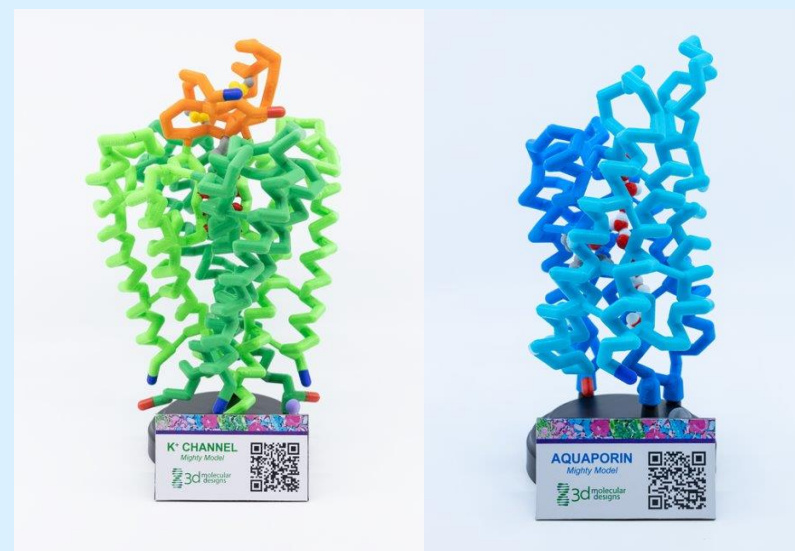




Introducing Mighty Models: Exploring the Molecular Basis of Heavy Metal Poisoning





Presenters:

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Workshop Goals

- Apply data from a case study to explain how water moves across the cell membrane to maintain homeostasis.
- Explore how physical and digital models foster an understanding of how channel proteins work.
- Encourage students to apply a wonder, explore, and explain mindset to their learning.

Possible student questions

- How does water in and out of the cell?
- What factors control how water passes through a membrane?
- Why do we need water channels?
- Why do we have so many different types of channels?

A young mother of two small children visits her doctor with complaints of

- trouble sleeping (insomnia)
- leg pain
- muscle weakness (paresis)
- tingling and numbness in her hands and feet (paresthesia and neuropathy)

Since this was not her first visit associated with these symptoms, the doctor ordered a urine and blood test

- *What conditions might cause the symptoms she was experiencing?*
- *What additional information do you need?*



The Results for the Urine Test come back quickly

Urine Test

- Appearance: Yellow
- pH: 6.9
- Specific Gravity: 1.010
- Protein: 100 mg/deciliter
- Glucose: 105 mg/dl
- RBCs: 3
- WBCs: 3
- Mercury: 23 mcg/L



*Interpret these results. Are the results within an acceptable range?
At first glance, does anything seem out of the ordinary?*



Over the next year the woman continued to experience the same worsening symptoms. She was also losing her eyesight. A new urine test was ordered.

Urine Test

Appearance: Dark Yellow
pH: 6.7
Specific Gravity: 1.050
Protein: 102 mg/deciliter
Glucose: 101 mg/dl
RBCs: 2
WBCs: 5
Mercury: 46.6 mcg/L

Acceptable Urine Test Results

Appearance: Clear to light yellow
pH: 4.5 to 7.2
Specific Gravity: 1.005-1.025
Protein: less than 150 mg/deciliter
Glucose: less than 130 mg/dl
RBCs: 0 to 3 RBCs
WBCs: less than 2-5 WBCs/hpf
Mercury: 5 mcg/L

*Interpret these results. Are the results within an acceptable range?
At first glance, does anything seem out of the ordinary?*

Home visit two to look for sources of mercury

The State Pollution Control Agency visited the home a year later and found the levels of Mercury in the home to have risen significantly.

Normal background Mercury Level= 200 ng/m^3



Home visit two to look for sources of mercury

Location	Level	How much higher?
Children's Bedroom	400 ng/m ³	
Towels	600 ng/m ³	
Washing machine	300 ng/m ³	

What might be causing the elevated values?



Activity Slide Deck Design

Urine Test

Over the next year the women continued to experience the same varying symptoms. Her neurologist looking for myelitis. A neurosurgeon not recommended.

Urine Test

Appearance: Dark Yellow

pH: 6.7

Specific Gravity: 1.050

Protein: 120 mg/decade

Bilirubin: 120 mg/dL

SGOT: 2

SGPT: 5

Mercury: 300 ng/g

Additional data needed. Do the results indicate a possible cause? If the patient, does anything come out of the analysis?

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Normal background Mercury Level: 200 ng/g

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Home visit two to look for sources of mercury

What might be causing the elevated levels?

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Skin whitening cremes

Whitening Cream	Amount of Mercury
Product 1	4,500 ppm (Open partially used bottle)
Product 2	7,440 ppm (Open partially used bottle)
Product 3	11,000 ppm (Open partially used bottle)
Product 4	18,000 ppm (Open partially used bottle)

How much mercury is in the cream? Where is the mercury going?

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Inorganic mercury in the cream is absorbed by the skin

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Mercury in the cream can become vapor and is inhaled.

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After it is inhaled, where does it go?

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Teacher Notes:

There are 13 different types of aquaporin. We are using Aquaporin-1 (AQP1) for our model. Most aquaporins are mercury sensitive.

Introductory biology students do not necessarily need to know that there are multiple types of aquaporin, but you know your students best. In the next slide, using a rat model, aquaporin-5 (AQP5) is found in the alveoli. The membrane of the capillary is studied with AQP1. A loose distribution and cellular localization patterns of proteins are dependent on species. Aquaporin water channels are involved in places that need high water permeability for fluid transport.

If you wish to know more about the variety of aquaporins, refer to the additional resources at the end of this slide deck.

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After it is inhaled, where does it go?

20

Teacher Notes:

Structure of Aquaporin

"A single polypeptide chain spans the membrane six times. The N- and C-terminal ends are both in the cell interior and there are three extracellular loops (A, C, and E) as well as two intracellular loops (B and D). The two halves of the dimeric subunit are arranged in a head-to-head orientation but are oriented oppositely in the membrane so that corresponding regions are found on opposite sides of the membrane. The E and G loops both contain the Asp-Pro-Ala (DPA) sequence that is characteristic of the major intrinsic protein of the lens (PI-LP) family of proteins, of which the AQPs are members." (Knepper, 1994)

Additional resource for teacher:

Knepper, M.J., FRAS. The aquaporin family of molecular water channels. LNCB, pp. 625-635.

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What is aquaporin-1?

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How does aquaporin-1 help maintain water homeostasis?

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Teacher Notes

For more information on aquaporin's structure check out these resources from the Center for BiMolecular Modeling:

[An Introduction to Aquaporin - YouTube](#)

[The Structure of Aquaporin - YouTube](#)

[Details of the Aquaporin Selectivity Pore - YouTube](#)

[Aquaporins in the Lung - BMC \(nih.gov\)](#)

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Where else is aquaporin-1 found?

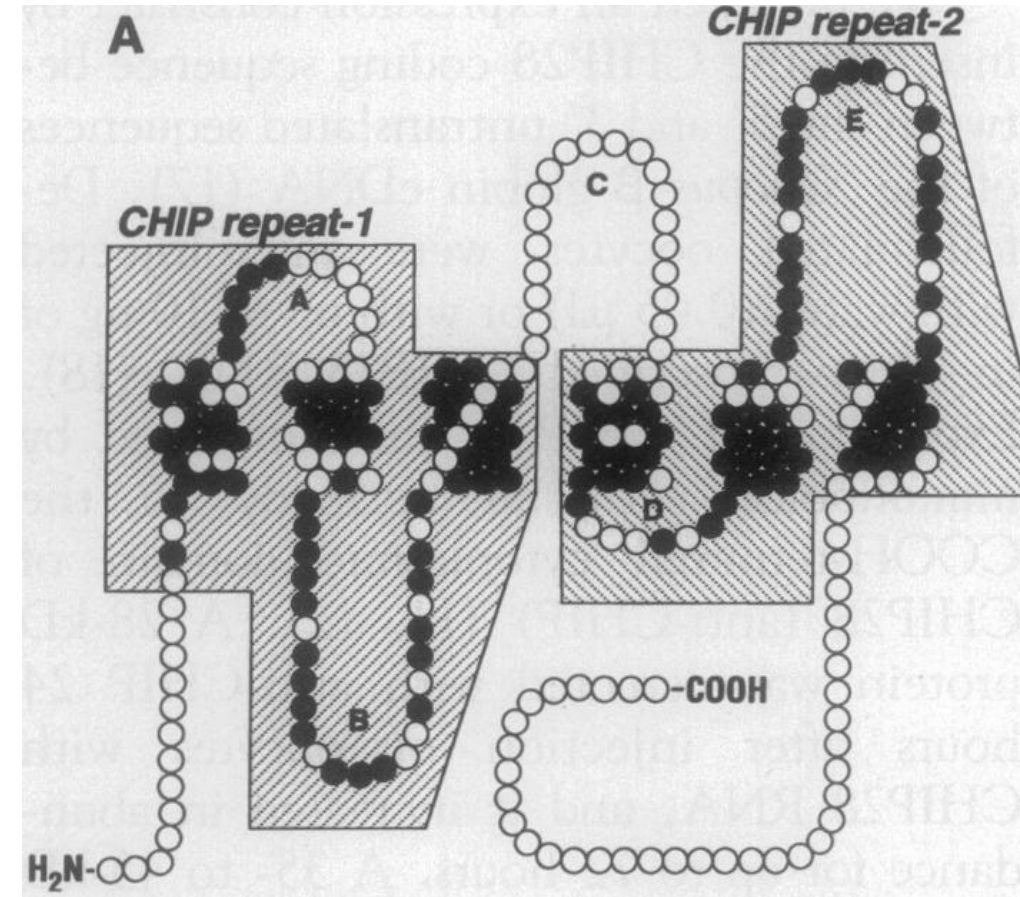
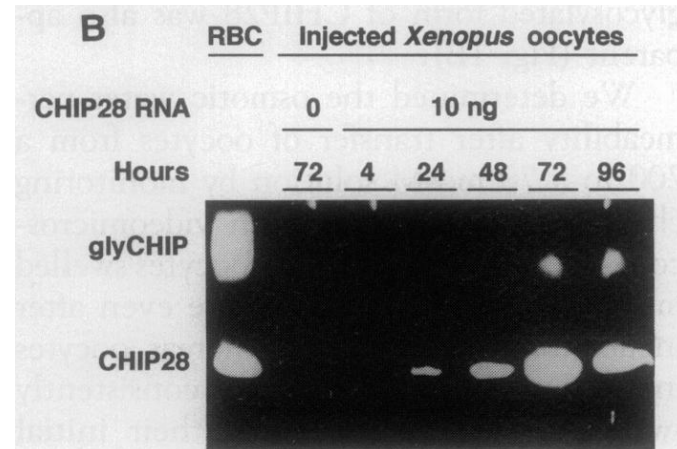
25

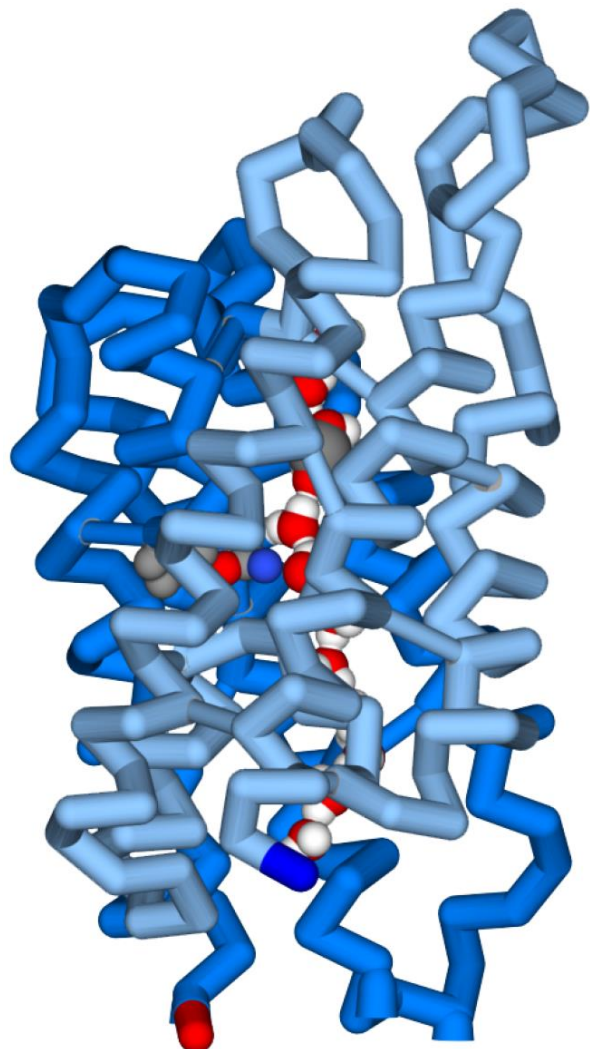
Stories Make Students Care

Appearance of Water Channels in *Xenopus* Oocytes Expressing Red Cell CHIP28 Protein

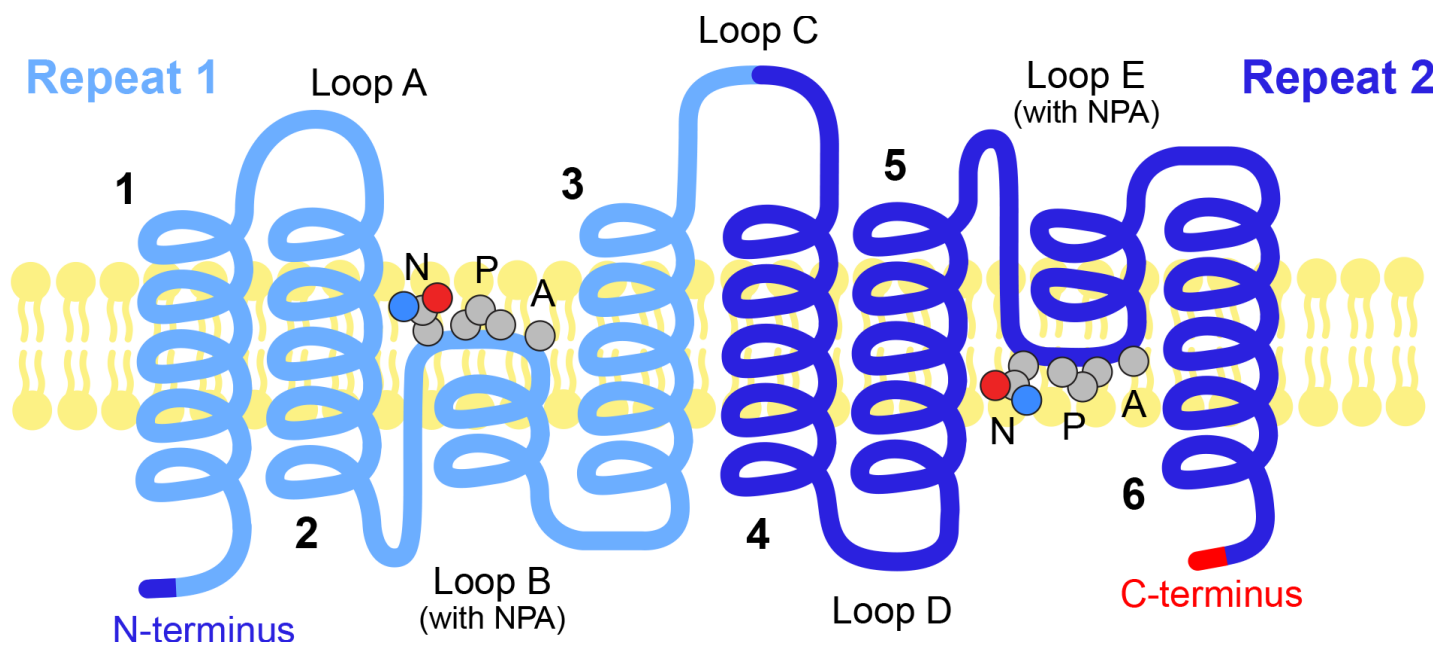
Gregory M. Preston, Tiziana Piazza Carroll,
William B. Guggino, **Peter Agre***

SCIENCE * VOL. 256 * 17 APRIL 1992

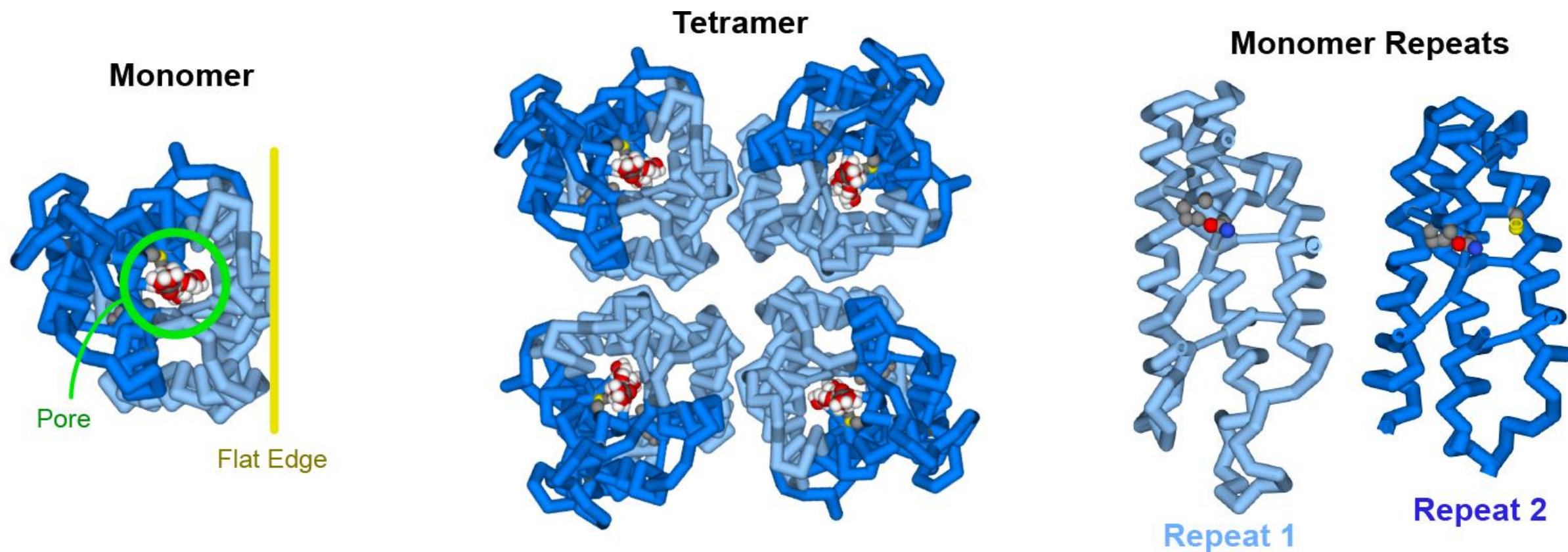




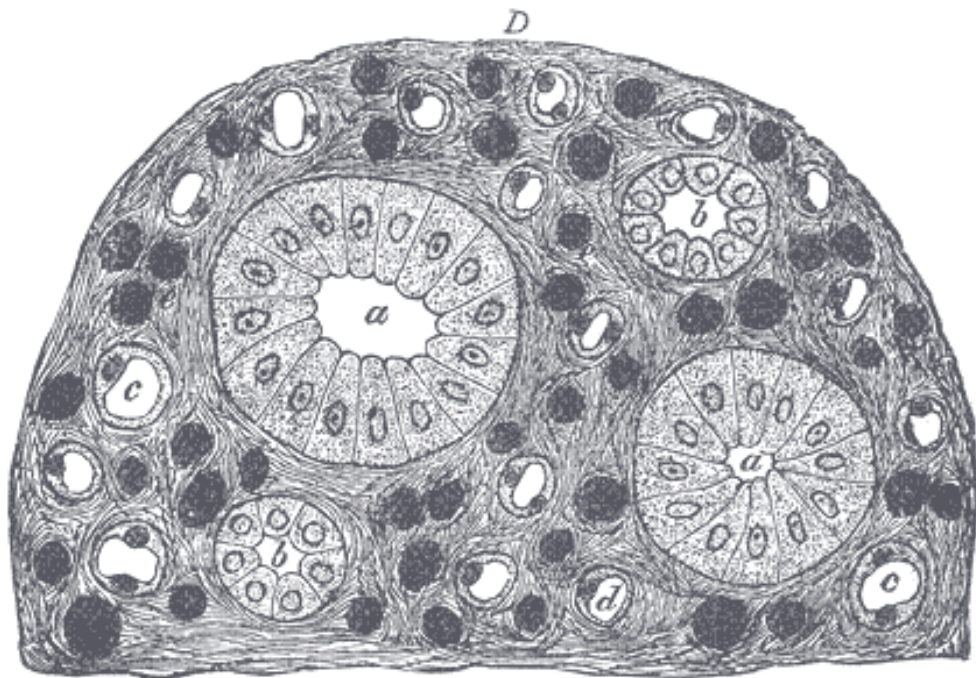
What is Aquaporin?



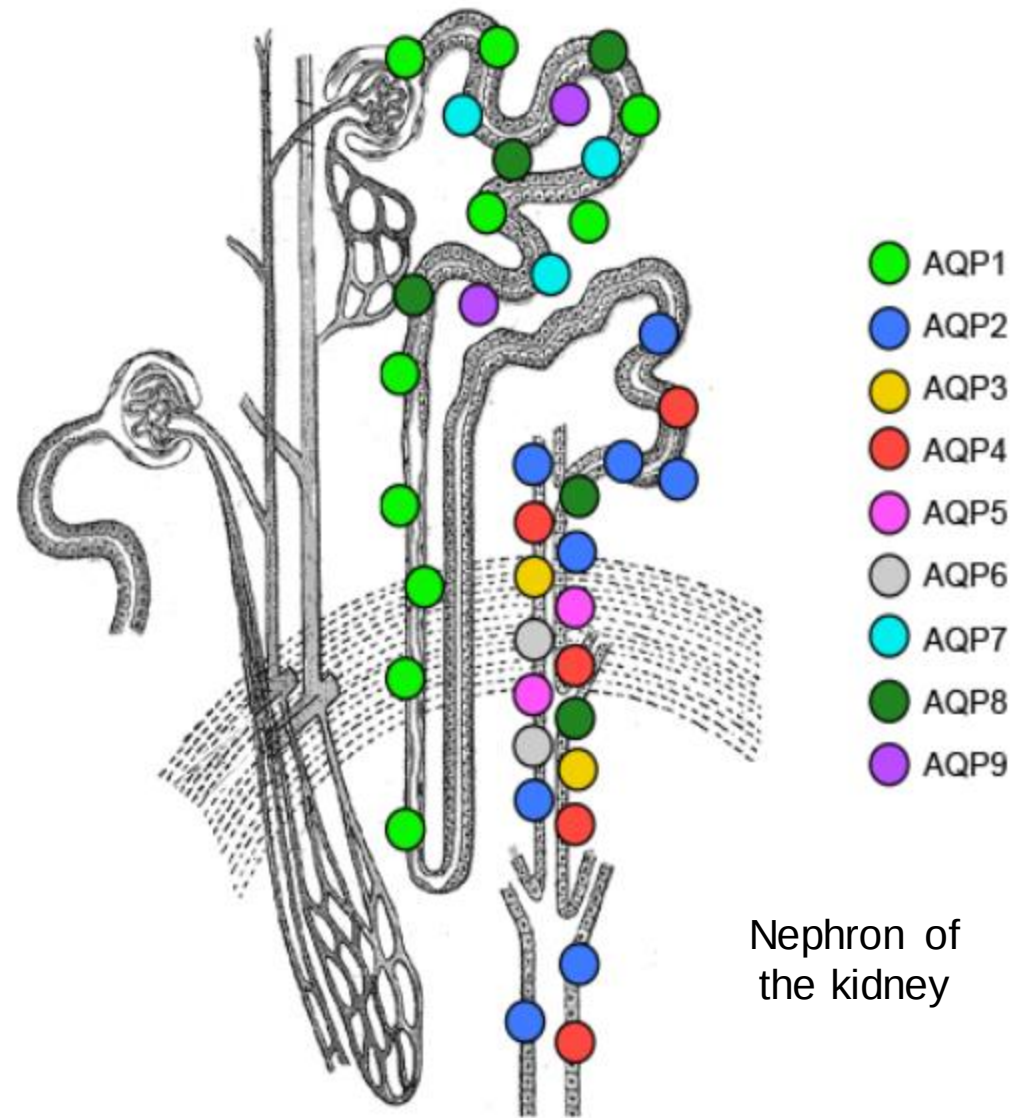
How does aquaporin-1 help maintain water homeostasis?



Where else is aquaporin-1 found?



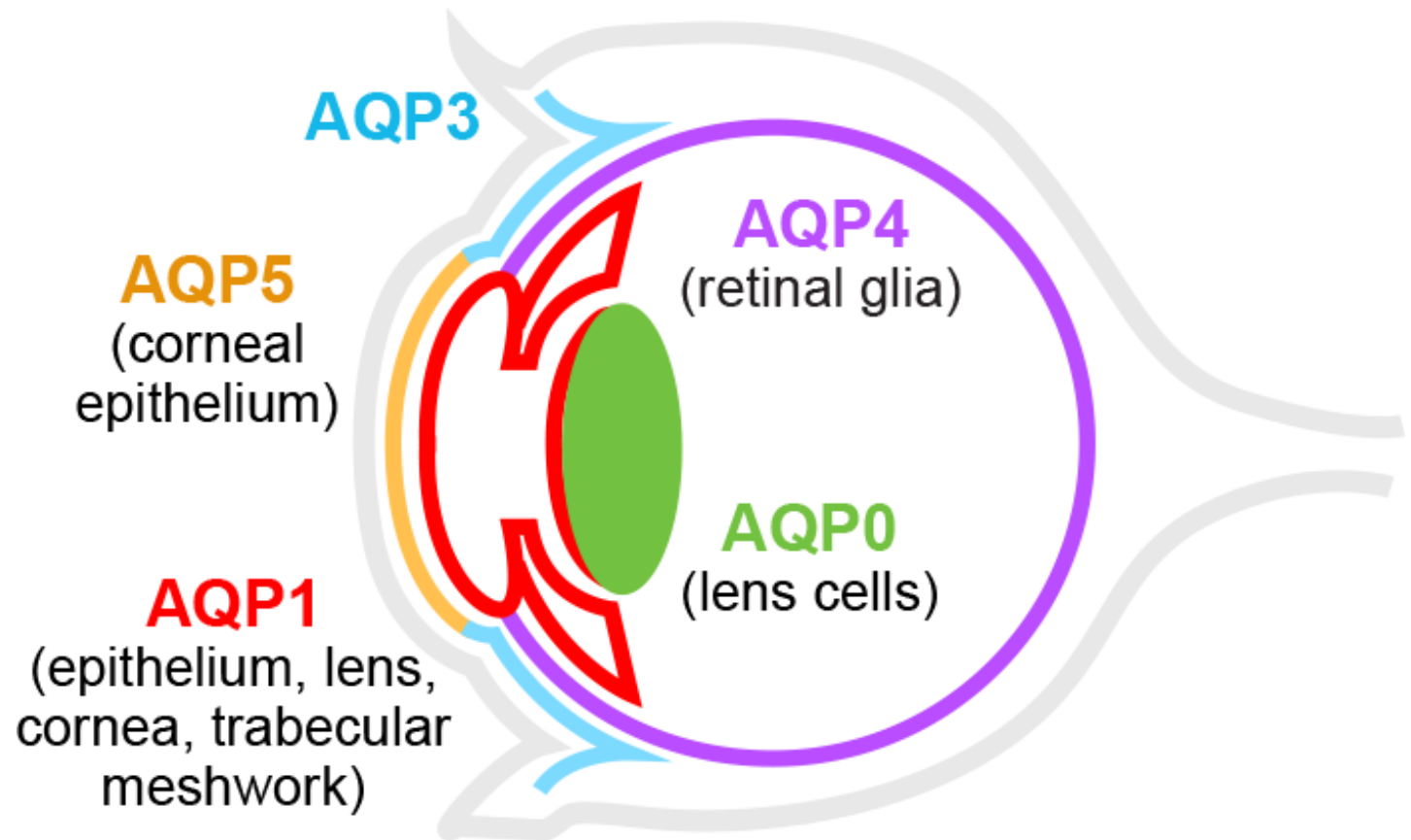
Cuboidal epithelium in the collecting ducts of the kidney



Nephron of the kidney

*Could damage to aquaporin
be responsible for the woman
losing her eyesight?*

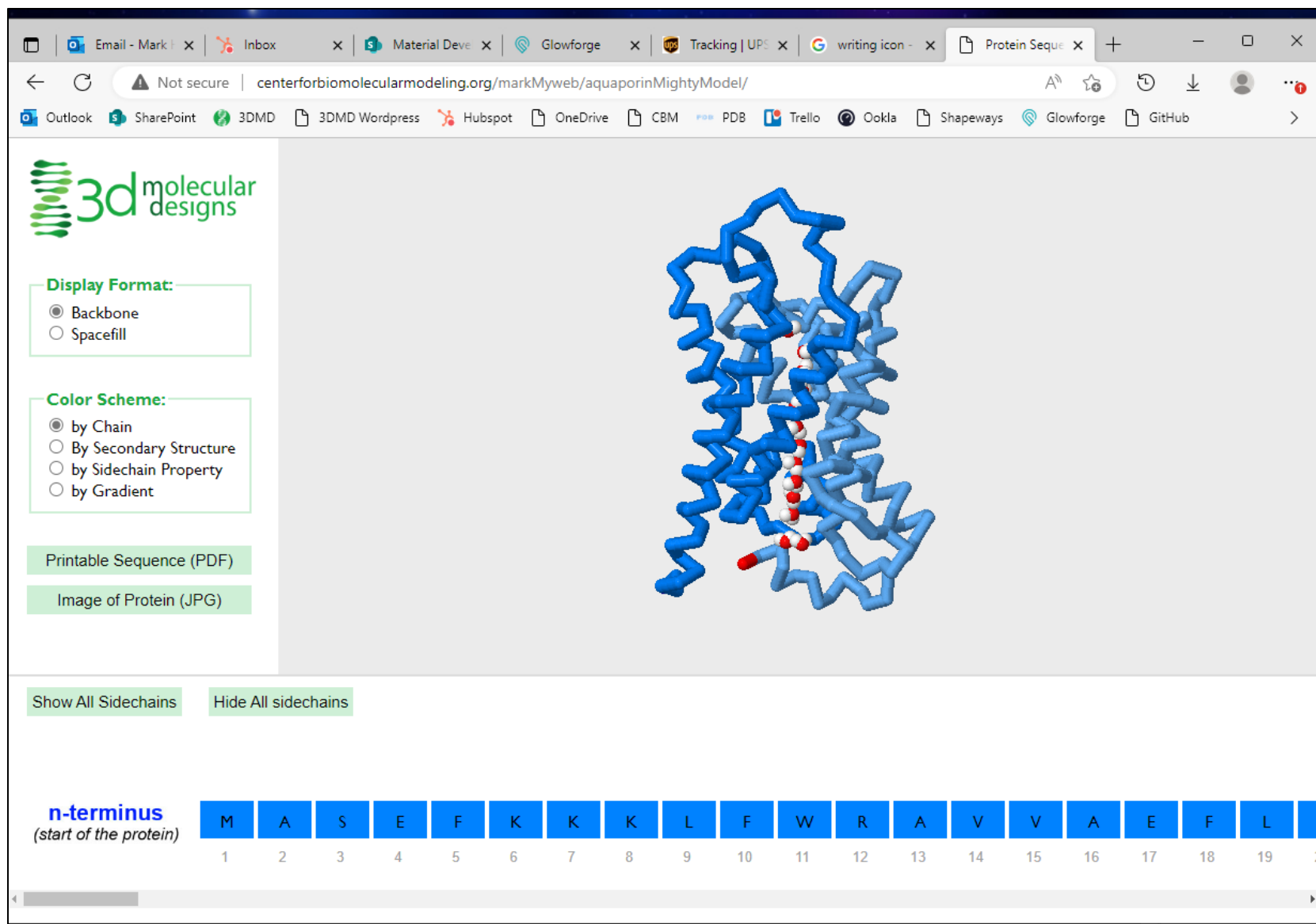
If so, which one?



Potassium channels

Sodium Channels

Protein Exploratorium



The screenshot shows a web browser window with the URL centerforbiomolecularmodeling.org/markMyweb/aquaporinMightyModel/. The page features the 3d molecular designs logo and a 3D ribbon model of a protein structure (Aquaporin) in blue, with a red and white stick model of a water molecule passing through the channel. On the left, there are controls for 'Display Format' (Backbone selected, Spacefill unselected) and 'Color Scheme' (by Chain selected, By Secondary Structure, by Sidechain Property, and by Gradient unselected). Below these are buttons for 'Printable Sequence (PDF)' and 'Image of Protein (JPG)'. At the bottom, there are buttons for 'Show All Sidechains' and 'Hide All sidechains', and a sequence viewer showing the n-terminus (start of the protein) with residues M, A, S, E, F, K, K, K, L, F, W, R, A, V, V, A, E, F, L.

Display Format:

- ☒ Backbone
- ☐ Spacefill

Color Scheme:

- ☒ by Chain
- ☐ By Secondary Structure
- ☐ by Sidechain Property
- ☐ by Gradient

Printable Sequence (PDF)

Image of Protein (JPG)

Show All Sidechains Hide All sidechains

n-terminus
(start of the protein)

M	A	S	E	F	K	K	K	L	F	W	R	A	V	V	A	E	F	L
1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19



NGSS Connections

Science and Engineering Practices	Cross Cutting Concepts	Disciplinary Core Ideas
Scientific Investigations Use a Variety of Methods	Stability and Change	HS-LS1-3
Developing and Using Models	Systems and System Models	HS-LS1-2
Constructing Explanations and Designing		

We value your opinion!
Let us know what you
think.

Scan the QR
Code and
complete this
short survey.



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