Prevention of scar formation in the skin using a topical FAK inhibitor

Geoffrey C. Gurtner, MD – Professor of Surgery and, by courtesy, Professor of Bioengineering and of Material Science and Engineering, Stanford University

Jayakumar Rajadas, PhD – Director of BIOADD and Assistant Director of CV Pharmacology, Biomaterials & Advanced Drug Delivery

Clinical Need

Injury to the skin in the craniofacial region from trauma, burns, radiation and surgery often results in hypertrophic scar (HTS) formation. HTS leads to airway edema, speech/swallowing dysfunction, sensory defects, disfigurement, and psychological distress to the patient. Approximately 2.5 million patients experience craniofacial wounds and 50,000 patients experience craniofacial burns each year in U.S. Burn wounds that are deep partial thickness or full thickness almost always result in HTS. While full thickness burns are surgically treated by skin grafts, there currently is no effective standardized therapy for patients with deep partial thickness injury.

Solution

Our solution is to provide accelerated and improved wound healing after craniofacial trauma or burns to the skin using our topical focal adhesion kinase inhibitor (FAK-I). During the past decade, Dr. Gurtner's lab has demonstrated that localized FAK-I treatment via a topical hydrogel scaffold decreases wound closure time, reduces hypertrophic scar formation, and restores hair follicles & skin appendages, leading to improved regeneration of the skin after injury and trauma. Our topical delivery mechanism can be applied with each dressing change of the wound and easily integrated within current wound care protocols.

Competitive Advantage

Our FAK-I compound has previously demonstrated human safety during a Phase I trial approved by FDA for oral anti-cancer therapy. Moreover, its pre-clinical efficacy in inhibiting pro-fibrotic cellular activities have been well-documented by us and others. To the best of our knowledge, we are the first group to pioneer research in this FAK-I molecule and the delivery mechanism for wound healing and scar mitigation applications.

Target Market

Approximately 2.5 million patients with craniofacial wounds and 50,000 patients experience craniofacial burns each year. We estimate the total global market size, at saturation, for the scar treatment market, and for all competitors, to be approximately $34.5B dollars (USD).[1] There currently are no effective pharmacological treatments for craniofacial burn wounds and HTS that are routinely used in the clinics. This makes topical FAK-I therapy a promising treatment approach from both a domestic and global market perspective. While there are medical devices in the market that physically modulate mechanical stress to reduce fibrosis, these are cumbersome to use in the craniofacial area. Moreover, burn injuries of the craniofacial area as well as other body parts that receive medical treatment at healthcare clinics in the U.S. have reached more than 400,000 each year. This makes a significant number of the burn patients the target segment who will use FAK-I therapy for wound care and scar management.

Regulatory Pathway

Combination product (drug-device) with the PMOA being the drug. Regulatory pathway will be IND with CDER as the lead agency.

Intellectual Property

We currently have two issued patents related to this technology: 9,655,967 and 9,636,362

Related Publications

Wong VW, Rustad KC, Akaishi S, et al. (2011) Focal adhesion kinase links mechanical force to skin fibrosis via inflammatory signaling. Nat Med 11;18(1):148-52. / Ma K, Kwon SH, Padmanabhan J, et al. (2018) Controlled delivery of a focal adhesion kinase inhibitor results in accelerated wound closure with decreased scar formation. J Invest Dermatol 138(11):2452-2460. Epub 2018 Jul 12.

Prevention of Scar Formation in the Skin using a Topical Focal Adhesion Kinase Inhibitor

Kellen Chen, PhD[1], Benjamin Levi, MD[2], Deepak Gupta, MD[3], Geoffrey C. Gurtner, MD FACS[1]

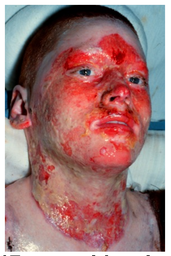
[1]Stanford University, [2]University of Texas Southwestern, [3]Santa Clara Valley Medical Center

DOCTRC DENTAL, ORAL, & CRANIOFACIAL TISSUE REGENERATION CONSORTIUM

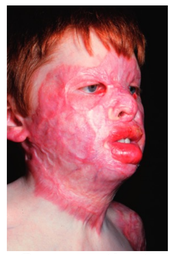
Michigan · Pittsburgh · Wyss Regenerative Medicine Resource Center

Annual Retreat 2020 | December 8, 2020

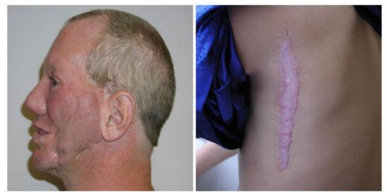
UNMET CLINICAL NEED



17-year-old male, flash burn at presentation



Same patient, six months later



- Injury to the skin in the craniofacial region from trauma, burns, radiation, and surgery leads to hypertrophic scar (HTS) formation[1]
- Over 400,000 patients experience burns each year in the U.S., with 20% being on the craniofacial area[2]
- **Currently no effective therapy for patients with deep partial thickness injury**

MARKET ANALYSIS

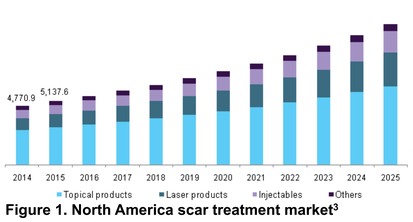


Figure 1. North America scar treatment market[3]

Foresight science & technology

"All of the end-users/experts we interviewed (8) viewed this technology very positively…"

"…huge need for new technologies like this that improve wound healing and reduce scarring…[develop] this technology for mass production…burn, surgical, and cosmetics"

- Global scar treatment market valued at **$13.8 billion (USD) in 2015** and estimated to reach approximately **$34.5 billion by 2025**[3]
- North America scar treatment market valued at **$5.138 billion in 2015**
- Currently no effective pharmacological treatments for craniofacial burn wounds and HTS in the clinic, making topical FAK-I therapy a promising treatment from both a domestic and global market perspective for many burn patients

INTELLECTUAL PROPERTY

Issued US Patent 9,655,967: Inhibition of focal adhesion kinase for control of scar tissue formation

"The formation of scars at a wound site is reduced by contacting the wound site with inhibitor of focal adhesion kinase (FAK) activity. Pharmacologic blockade of FAK significantly reduces scar formation in vivo."

Issued US Patent 9,636,362: Pullulan regenerative matrix

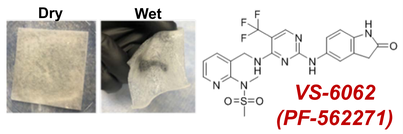
"…manufacture and use of a pullulan-based collagen hydrogel with controlled porosity"

Provisional U.S. Patent Application No. 63/000,309: Methods for Tissue Regeneration and Kits Therefor. Filing Date: March 26, 2020

Issued license agreement with Verastem and side letter

RESULTS

Technology: Porous pullulan-collagen hydrogel for FAKI delivery



- FAKI (focal adhesion kinase inhibitor) physically encapsulated
- Topically applied hydrogel patches release FAKI in a controlled and sustained manner

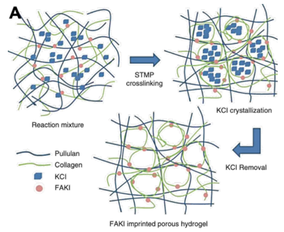


Figure 2. VS-6062-releasing pullulan-collagen hydrogel[4].

Porcine Partial Thickness Model Demonstrates Safety and Efficacy

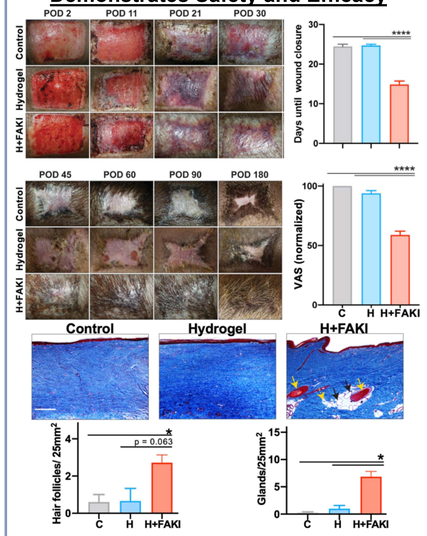


Figure 3. FAK-I hydrogel accelerates porcine wound closure, reduces scar, and promotes hair and gland regrowth[6].

Split Thickness Skin Graft (STSG) Porcine Model Demonstrates Safety and Efficacy

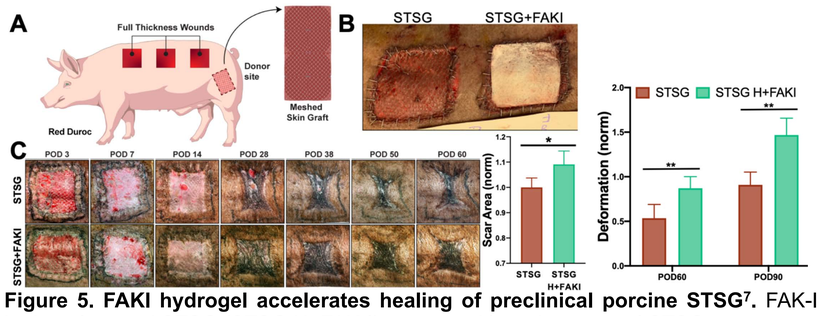
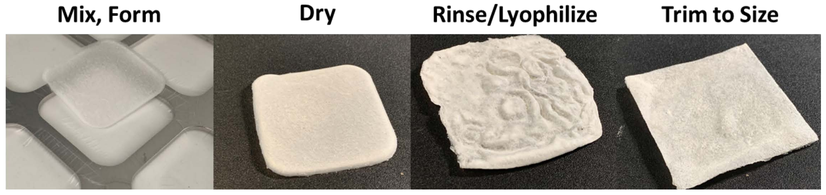


Figure 5. FAKI hydrogel accelerates healing of preclinical porcine STSG[7]. FAK-I hydrogel treated STSG (STSG H+FAK-I) contracted less than normal STSG.

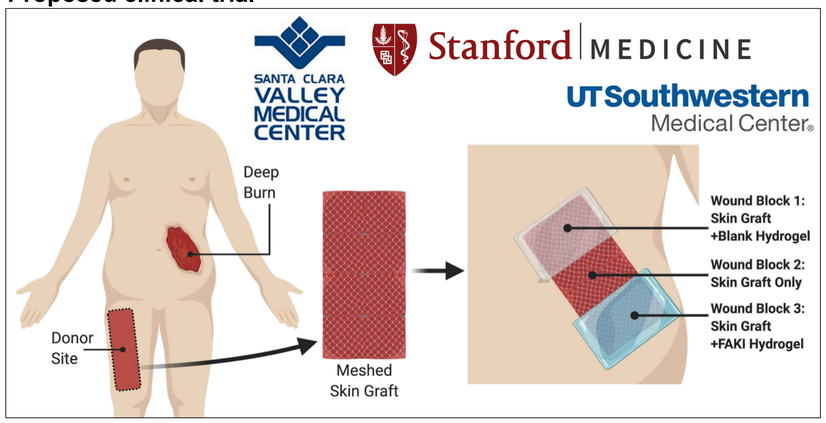
MANUFACTURING



- **GMP-compliant manufacturing of FAK-I hydrogels for human clinical use.** Clinical-grade FAK-I hydrogel was produced under GMP guidelines to assure consistent therapeutic quality.
- We have developed GMP methods to meet all regulatory standards (drug content, identification, dissolution procedures). Quality of sample patches are being evaluated.

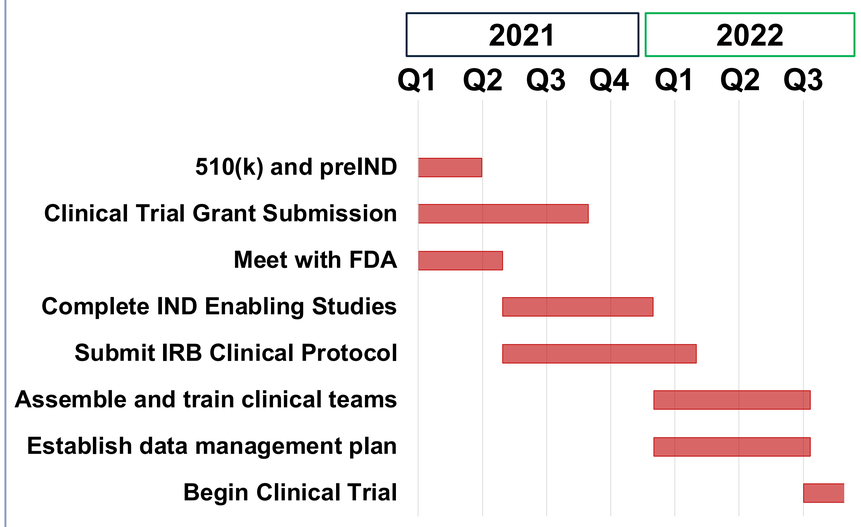
REGULATORY PATHWAY

Proposed clinical trial



- Compiling all written documents to construct briefing packet to request a **Type B meeting with FDA** by **January 2021**
- Predicted and conducted FDA-recommended cytotoxicity studies
- **510(k)-submission pathway:** multiple predicates utilizing collagen hydrogel dressings

TIMELINE & FUTURE DIRECTIONS



REFERENCES

[1]Berman, B. *et al. J Craniofac, Surg.* (2008).
[2]https://ameriburn.org/who-we-are/media/burn-incidence-fact-sheet/
[3]https://www.grandviewresearch.com/press-release/global-scar-treatment-market
[4]Ma, K. *et al. J Invest Dermatol* (2018).
[6]Chen, K. *et al. In Review.*
[7]Chen, K. *et al. In Preparation.*

This work was supported by the Center for Dental, Oral, & Craniofacial Tissue & Organ Regeneration Interdisciplinary Translational Project Awards supported by the National Institute of Dental & Craniofacial Research (U24 DE026914).