Advances in Biomaterial Design and Application for Glaucoma Therapy

Jui-Yang Lai, Ph.D.
Department of Biomedical Engineering,
Chang Gung University, TAIWAN

CONTROLLED RELEASE SOCIETY
CRS 2023 ANNUAL MEETING & EXPOSITION
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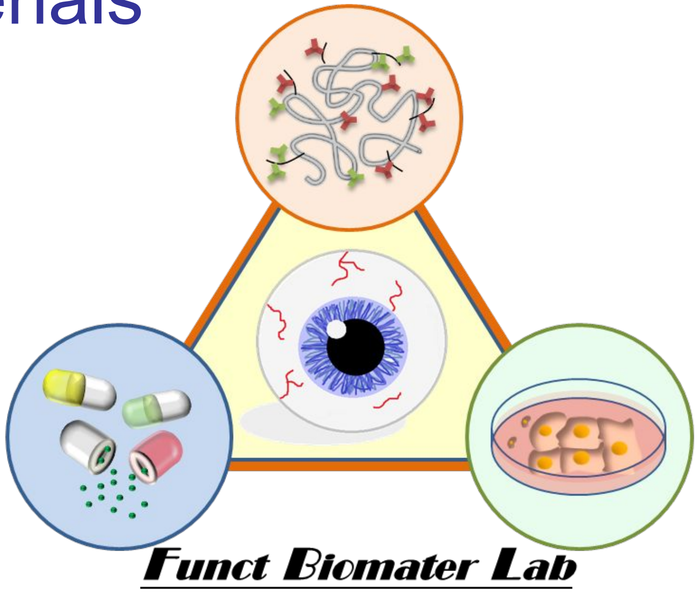
THE FUTURE OF DELIVERY SCIENCE

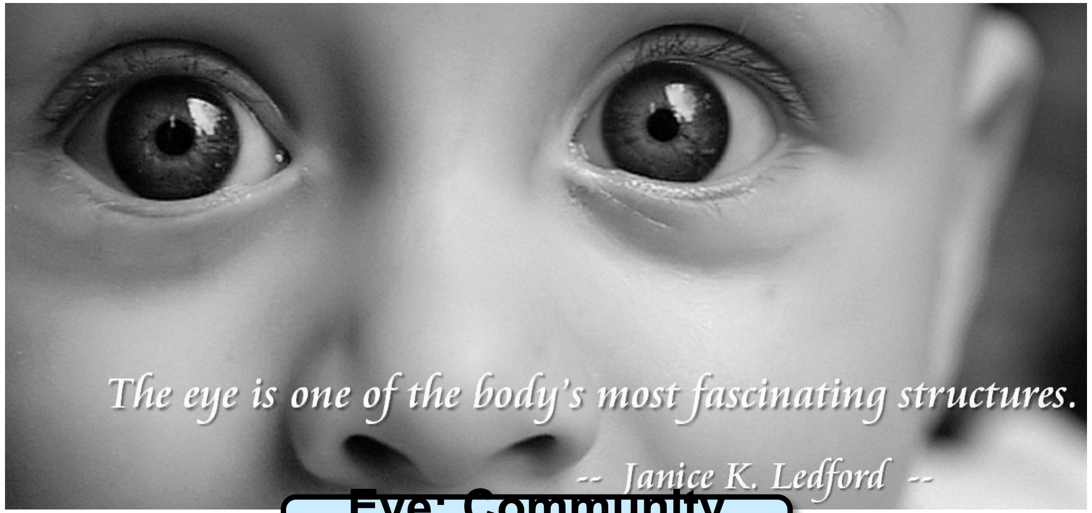
Functional Biomaterial Lab

Research Interest

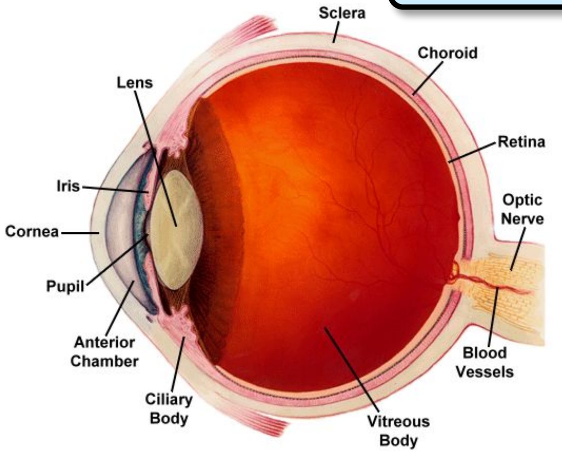
- Ophthalmic Biomaterials
- Drug Delivery
- Nanomedicine
- Tissue Engineering

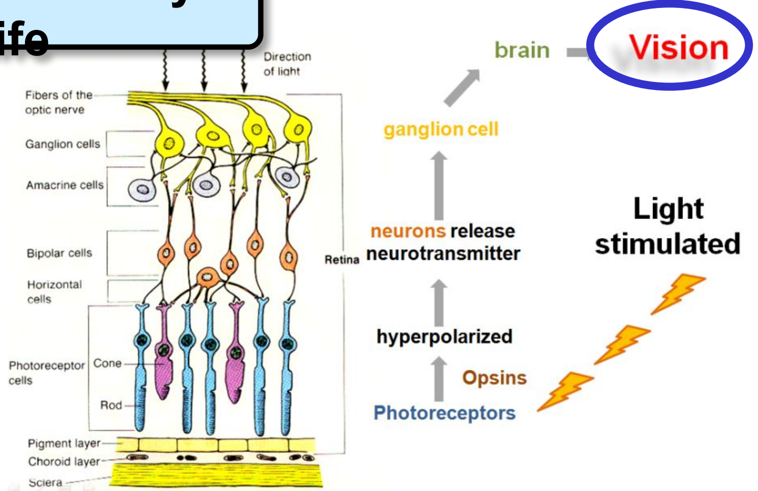


Eye



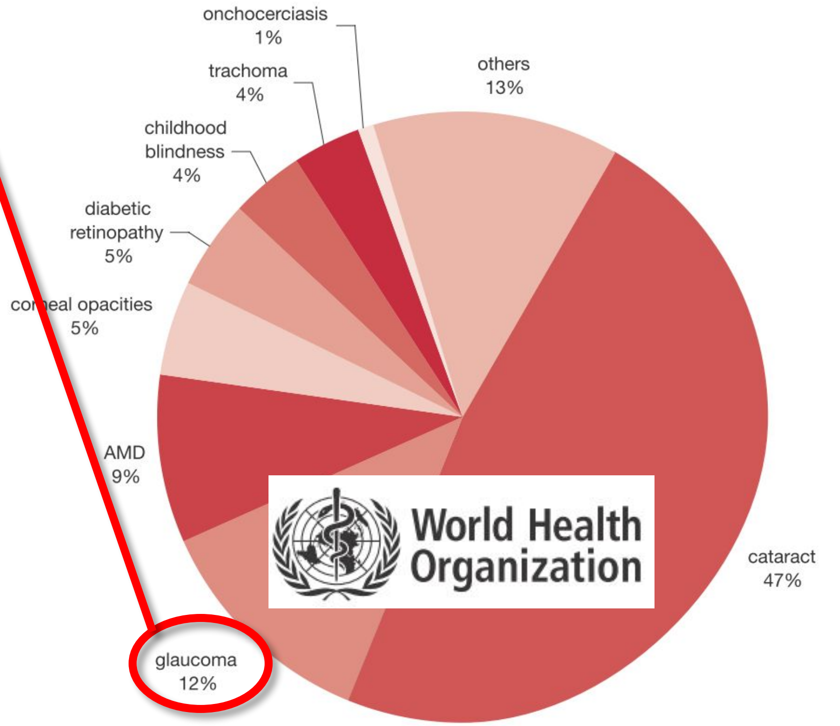
Eye: Community Life





http://www.nei.nih.gov/health/eyediagram/eyeimages4.asp

2nd global leading cause of blindness



http://www.who.int/Blindness/Vision2020_report.pdf

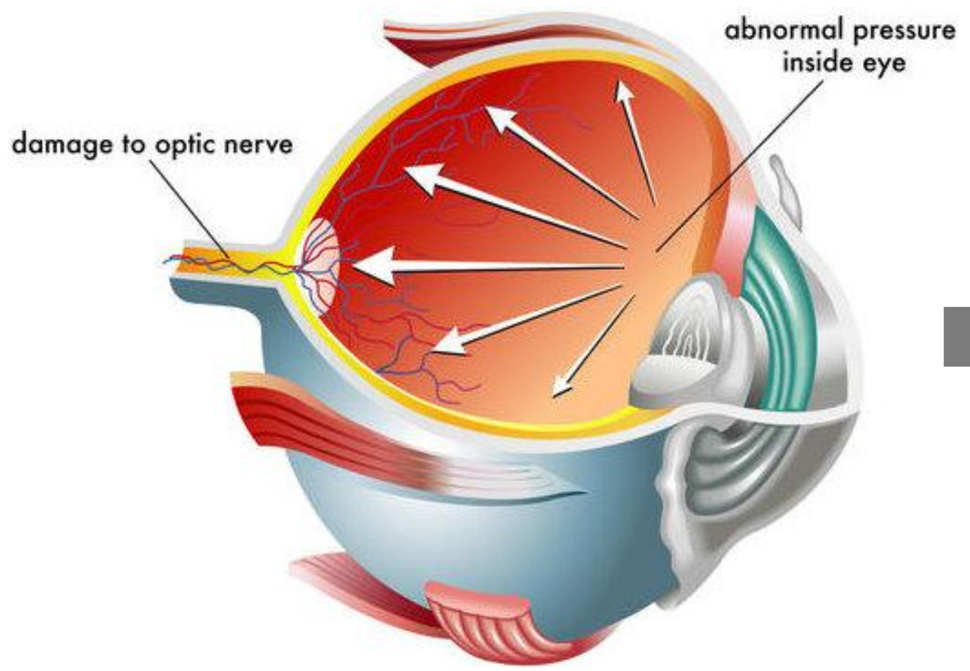
Glaucomatous Case Number ↑

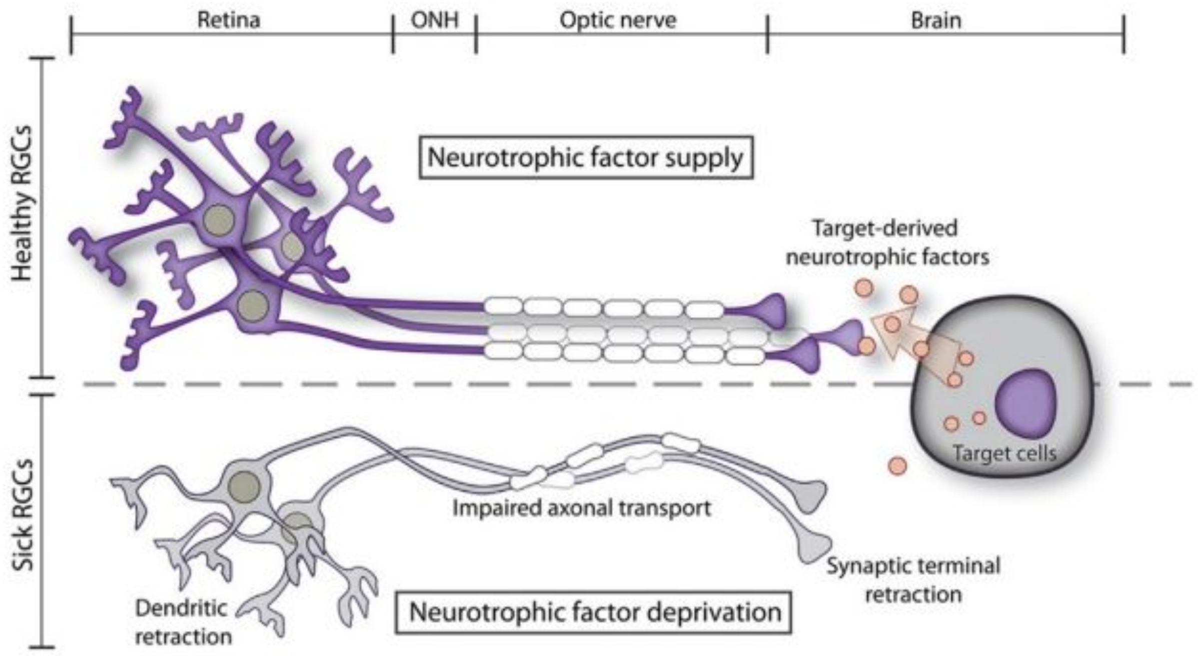
Funct Biomater Lab

Glaucoma: Feature

- Elevated eye pressure
  (> 21 mmHg)

Retinal ganglion cell apoptosis

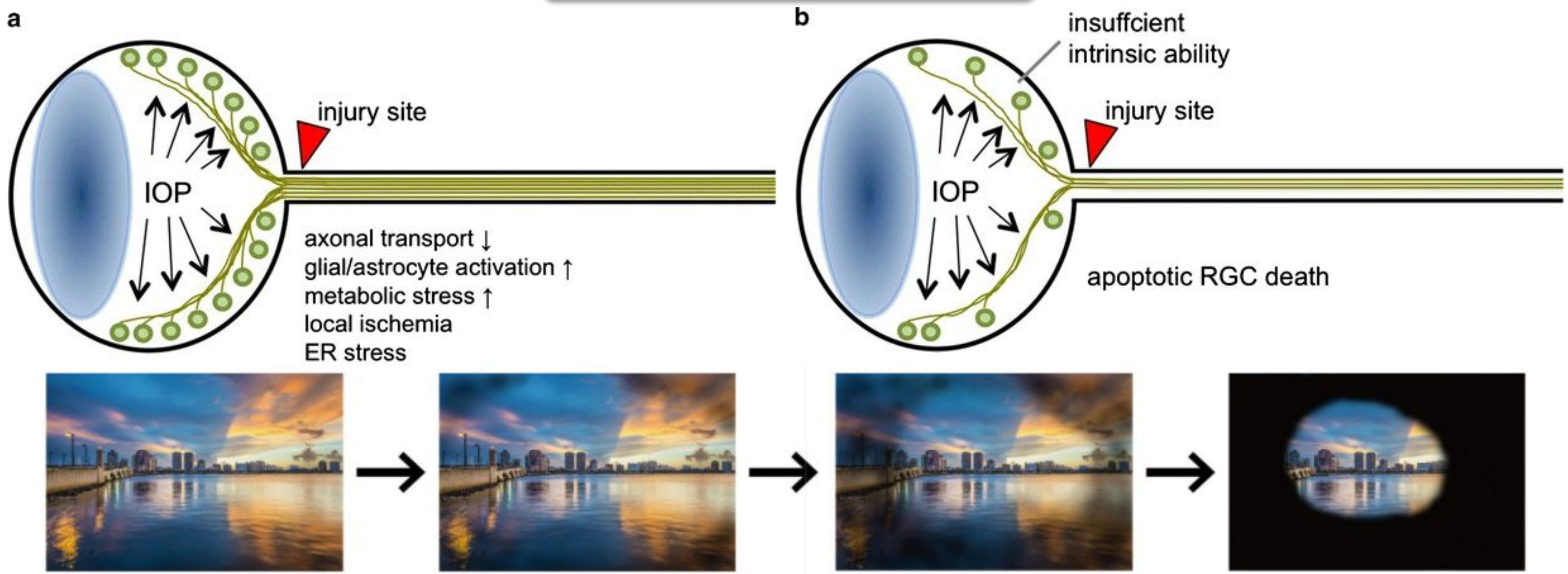




https://edc2.healthtap.com/ht-staging/user_answer/avatars/1106716/large/open-uri20130505

Glaucoma: Outcome

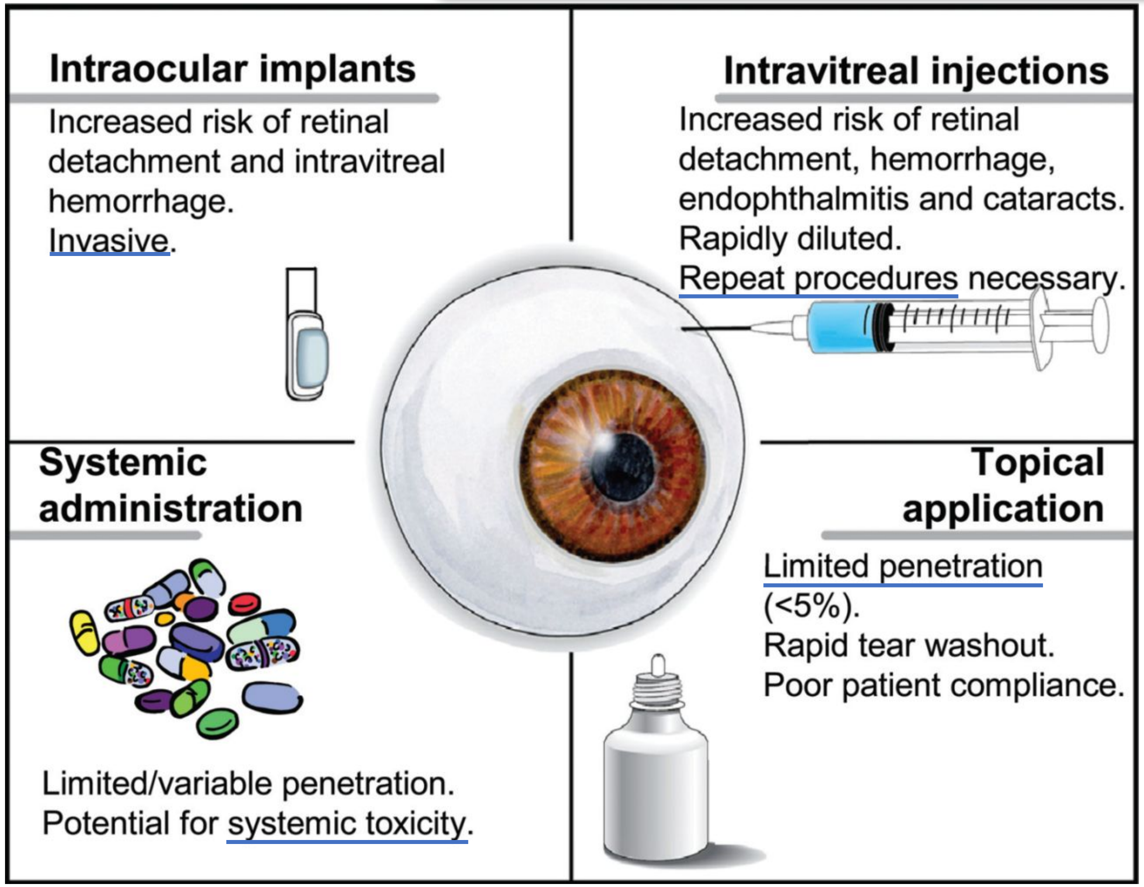
Optic nerve depression



https://www.cceye.com.tw/eyecare/view/446

Ophthalmic Drug Formulations

Functional biomaterial carrier as DDS



Short, Toxicol. Pathol. 2008;36:49-62

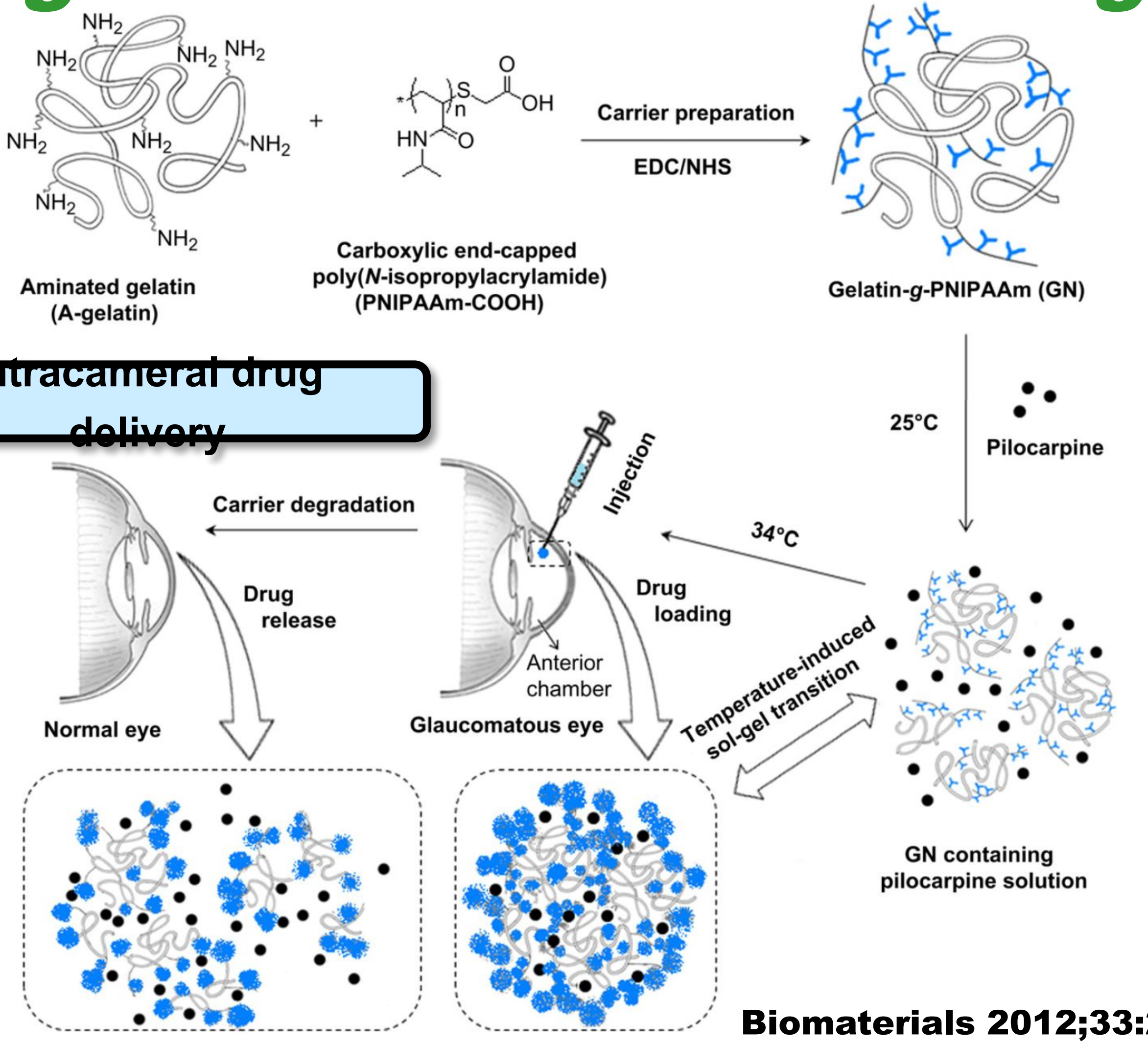
- **Injectable Thermogel**
- **Nanoceria Eye Drop**

→ Improve bioavailability

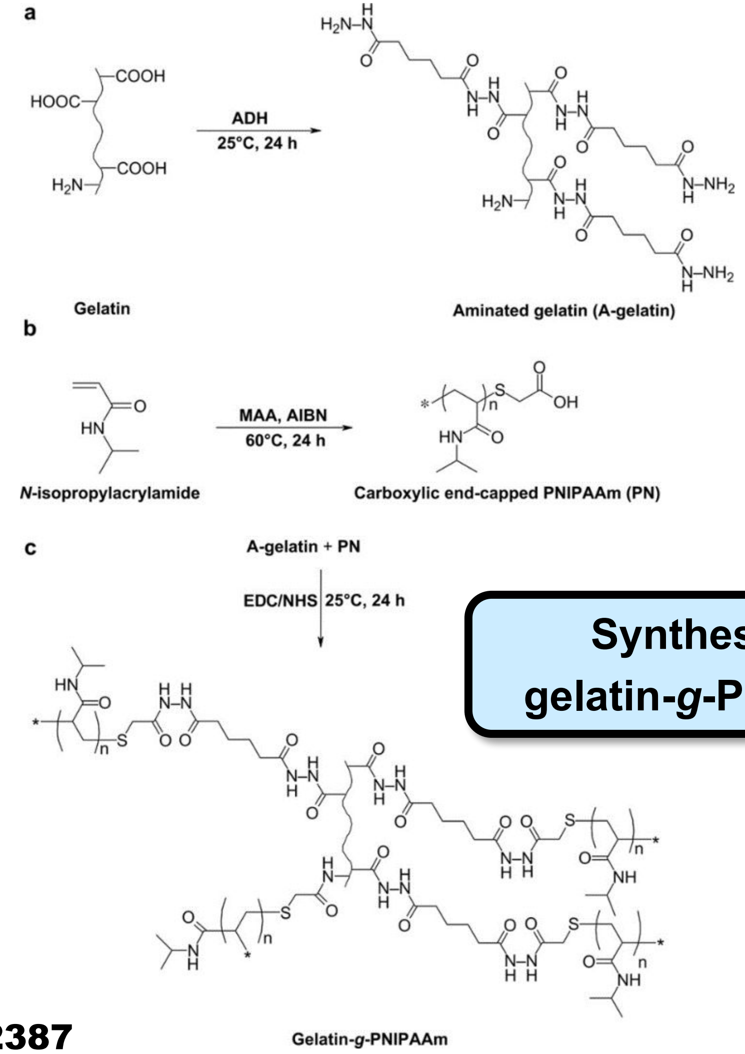
→ Completely alleviate symptoms

Biodegradable In Situ Forming DDS

Intracameral drug delivery

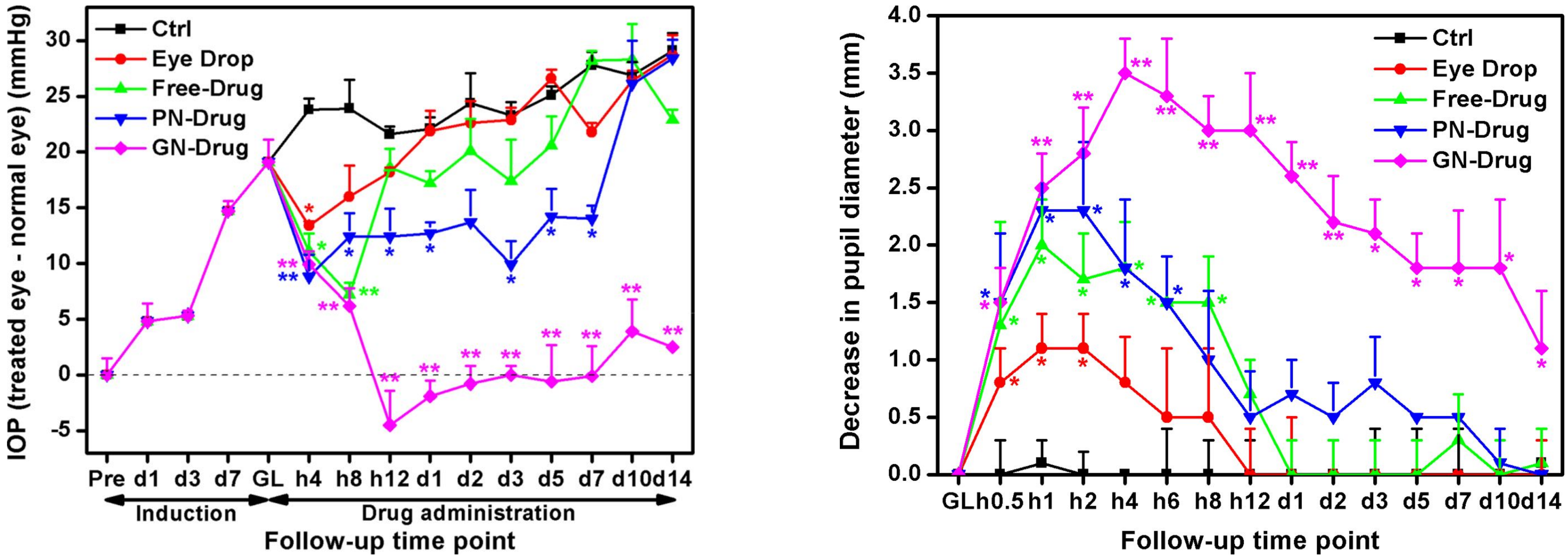


Synthesis of gelatin-g-PNIPAAm



Biomaterials 2012;33:2372-2387

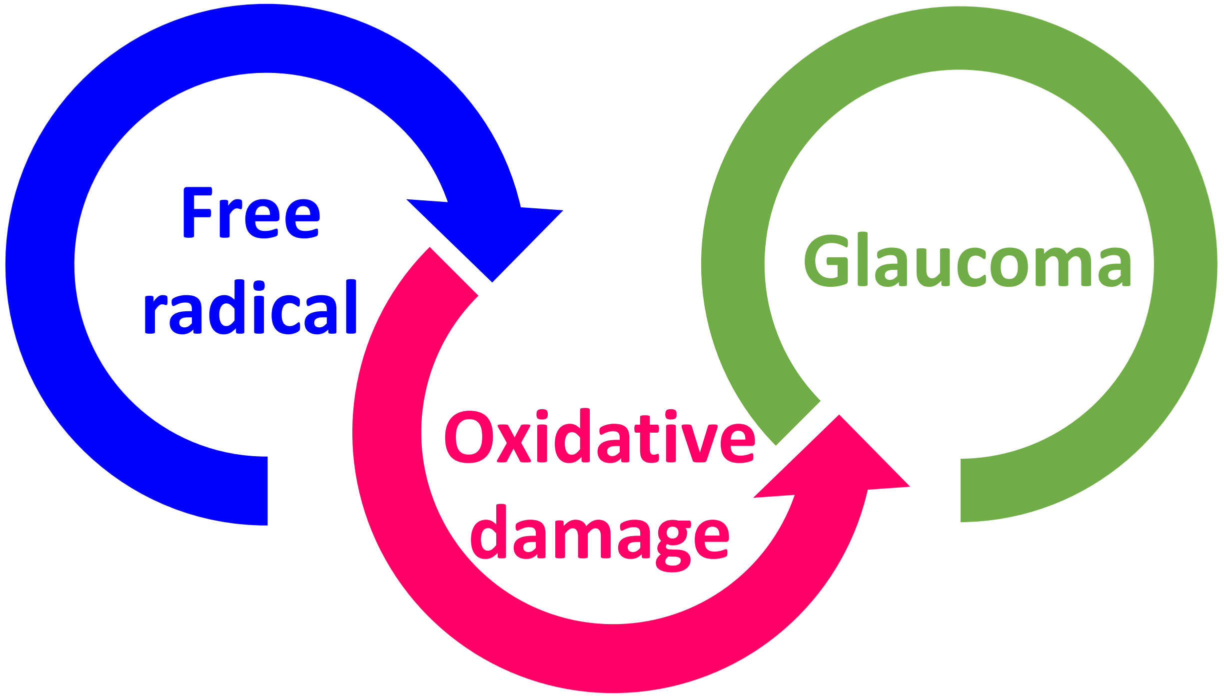
Intraocular Pressure & Pupil Diameter



- GN-Drug: significant decreases in IOP & pupil diameter were noted over 2 weeks, suggesting intense pharmacological activity and high ocular drug bioavailability

Next Stage

- Our findings support the hypothesis that the combination of **degradable** with **temperature-sensitive** features of carriers increases drug delivery performance



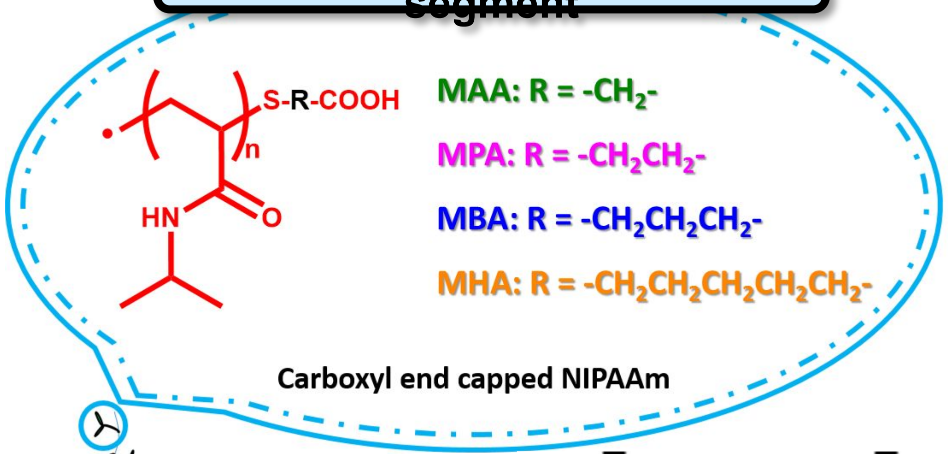
Extended Release

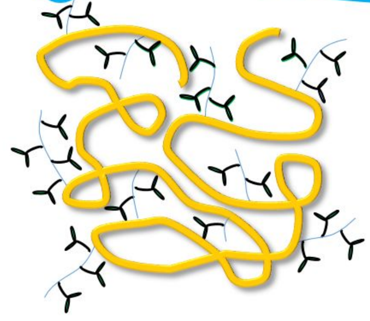
Functional Boost

Extended Release

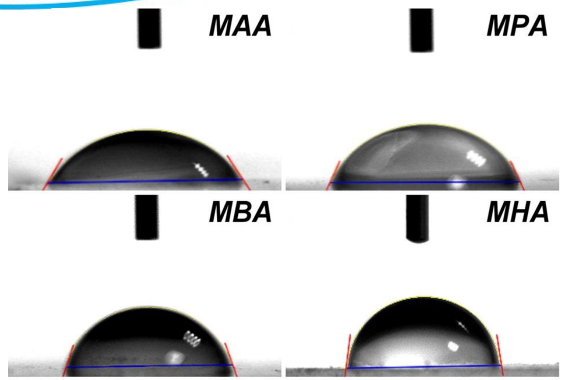
Chain Length of Monothiol-Terminated Alkyl Carboxylic Acid

Carbon number of PN segment

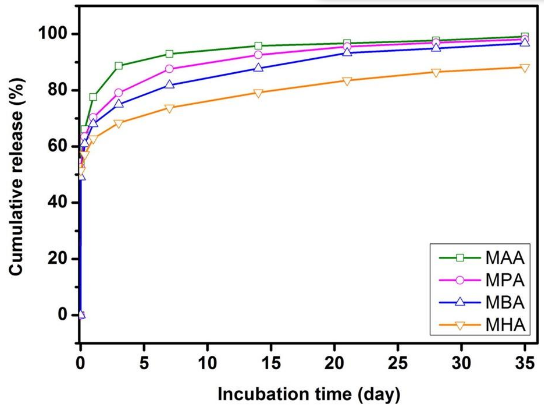


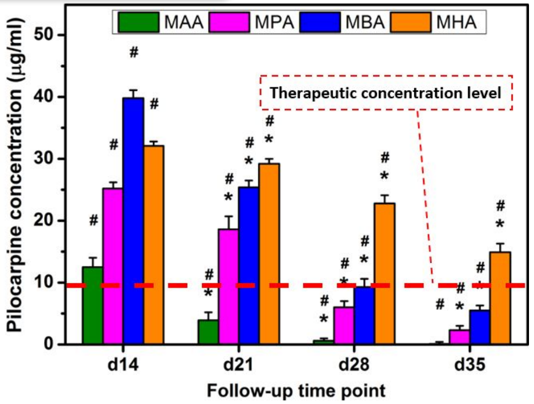


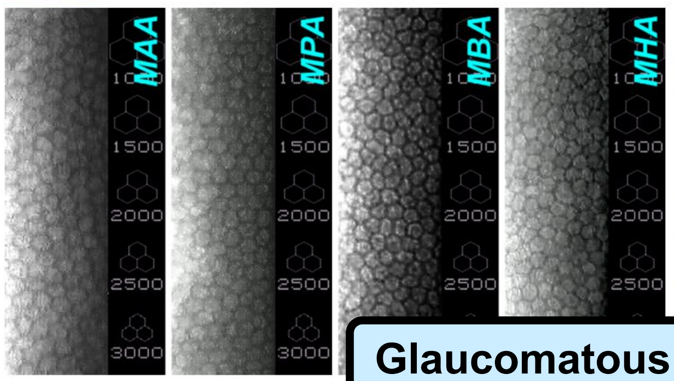
Gelatin-*g*-PNIPAAm (GN)

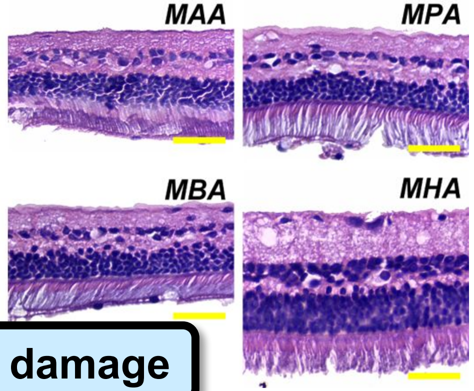


In vivo release profile









Glaucomatous damage

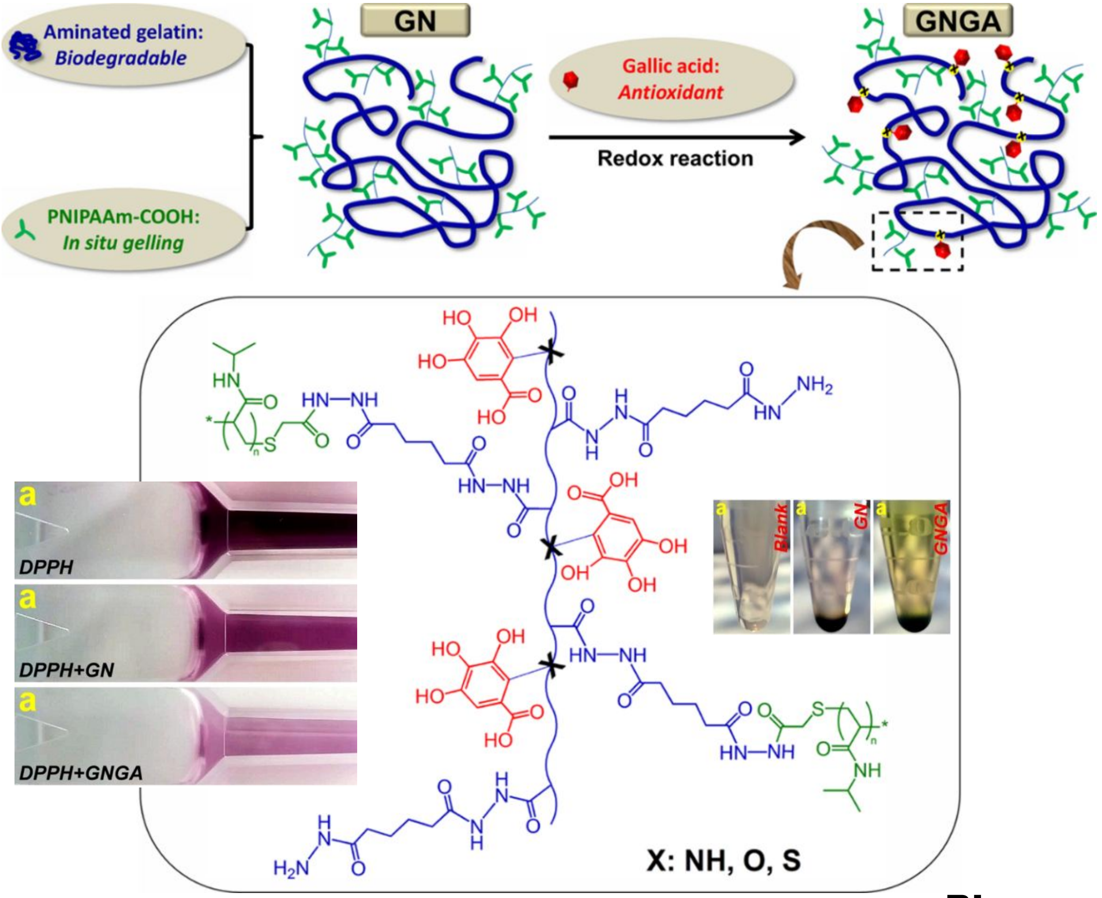
Acta Biomater. 2017;49:344-357

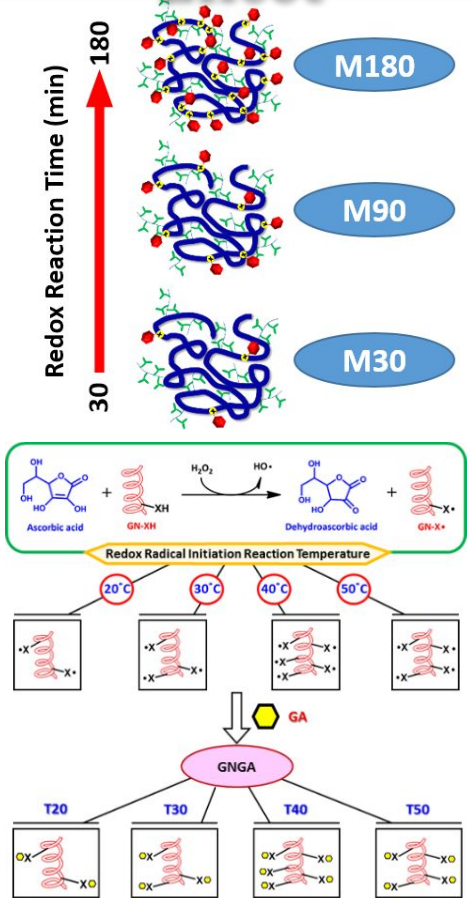
Functional Boost

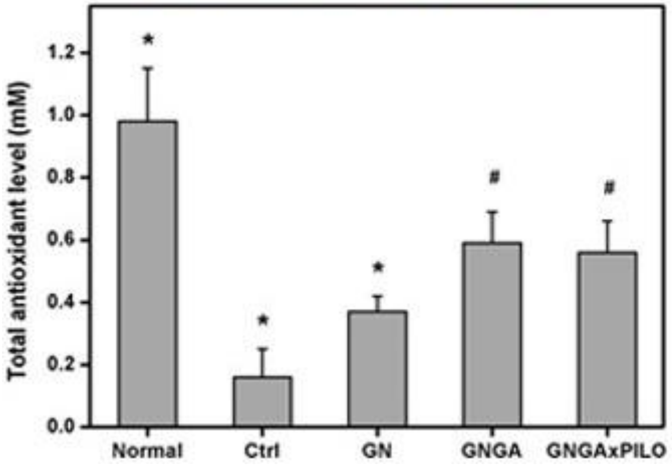
Cytoprotective Antiglaucoma DDS

GA Grafting Effect

Improved Antioxidant

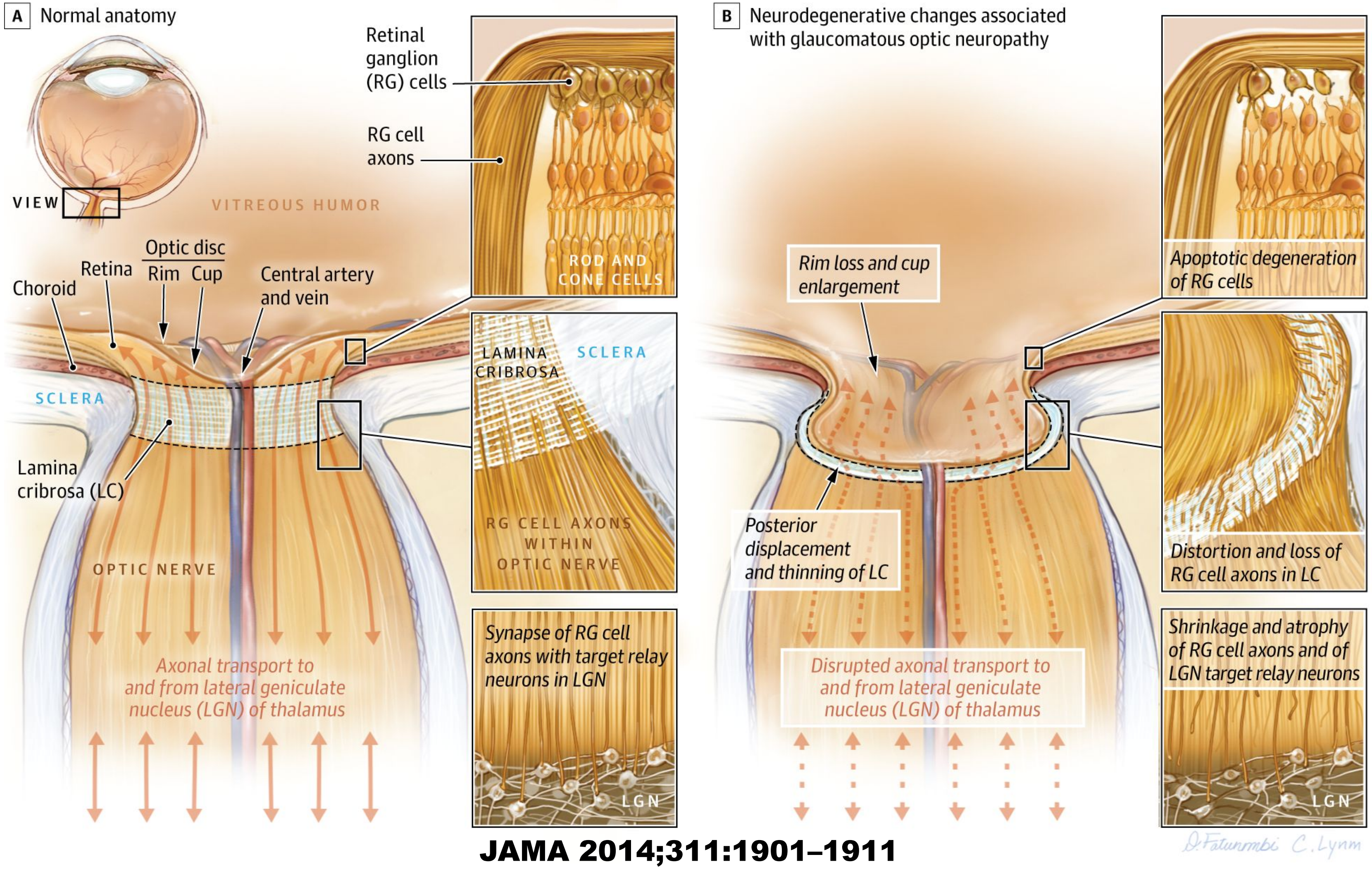






Biomacromolecules 2015;16:2950–2963

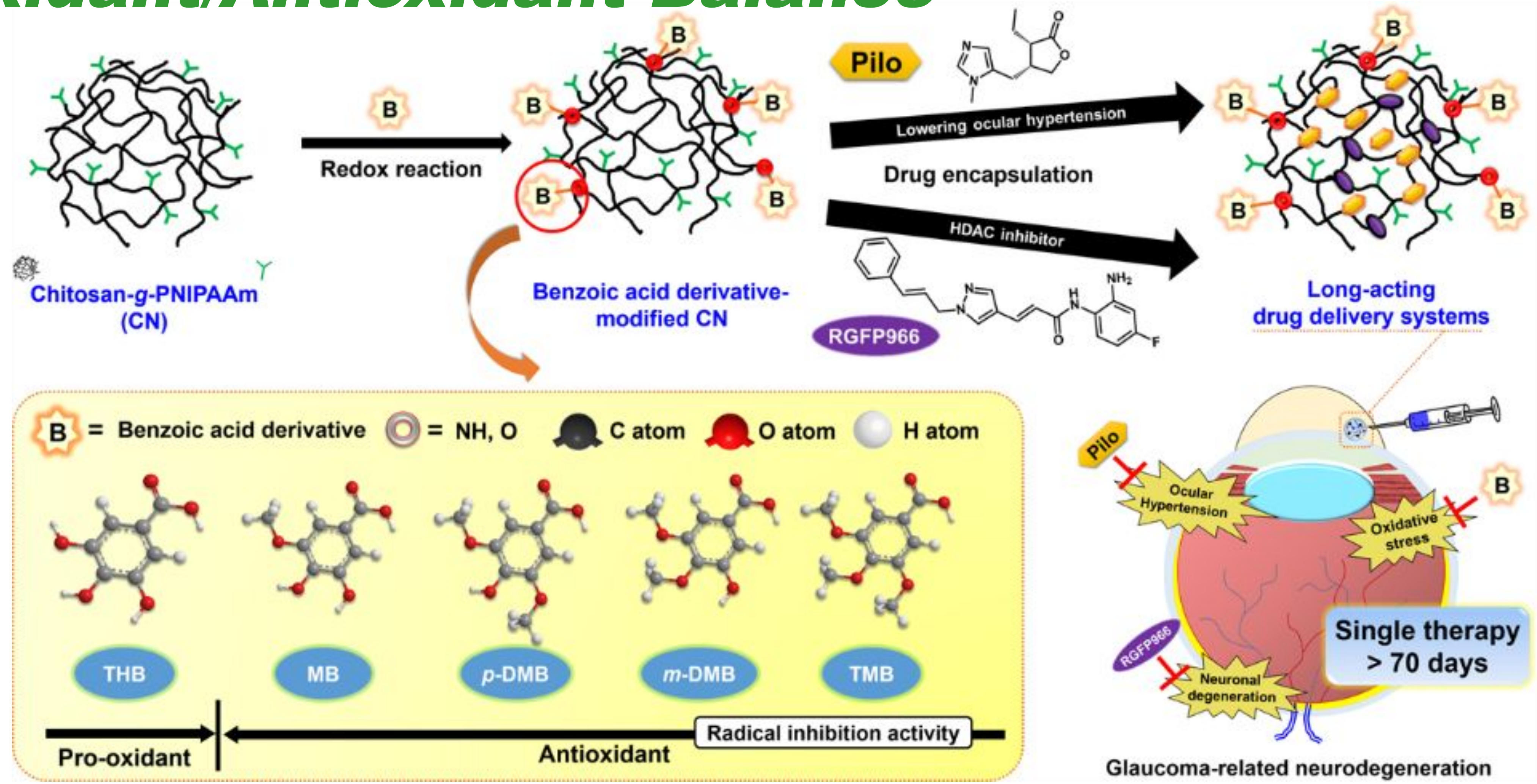
Glaucomatous Optic Neuropathy



JAMA 2014;311:1901–1911

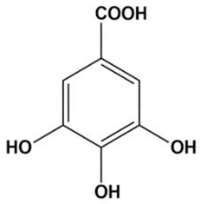
- The optic disc is composed of neural, vascular, and connective tissues
- Glaucomatous optic neuropathy involves damage and remodeling of the optic disc tissues and lamina cribrosa that lead to vision loss

Prooxidant/Antioxidant Balance

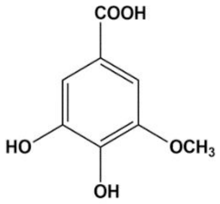


J. Control. Release 2020;317:246-258

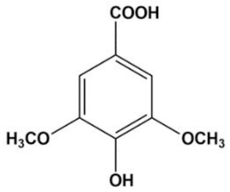
Characterization



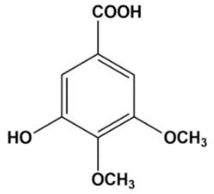
3,4,5-trihydroxybenzoic acid
(THB)



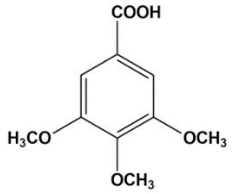
3,4-dihydroxy-5-methoxybenzoic acid
(MB)



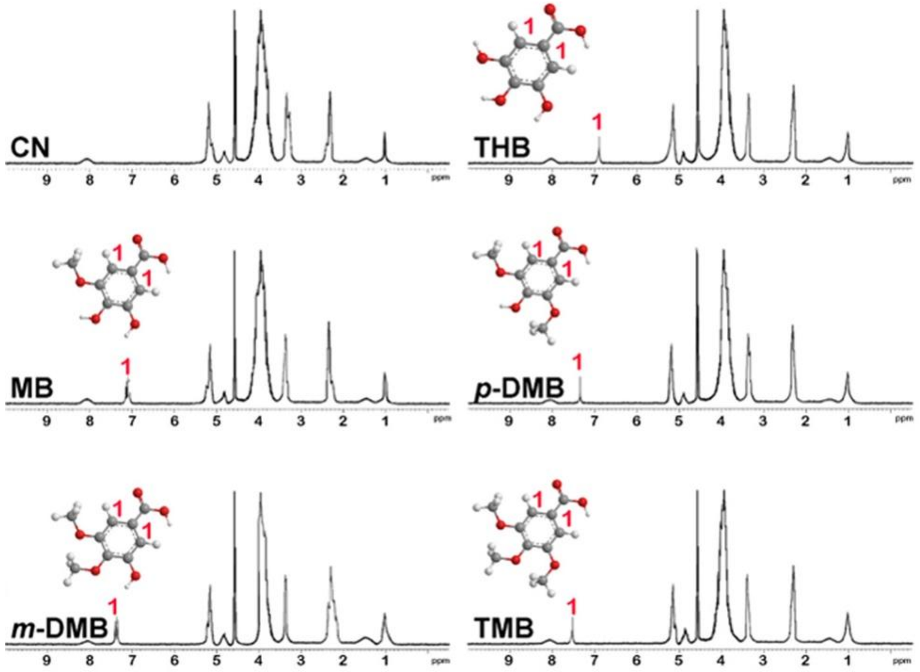
4-hydroxy-3,5-dimethoxybenzoic acid
(*p*-DMB)

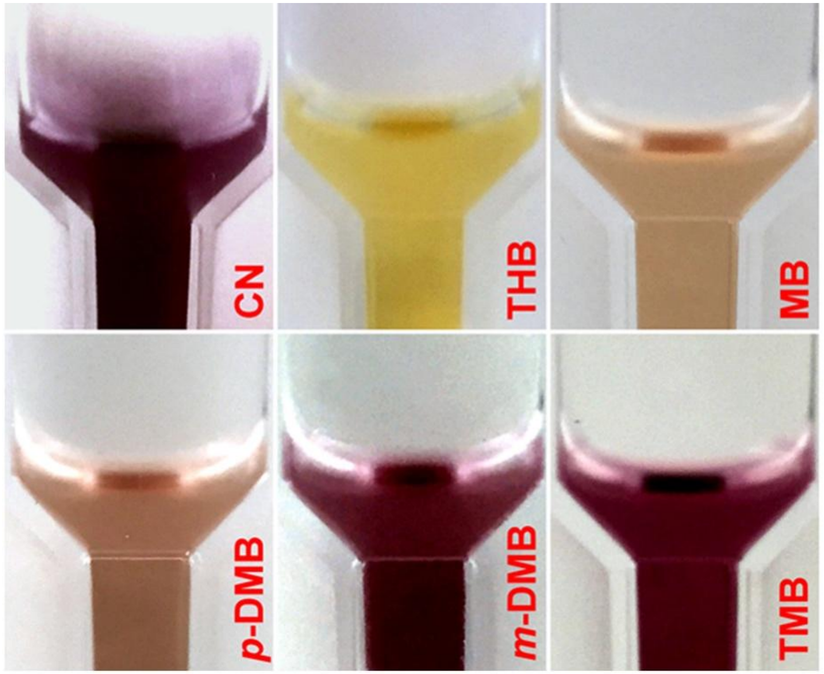


3-hydroxy-4,5-dimethoxybenzoic acid
(*m*-DMB)



3,4,5-trimethoxybenzoic acid
(TMB)

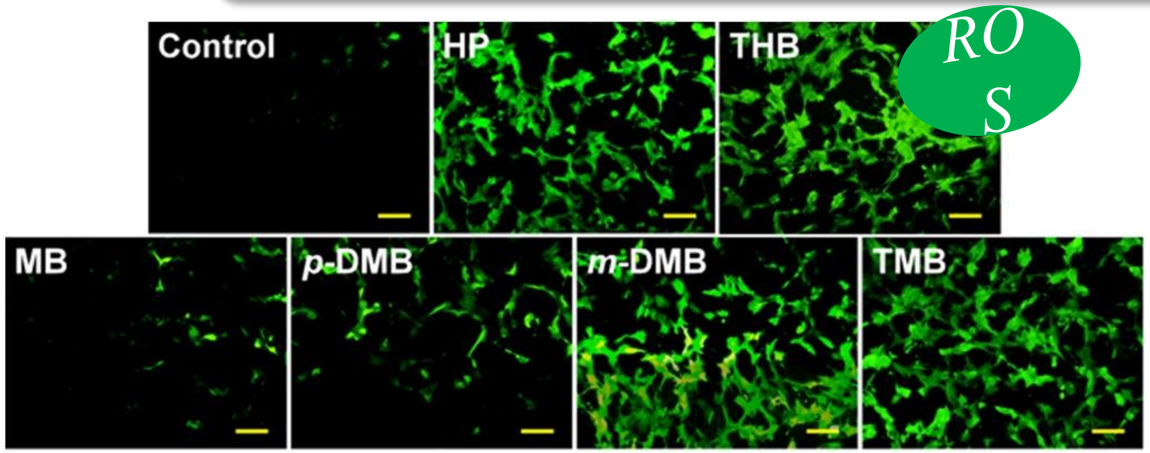


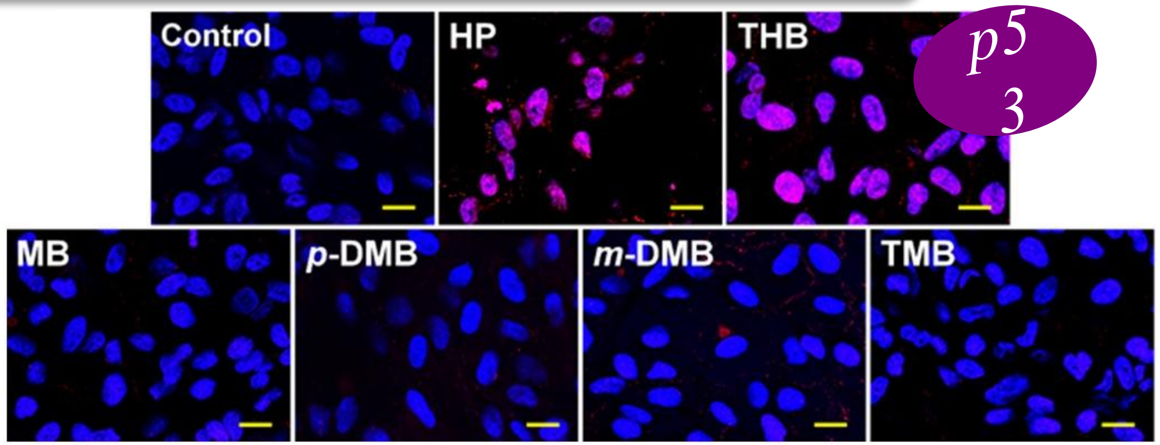


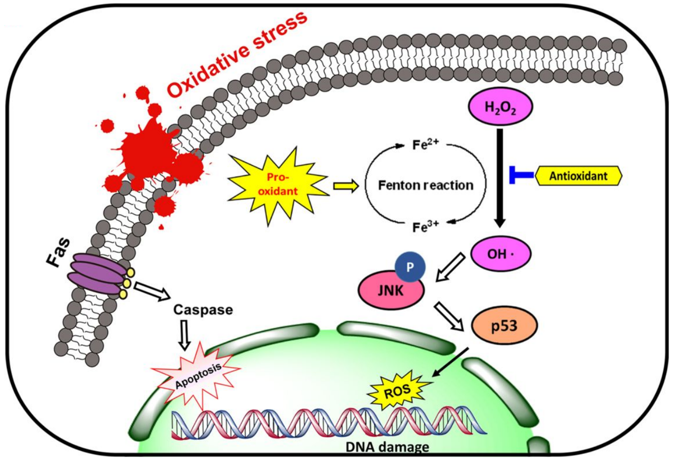
- **Increasing the number of methylation of OH groups induces a hypsochromic shift**
- **An additional spectral peak was noted in the range of 7.0-7.5 (2H, s, 2-H and 6-H) ppm**

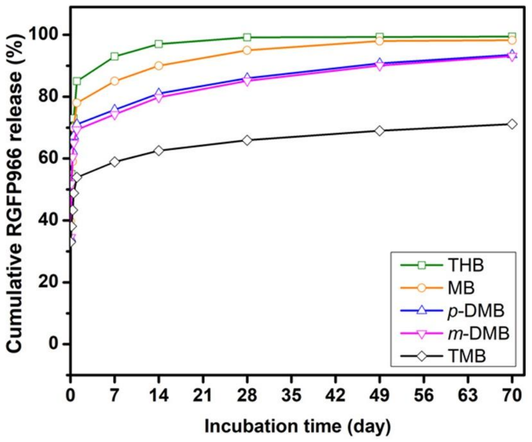
Cellular Response

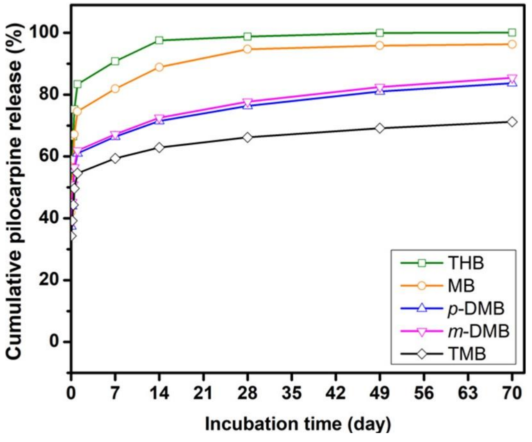
THB has strong antioxidant activity but also could act as pro-oxidant



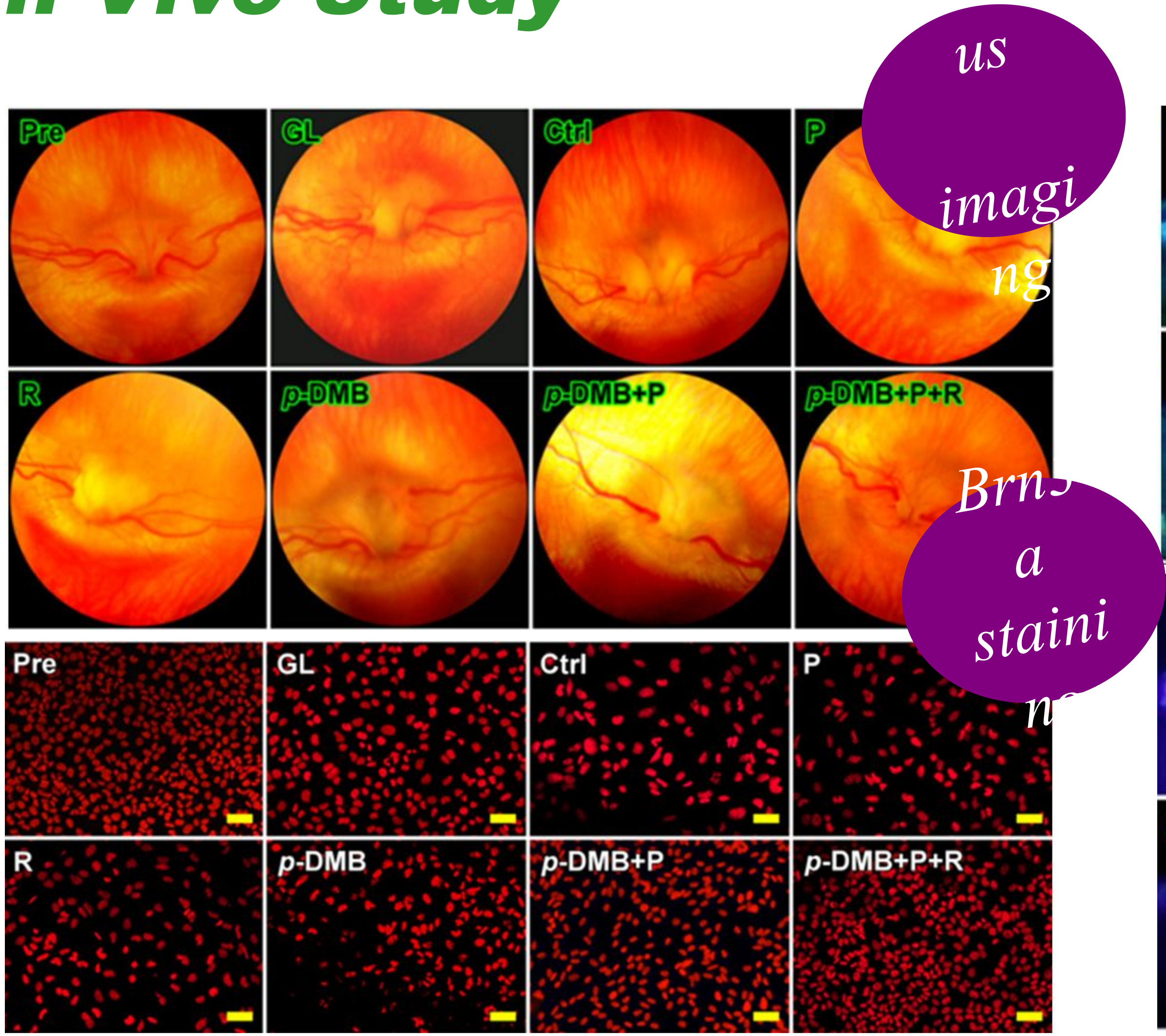


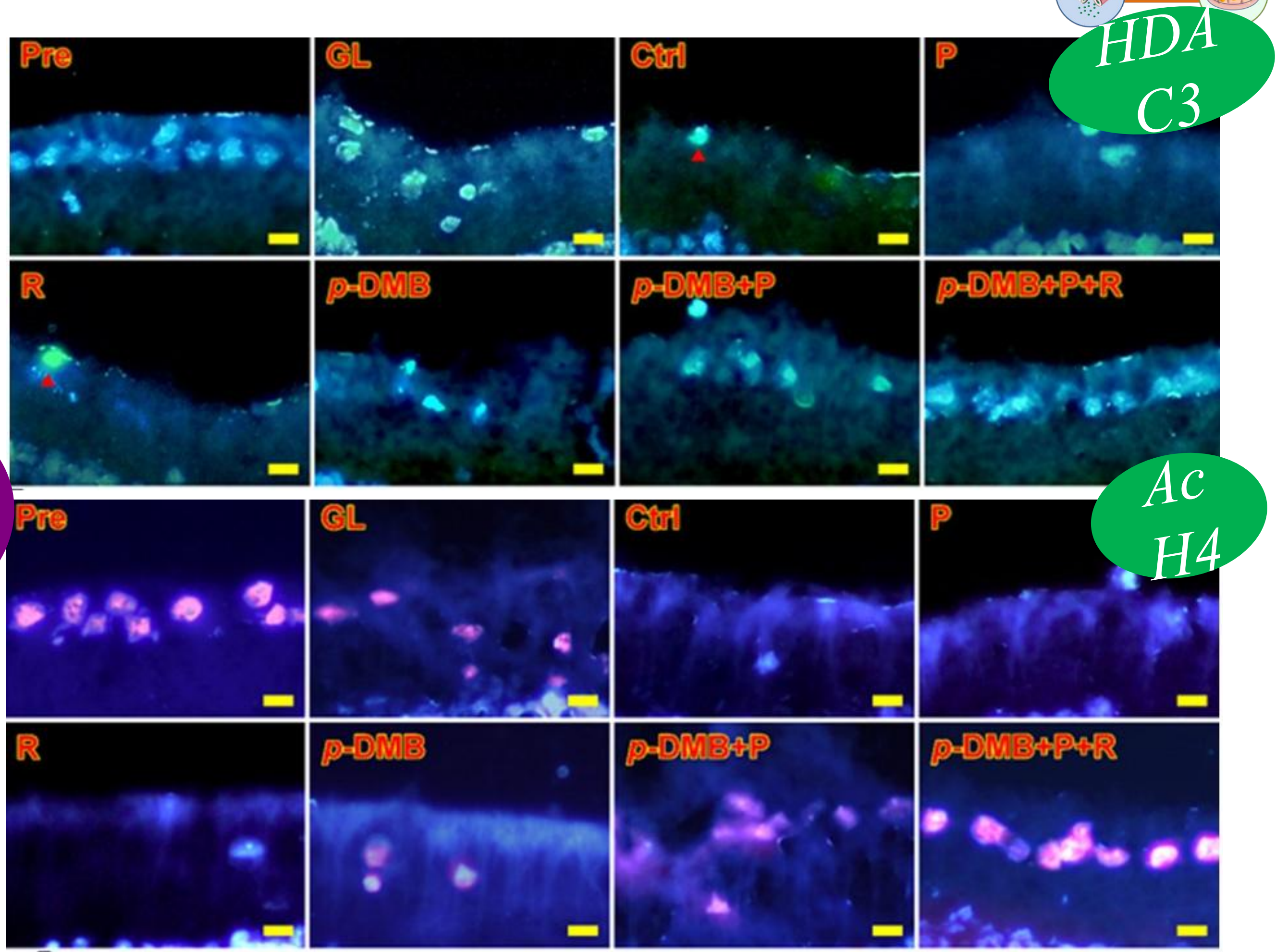




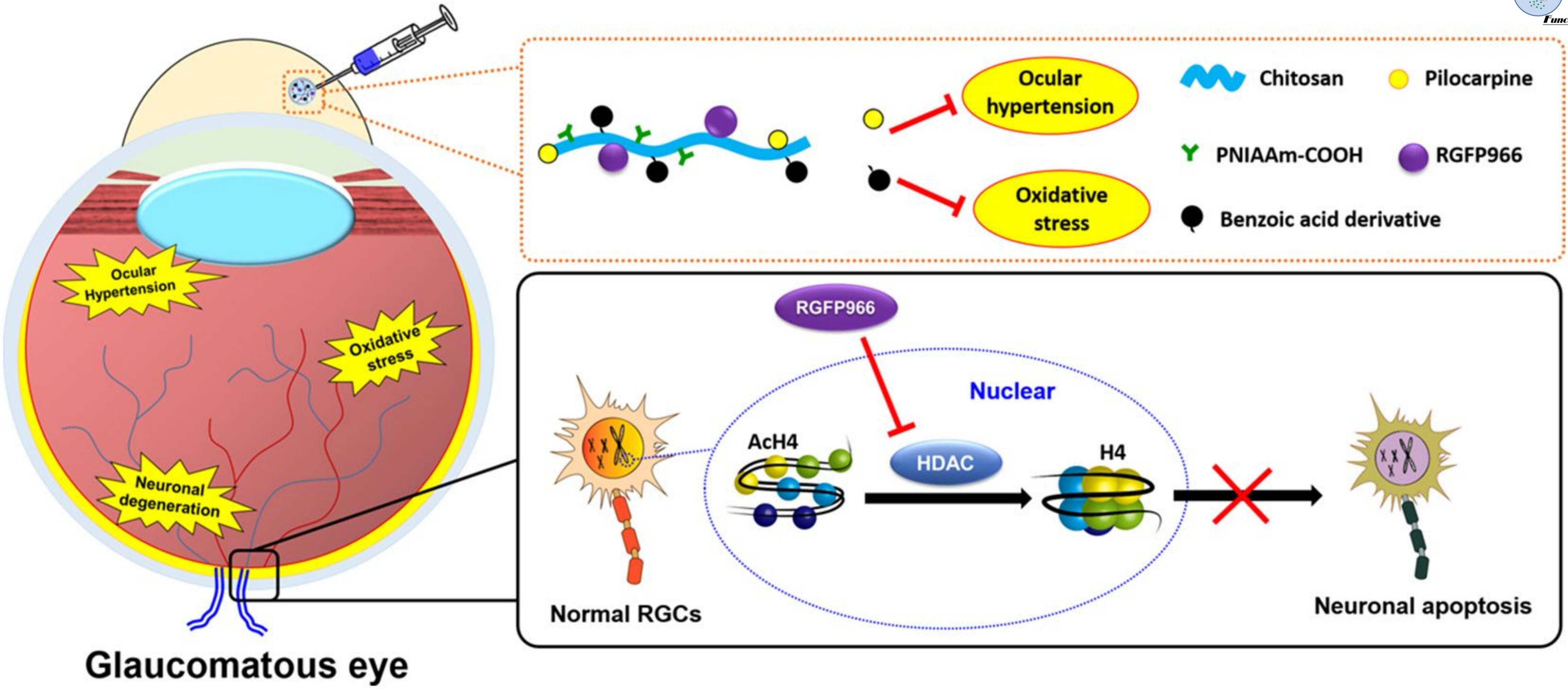


In Vivo Study



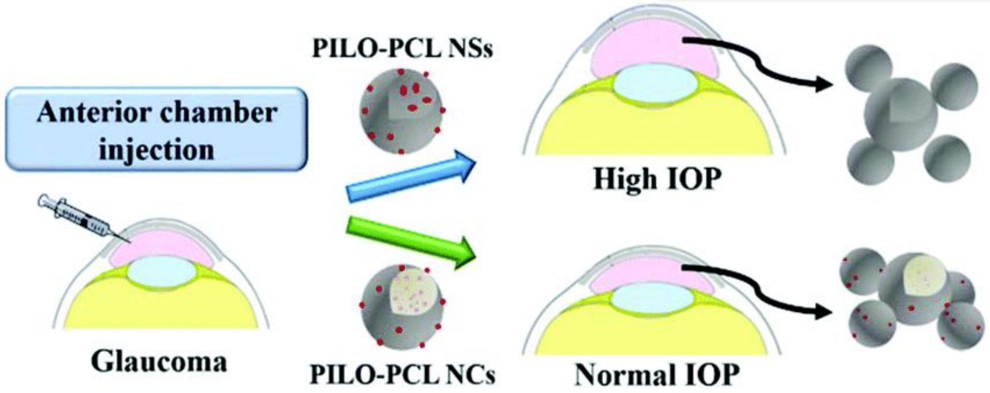


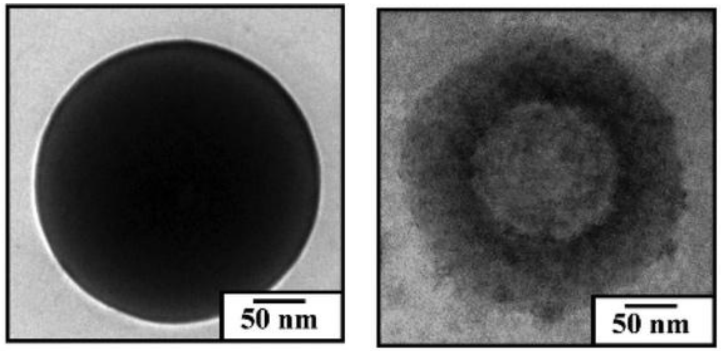
In Vivo Study

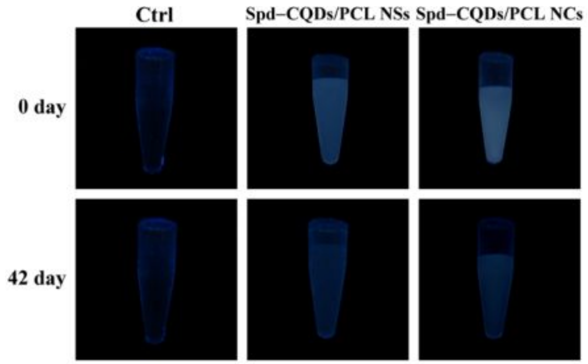


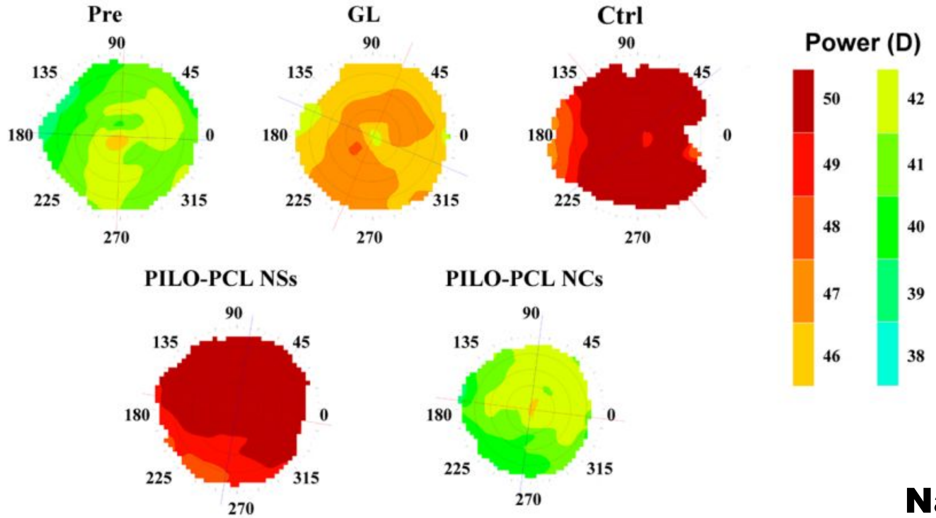
Nanocapsular System

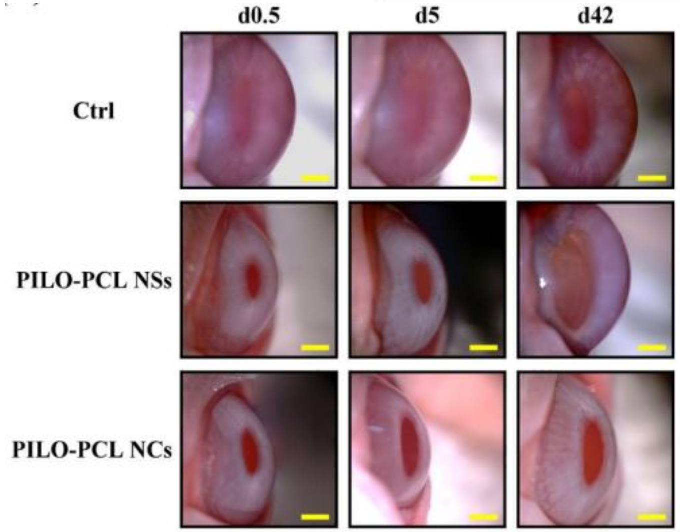
Polyester-Based Hollow Nanocarrier

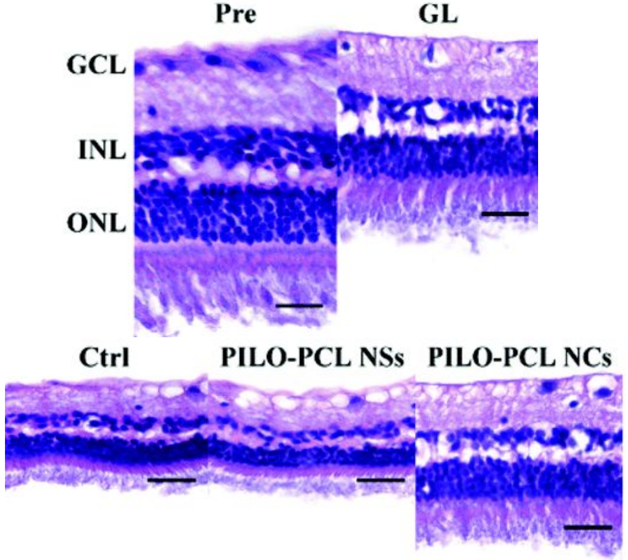






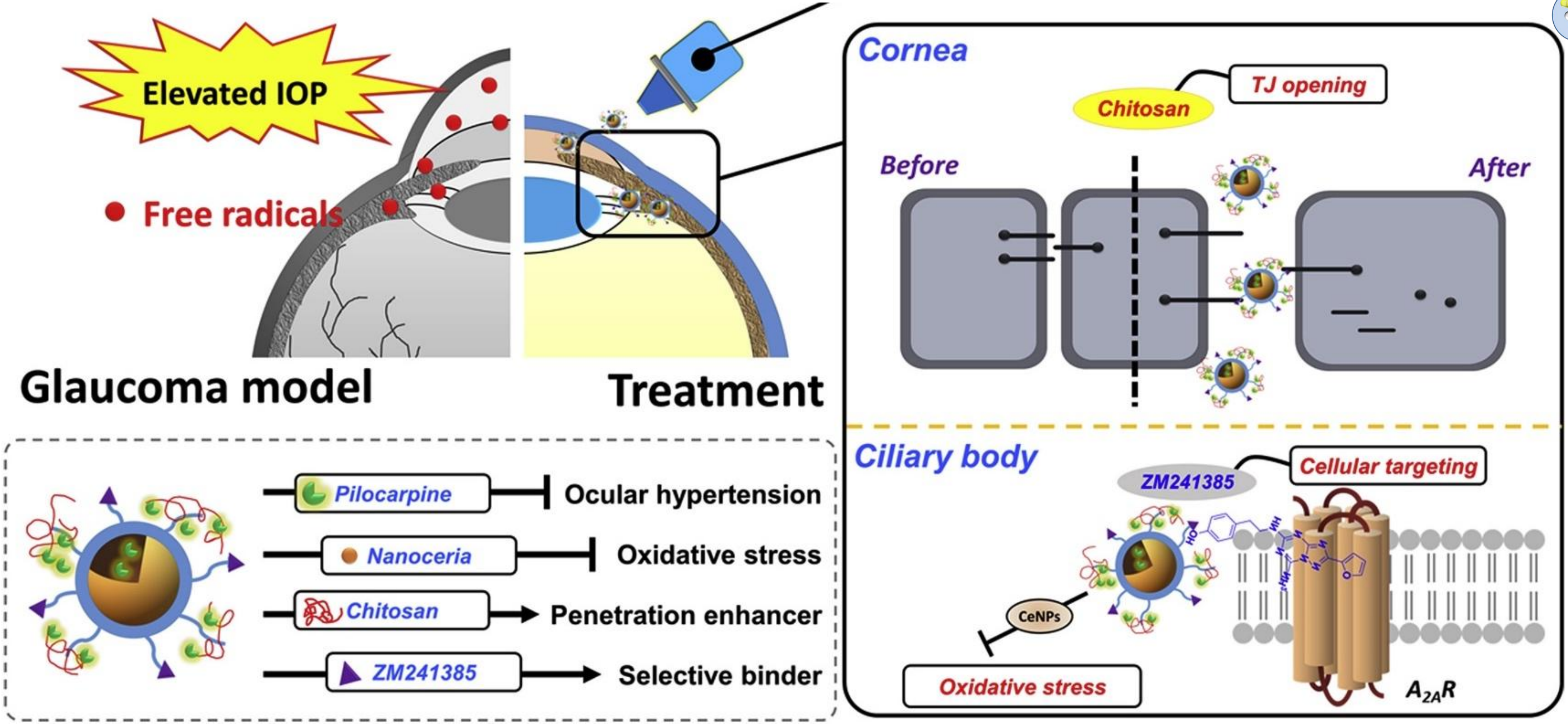






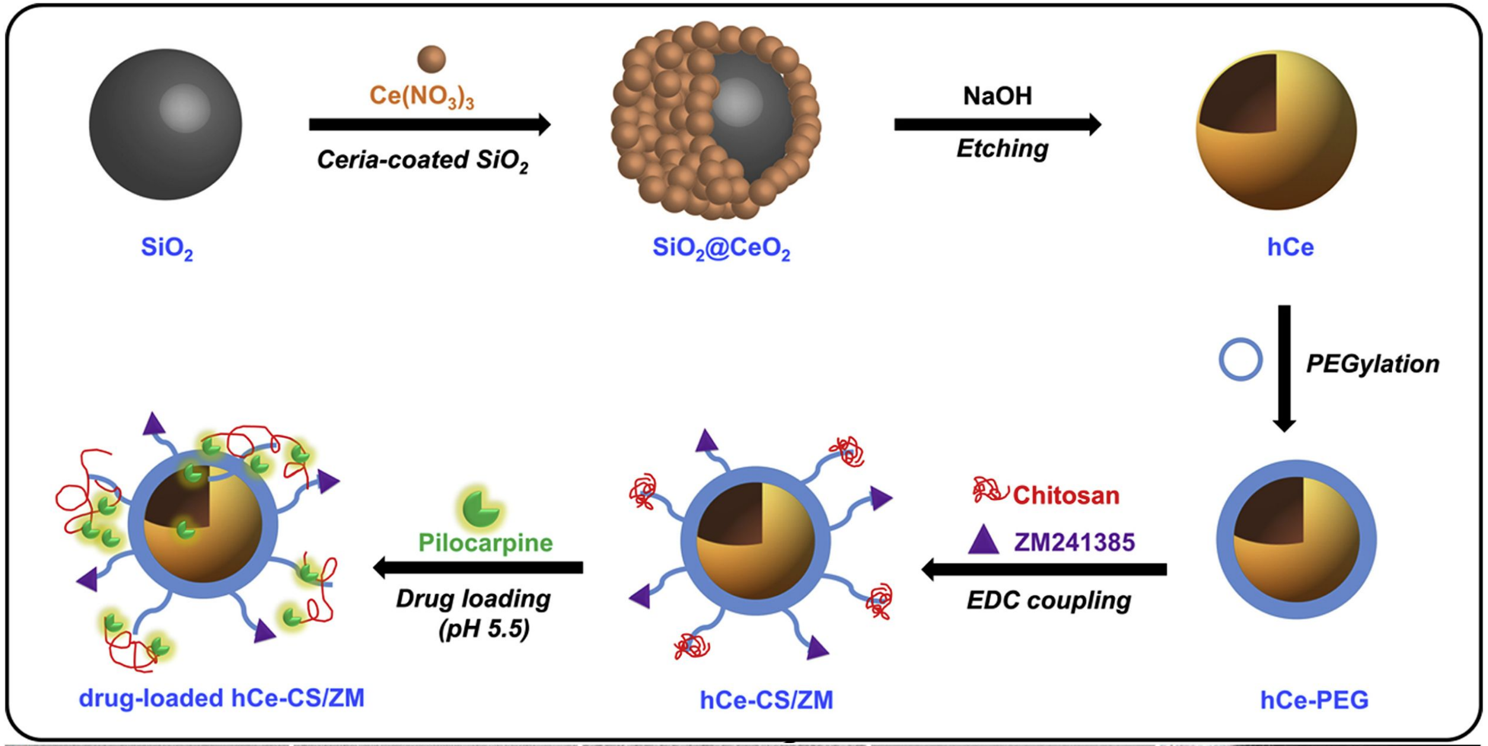
Nanoscale 2017;9:11754-11764

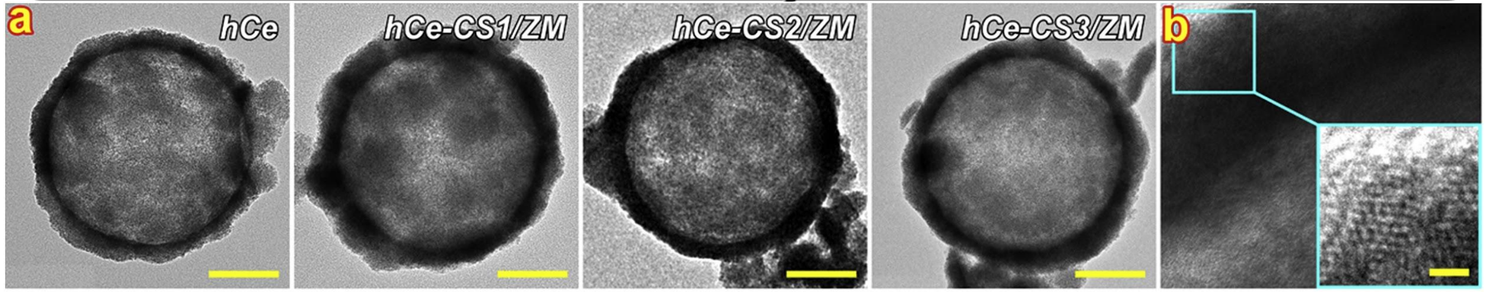
Eye Drop

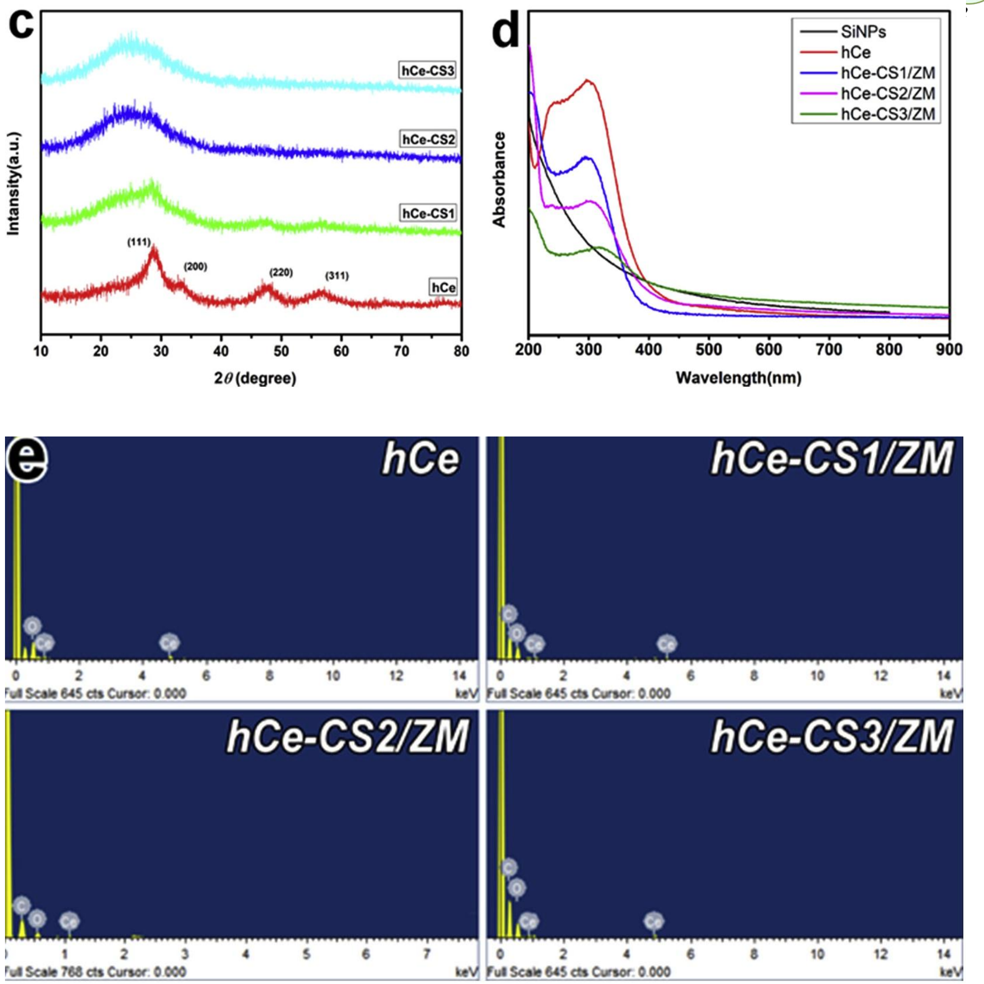


Biomaterials 2020;243:119961

Characterization

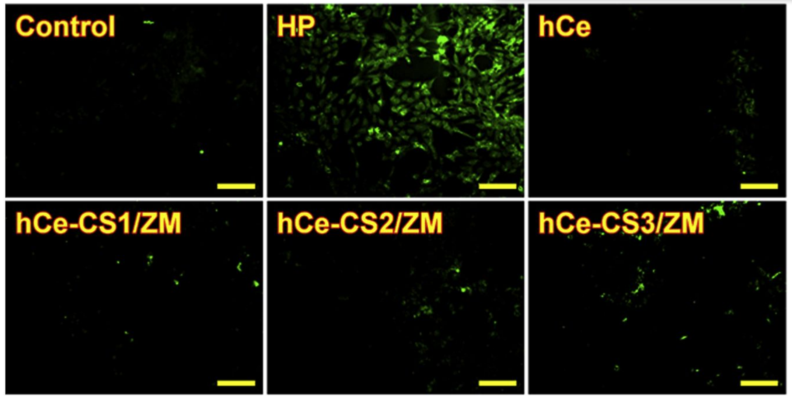


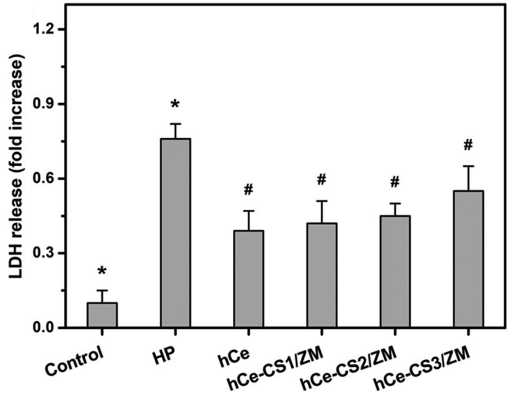




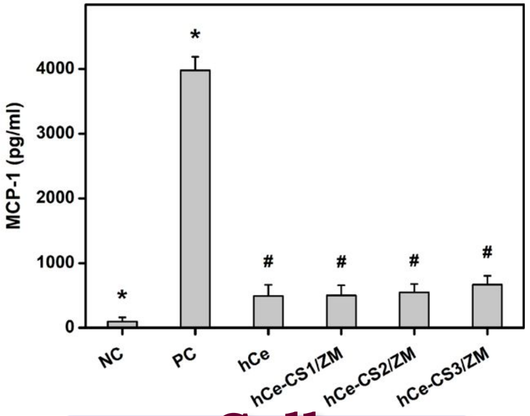
Functional Assay

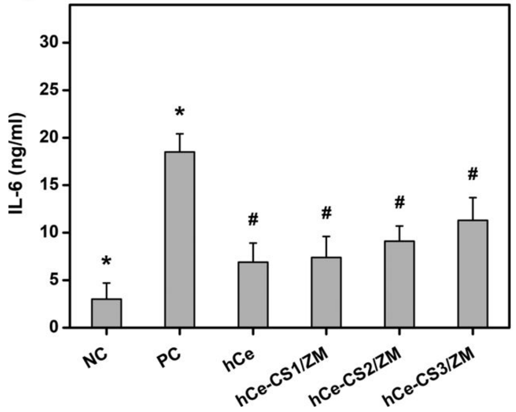
Anti-Oxidant



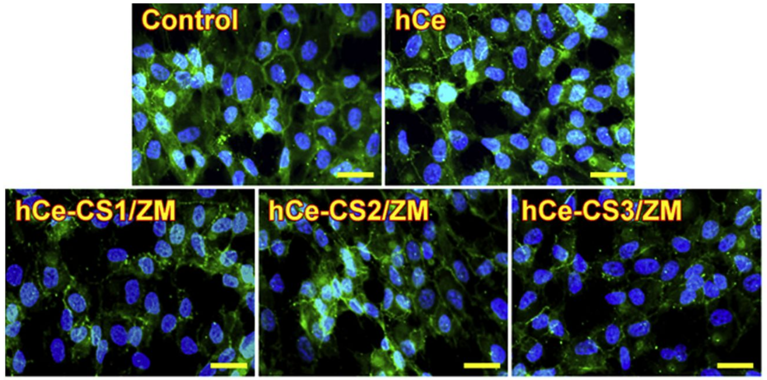


Anti-Inflammatory

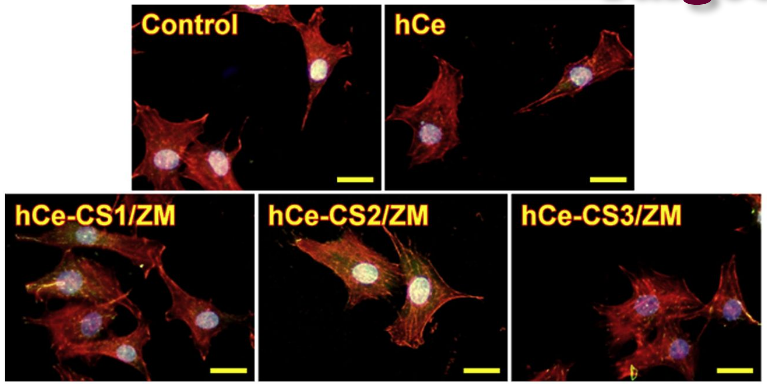


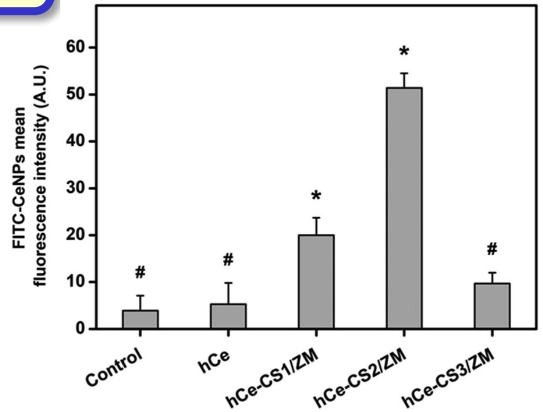


TJ Opening

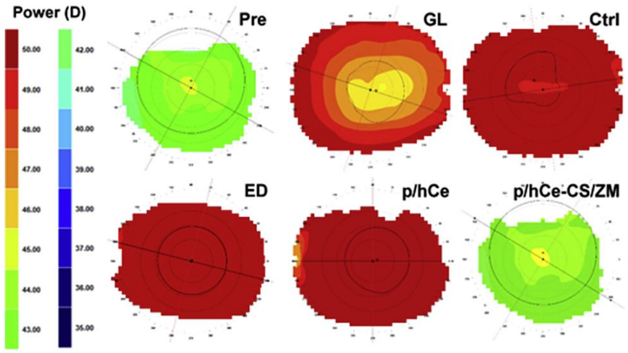


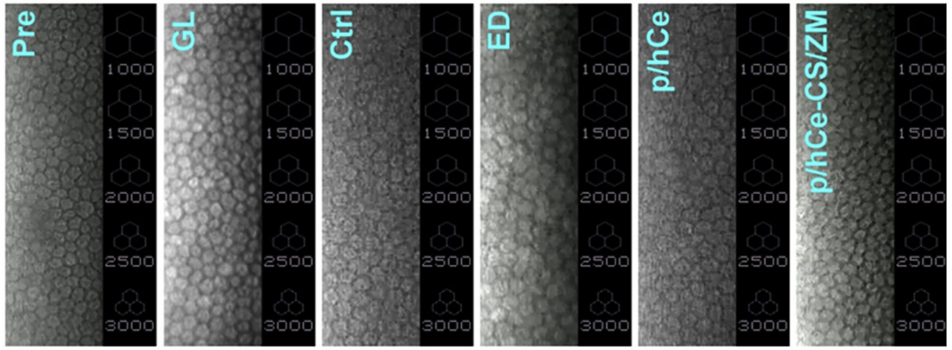
Cell Targeting

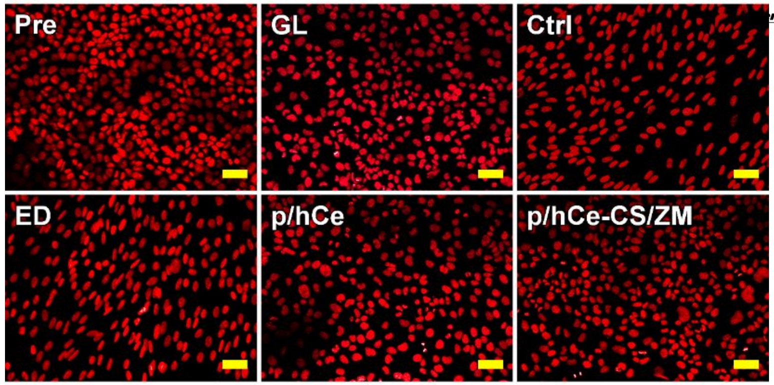


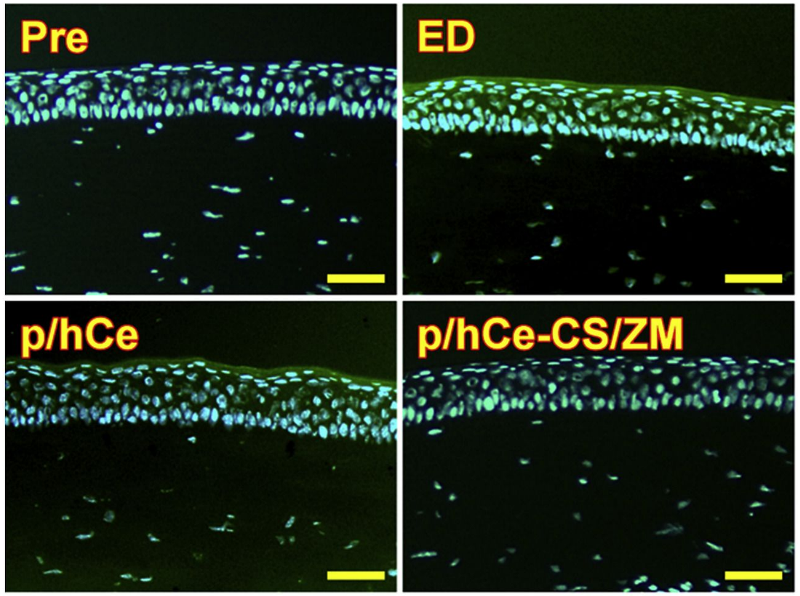


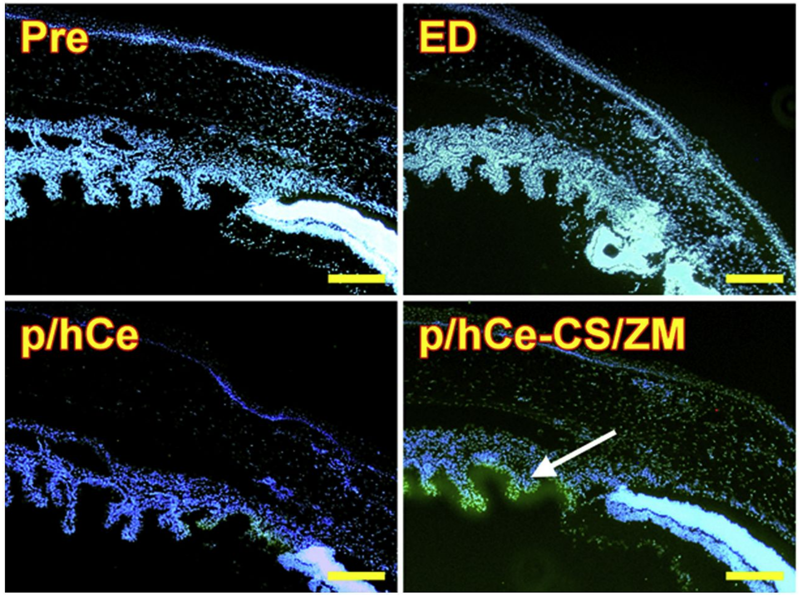
In Vivo Study

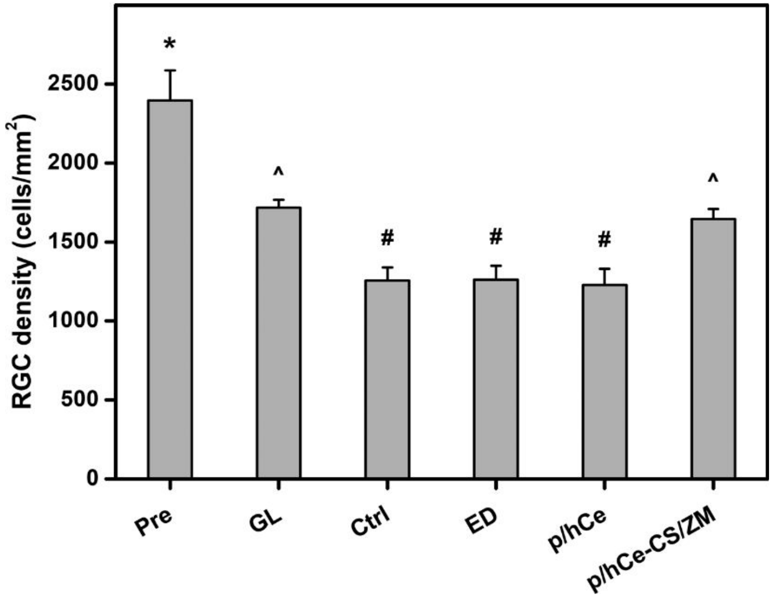




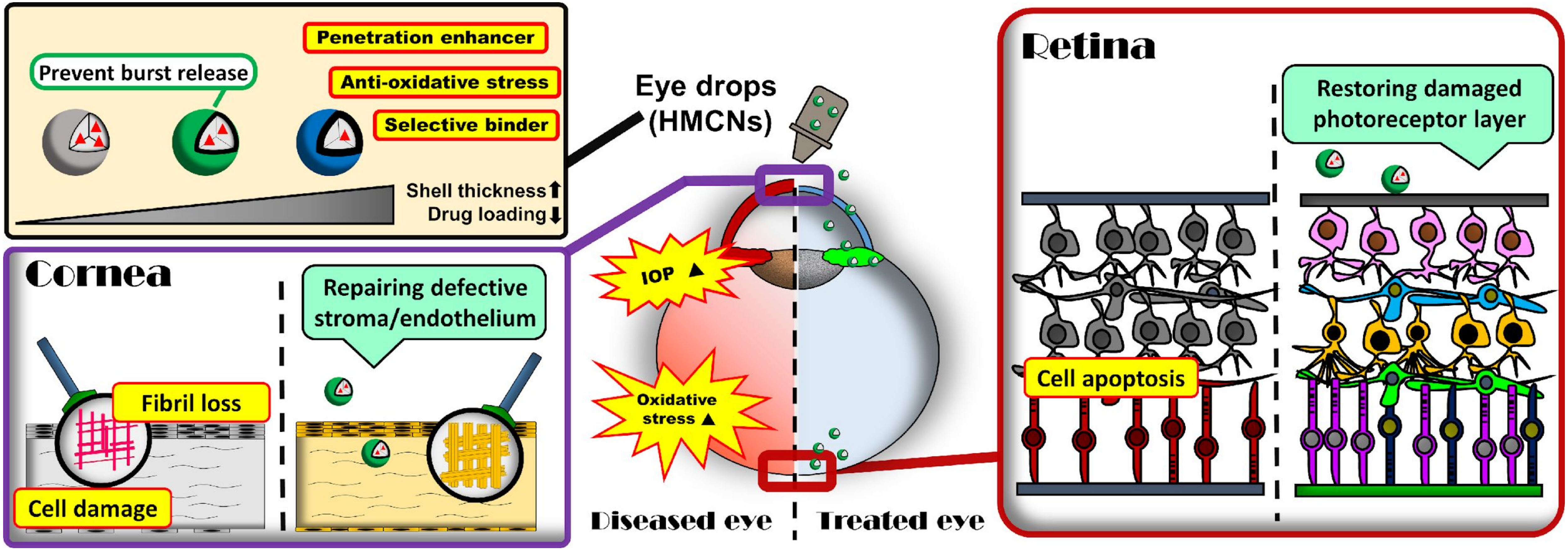








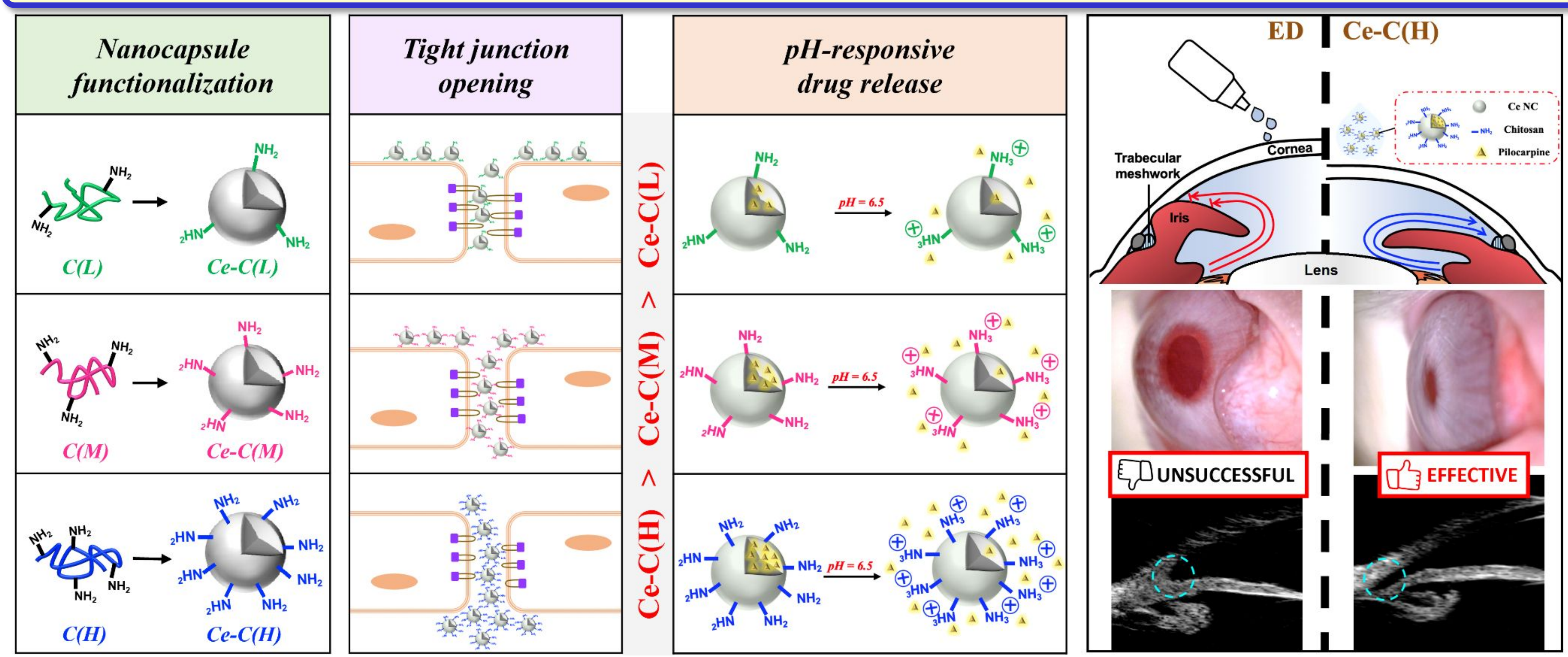
Effect of Shell Thickness



Theranostics 2021;11:5447-5463

Effect of Chitosan DD

Amination-Mediated Drug Delivery Performance for Acute Glaucoma Therapy

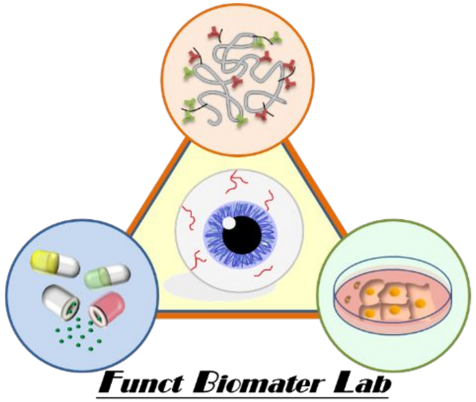


Chem. Eng. J. 2023;451:138620

Concluding Remarks

- Our findings suggest that multifunctional biomaterials may have potential for application as **injectable depot** or **eye drop** formulation for intraocular drug delivery

- Structure-property-function relationship can be tailored to the needs of **therapeutic DDS** for treating ocular diseases



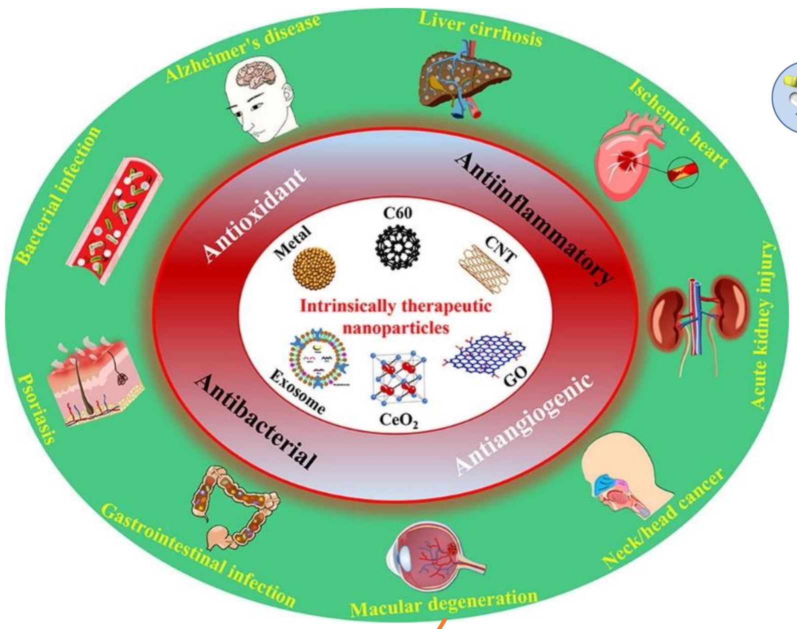
Acknowledgments

Group member: graduate students

Financial support: NSTC & NHRI

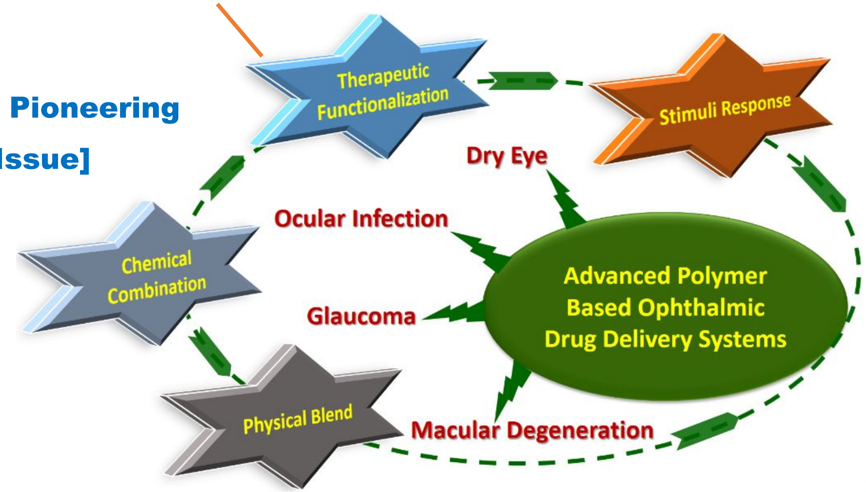
Disease Treatment: DDS/ITNP

[WOS Highly Cited Paper]



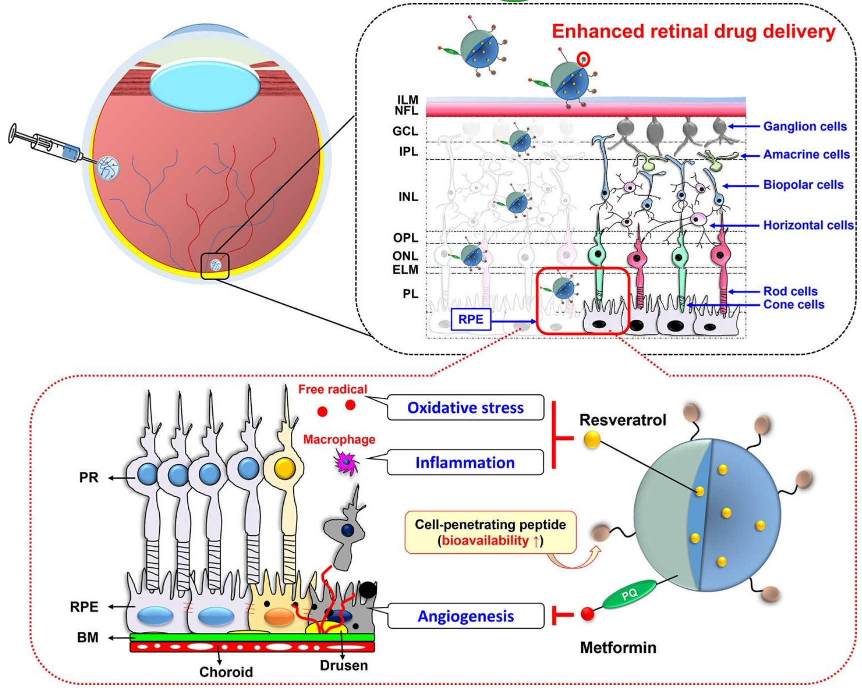
The development of efficient therapies for ocular diseases remains a significant challenge because of the static and dynamic barriers in the eye. A variety of pharmaceutical strategies have been explored to overcome these ocular physiological barriers and thereby improve therapeutic bioavailability in both anterior and posterior ocular tissues. This mini-review summarizes, analyzes, and discusses recent advances in the field of ophthalmic drug delivery systems (DDSs). Specifically, the focus is on design strategies using stimuli-responsive polymers and their applications for the treatment of prevalent ocular diseases such as dry eye, ocular infection, glaucoma, and age-related macular degeneration. The stimuli-responsive polymers are categorized according to their responses in various ocular environmental conditions (such as temperature, pH, and ions). Additionally, general strategies and methodologies for the construction of effective ophthalmic stimuli-responsive DDSs are investigated by exploiting key parameters such as the stimuli-response type, ocular biocompatibility, ocular biodegradability, drug encapsulation and release, as well as the modifiable structure of the polymers. Also discussed in this review are the interrelationships among the designed structures, properties, and functions of the stimuli-responsive DDSs and their pharmacological treatment efficacies. In summary, we believe that the recent progress in the field of stimuli-responsive DDSs constitutes a significant advance for the development of effective pharmacological treatments for eye disorders.

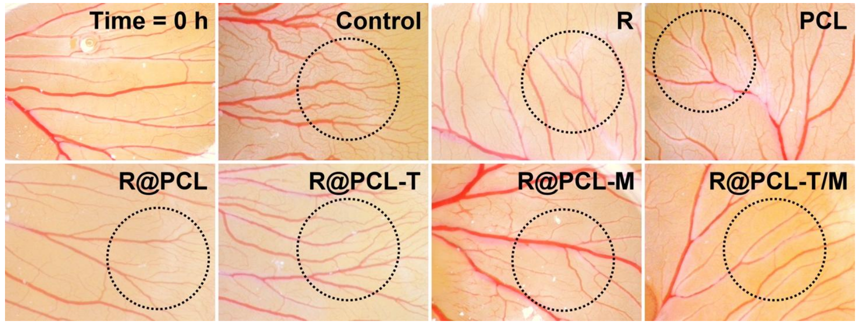
[Polymer Chemistry Pioneering Investigators Issue]

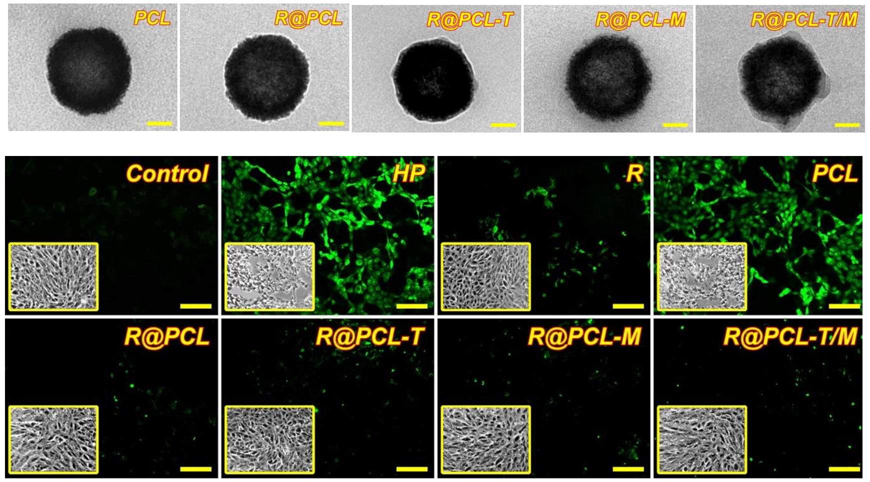


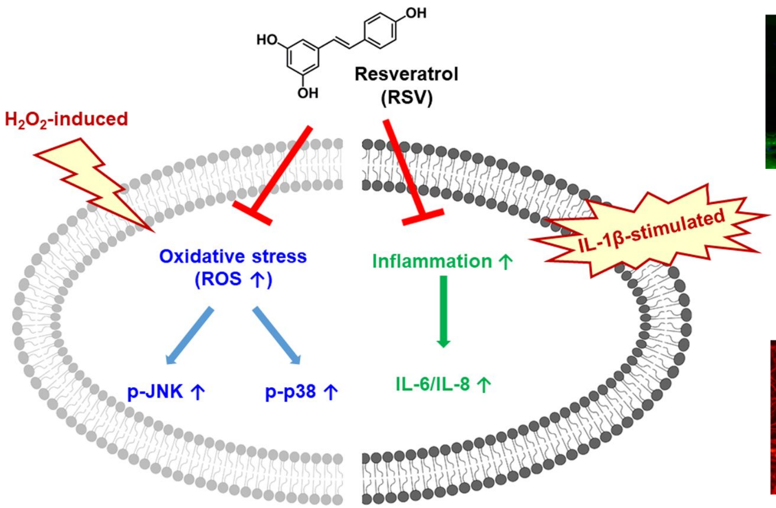
Intrinsically therapeutic nanoparticles (ITNPs) are a special class of nanomaterials with capabilities of self-triggering bioactive activities (without drug) when interacting with biological entities of interest. Typical bioactive features of ITNPs are antioxidant, antiinflammatory, antiangiogenic, and antibacterial properties, which can be medicinally exploited to treat a variety of diseases. Recently, ITNPs have considerably contributed to the development of numerous therapeutic modalities, simplified the formulation of nanotherapeutics, and promoted the translations of these intriguing biomaterials from bench to bedside. Therefore, this review summarizes, analyzes, and discusses recent advances of ITNPs in the treatment of diseases associated with four main risk factors: oxidative stress, inflammation, angiogenesis, and infection. Specifically, an update on the syntheses, bioactive properties, and biomedical assessments of ITNPs is provided. Moreover, therapeutic efficacies of ITNPs in pre/clinical trials are deliberated with respect to their physical/chemical characteristics; challenges and perspectives toward the clinical translation of ITNPs are also highlighted.

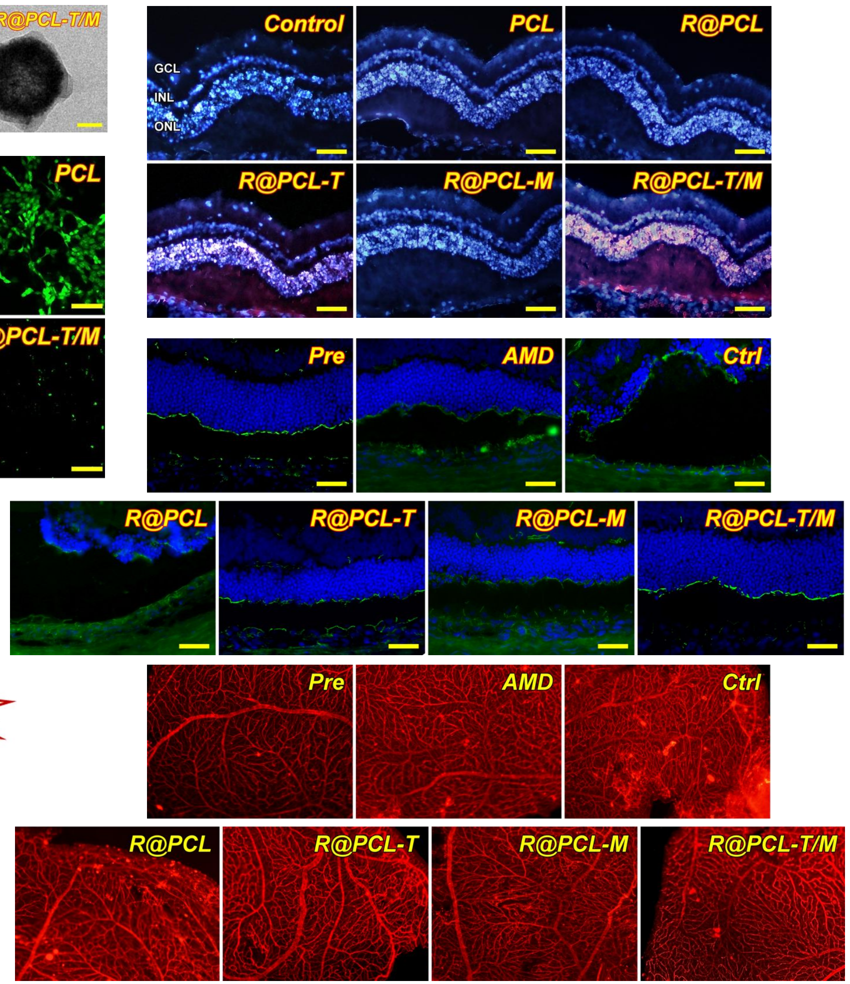
Macular Degeneration: Nanotherapeutics











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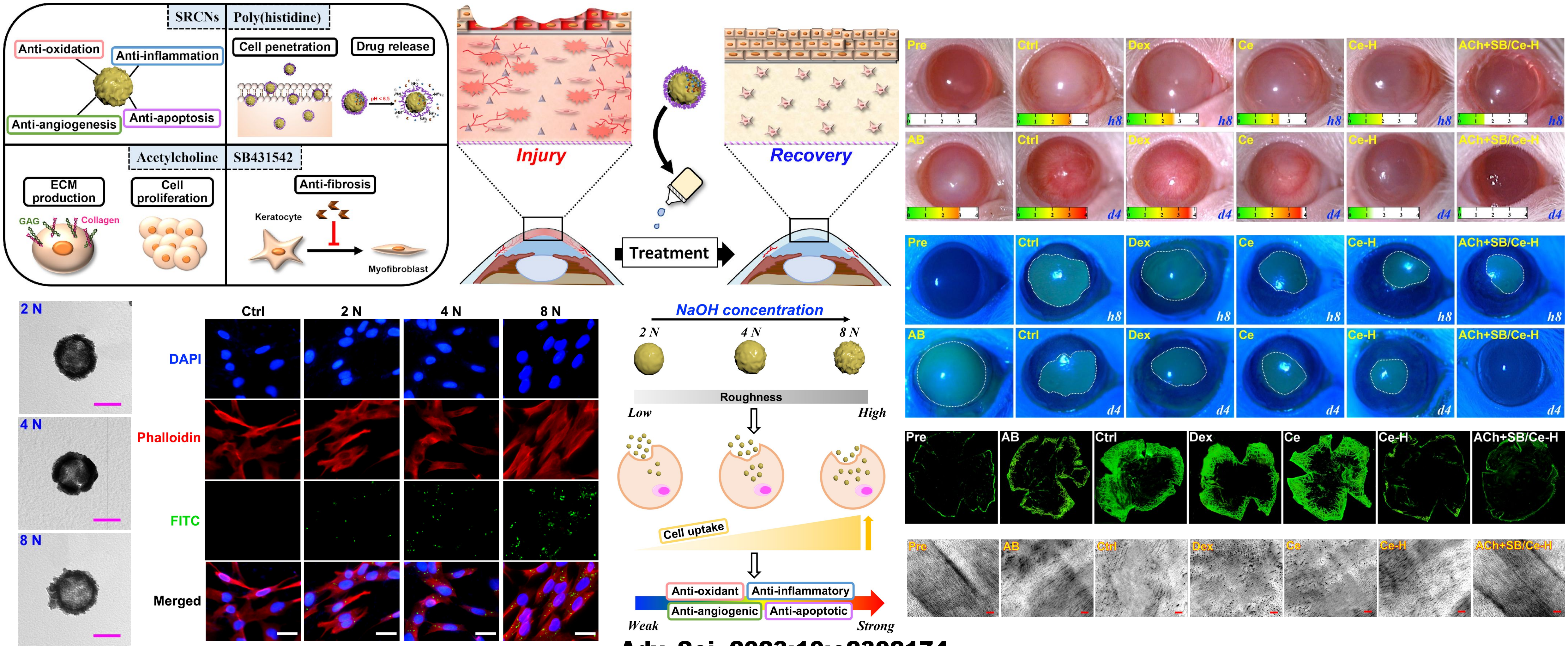
Corneal Alkali Burn: Nanomedicine



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