Payload Delivery Using Poly(glycerol ester) Polymers

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Thank you for joining us and welcome

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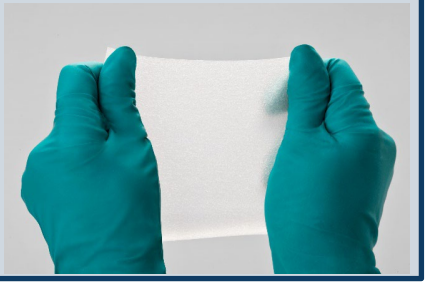
1. Secant Group Overview
2. Cationic PGE and Delivery to Cells
3. Applications: Delivery to Ocular Cells and iPSCs
4. Wrap-Up

Secant Group Overview

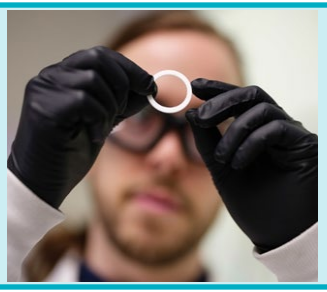
Secant Group focuses on polymer development for next-generation drug delivery and tissue engineering solutions for the medical device and pharmaceutical industries by engineering technologies that enable repair, recovery, and regeneration of the human body.

- *Decades of expertise in biomaterial research*
- *Development of proprietary, patent-protected polymer platforms*
- *Analytical testing & method development*
- *ISO 13485:2016 certified QMS*
- *ISO 14644:2013 Class 7 & 8 cleanrooms*

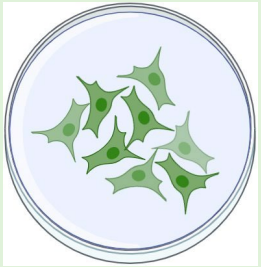
Poly(glycerol sebacate) (PGS is a tunable polymer used to enhance medical device implantation by promoting healthy tissue growth.



Hydralese ® is a tunable polymer platform for controlled release drug delivery of small and large molecules that originated with the development of poly(glycerol sebacate) urethane.



PGE+ Polyplex is a customizable poly(glycerol ester) for delivery of biological payloads .



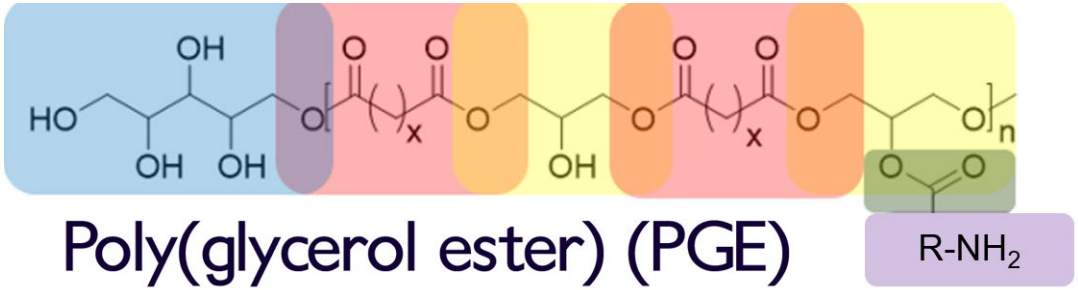
PGE Polyplex – Easy-to-use Delivery Vehicle

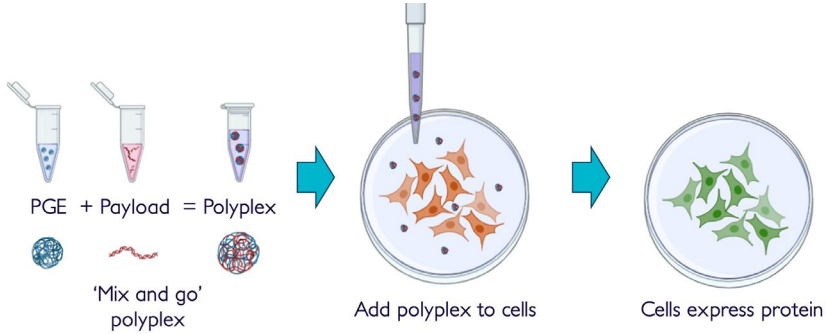
End-group chemistry:
- tunes hydrophilicity
- incorporate targeting ligands

Diacid selection:
- tunes hydrophobicity and particle assembly
- impacts stability

Glycerol modification:
- controls branching
- provides site bioconjugation

Amine attachment:
- impacts complexation
- affects biocompatibility
- release of payload

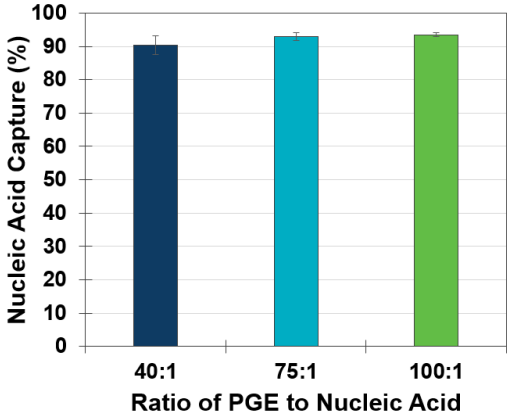




Poly(glycerol ester) (PGE) polyplex reagents are single component … no additives or enhancers required

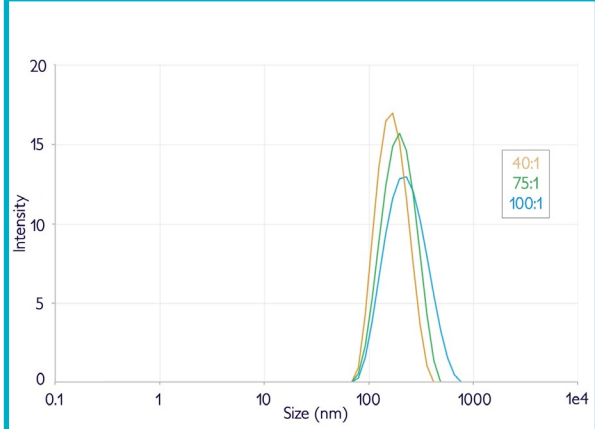
PGE Can Complex with Nucleic Acids

PGE Can Efficiently Capture Nucleic Acid Payloads



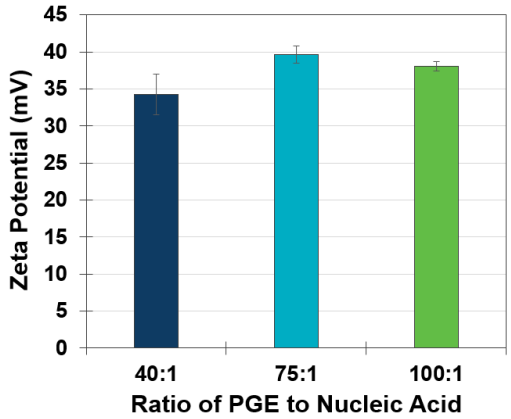
Nucleic acid capture with PGE is above 90% (PicoGreen Assay)

PGE Nanoparticles Are Sized Well for Cellular Uptake



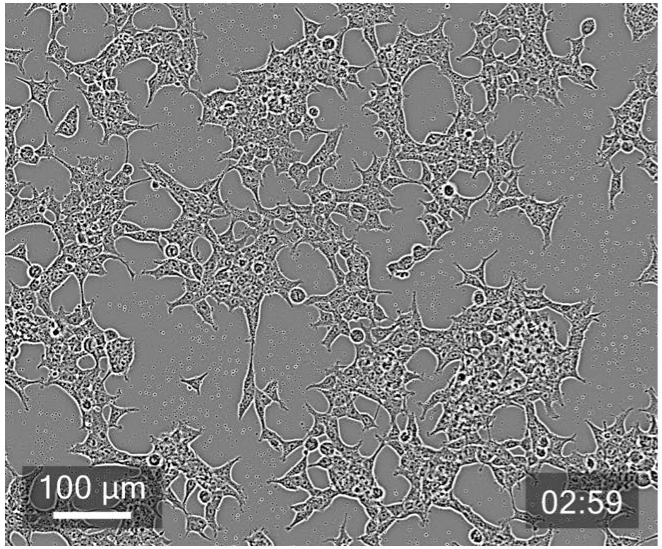
Polyplex size when complexed with 1 µg pDNA is between 150 to 250 nm at PGE:pDNA mass ratios ranging from 40:1 to 100:1

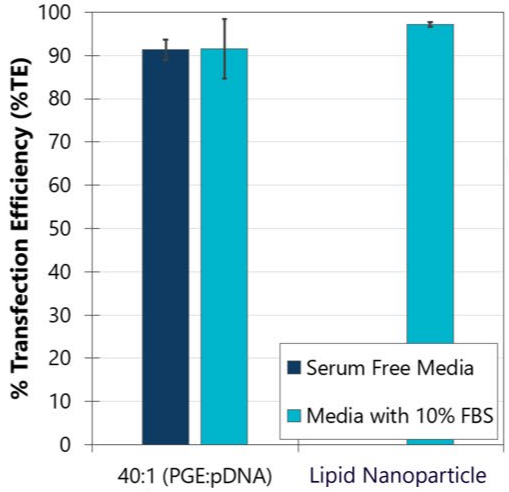
PGE Charge Enables Binding to Cell Membrane

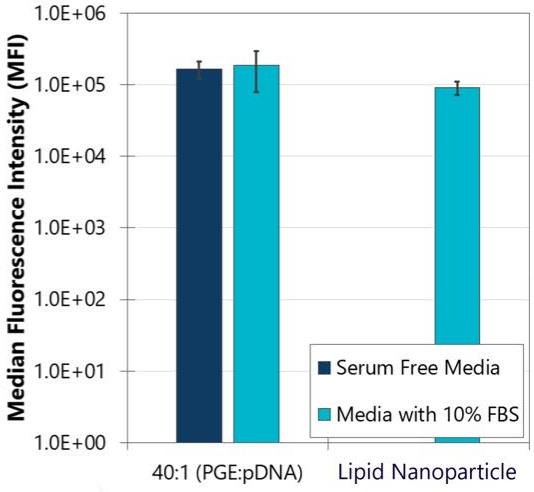


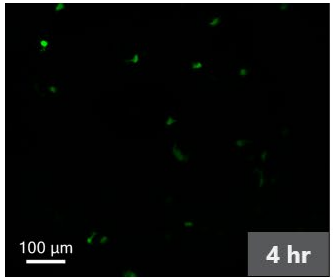
Positive zeta potential of PGE nanoparticles can bind to negatively charged cell membrane

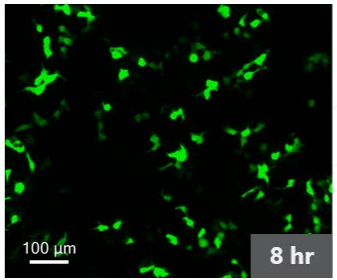
PGE Can Successfully Transfect HEK293T Cells

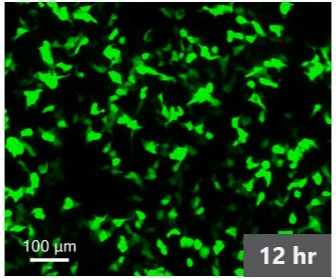


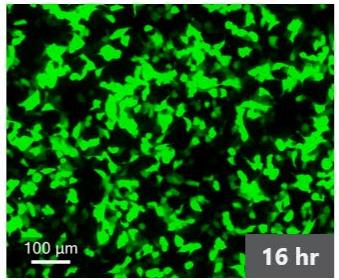


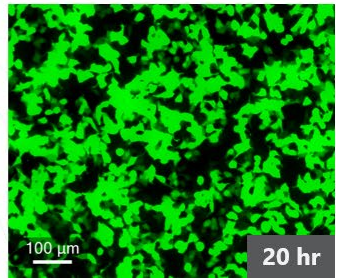






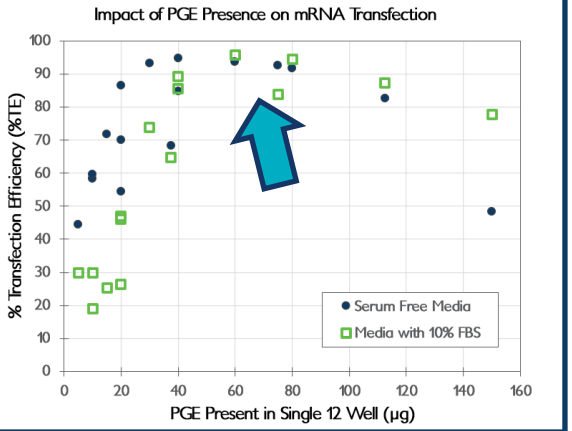






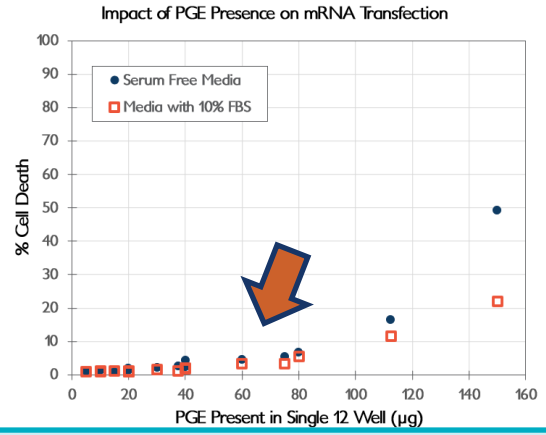
PGE Polyplex Efficacy Can Be Tuned

Optimal Concentration of PGE per Well Maximizes %TE



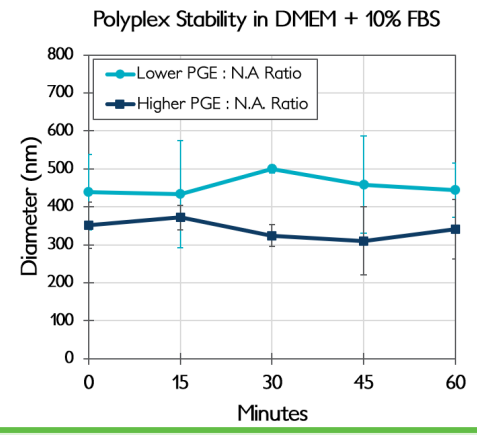
Concentration of PGE used yields maximal %TE at intermediate PGE levels.

Predictable Cytotoxicity Profile with PGE Use



PGE polyplex has low cytotoxicity at concentrations that maximize %TE. Very low cytotoxicity seen at lower concentrations that have moderate %TE.

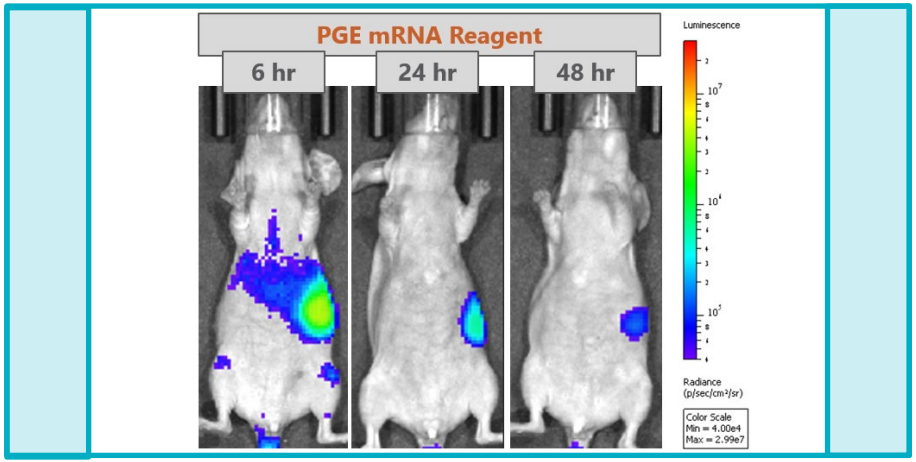
Particles Have Good Stability when Added to Media

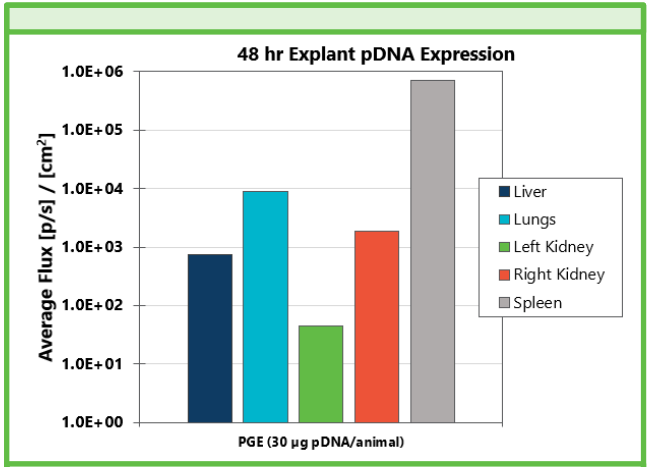


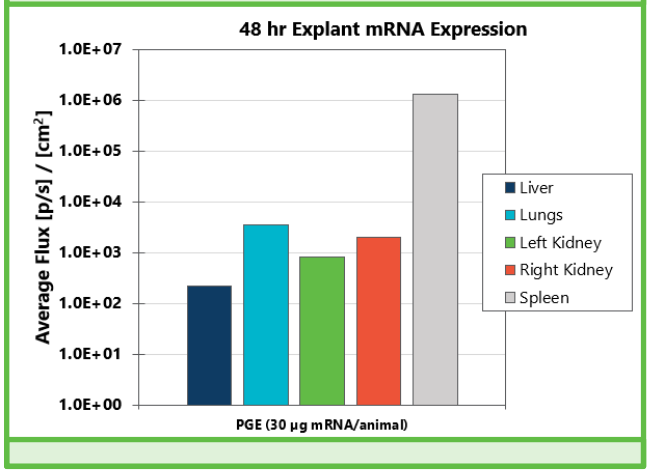
PGE polyplex does not show significant change in particle size over time upon addition to cell culture media containing serum.

PGE Polyplex Can Deliver *In Vivo*

- Testing Parameters:
  - Dosage: 20 µg/mRNA or pDNA per animal.
  - Tail vein injection into NCr nu/nu female mice.
  - Whole animal imaging at 6 hr, 24 hr, and 48 hr.
  - Ex-vivo imaging of organs after 48 hr timepoint.
- Success delivering **both mRNA and pDNA** in mouse model
- Expression primarily in spleen for both payload types
- No adverse response by any animals

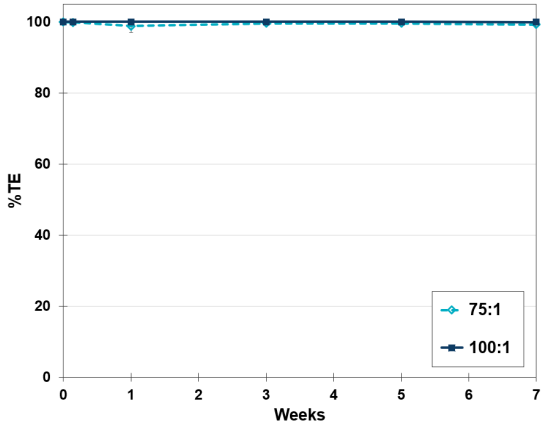


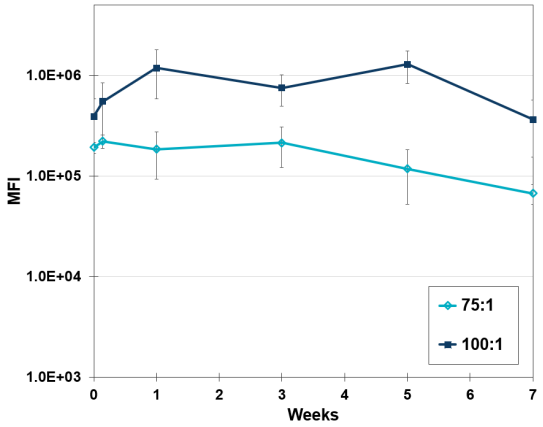




PGE Can Be Pre-complexed and Used After Storage

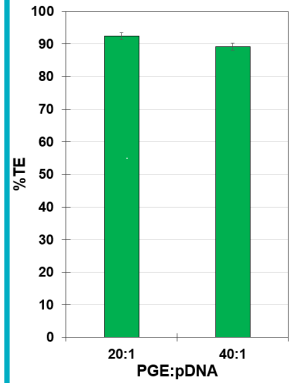
No Loss in Transfection Efficiency after Storing Pre -complexed PGE Polyplex

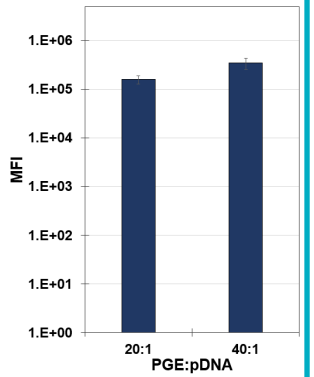




Plasmid DNA was pre-complexed with PGE and stored at 4 °C prior to use with HEK293T cells. Pre-complexed nanoparticles maintain high delivery efficiency and green fluorescent protein (GFP) reporter expression levels for at least seven weeks.

Loaded PGE Nanoparticles Can be Freeze Dried

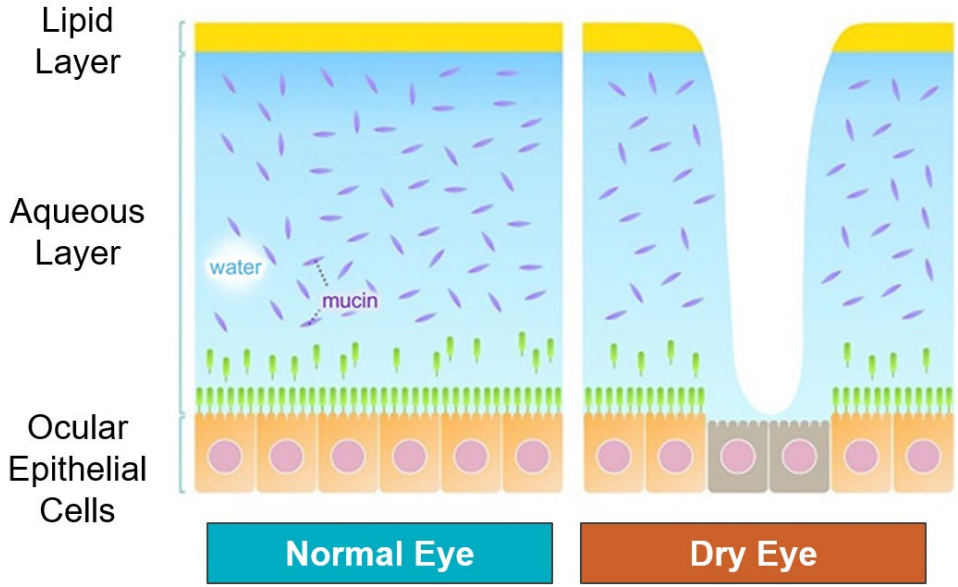




PGE complexed with pDNA was freeze dried and then reconstituted with media following one week storage at -80°C

PGE As a Candidate Material for Dry-eye Treatments

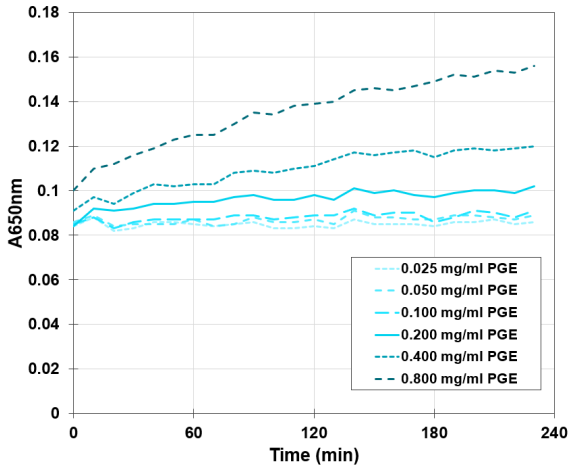
- We are focused on determining if PGE can have a benefit in the ocular space through interactions with mucin and epithelial cells
  - Positive zeta potential of PGE nanoparticles can help PGE interact with both
  - Help restore tear film layer
  - Improve retention time of APIs
- One area of interest to us is improving treatments for dry eye
  - Epithelial cells during dry eye are damaged and have difficulty returning to normal physiological state
  - PGE has shown to be friendly to cells during nucleic acid delivery



Collapse of the Glycocalyx in Dry Eye
https://www.glycoforum.gr.jp/article/26A15.html

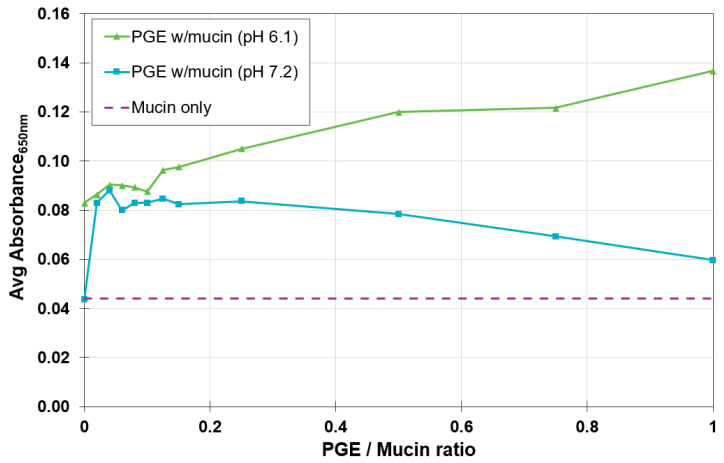
PGE Has a pH Dependent Interaction with Mucin

PGE Shows Increasing Interaction with Mucin Over Time



PGE remains ‘sticky’ to mucin over time in a concentration-dependent manner.

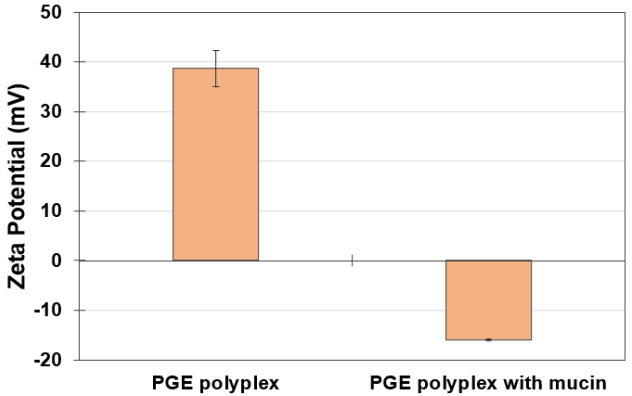
PGE Shows Interaction with Mucin Across a Range of Concentrations

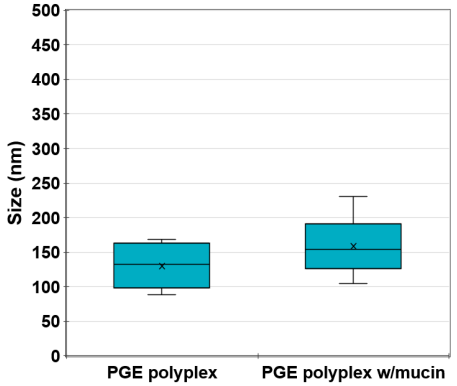


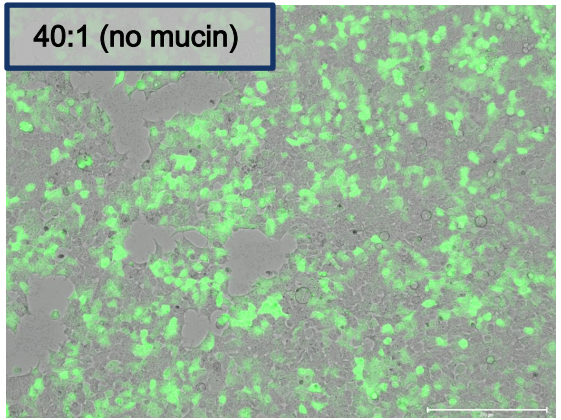
PGE has improved interaction with mucin at lower pH as concentration increases. PGE has best interaction with mucin near neutral pH when PGE concentration is low.

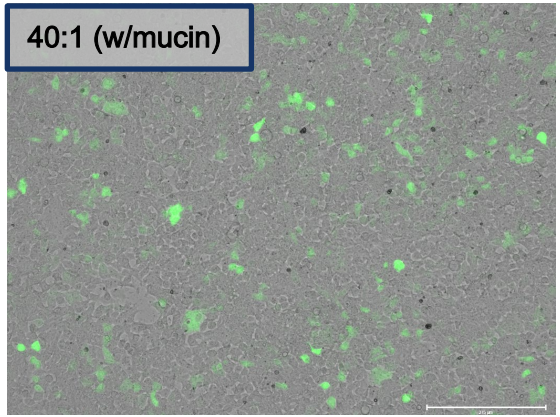
PGE Delivers in the Presence of Soluble Mucin

- **PGE was able to deliver payload when soluble mucin added to media:**
  - Testing in presence of 0.05 wt% mucin
  - HEK293T cells w/serum present
  - Assessment 24 hr post-transfection with GFP reporter pDNA



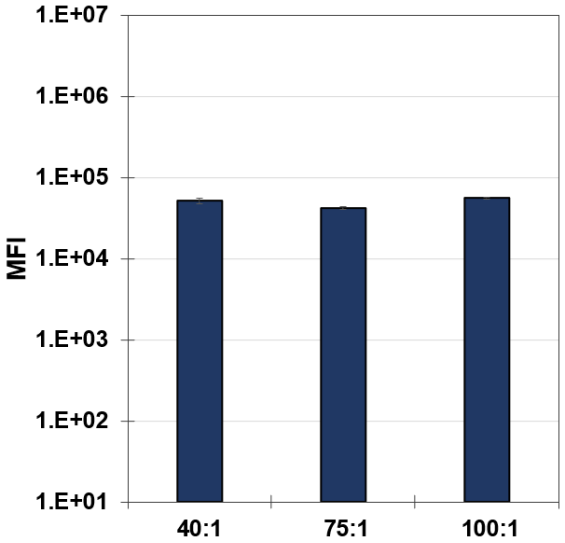


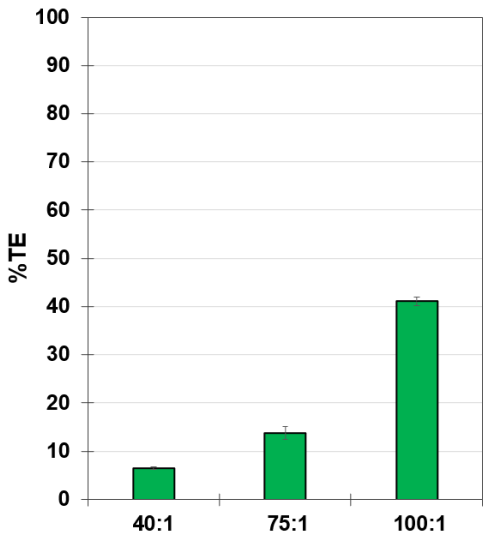


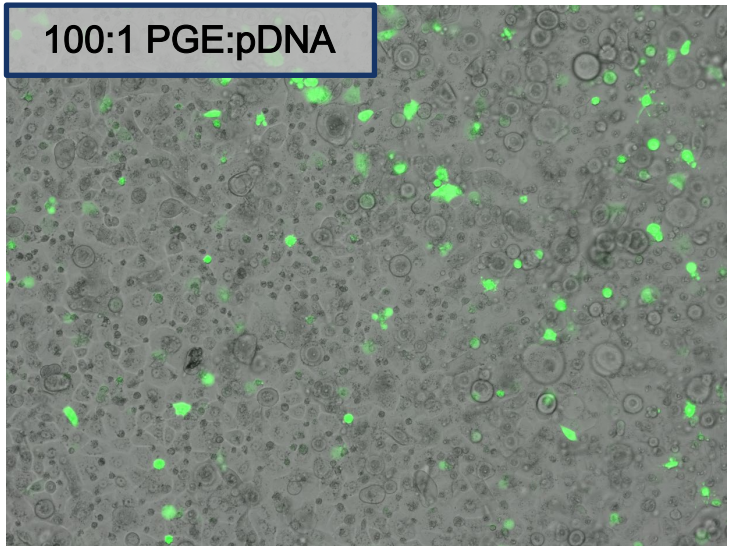


PGE Can Deliver to Corneal Cells

PGE Can Deliver to Cells that Express Membrane -bound Mucin



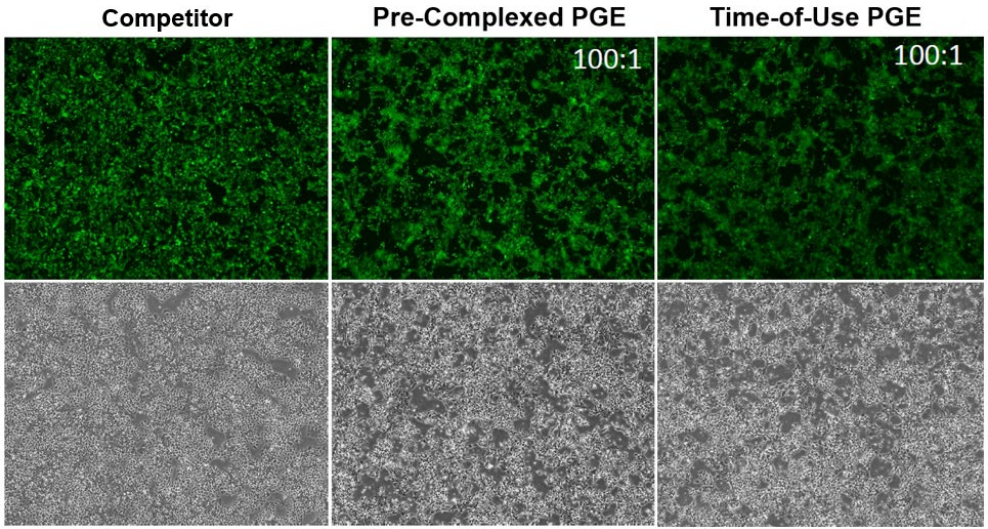


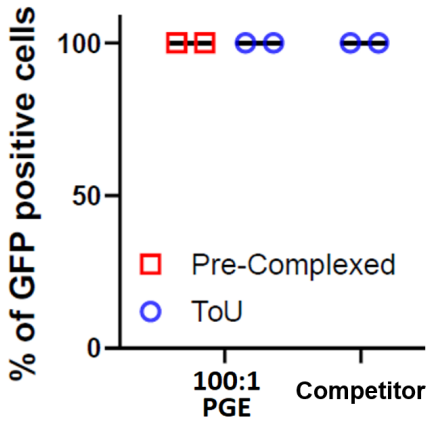


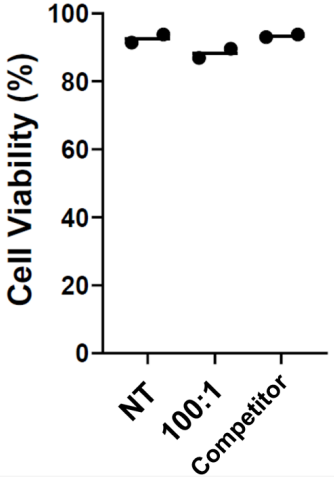
Higher ratios of PGE to nucleic acid improves the percentage of cells expressing green fluorescent protein (GFP) reporter.

PGE Can Deliver mRNA to Polyclonal iPSCs

- Study performed in collaboration with Pluristyx (Seattle, WA)
- Compared PGE with commercial reagent
- Delivery of 1000 ng GFP mRNA per well to iPSCs
- Similar performance of PGE polyplex when used immediately (ToU) or after 24 -hours storage (4°C) following complexation with mRNA



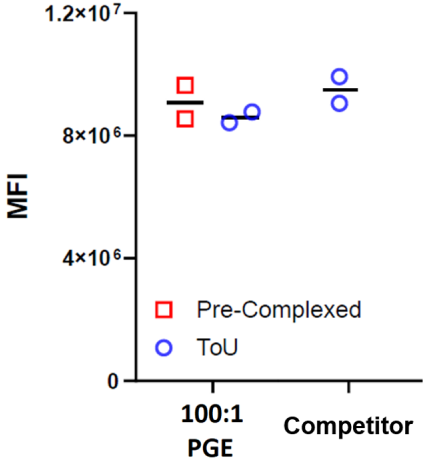


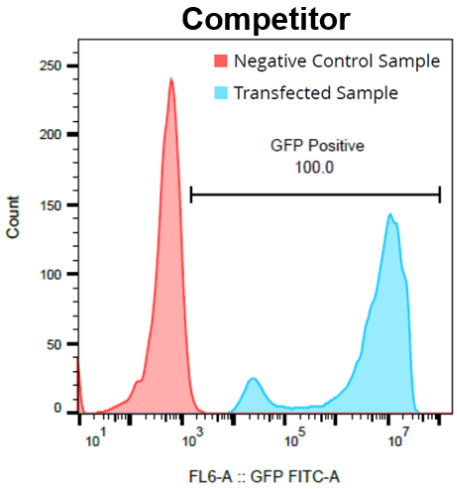


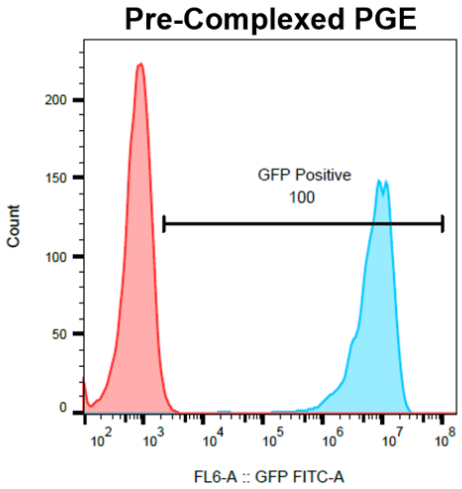
PGE Can Deliver to Polyclonal iPSC Subpopulations

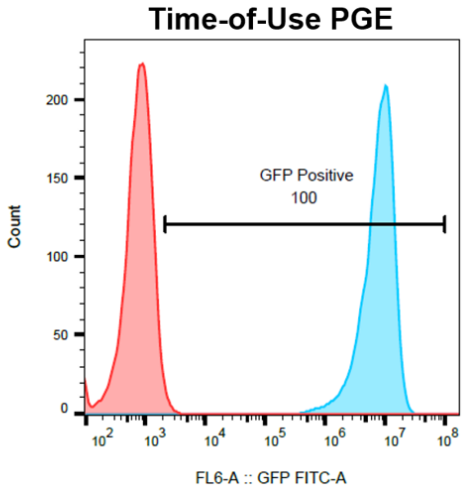
- **Similar levels of mRNA expression** between PGE and commercial reagent
- mRNA delivery with **PGE** ensures uniform, high-level protein expression **across the entire cell population**

pluristyx®









Poly(glycerol esters) (PGEs) are a new biodegradable polyplex reagent that can be used to deliver biologics.

- ✓ Cationic PGE can deliver both pDNA and mRNA
- ✓ Able to deliver payload to multiple cell types
  - ✓ HEK293T, primary corneal, iPSC
- ✓ Able to protect mRNA and deliver *in vivo*
- ✓ Can beneficially interact with mucosal layers

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Partner With Secant Group

We are actively looking for partners interested in beta-testing this polyplex technology to address your specific needs and payloads

Thank you for your time!

Questions?
Please visit us at booth #104

Interested in more from Secant Group?
Track 3B: Novel Device Technologies @ 6:00PM – 6:15PM
Enabling Accelerated Development of a Drug-Loaded Polyester-Based Implants Through Multiphysics Modeling
Presented by Victor Mishin, Scientist II, Translational PD