Ultrastable™ bFGF

The Most Stable Growth Factor for Regenerative Repair of Corneal Injuries.

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Disclaimers And Conflict of Interest

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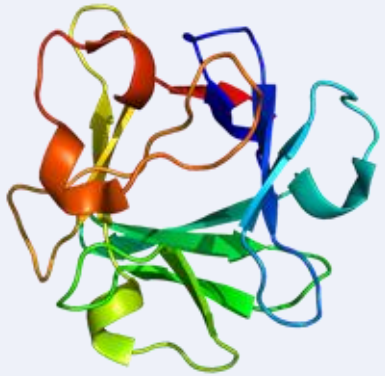
Patent filed: Ultrastable Basic Fibroblast Growth Factor Variants and Methods of Use – PCT/US26/25294

Problem Statement

- About 10% of all battle-related injuries to our troops are corneal, resulted from mechanical or chemical insults
- Approximately 3% of all visits to the emergency department are due to corneal injury
- Corneal injuries can lead to not only extreme pain but also compromised vision or even blindness
- Current treatment primarily focuses on symptomatic management, prevention of infections, as there are no approved therapies available to enhance the rate of healing or the clarity of the cornea

Source: Tactical Life

bFGF is a Critical Growth Factor in the Regenerative Medicine Field.



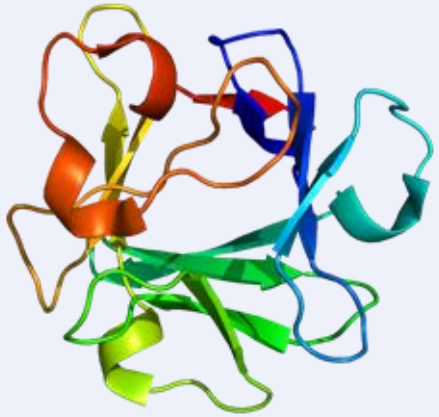
Basic fibroblast growth factor (bFGF) is a potent growth factor with **tissue repair, anti-inflammatory, and neurotrophic effects**, making it a promising agent for treating various ocular surface injuries, including corneal abrasions, dry eye with corneal damage, and post-surgical surface damage

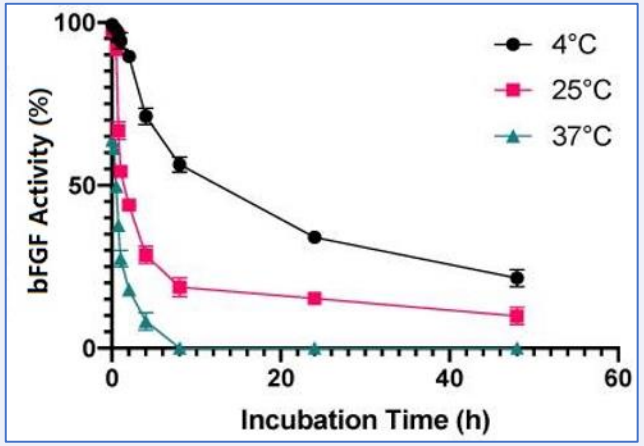
bFGF promotes:

- **Epithelial cell proliferation and migration** to accelerate wound healing
- **Angiogenesis regulation** (in corneal neovascularization contexts)
- **Anti-inflammatory effects** by reducing tear inflammatory markers like IL-1β and IL-18
- **Neurotrophic support** for ocular surface nerves

Chen et.al, *Front Pharmacol*, 2020
Zhao et.al, *Alt. Therapies in Health and Medicine*, 2023

bFGF is a Critical Growth Factor in the Regenerative Medicine Field, but Instability Remains a Core Limitation





- bFGF (basic fibroblast growth factor) has strong mitogenic activity
- The instability of currently available bFGF prevents its application in the healing of corneal injuries
- bFGF must be stabilized before clinical translation as a regenerative therapy

Hypotheses & Research Aims

Hypothesis

- The robustness of bFGF can be substantially improved for clinical relevance in practice
- Algae derived bFGF has improved biosafety and economics
- The enhanced bFGF will facilitate reliable evaluation on its potential in corneal treatment

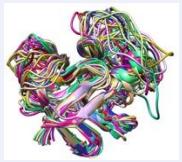
Specific Aims

- Develop a stable bFGF through AI-enabled iterative design.
- Evaluate the efficacy of the designer bFGF in the treatment of corneal injuries using animal models.

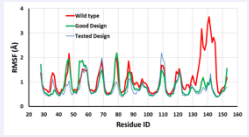
Technology Platforms

AI + molecular-dynamics (FEP) pipeline to engineer stable growth factors

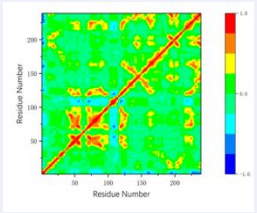
bFGF MD conformations



Identify unstable amino acids and their correlated residues



Unstable amino acids



Correlated residues

AI-based mutation scan
Free-energy ranking across residues

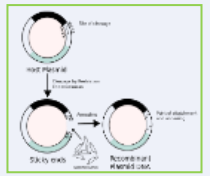
Stabilizing amino-acid mutations

MD-based free-energy perturbation (FEP) calculations

Wet-lab validation

SynBio-enabled algae production platform

Animal-free, endotoxin-free, and cost-efficient



Expression Vector

Transformation

Selection

Production

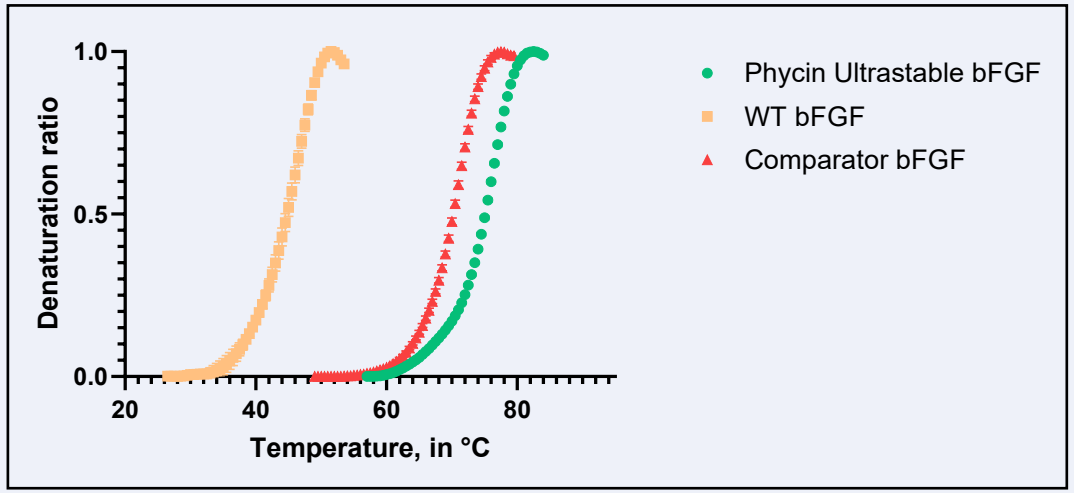
Protein Purification

Final Product

7

Phycin's Ultrastable™ bFGF Demonstrates Both Superior Stability and Potency

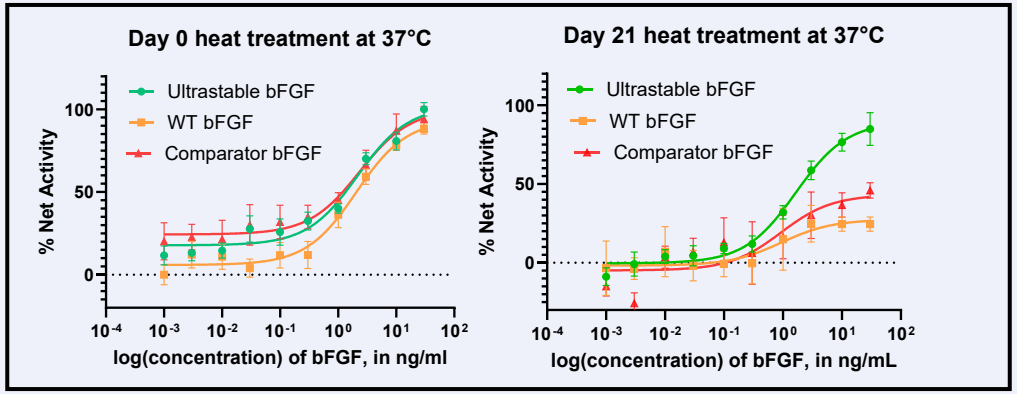
An order of magnitude higher intrinsic thermal stability



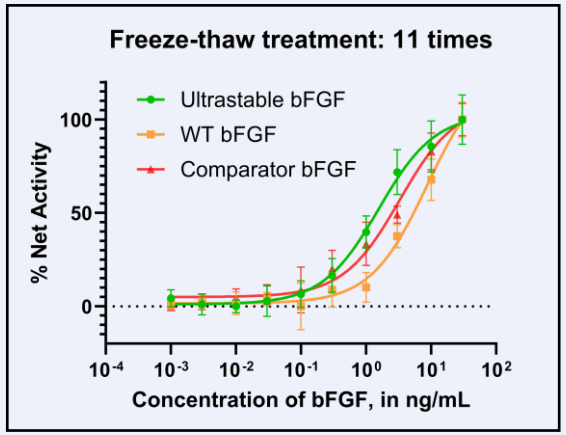
ΔTm +5.5°C vs comparator's HS-bFGF (DSF) can correspond to multi-fold (up to ~10×) higher intrinsic stability than comparator

Melting curves by DSF

Ultrastable™ bFGF retains functional activity after 21 days at 37˚C



Ultrastable™ bFGF retains higher functional activity after 11 freeze thaw cycles

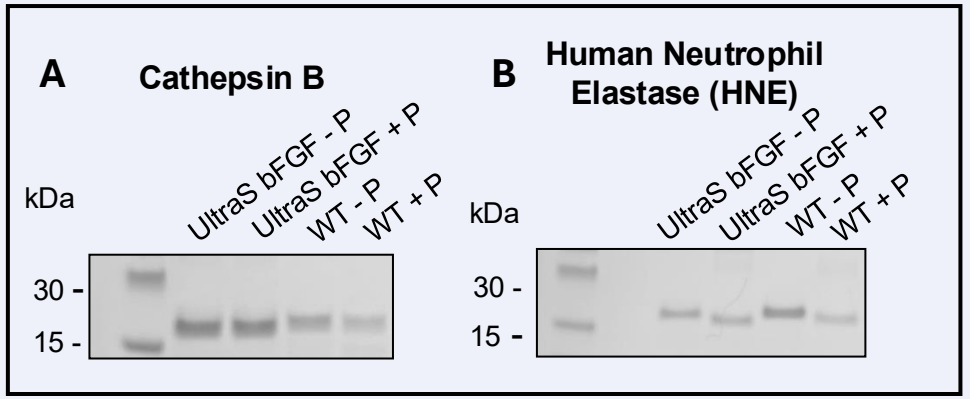


3T3 fibroblast proliferation assay

Phycin's Ultrastable™ bFGF demonstrates both superior physiological protease resistance

- Protease dynamics underpin the progression from acute injury to chronic wounds through intricate regulation of inflammation, cell migration and extracellular matrix remodelling.
- In healthy healing, a tightly controlled cascade of proteases—chiefly matrix metalloproteinases and serine proteases—facilitates debridement and tissue regeneration, tempered by endogenous inhibitors.
- Chronic wounds arise when this balance is disrupted by persistent inflammation, pathogenic biofilms or systemic factors, resulting in excessive proteolytic activity that degrades growth factors, matrix proteins and cell-surface receptors.

Ultrastable™ bFGF presents higher resistance to physiological wound site proteases



Ultrastable bFGF Facilitates Similar Growth Rate of iPSCs and Activates the Canonical FGF Signaling Pathway

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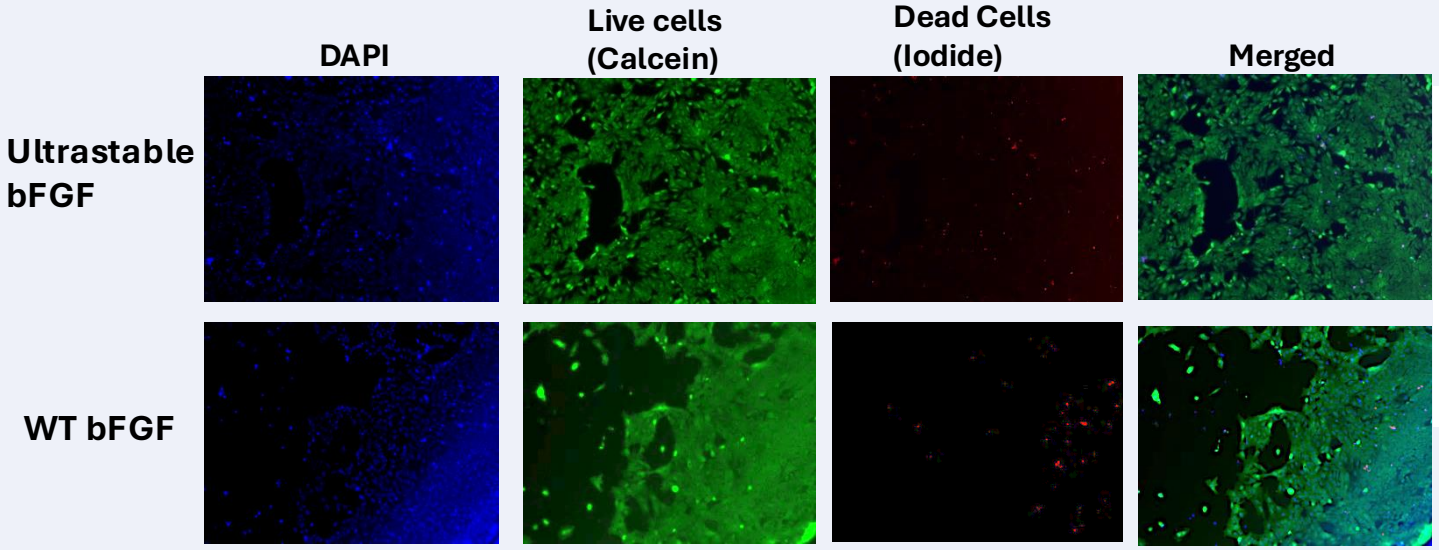
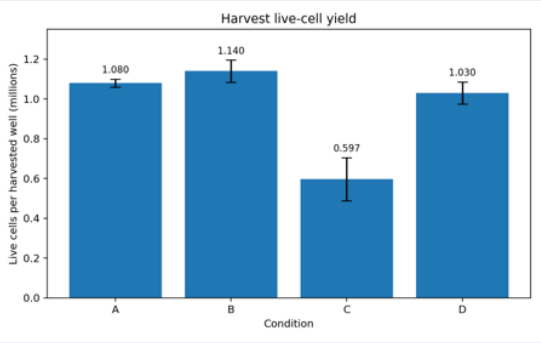
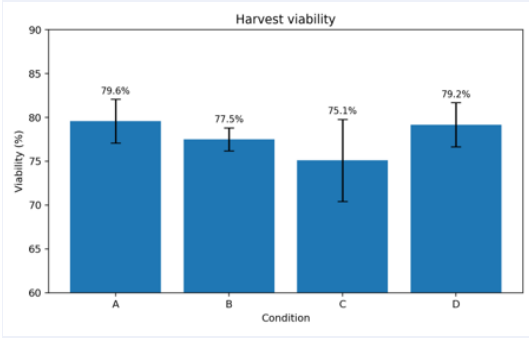
Live-Dead Cell Imaging

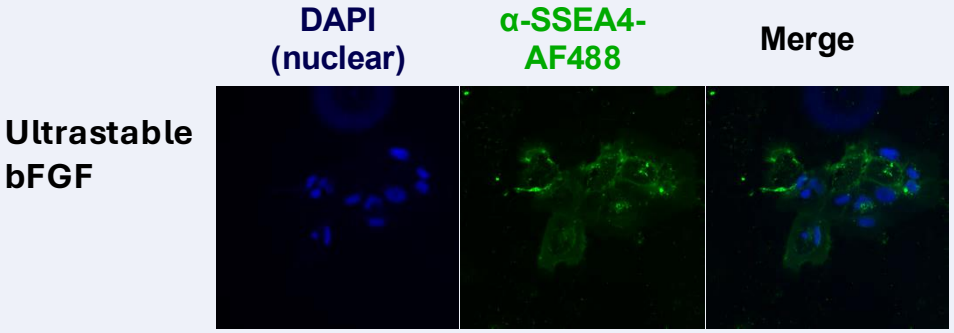




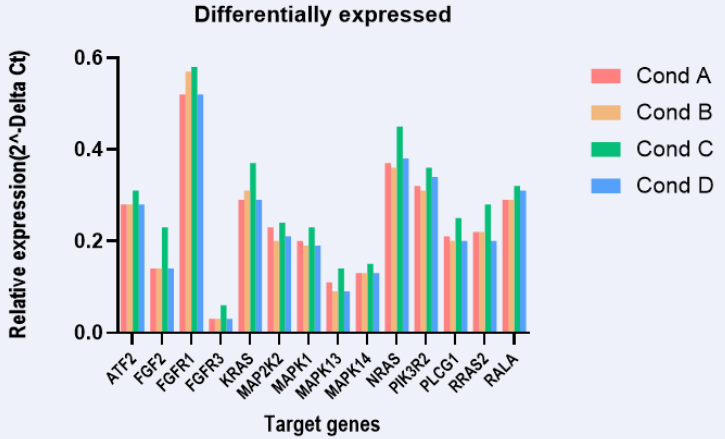


Cond A: Ultrastable bFGF
Cond B: Comparator bFGF
Cond C: WT bFGF 24 hr media change
Cond D: WT bFGF 48 hr media change

Maintains Pluripotency



Activates Canonical FGF Pathway (preliminary)



Accelerated Healing of Mechanical Corneal Injury

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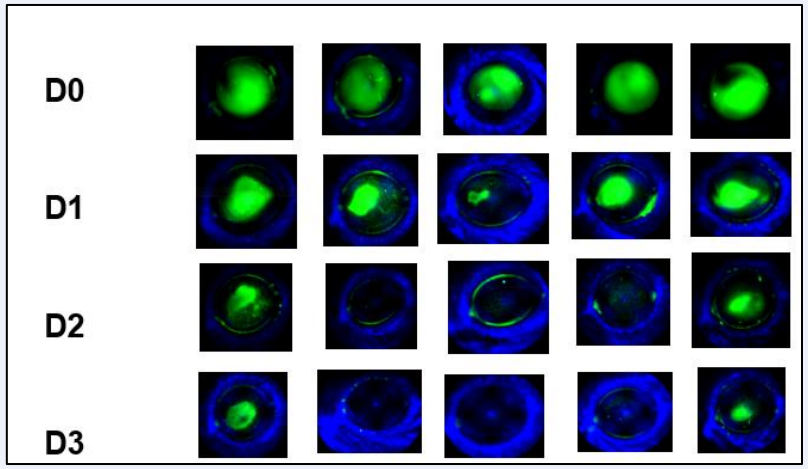
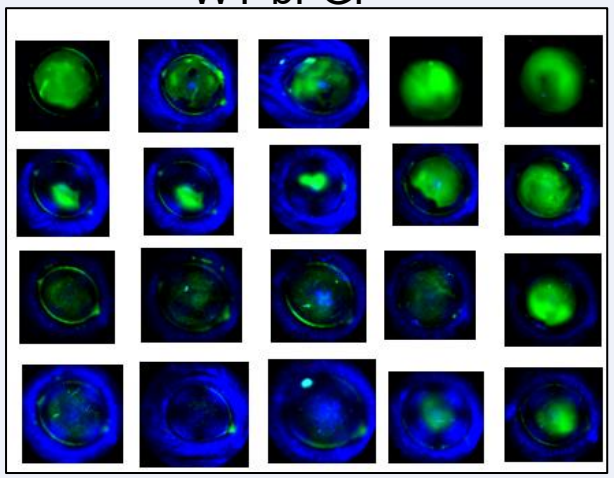
Manual scraping (Croneal Rust Ring Remover (BR2-5 1/2mm) Diamond instrument was used to induce mechanical injury in **C57BL/6J mice** eyes. 5 µL of stabilized bFGF (20 µg/mL) was applied daily to each injured eye.

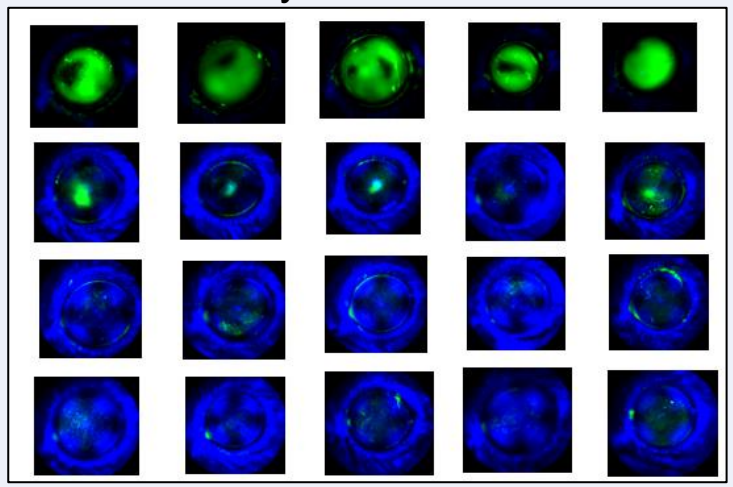
PBS

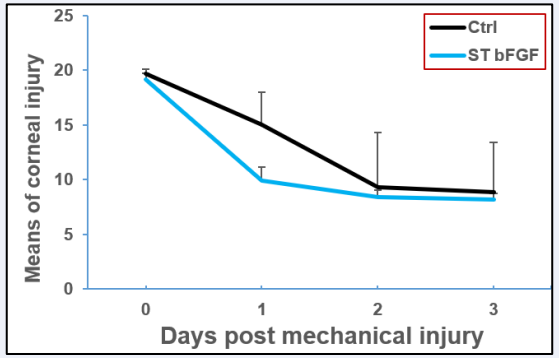


WT bFGF



Phycin bFGF



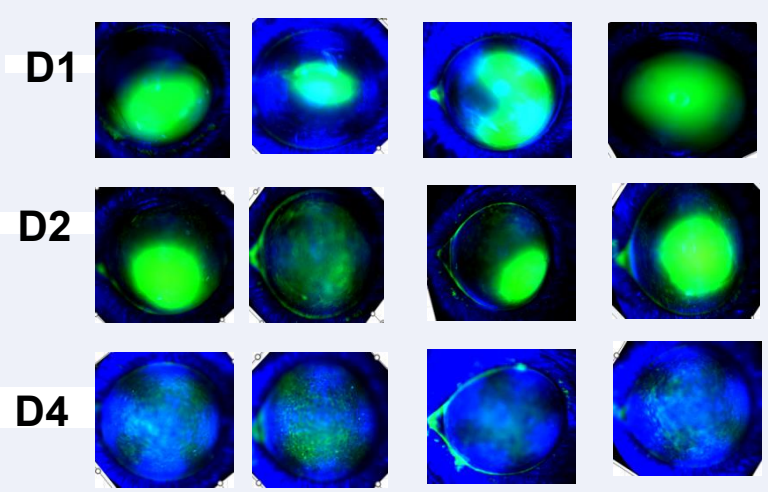


Shao Lab, Ophthalmology & Visual Sciences, University of Louisville

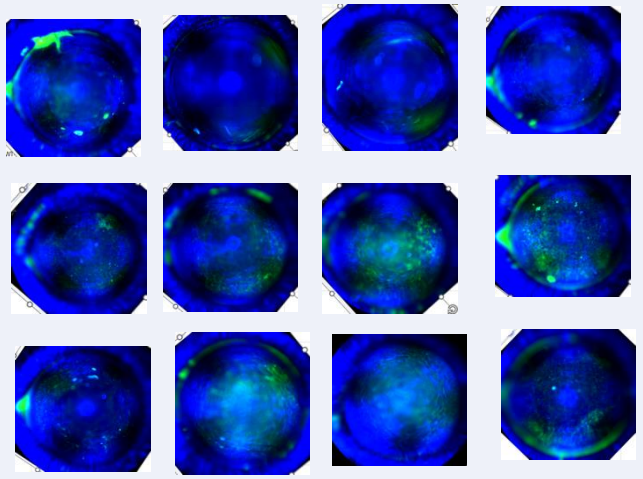
Accelerated Recovery of Chemical Corneal Injury

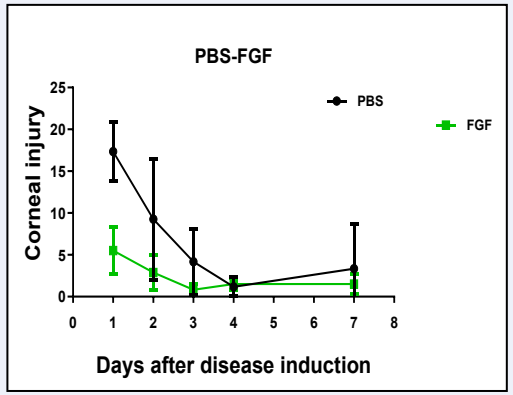
1.5% nitrogen mustard was used to induce corneal burns in B6 female mice eyes.
5 µL of stabilized bFGF (20 µg/mL) was applied daily to each injured eye.
Images on day 0 (day of injury) were not taken to avoid stress from repeated anesthesia.

PBS



Phycin stable bFGF





Improved Healing of Mechanical Corneal Injury

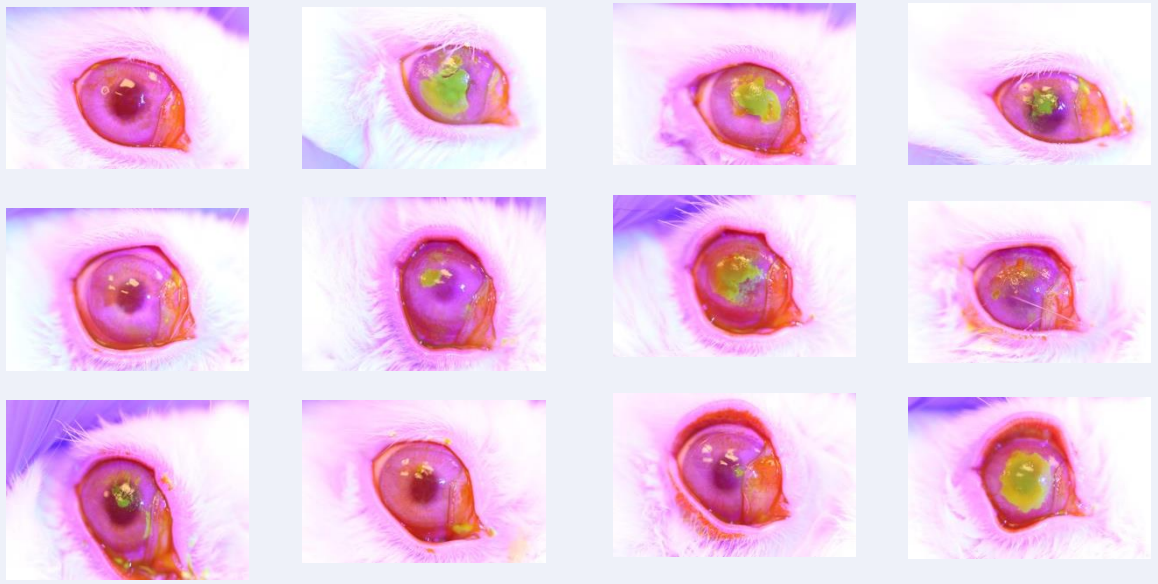
A diamond dusted burr was used to induce mechanical injury in **New Zealand rabbit** eyes. 20 µL of stabilized bFGF and EGF (20 µg/mL) were applied twice a day to each injured eye.

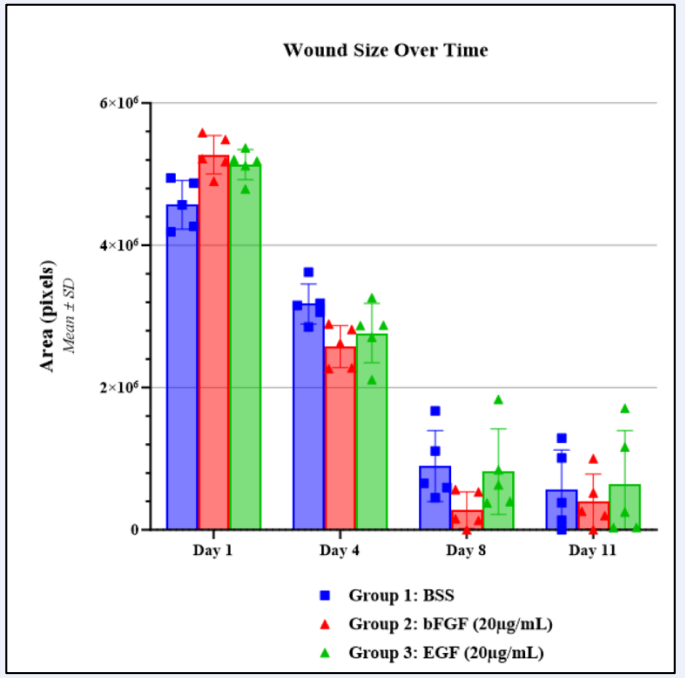
Day 11 after injury

PBS

Stable bFGF

EGF





Dr. Esen Akpek and Powered Research LLC

Risks and Mitigations

Risk: bFGF may lead to NV

Mild to moderate NV was observed in the bFGF treated eyes

Possible Causes

- The enhanced stability of the Phycin variant may increase its local duration of activity, potentially increasing angiogenic exposure at the tested dose and dosing frequency.
- Corneal neovascularization following injury or growth factor treatment may be transient and may regress over time

Mitigation

- Determine the optimal concentrations and dosing frequency of the stable bFGF empirically.
- Monitor vascular changes following discontinuation of bFGF treatment.

Accomplishments

Phycin aims to develop bFGF into a therapy suitable for the treatment of corneal injuries in both military personnel and civilians.

- The first and only bFGF suitable for room temperature storage and transportation
- Production of inexpensive bFGF that is free of animal components and endotoxins
- Enhanced corneal epithelization by stable bFGF when administered topically in the eyes of animal models.

Future Plan

- Test the enhanced bFGFs in corneal injuries of larger animals, such as rabbits and pigs, to confirm its therapeutic effects in multiple and various species
- Test the effective bFGF concentrations and dosing to counteract mechanical and chemical corneal injuries in human corneal fibroblast culture to validate its application in human ocular disease
- Define the molecular mechanism of bFGF in enhancing corneal healing following mechanical and chemical corneal injuries
- Address the neovascularization concern by dosage optimization, or to employ EGF as the combination reagent.
- Develop and follow regulatory strategies to prepare for Investigational New Drug (IND) submission.

Traction & Partnerships

Phycin

Funding

Medical Technology Enterprise Consortium (MTEC)

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Maryland Stem Cell Research Fund (MSCRF)

Research Partners

Johns Hopkins University School of Medicine

Walter Reed Army Institute of Research

Advanced Regenerative Manufacturing Institute

Kennedy Krieger Institute

Duke University School of Medicine

Powered Research, LLC

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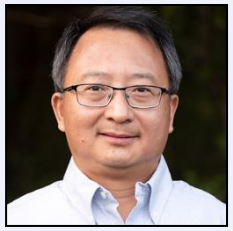
- Hui Shao, PhD, MD, Ophthalmology & Visual Sciences, University of Louisville

Our team at Phycin



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Ultrastable™ bFGF — the stable core of regenerative biotech.

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