

Starting a career in start-ups (during a global pandemic)

Laura Ensign, Ph.D.

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Advanced Delivery Science



Starting a career in start-ups (pandemic edition)

- Freya Biosciences, March 2020



- NovusBio, LLC, March 2021

NOVUS

- Novus Vision Inc, July 2021

VISION

- Zephyrus Therapeutics, LLC, April 2022



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“Growing up” in the right environment

“Mucus-penetrating particle” technology

- Founded at JHU in 2009
- Joint patents filed 2011/2012
- IPO 2017
- First product approved 2018
- Second product approved 2020



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“Growing up” in the right environment



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“Growing up” in the right environment



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Learning a new skill set

- The key to doing anything new is to learn from people who know what they are doing (apprenticeship)
- In research, we naturally seek to collaborate with those who have complementary skillsets
- The best collaborations are based on trust and mutual respect of skillsets



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Many (non-research) competencies needed for successful start-ups

- Legal (formation documents, confidentiality agreements, consulting agreements, board agreements, partnerships, intellectual property, licensing, etc.)
- Fundraising
- Business development
- Administrative (taxes, accounting, ordering)
- Regulatory
- Clinical trial design
- Marketing/brand development



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Novus Vision mentors (and co-founders)



Justin Hanes, Ph.D.
Founder, Director, CEO

Founder of Kala Pharmaceuticals (Nasdaq: KALA), GrayBug Vision (Nasdaq: GRAY; former CEO & CSO), Neuraly (acquired), Theraly Fibrosis (acquired), Orpheris, and Ashvattha Therapeutics.

Co-inventor of OcuGel



Jerry Cagle, Ph.D.
Founder, President
Chief Operating Officer

Long time Global Head of Alcon Research and Development.

Experienced in developing topical and intraocular products across broad therapeutic classes.

Brought over 300 ophthalmic products to market



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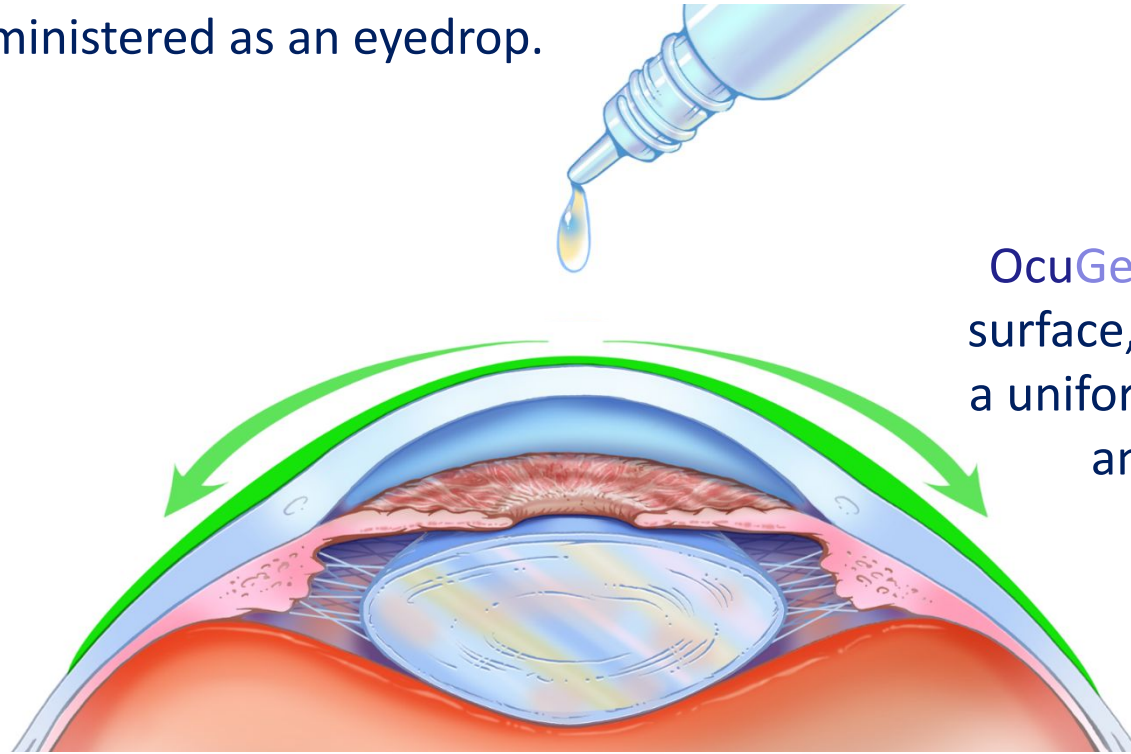
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The technology: OcuGel

OcuGel can be paired with a wide variety of drugs into water-based solutions that are easily administered as an eyedrop.



OcuGel spreads over the ocular surface, then subsequently forms a uniform thin gel that traps drug and slowly releases it.



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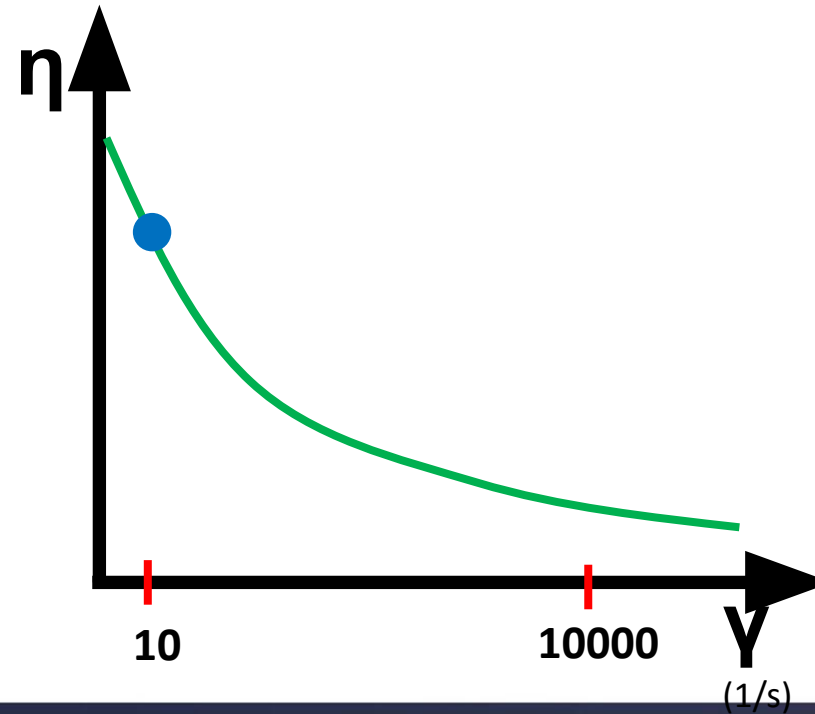
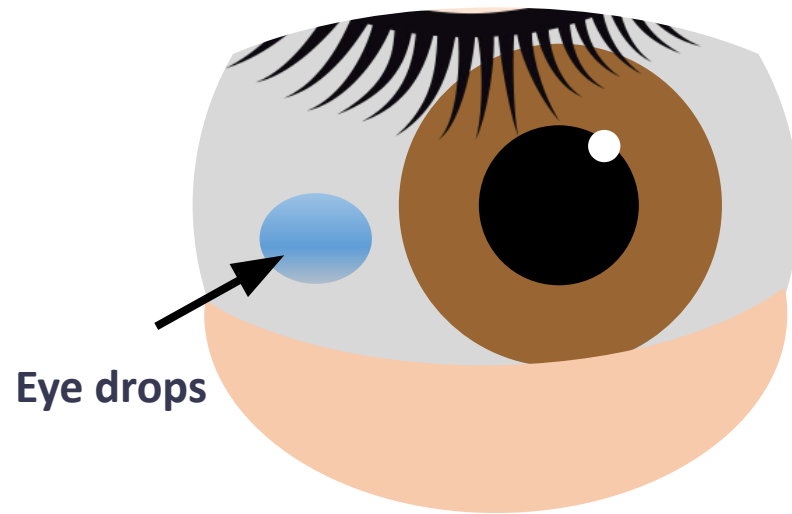
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Why do we have to use eye drops so often?

Blinking 12-20 times/min + reflexive blinking and tear production

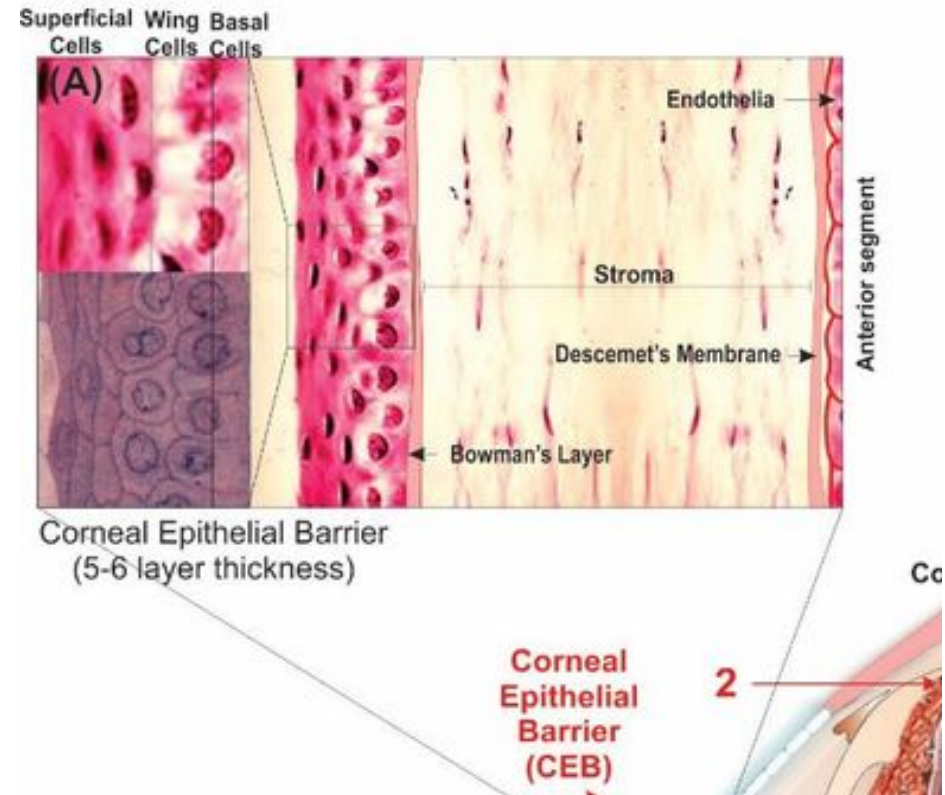


Why do we have to use eye drops so often?

Nasolacrimal drainage



Corneal barrier



<https://ocvermont.com/tear-duct-surgery/>

https://www.researchgate.net/figure/Schematic-demonstration-of-the-anatomy-and-the-biological-membranes-and-barriers-of-the_fig1_304186889

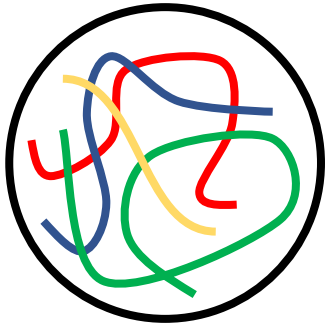


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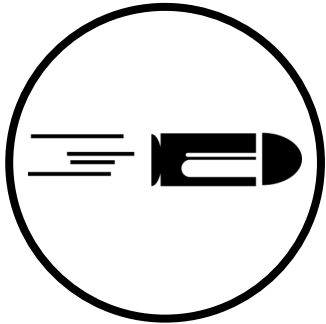
Strategies for improving topical ocular drug delivery



Viscosity Enhancer: Improve corneal residence time and to improve bioavailability

Materials: Polyacrylic acid (polycarbophil), Gellan Gum, Poloxamer.

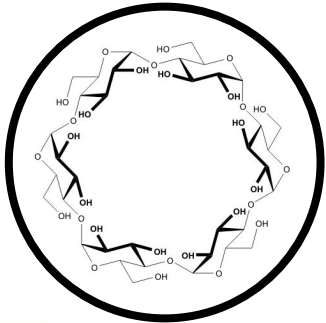
Example: Ocular ointments, creams, and in-situ gel.



Penetration Enhancer: Enhance corneal absorption by modifying corneal integrity

Materials: Chelating agents (EDTA), preservatives (benzalkonium chloride).

Example: Selected in some commercial eye drop formulation as preservatives.



Solubility Enhancer: Increase the hydrophobic drug solubility

Materials: Cyclodextrins (2-hydroxypropyl-cyclodextrin), surfactants

Example: Clorocil[®] (Chloramphenicol), Pazeo[®]



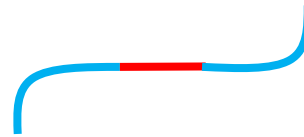
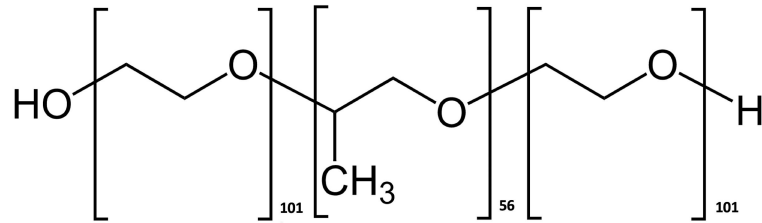
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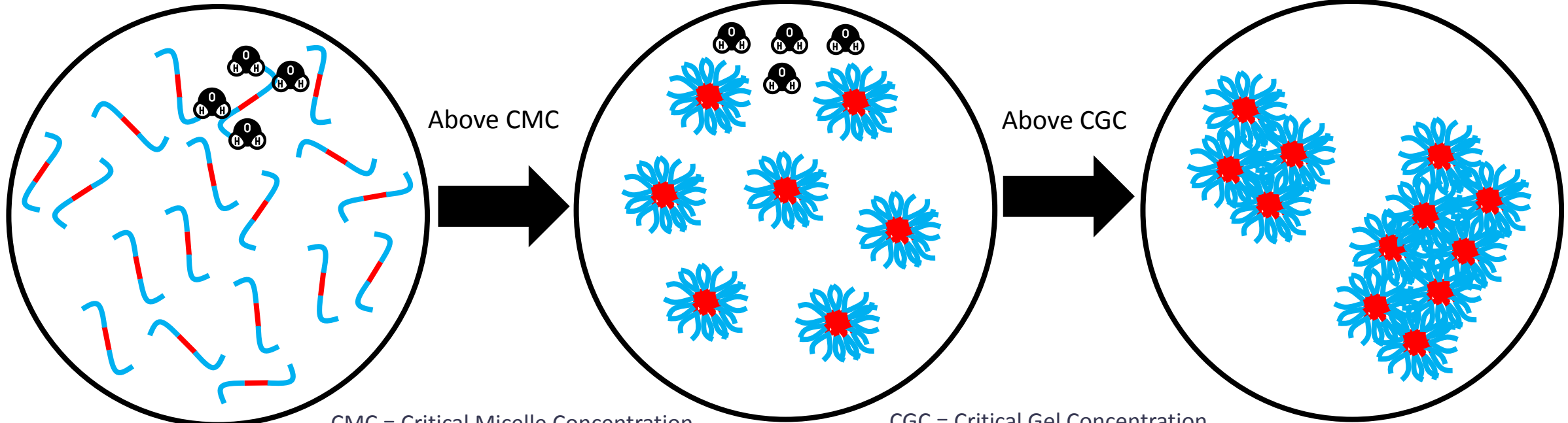


Pluronic/Poloxamer thermogels



$$\Delta G = \Delta H - T \Delta S$$

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CMC = Critical Micelle Concentration

CGC = Critical Gel Concentration

Bodratti, A., (2018). *J functional biomat*, 9(1), 11.



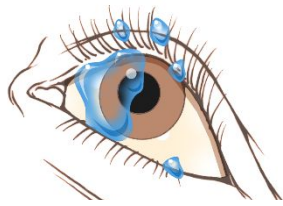
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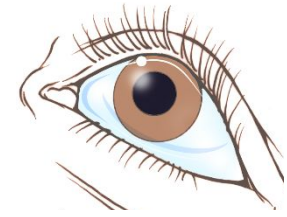
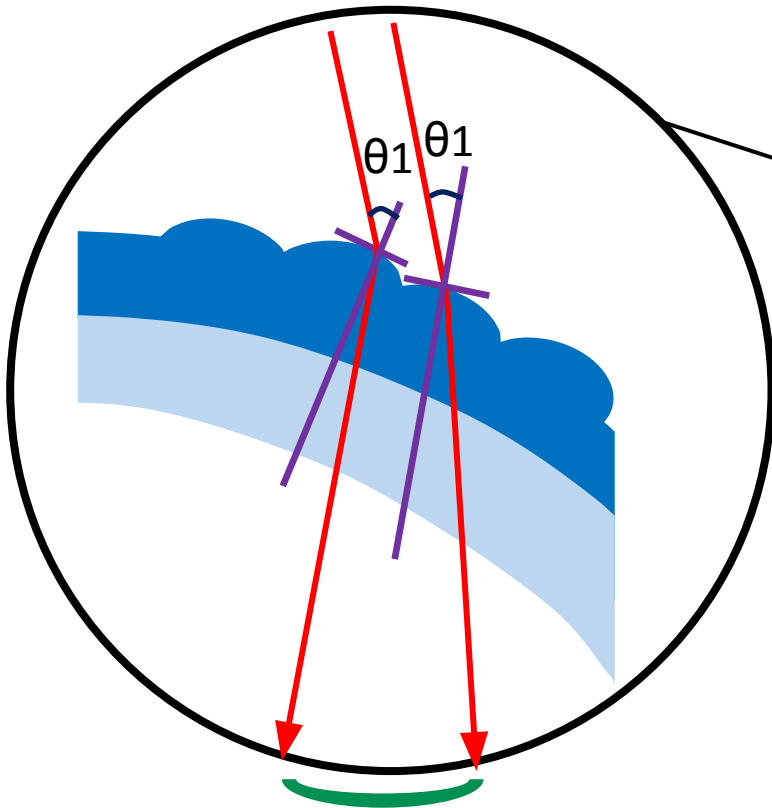
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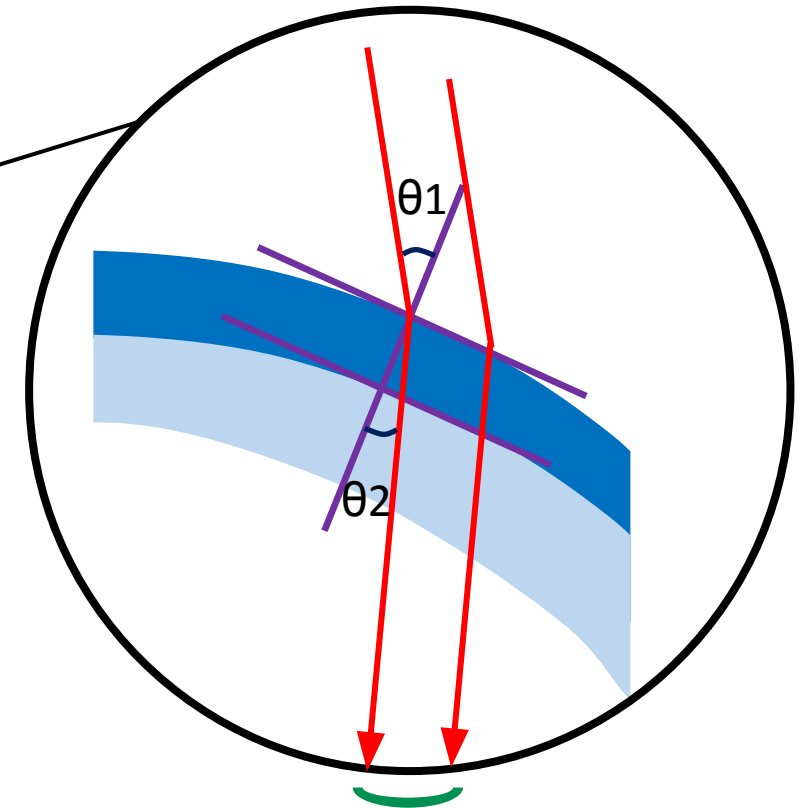
Gels and vision



Uneven gel/ointment layer



Uniform layer



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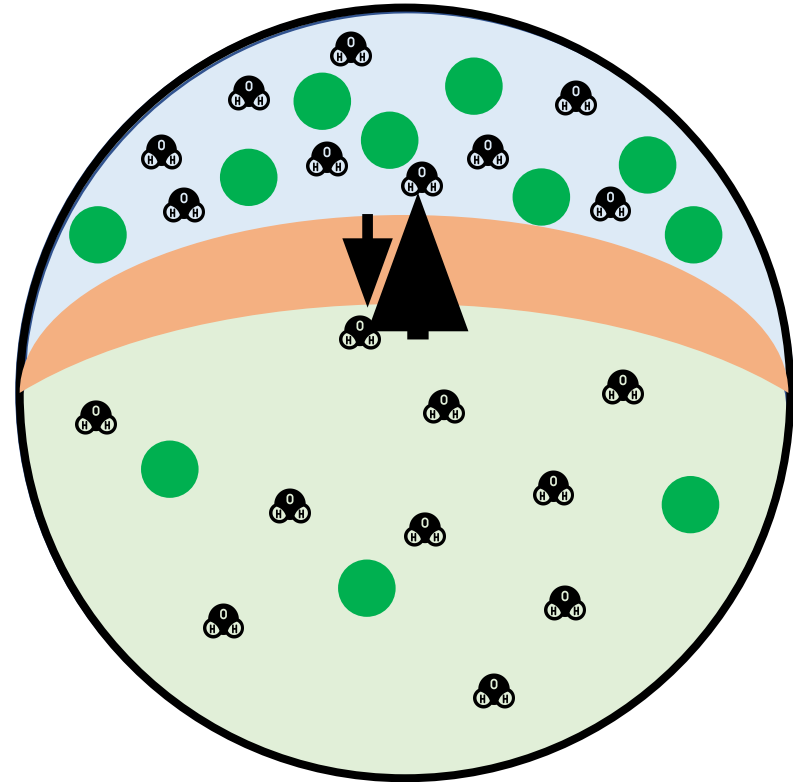
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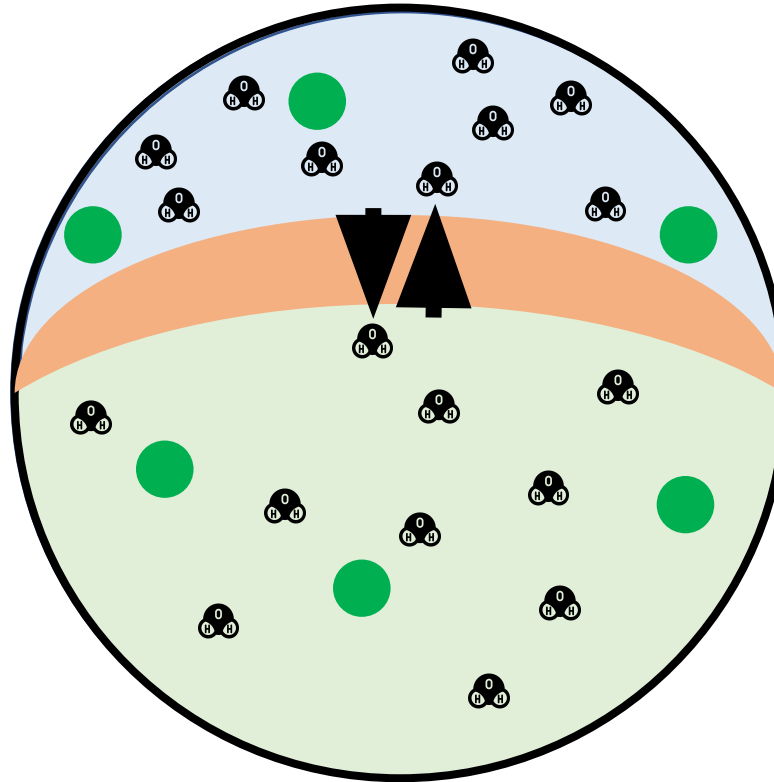


Osmotic pressure regulates ion balance

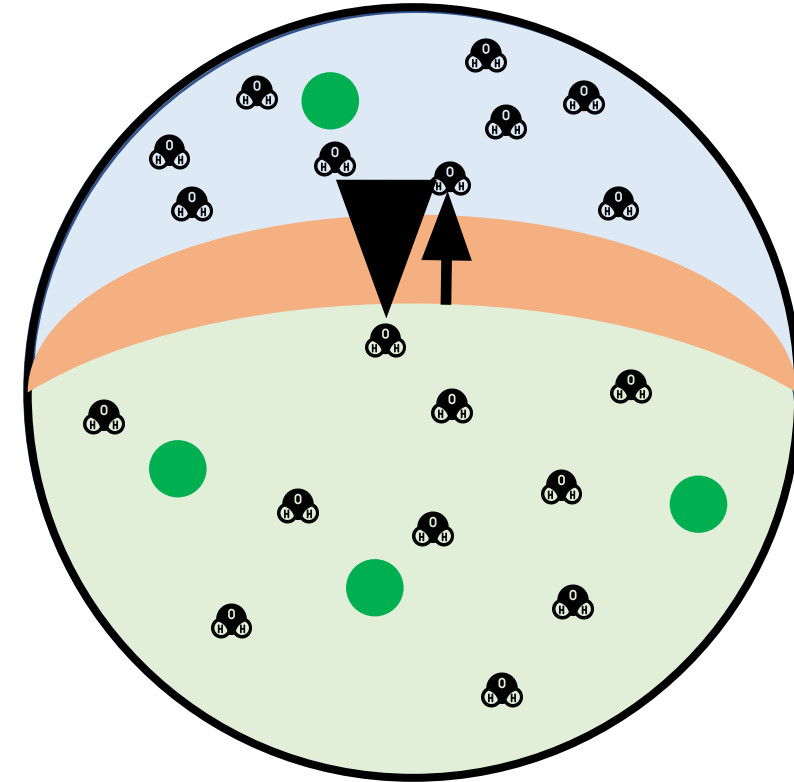
Hypertonic formulation



Isotonic formulation



Hypotonic formulation



 Solute/ion

 Water molecule



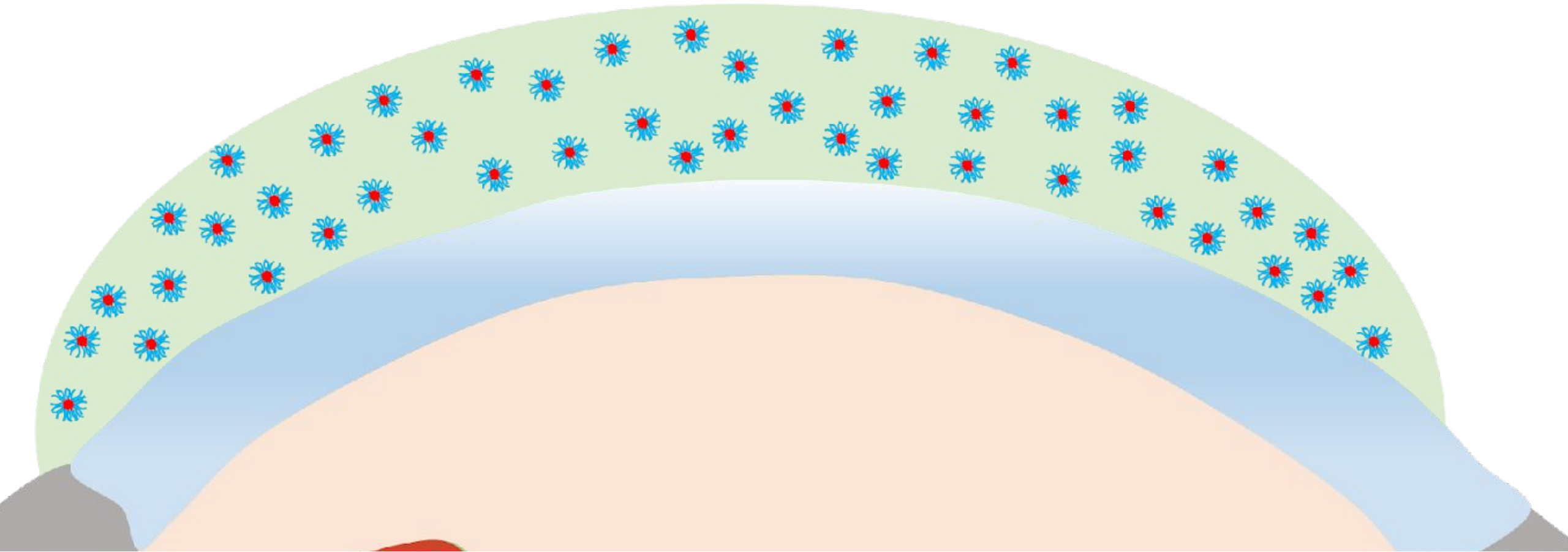
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Pluronics in a hypotonic vehicle, below the CGC



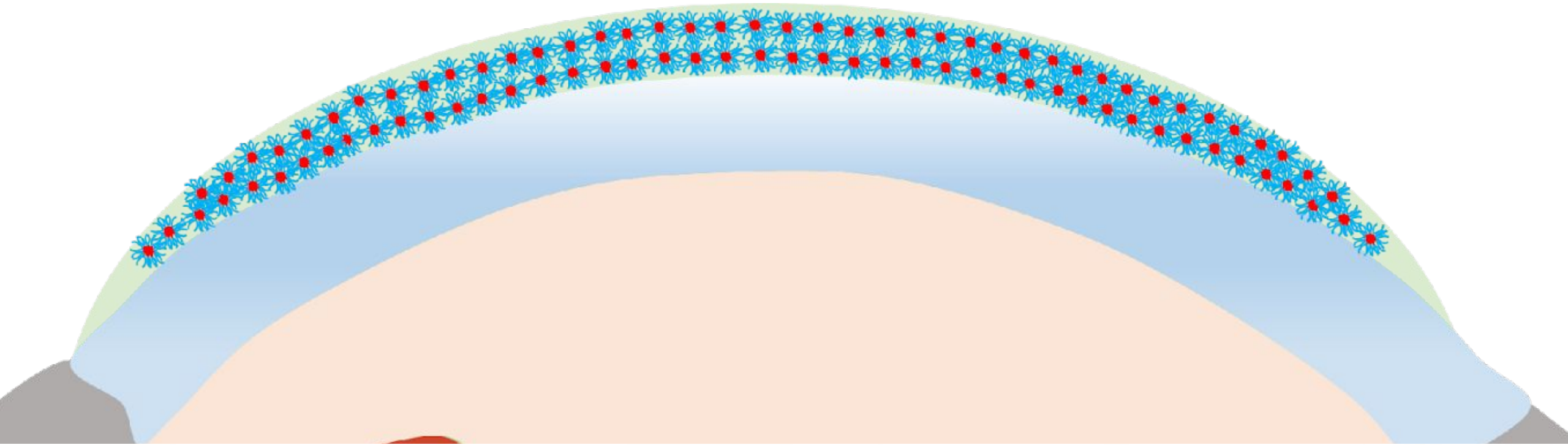
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Pluronics in a hypotonic vehicle, below the CGC



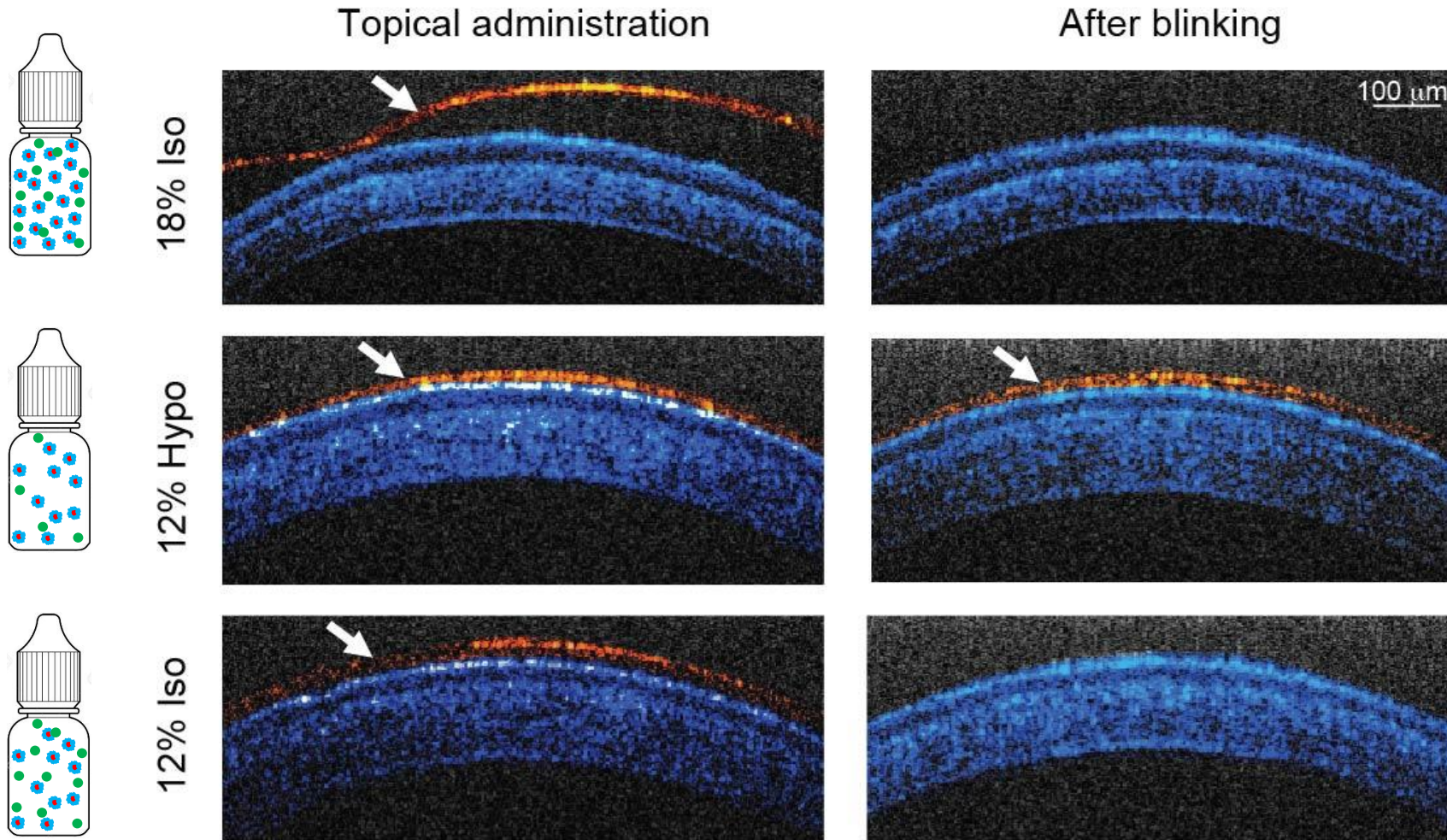
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Eye drop distribution in vivo



Kim et al, *Nature BME*, 2020



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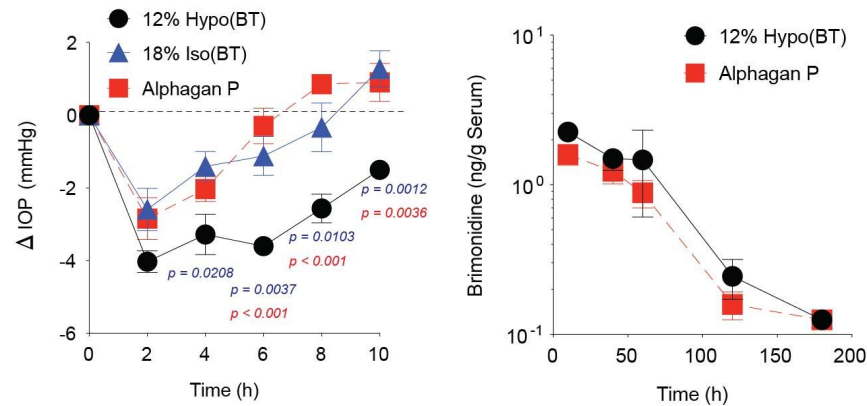
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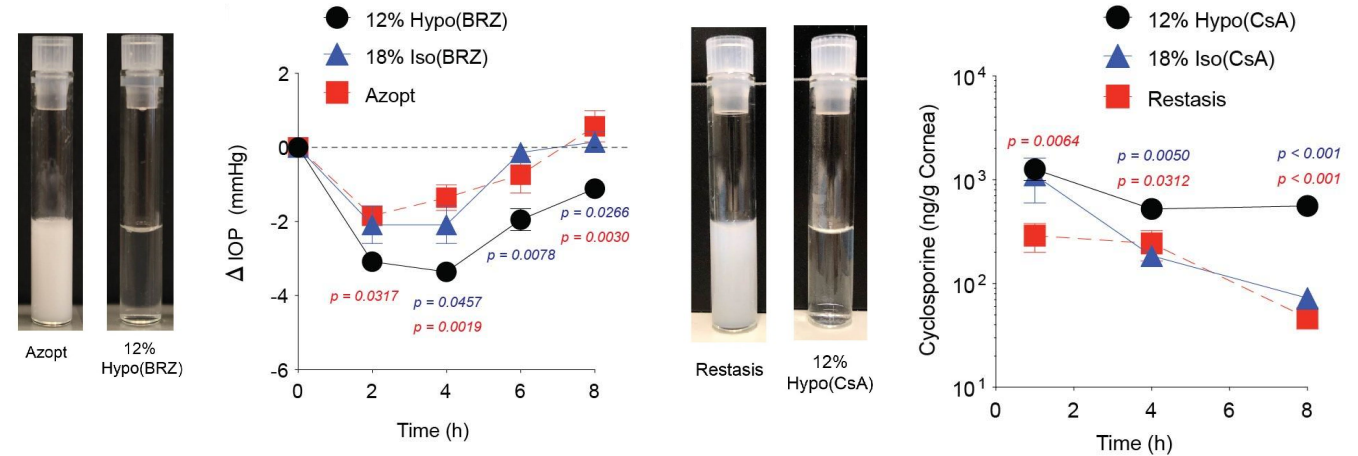


Broad impacts on eye drop performance

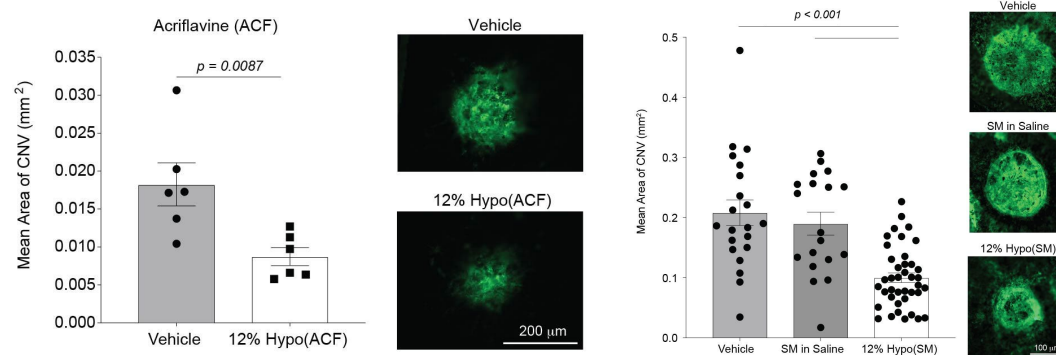
Improved delivery of water soluble drugs without increasing systemic exposure



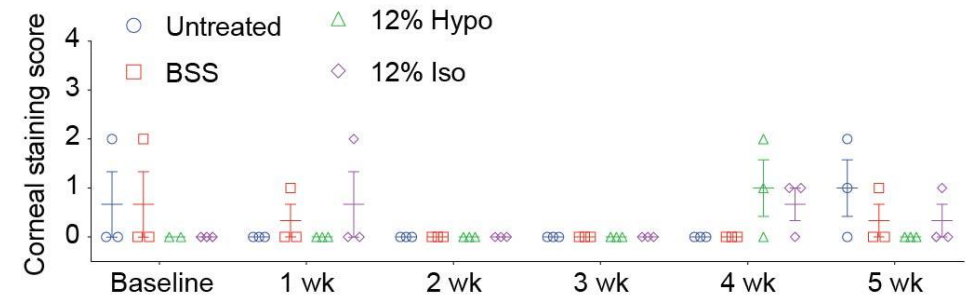
Solubilization and improved delivery of low solubility drugs



Improvement in posterior drug delivery



Biocompatible in sensitive model with repeated dosing



Kim et al, *Nature BME*, 2020



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Why was this technology well-suited for clinical development?

- Patents!
 - Surprising, unexpected, not obvious
 - Broad (awarded) claims that are not easy to circumvent
- Addresses a range of unmet needs
 - Current therapies with significant drawbacks and/or diseases that are unaddressed
- Room in the market/differentiation from competitors
- Materials with a history of safety/extensive preclinical safety data
- Initial development pathways that are relatively fast/inexpensive



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Learnings based on my limited experience

- Do not be intimidated by working outside your comfort zone
- Find and work closely with people who are experienced and know what they are doing
- Figure out what roles you do and do not want to fill
- Find the right people to fulfill vacant roles and trust them to do their job
- Be prepared to incentivize people appropriately
- Do not let your attachment to your invention impede progress (align your priorities with your end goal)



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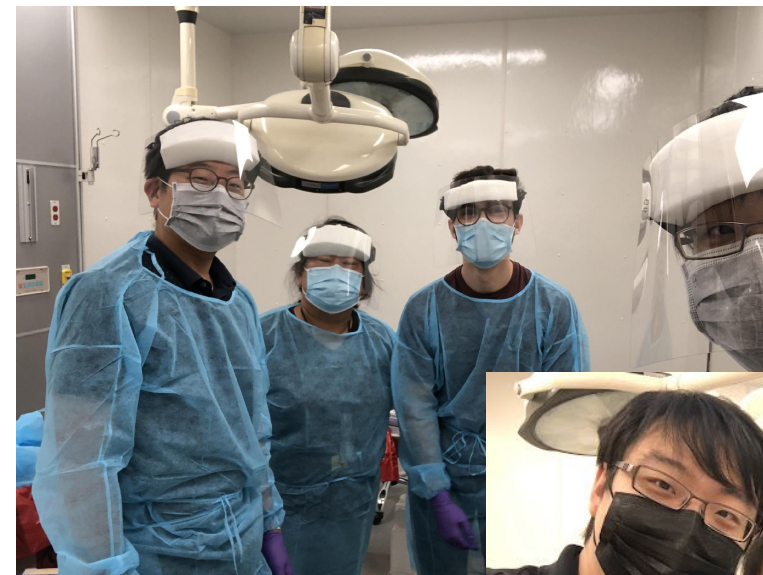
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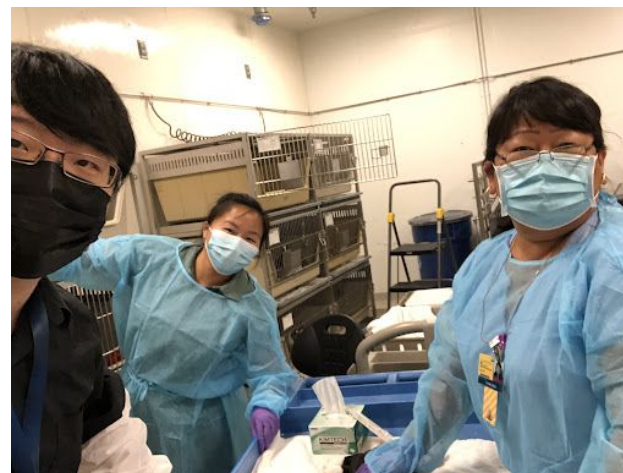
Matthew Shin

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Stay tuned!



NOVUS VISION



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