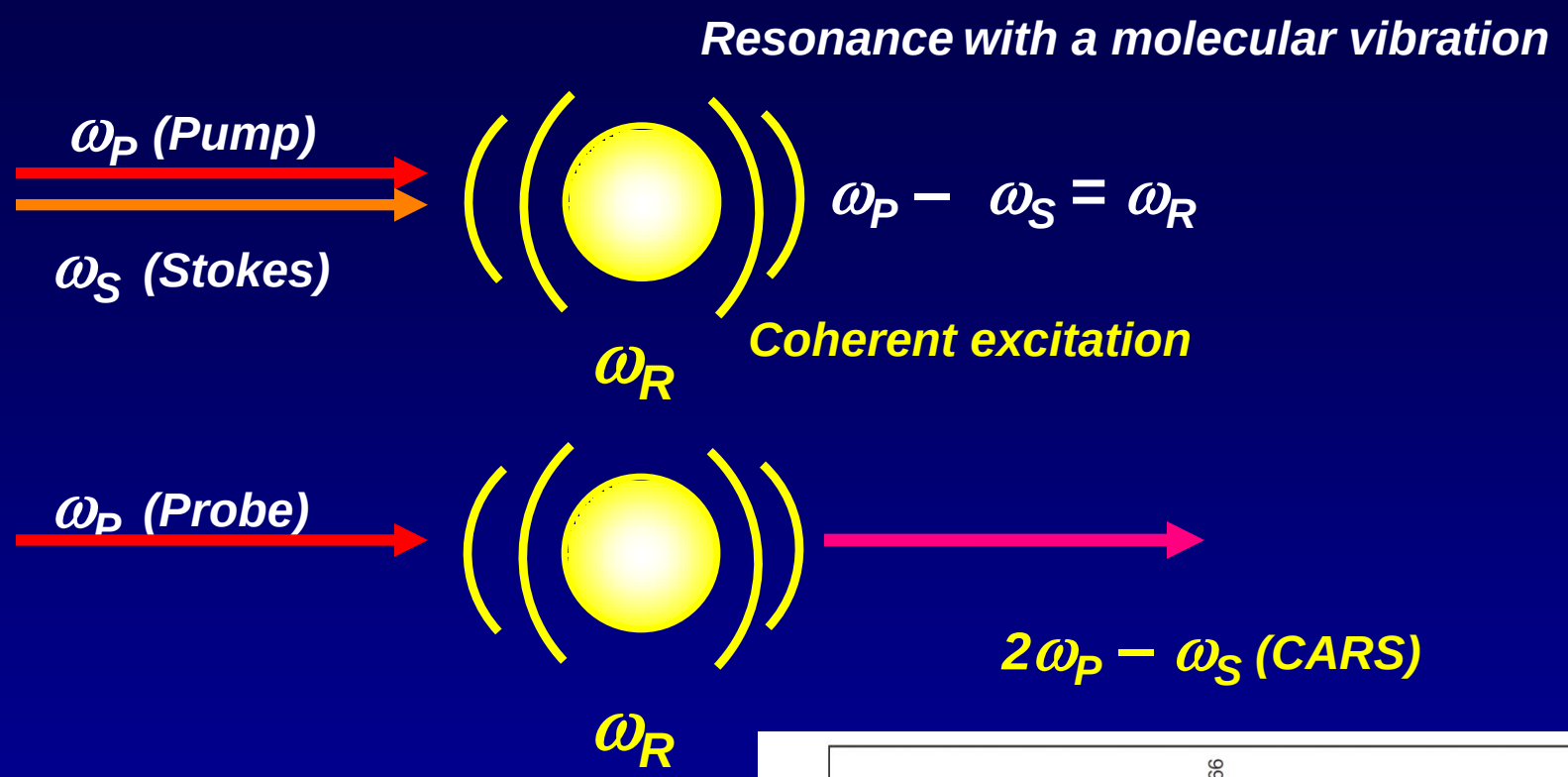
$\omega_i - \omega_{OHvibration}$

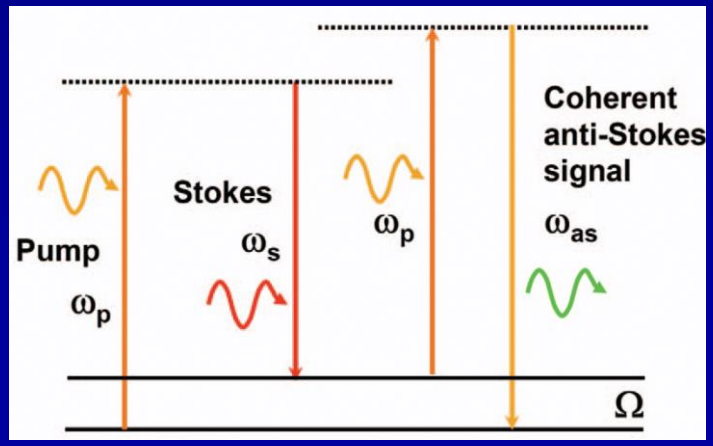
$\omega_i + \omega_{OHvibration}$

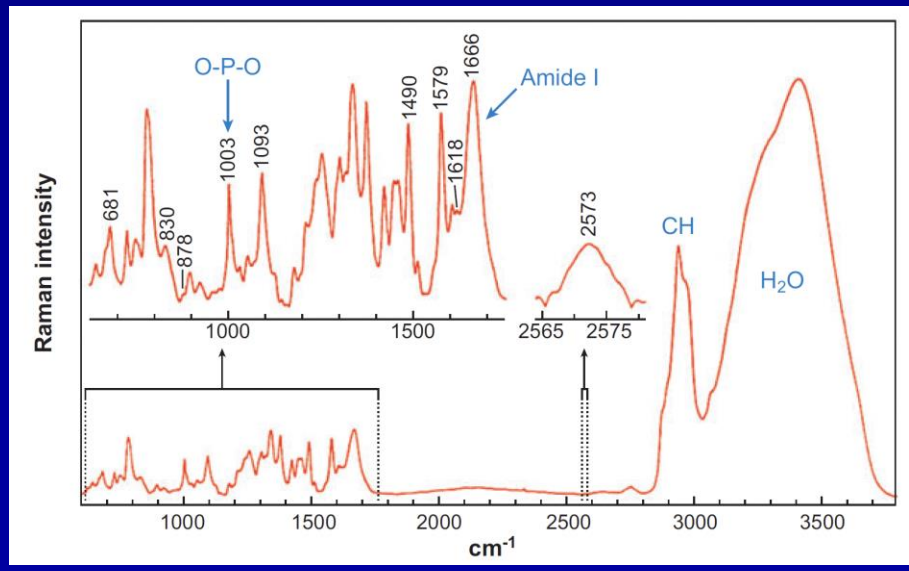




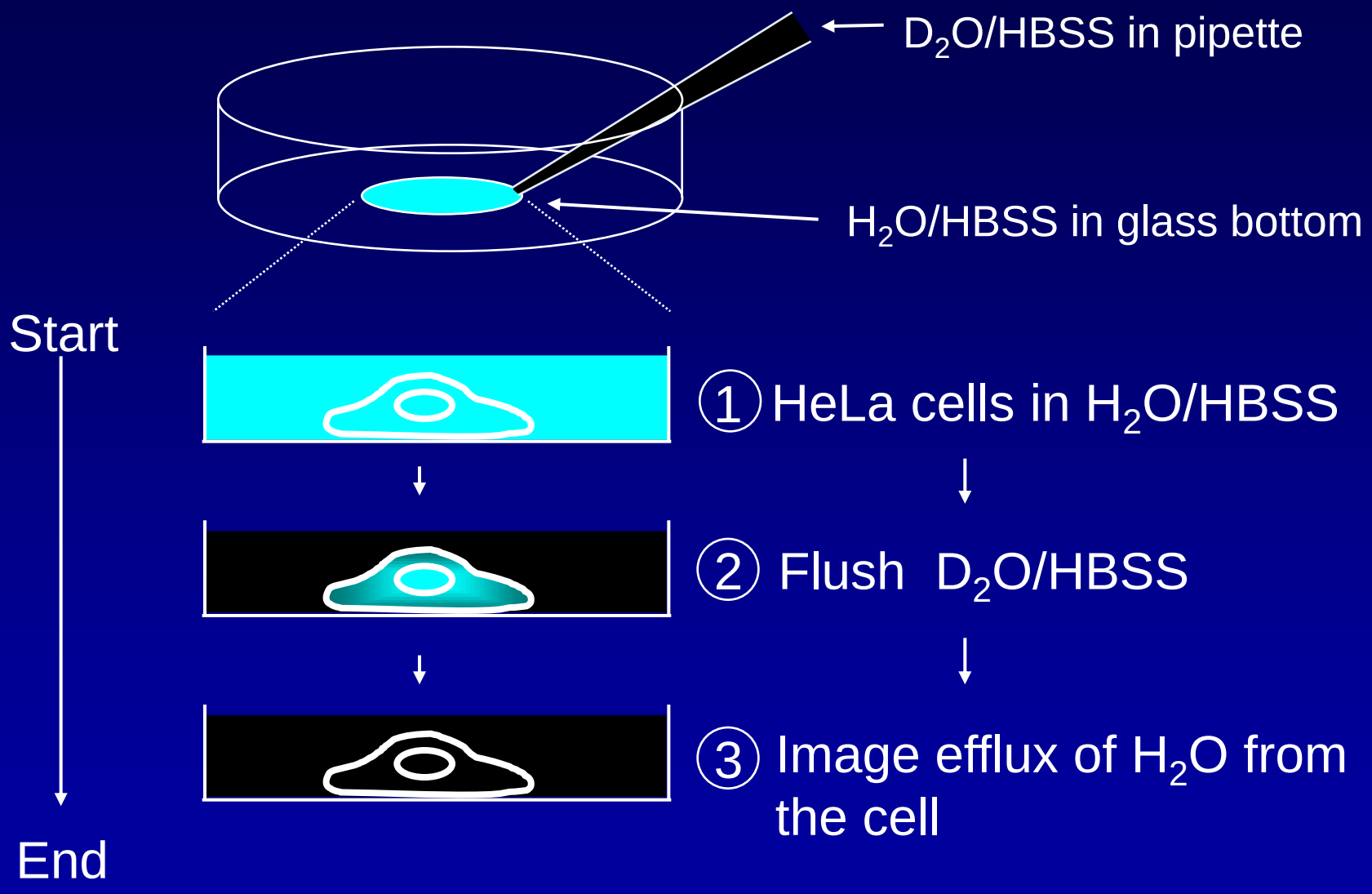
Principles of CARS



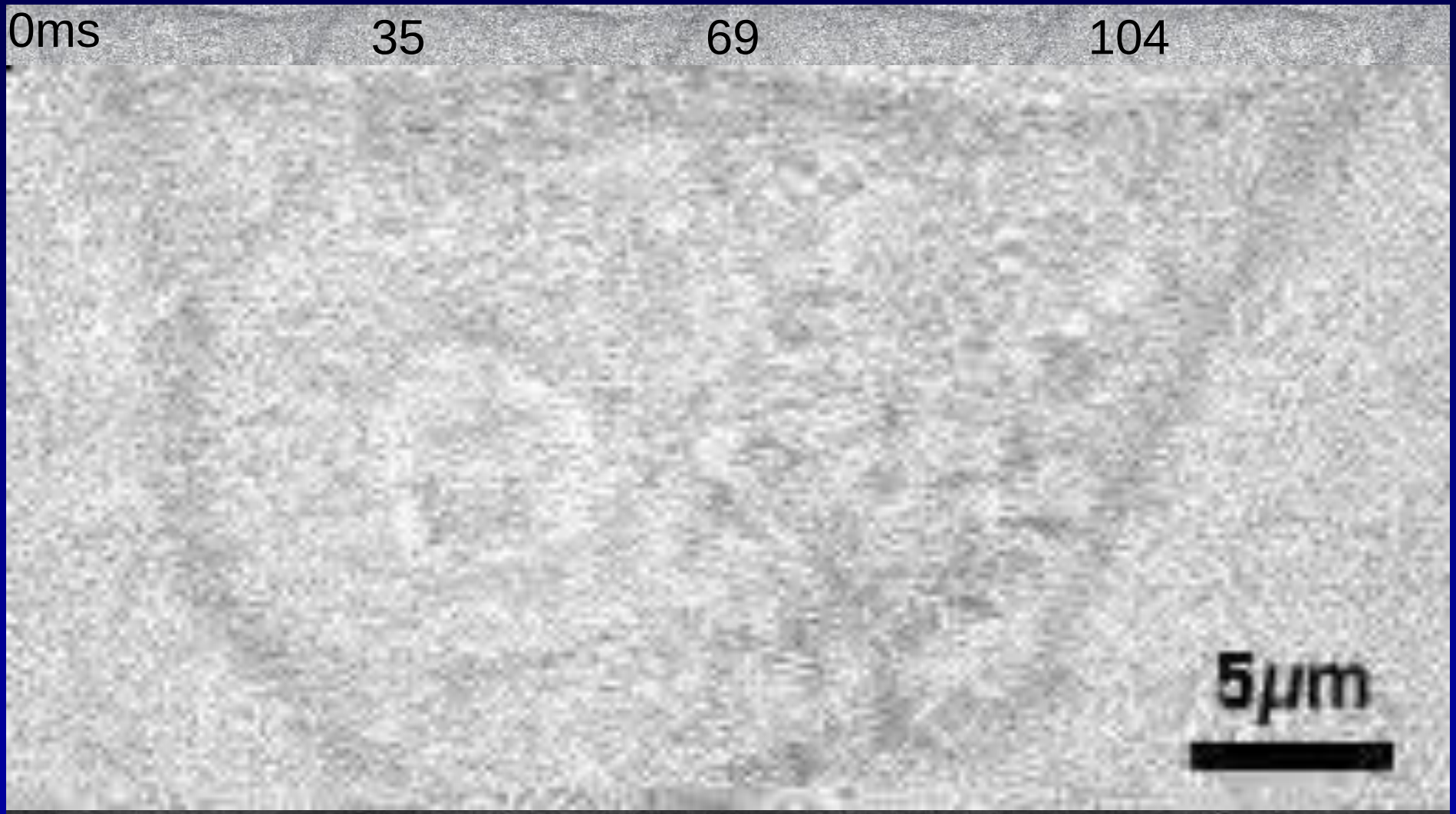




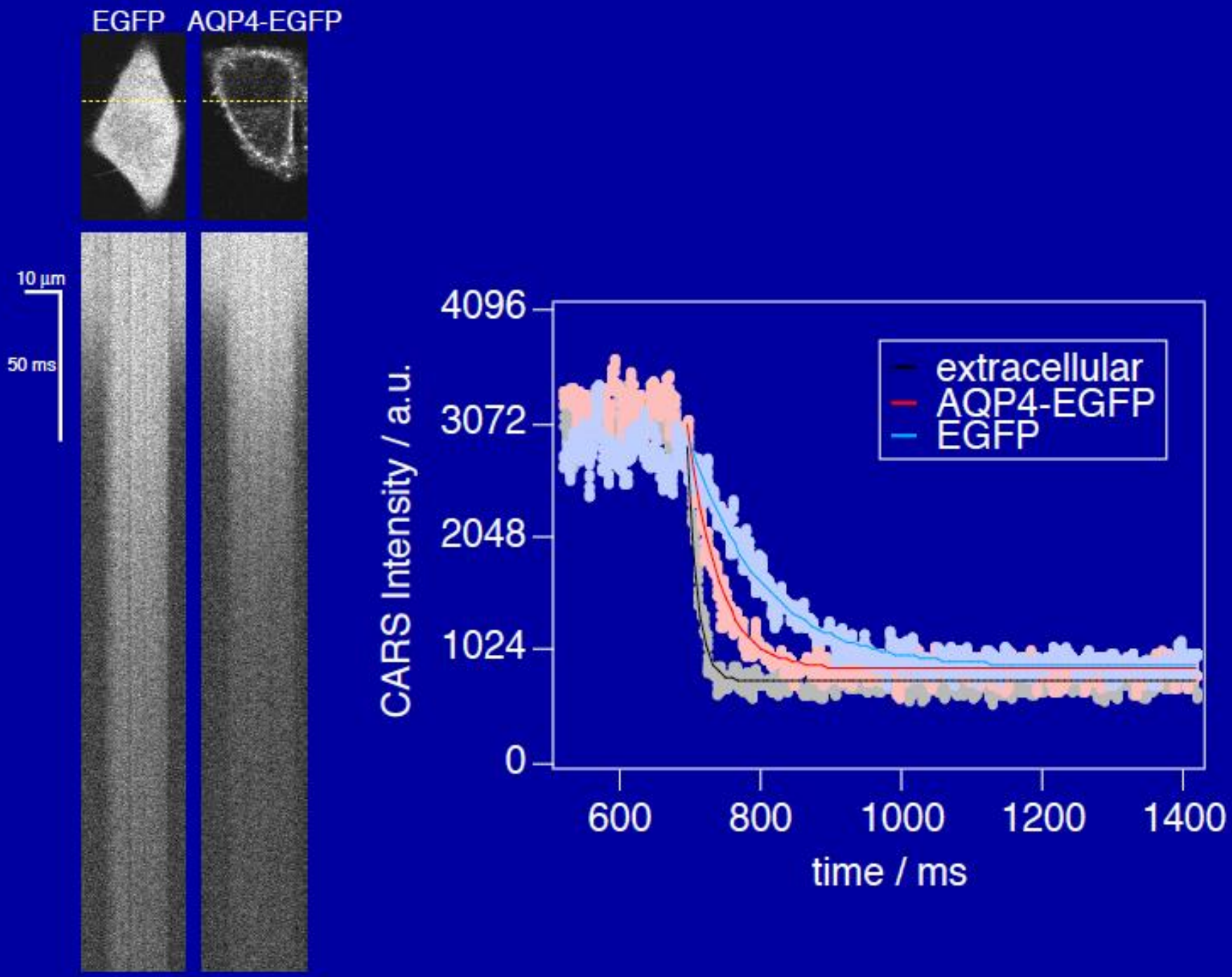
Experimental procedure for flushing isotonic D_2O/HBSS

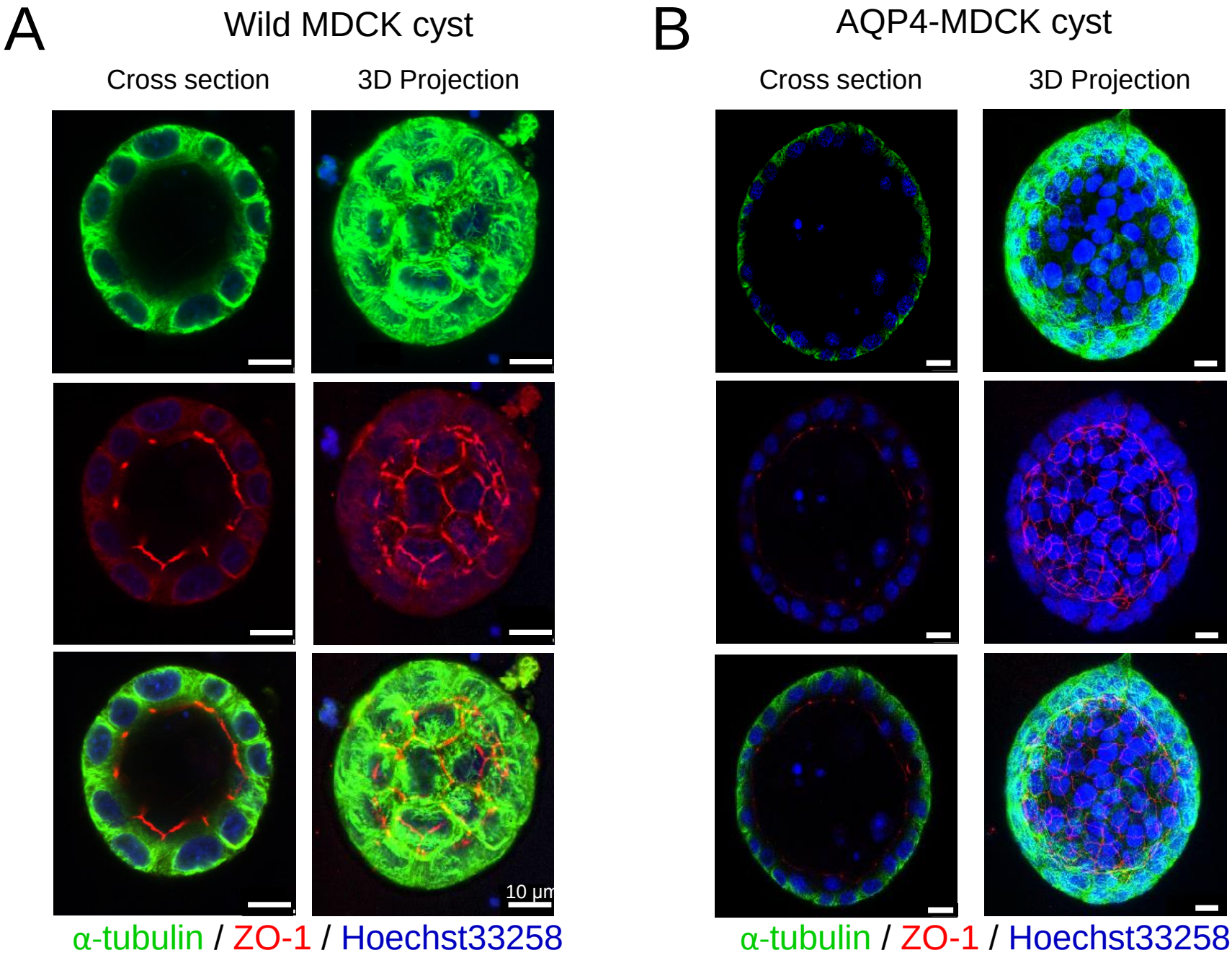


Frame by frame pictures of H_2O efflux from single cell



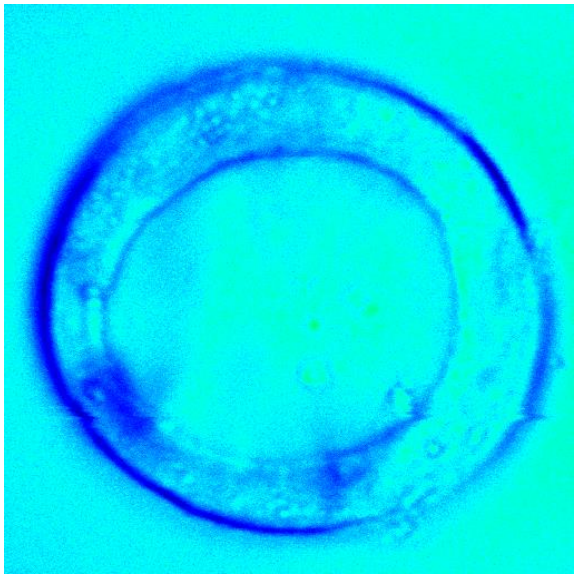
Ibata, *et al*, 2011)


EGFP
AQP4-EGFP
10 µm
50 ms
4096
3072
2048
1024
0
CARS Intensity / a.u.
extracellular
AQP4-EGFP
EGFP
600
800
1000
1200
1400
time / ms


A
Wild MDCK cyst
Cross section
3D Projection
10 µm
α-tubulin / ZO-1 / Hoechst33258
B
AQP4-MDCK cyst
Cross section
3D Projection
α-tubulin / ZO-1 / Hoechst33258

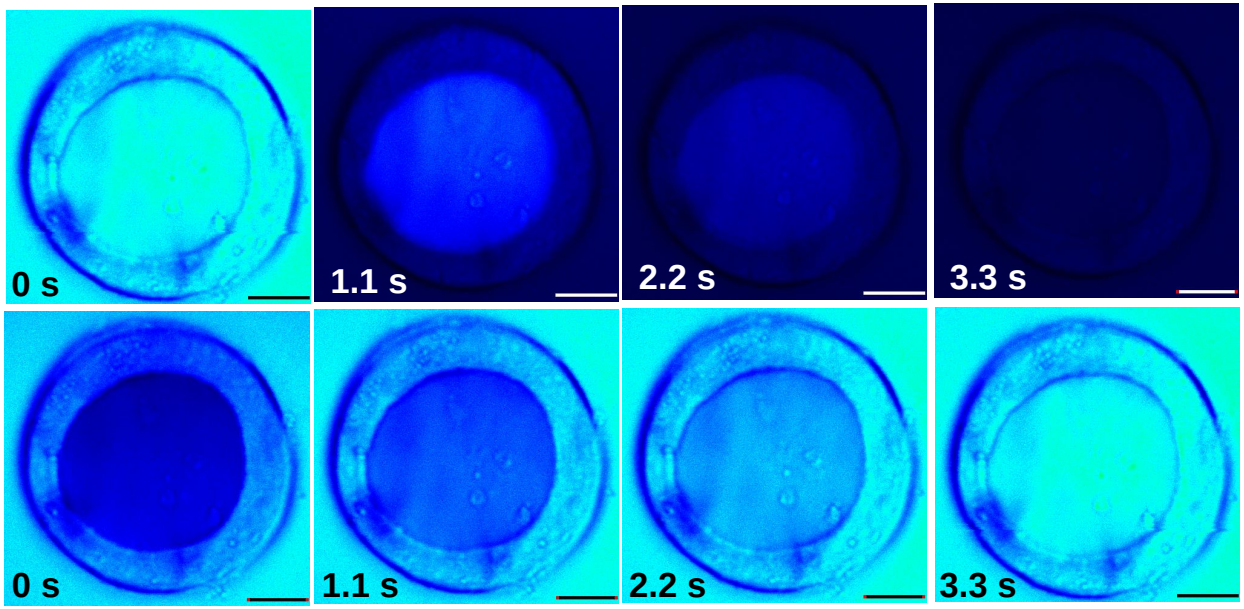
H_2O/D_2O Exchange Experiment

WT-MDCK cyst



10 μm

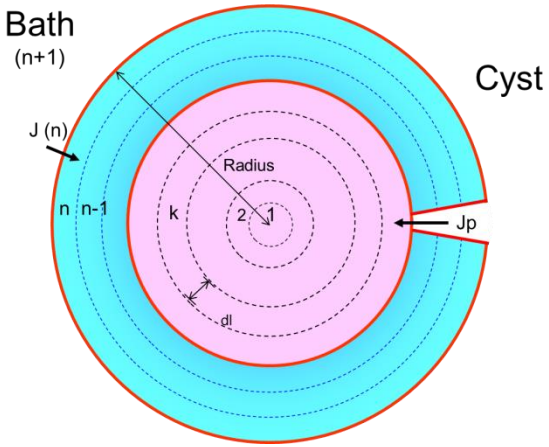
X-Y scan mode



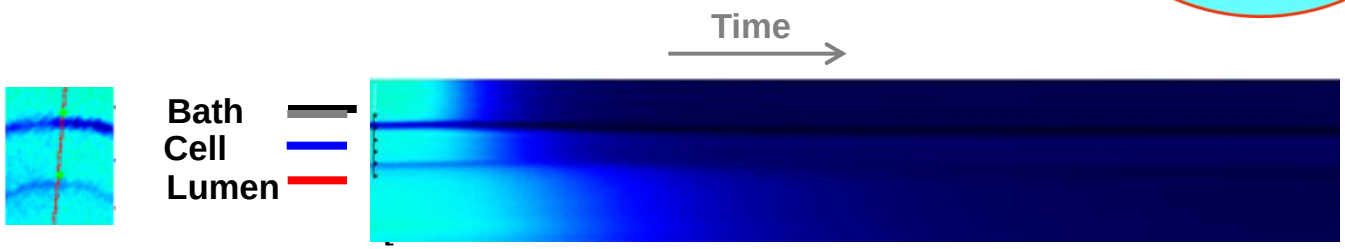
（Yu *et al. Sci. Rep*. 2013）

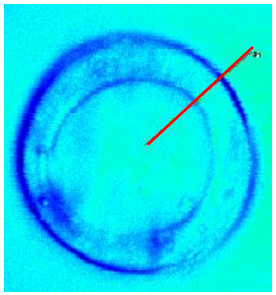
H_2O/D_2O exchange experiment

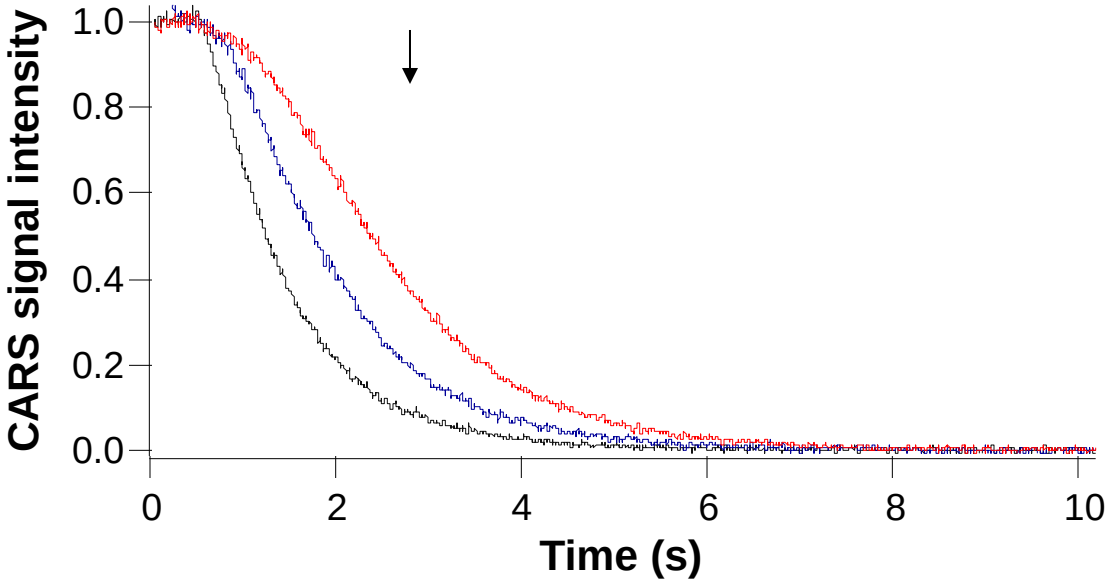
Multi-shelled three compartment model



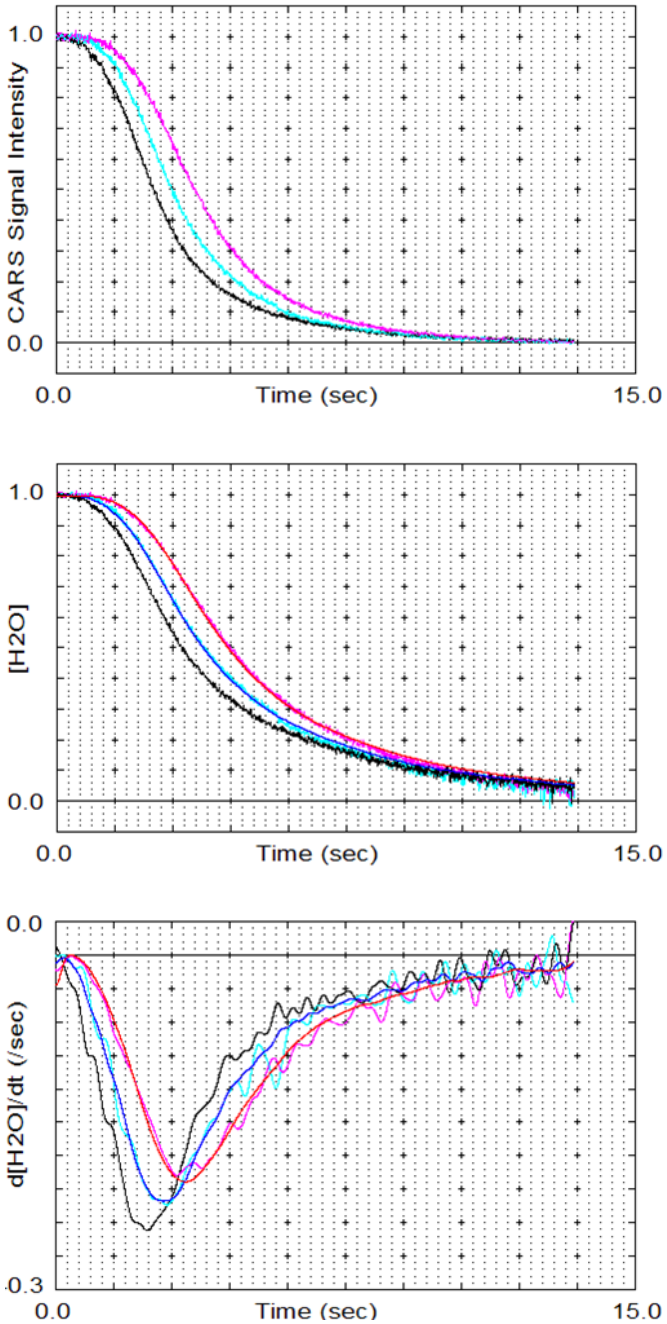
Line scan mode

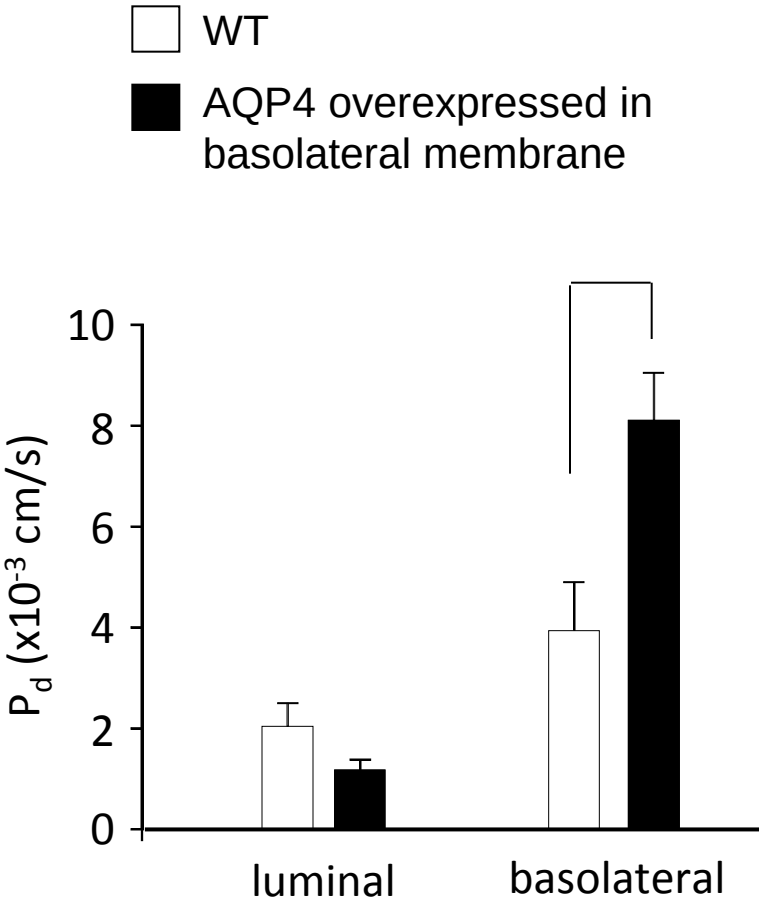






AQP4 overexpression increased water permeability in basolateral membrane



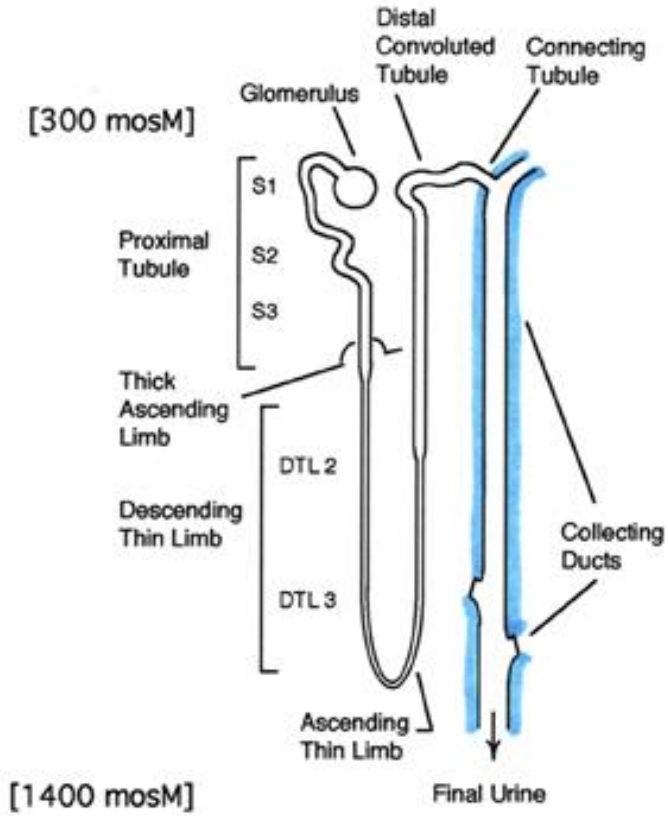


（Yu *et al. Sci. Rep*. 2013）

AQP2—A regulated water channel

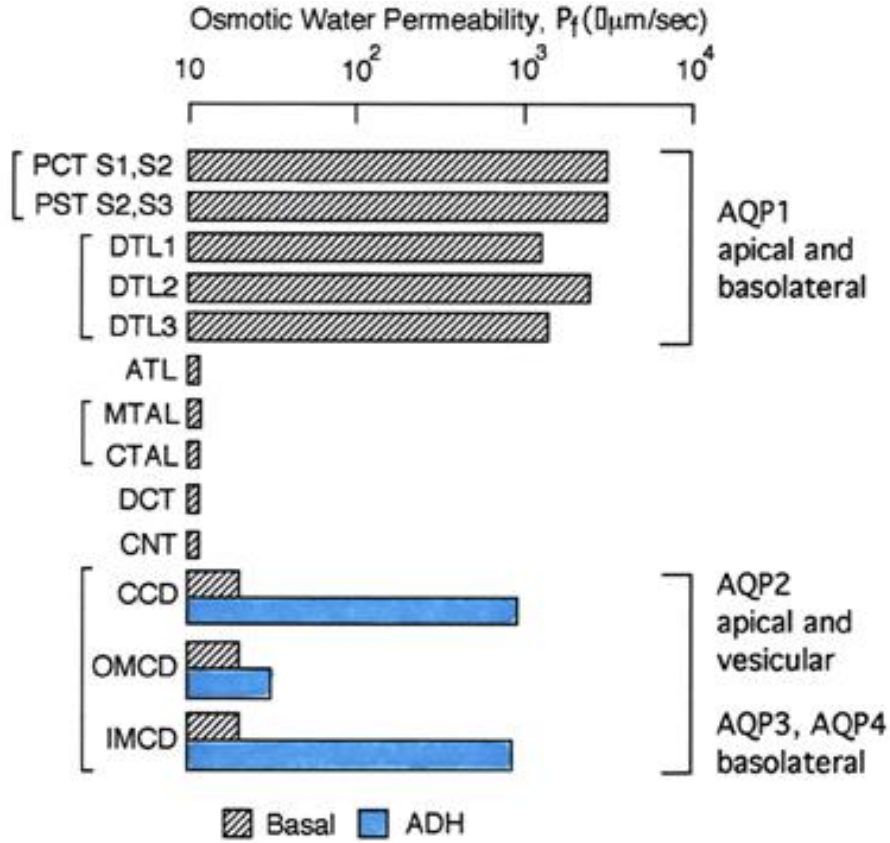
cDNA cloned by homology

(Fushimi *et al., Nature,* 1993)



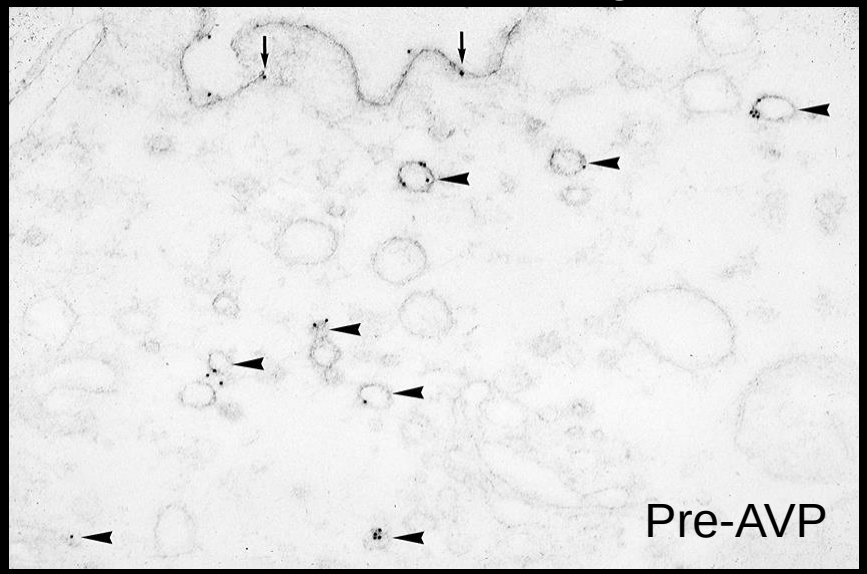
AQP2 localization in kidney

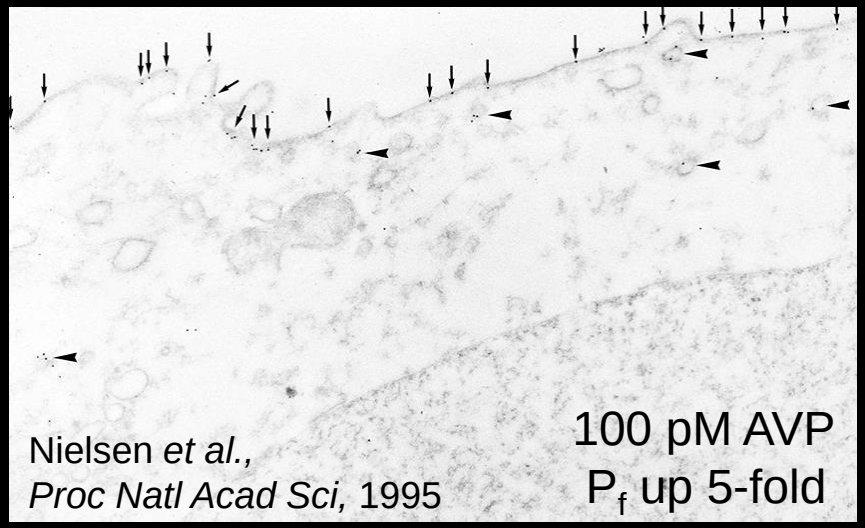
(Nielsen *et al., Proc Natl Acad Sci,* 1993)



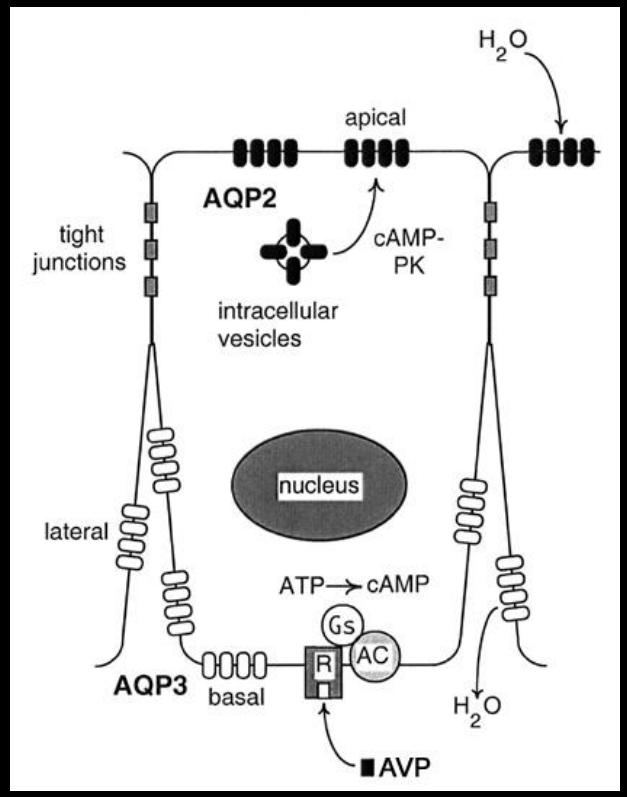
AQP2—Acute regulation by AVP

Isolated renal collecting ducts





Nielsen *et al.*, *Proc Natl Acad Sci*, 1995



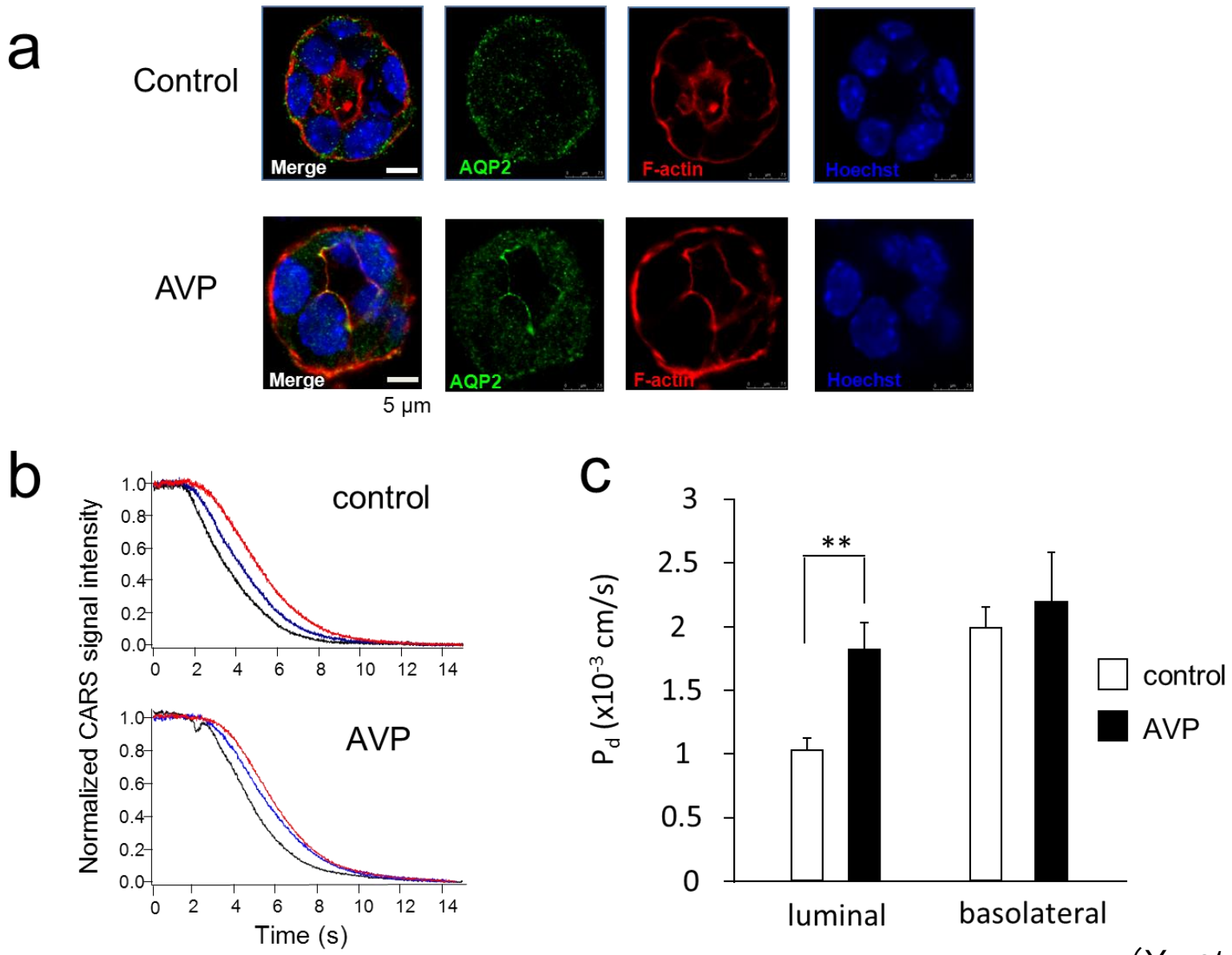
Inherited defects (rare)

- Nephrogenic DI (severe)

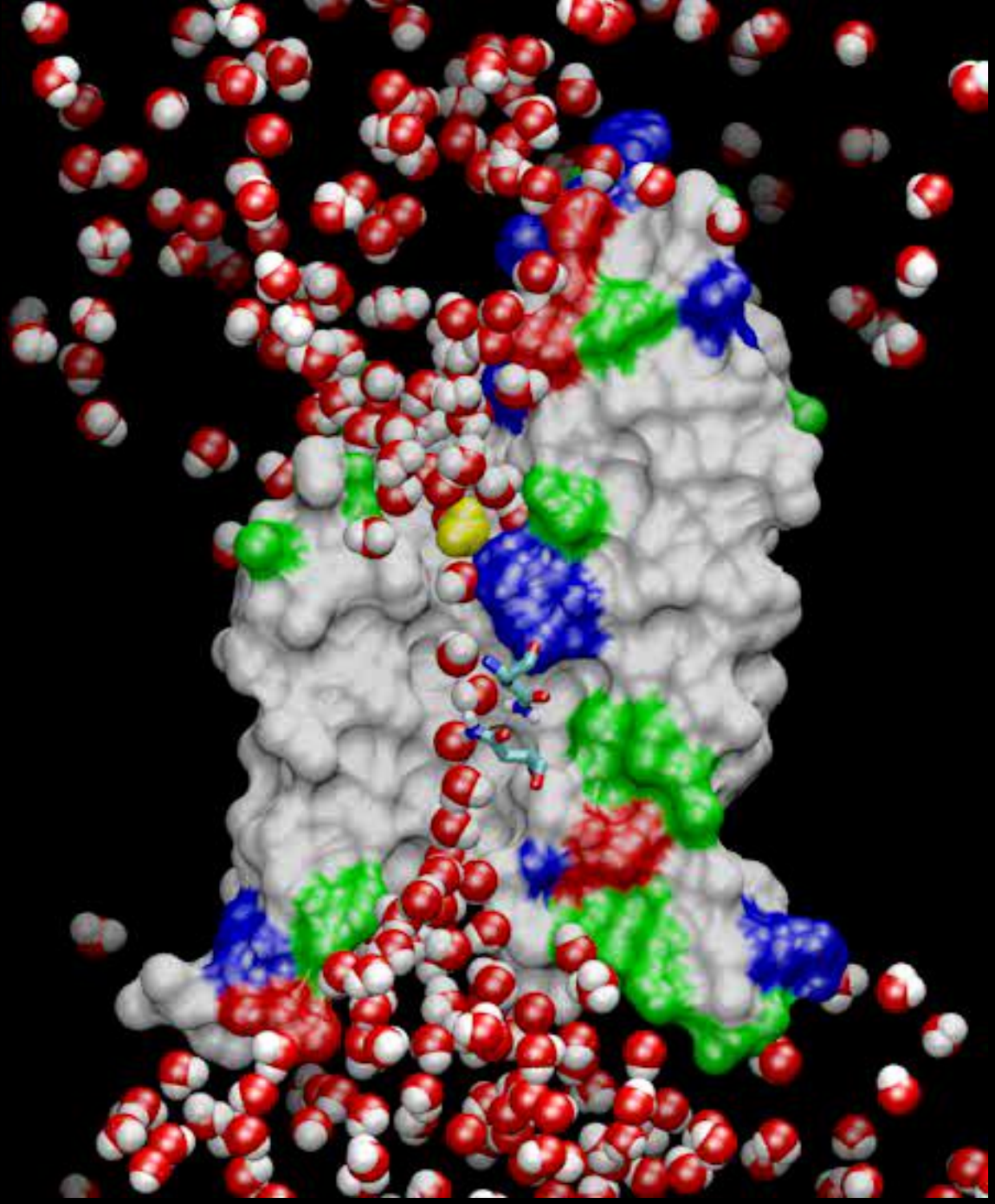
Acquired defects (very common)

- Overexpression—Fluid retention
- Underexpression—Enuresis

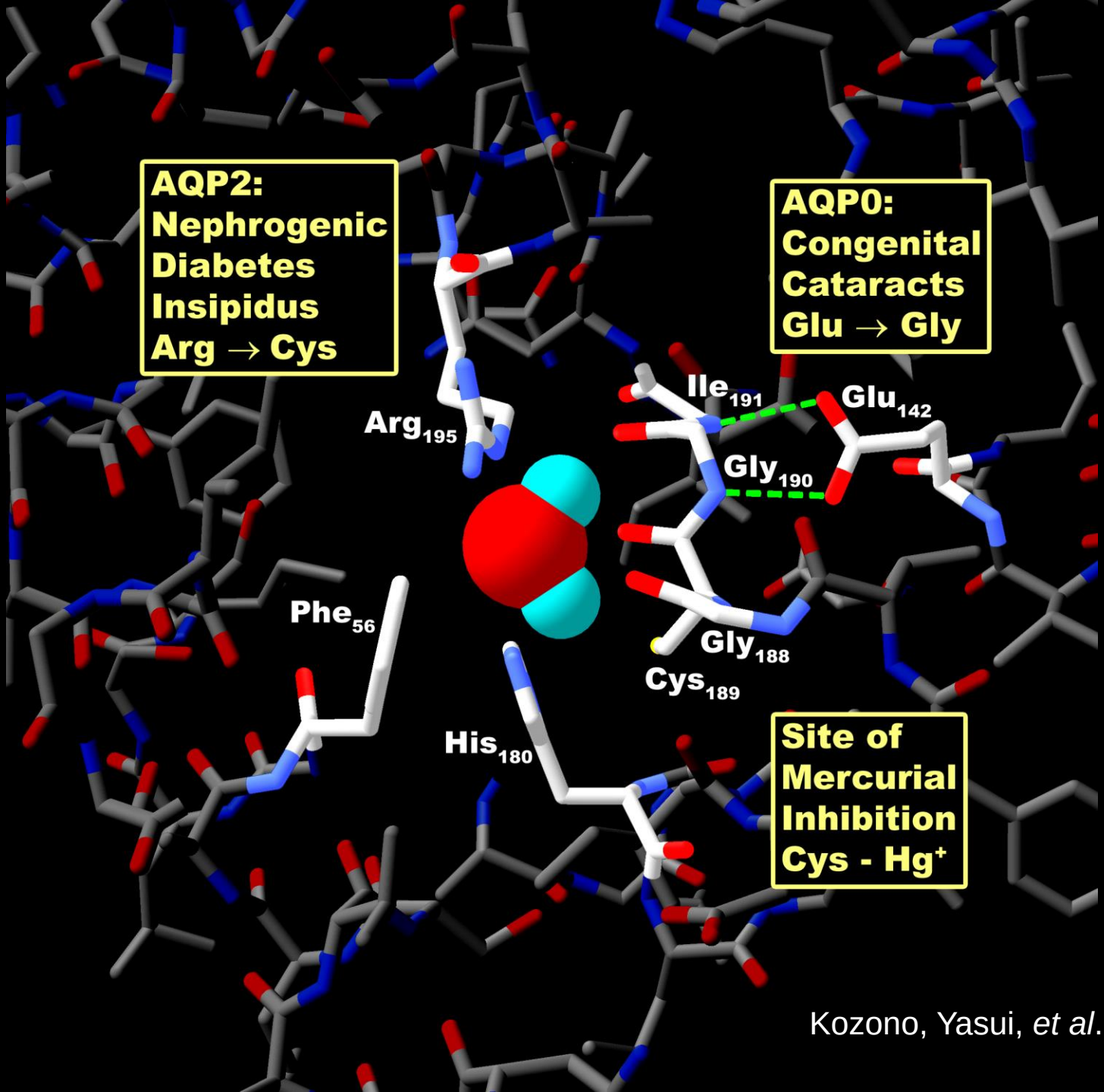
Vasopressin promoted AQP2 expression and increased water permeability in luminal membrane of M-1 cysts



（Yu *et al.* 2013）

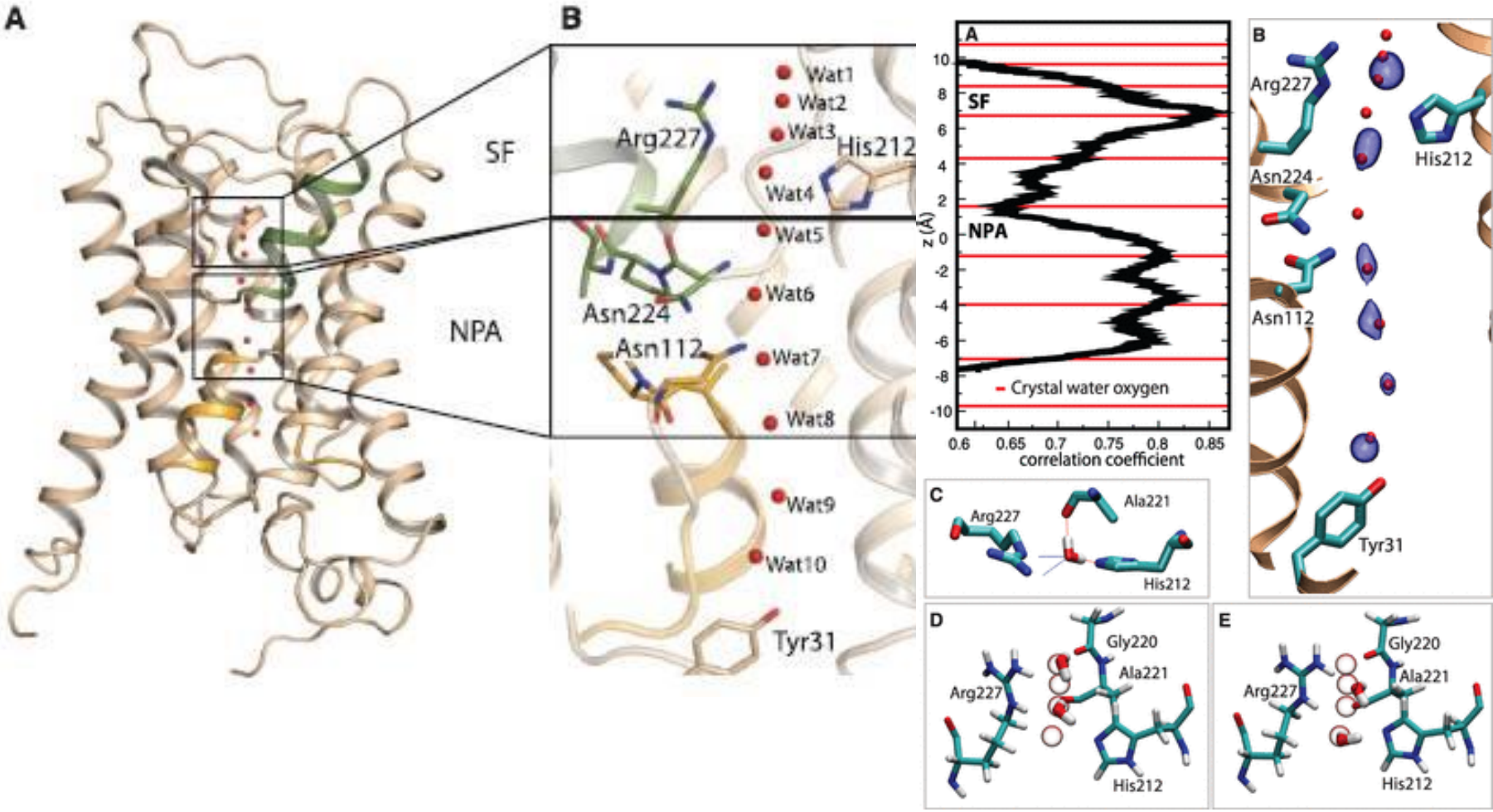


http://www.ks.uiuc.edu/Research/aquaporins/



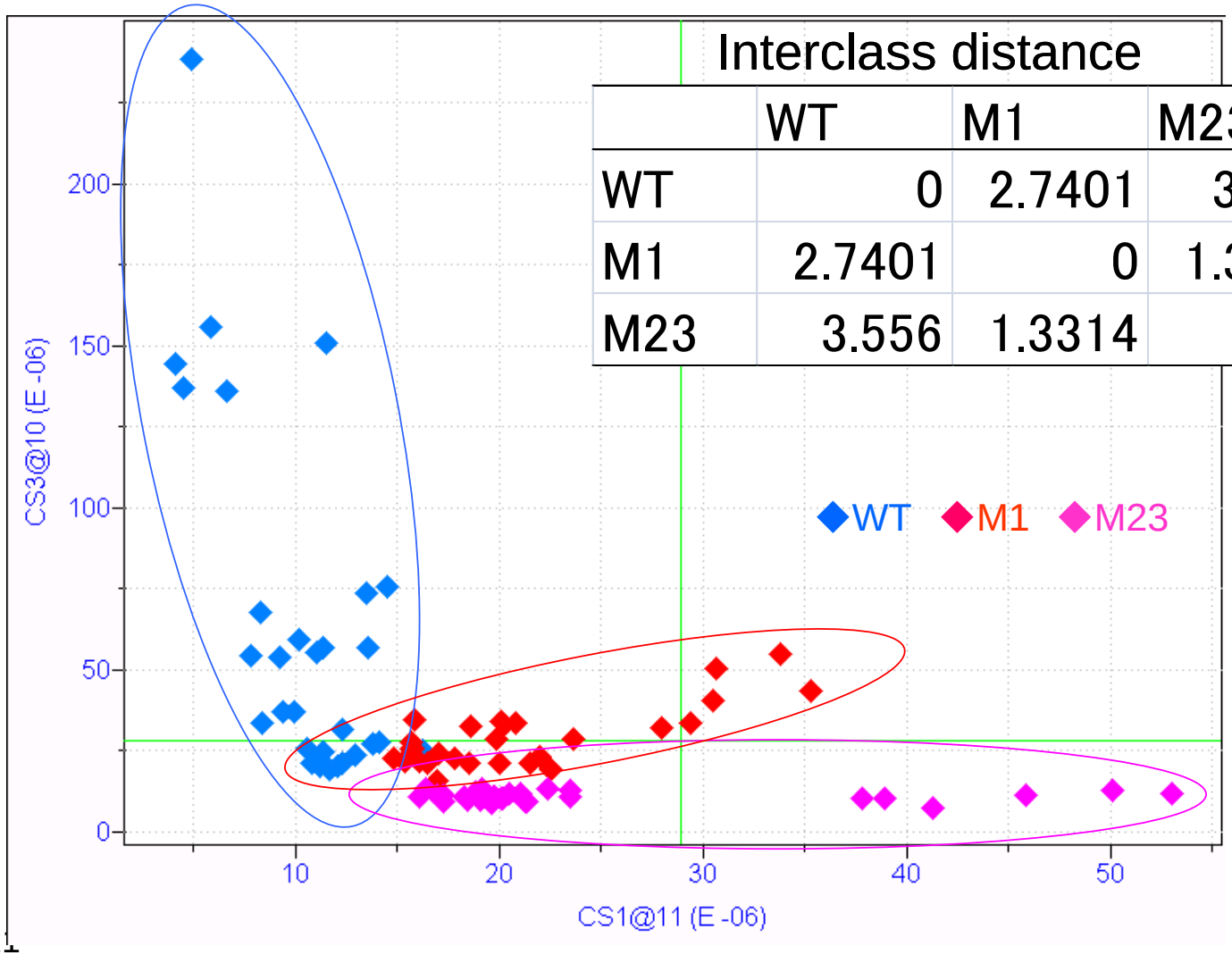
Kozono, Yasui, *et al*., 2002

Mechanisms of Selective filter for H_2O



Kosinka *et al., Sceince* 2013

SIMCA (1300-1600nm, transform : MSC)

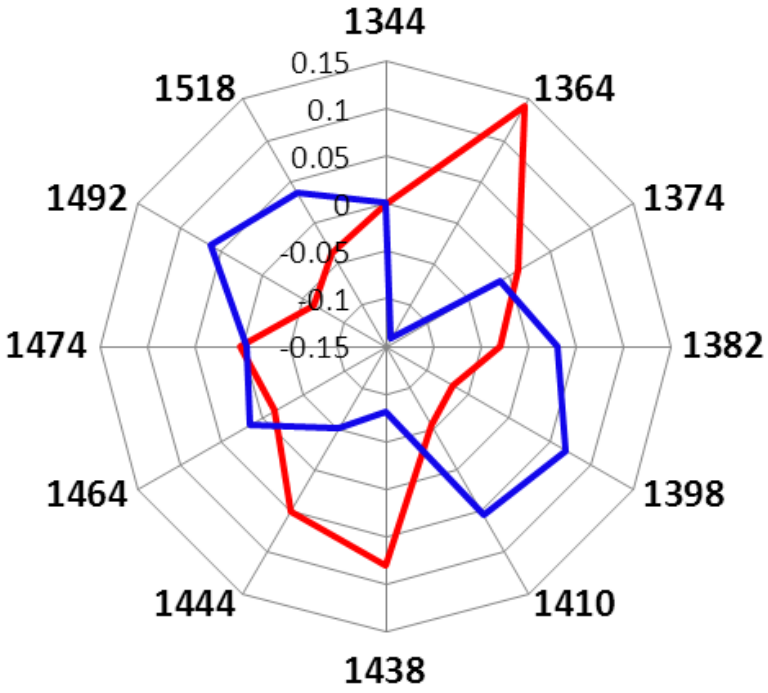


Interclass distance

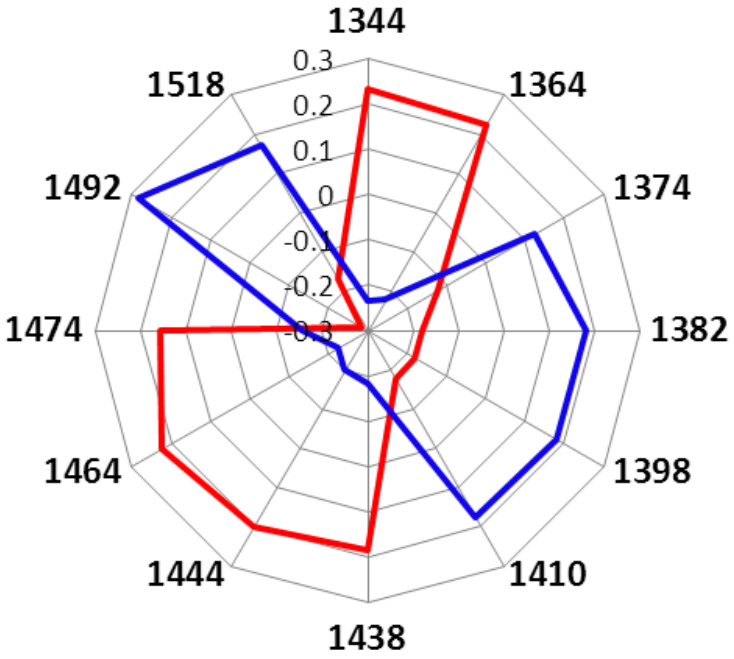
	WT	M1	M23
WT	0	2.7401	3.556
M1	2.7401	0	1.3314
M23	3.556	1.3314	0

Aquagram shows the difference in water structures with and without AQP

METABOLITES

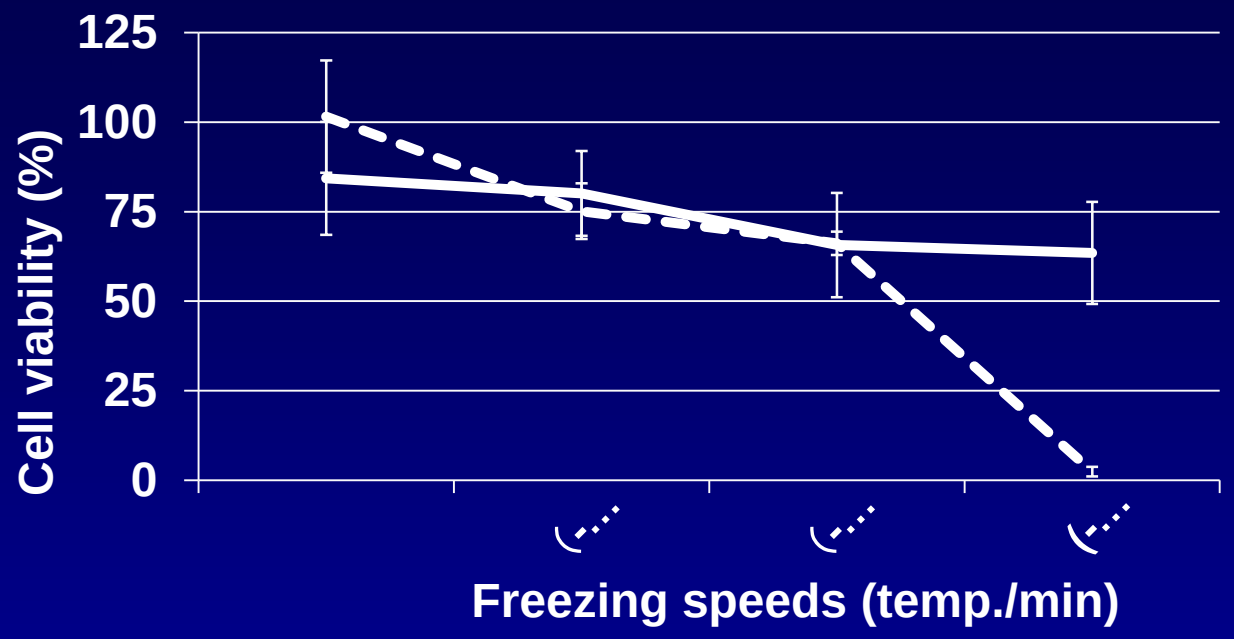


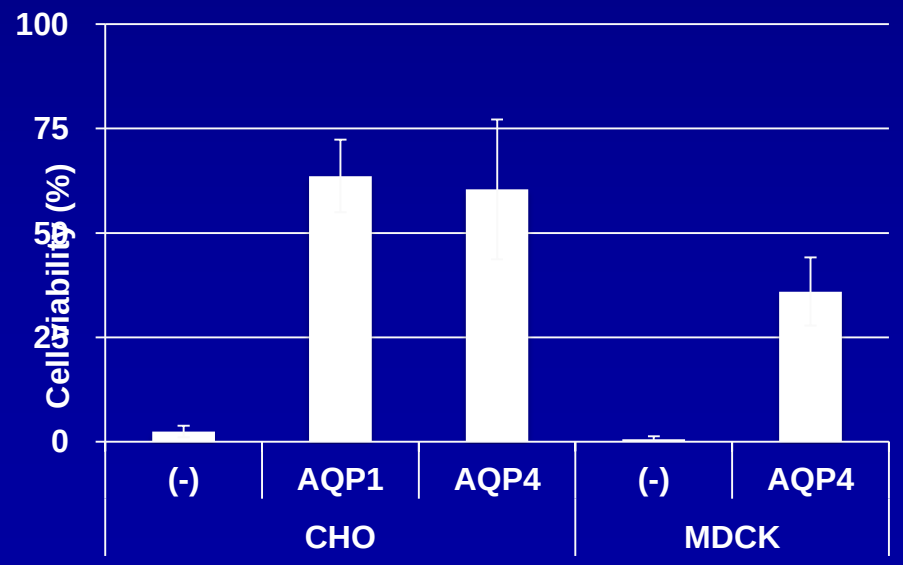
CELLS in HF-12



No AQP
AQP

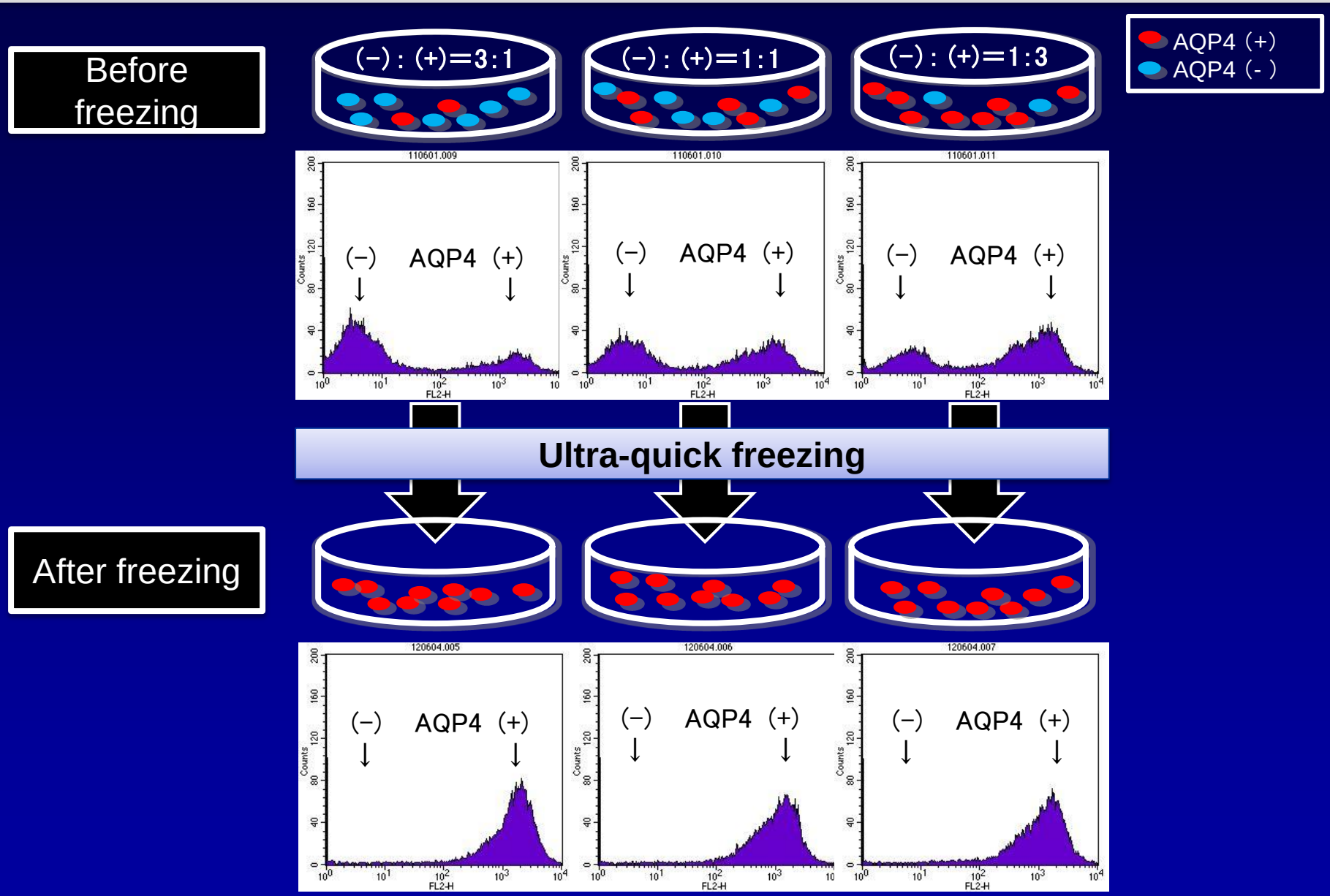
AQP expression increase cell survival rate after freezing





(unpublished)

Anti-freezing feature of AQP



Acknowledgements

Olympus
Shinichi Takimoto

Kobe Univ.
Prof.Roumiana Tsenkova

RIKEN BSI
Dr. Atsushi Miyawaki
Dr. Keiji Ibata