Michigan • Pittsburgh • Wyss
Regenerative Medicine Resource Center

2019 Annual Report

Letter from the Leadership

Formally launched in March 2017, the Michigan-Pittsburgh-Wyss Regenerative Medicine Resource Center continues to shepherd promising regenerative medicine technologies towards initiation of clinical trials and beyond. In collaboration with our sister consortium, C-DOCTOR (Center for Dental, Oral, & Craniofacial Tissue & Organ Regeneration), and our sponsor, National Institute of Dental and Craniofacial Research (NIDCR), we have forged strategic partnerships, built infrastructure, and provided expertise to support 19 Interdisciplinary Translational Projects (ITPs).

This has been a particularly exciting year, with the concurrent implementation of 3 cycles of ITPs. The projects represent a balanced portfolio across therapeutic indications and technology types, with corresponding regulatory pathways. We continue to be inspired by these projects and their strong potential to address unmet needs in dental, oral, and craniofacial medicine.

We share with you our enthusiasm, as well as the impact of the Michigan-Pittsburgh-Wyss Regenerative Medicine Resource Center in this report. Through the accelerated clinical translation of dental, oral, and craniofacial regenerative therapies, the Resource Center and the ITPs make progress towards improved patient care.

Sincerely,

David H. Kohn, PhD | **William V. Giannobile**, DDS, DMSc
University of Michigan

Charles S. Sfeir, DDS, PhD | **William R. Wagner**, PhD
University of Pittsburgh

David J. Mooney, PhD
Wyss Institute

UNIVERSITY OF MICHIGAN

University of Pittsburgh

WYSS INSTITUTE

The MPWRM Resource Center is supported in part by the National Institute of Dental & Craniofacial Research of the National Institutes of Health under Award Number U24DE026915. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Michigan • Pittsburgh • Wyss
Regenerative Medicine Resource Center

Resource Center Impact

The MPWRM Resource Center is comprised of more than 70 members with expertise that span the spectrum of translational research and commercialization. With the majority of the members serving on an ITP advisory team, each project receives broad and customized guidance. In addition, all ITP teams are working with the market assessment core to understand customer needs to position the technology for successful commercialization and clinical adoption. Below are some examples of how the MPWRM Resource Center is impacting the translational trajectory of dental, oral, and craniofacial technologies.

The impact of these efforts will be a catalysis of translation in the dental, oral, and craniofacial arena never previously achieved in an NIH extramural program, resulting in the transformation of dental, oral, and craniofacial medicine.

REGULATORY & QA QC

Identify strategic regulatory pathways for a potential product

Develop experimental requirements to streamline execution of regulated studies

Conduct prequalification of contract research organizations prior to engagement

SCIENTIFIC & CLINICAL

Propose preclinical models and connect teams with surgical expertise

Suggest experimental techniques and data analysis methods to facilitate clinical translation

Review statistical rigor for studies and provide recommendations

BUSINESS & MARKET

Facilitate discussions amongst company representatives, principal investigators, and home institution offices to cultivate partnerships

Conduct interviews with key opinion leaders to understand clinical and industry needs

$ FUNDING

Leverage ITP support in garnering additional funding (equity financing, SBIR)

Connect investigators to new funding and training opportunities

Interdisciplinary Translational Projects

APPLICATION AND REVIEW PROCESS

Total Number of Applications Reviewed **82**

Total Number of Interdisciplinary Translational Projects Supported **19**

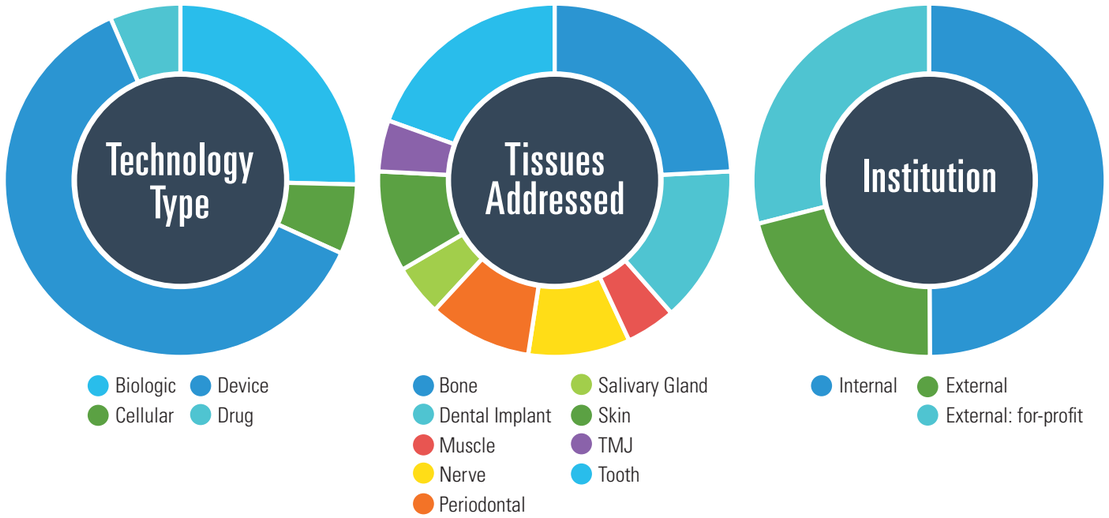
Total Number of Currently Active Interdisciplinary Translational Projects **14**

ITP APPLICANT DEMOGRAPHICS

% of Applications with Female | Minority (co-) Principal Investigator ..... **30% | 11%**

% of ITPs Supported with Female | Minority (co-) Principal Investigator ..... **32% | 16%**

CURRENTLY ACTIVE INTERDISCIPLINARY TRANSLATIONAL PROJECTS (n=14)



100%

ITP teams with issued or pending patent/ applications

57%

ITP teams with FDA submissions

From the ITP Teams...

"I am not aware of another grant mechanism by which one can accomplish IND-enabling studies that de-risk the technology and make it much more attractive for private investment. In particular, the ITP program serves as a bridge between R01, non-GLP lab research, and the UG3/UH3 clinical trial grant program and thus serves a critical role in clinical translation."

Michael Passineau, PhD
(Allegheny Health Network)

Isabelle Lombaert, PhD
(University of Michigan)

"The clear and fast communication with the Resource Center has been speeding up the decision making process… In addition, the resource center has put us in contact with the Avenues company who would like to help us develop an integrated strategy that will include clinical, regulatory, and R&D, as well as market and business development. This will allow us to focus our efforts and move forward as effectively as possible."

Luiz Bertassoni, PhD, DDS
(Oregon Health & Sciences University)

Pamela Yelick, PhD
(Tufts University)

"The ITP provides a unique format that brings a variety of resources to a small business that are NOT available via traditional SBIR systems. The auxiliary services provided are just as critical to commercial success as the basic R&D services that can be covered under a traditional SBIR grant. By this I mean regulatory issues, market development and the opportunity to collaborate with scientific colleagues in a much more personal and interactive format."

Stephen LeBeau, PhD
(President, nanoMAG)

Andrew Brown, PhD
(President, Emergence Dental)

FEATURED INTERDISCIPLINARY TRANSLATIONAL PROJECT

LaunchPad Medical is an early-stage medical device company developing Tetranite® (TN), an injectable, synthetic osteoconductive adhesive for bone repair. Now in its second year of ITP support, TN is positioned as a next generation bone graft since it does not require ancillary containment devices. To ensure a market competitive product, the TN formulation is being optimized to ensure the timescale of its replacement by nascent regenerated bone is commensurate with existing dental bone graft materials. Work under the ITP program complements the company's various efforts; in addition to raising $9.5M in a round of equity financing in March 2019, LaunchPad Medical recently received FDA approval and initiated a clinical study to investigate TN for dental implant stabilization, and won an NIH HEAL grant, a phase I SBIR grant (1R43DE029369-01), for the development of non-opioid pain medication-releasing TN for bone graft application. Leveraging its successes of the ITP program, the LaunchPad Medical team is garnering additional support to enhance the clinical utility of TN in dental applications.

LaunchPad Medical

Achievement Over the 3 Years

2017

March The Michigan-Pittsburgh-Wyss Regenerative Medicine Resource Center (MPWRM RC) is founded with the award of the U24 grant (U24DE026915) (https://www.nidcr.nih.gov/news-events/nidcr-news/2017/nidcr-funds-consortium).

May First Request for Applications of the ITP program is released.

June Multi-site (online) MPWRM RC launch meeting is held. Charges for the Operating Committee, Advisory Groups, Assessment Teams, and Cores are established.

November First Semi-Annual meeting is held in Ann Arbor, Michigan. Evaluation results for the first group of ITP proposals are reviewed, and funding selections are made for first cycle of ITPs (ITP01). Concurrently, strategic planning session is held to outline future initiatives for the MPWRM Resource Center.

Second Request for Applications of the ITP program is released.

2018

January First Cycle of ITPs/ITP01 is launched.

March MPWRM RC and C-DOCTOR host a symposium at the American Association of Dental Research annual meeting in Fort Lauderdale, FL.

An editorial authored by the MPWRM RC and C-DOCTOR principal investigators is published in Journal of Dental Research (JDentRes 2018, 97(4)361-3).

May Third Request for Applications of the ITP program is released.

July First Annual Stakeholder's Summit is held in Pittsburgh, PA. Program included 3 practicum sessions, presentations by ITP01 teams, and online pitches by Cycle 2 applicants. Funding selections are made for second cycle of ITPs (ITP02). Meeting was open to all Resource Center members, and was sponsored by 4 corporate partners.

September Second Cycle of ITPs/ITP02 is launched.

October Request for Applications for ITP01 renewal project is released.

AxoMax™ is registered.

November MPWRM RC is featured on the programming of Materials Research Society TV for the 2018 MRS Fall Meeting in Boston, MA.

GreenMark Biomedical wins funding at Accelerate Michigan.

2019

January Second Semi-Annual Meeting and Operating Committee Strategic Meeting are held in Ann Arbor, MI. Meeting was open to all Resource Center membership and corporate partners, with >70 attendees. In addition to the 3 practicum sessions, meeting included presentations by ITP02 teams, in-person pitches by Cycle 3 applicants, and 23 partnering forums for funded ITP teams to discuss their project in depth with Resource Center marketing and regulatory experts. Funding selections are made for third cycle of ITPs (ITP03).

Emergence Dental is founded.

February LaunchPad Medical raises $9.5M in equity financing.

March Third Cycle of ITPs/ITP03 is launched.

GreenMark Biomedical completes $1.2M series seed preferred stock round.

June DOCTRC Stage 3 proposal is submitted in response to RFA-DE-19-010.

MPWRM RC and C-DOCTOR host a symposium at the International Association of Dental Research meeting in Vancouver, BC. Two teams from each of the Resource Centers presented their ITP.

July Request for Applications for all ITP renewal projects is released.

September Second Annual Stakeholder's Summit is held in Pittsburgh, PA. Meeting was open to all Resource Center membership and corporate partners (>70 attendees), and included a day-long regulatory training session for the ITP teams and Resource Center members, and presentation by the FDA. All ITP teams provided a presentation to open session attendees, and concluded 25 partnering sessions with the Resource Center experts.

October LaunchPad Medical initiates clinical trial of Tetranite® for dental implant stabilization.

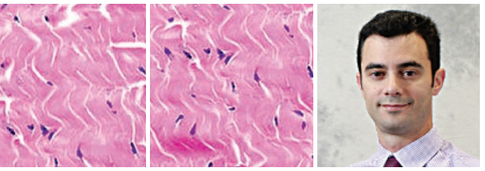
GreenMark Biomedical secures Phase II SBIR.

November Ostiio closes $520k in Series A equity round.

LaunchPad Medical wins NIH HEAL grant.

December Operating Committee meeting is held to review evaluation results of the ITP renewal projects to prioritize any future funding decisions.

Extracellular Matrix Scaffold for TMJ Disc Repair



ALEJANDRO ALMARZA, PHD

University of Pittsburgh

"This technology will provide an off-the-shelf solution for the repair of the TMJ disc."

www.dental.pitt.edu/person/alejandro-j-almarza

CLINICAL NEED

Individuals suffering from severe temporomandibular joint (TMJ) disc disease experience painful clicking or locking that can dramatically affect quality of life. Total TMJ reconstruction is often the last-resort surgical intervention for the irreparably damaged joint. Current therapies include joint replacement using alloplastic implants or autogenous grafts; however, long term outcomes with alloplastic implants are unclear, while autogenous grafts are associated with donor site morbidity.

SOLUTION

University of Pittsburgh team of Alex Almarza, PhD, Stephen Badylak, DVM, PhD, MD, William Chung, DDS, MD, and Bryan Brown PhD is developing an extracellular matrix (ECM)- based scaffold device for the reconstruction of the TMJ. In particular, the device is designed to replace the meniscus of the TMJ by inducing the formation of new, patient-specific, functional tissue formation.

COMPETITIVE ADVANTAGE

Unlike currently available alloplastic implants, ECM-based device is biodegradable, and mimics the shape and size of native TMJ meniscus, without the need for autologous tissue harvesting. The device has been validated in canine and porcine models, where the scaffold demonstrated rapid transformation into a fibrocartilaginous tissue with biomechanical and biochemical properties similar to the native TMJ disc, as well as elicited formation of near-normal tissues in only one month following implantation.

ITP SUPPORT

The long-term objective of this program is the development of a safe and effective therapeutic option for reconstruction of the TMJ disc. In preparation for submission to the FDA, the ITP program will support the validation of devices made in a GMP facility, and for the submission of a pre-IDE application to the FDA.

CLINICAL TRANSLATION PATHWAY

Publications:
Extracellular matrix as an inductive template for temporomandibular joint meniscus reconstruction: a pilot study. J Oral Maxillofac Surg 2011.

Inductive, scaffold-based, regenerative medicine approach to reconstruction of the temporomandibular joint disk. J Oral Maxillofac Surg 2012.

Intellectual Property:
US 9,314,340 Joint bioscaffolds

Regulatory Pathway:
Anticipated:
Device, IDE
to enable PMA

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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A Smart, Fully-Implantable Craniomaxillofacial Distractor

CLINICAL NEED

Distraction osteogenesis (DO) is a technique used to generate new bone at the site of a surgical cut by slowly separating plates attached to two opposing fragments. While the procedure is increasingly used in the treatment of various congenital craniomaxillo-facial (CMF) deformities including undergrowth of the mandible in patients with disease such as, craniosynostosis or hemifacial microsomia, limitations exist in its current form, including the component that protrudes through the skin for manual engagement of the device.

SOLUTION

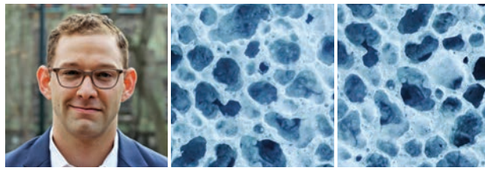
Ostiio is developing a fully-buried, remote-controlled DO system for the craniomaxillo-facial skeleton. This device is intended to be applicable to all patients who would be treated with traditional DO systems, but is completely implanted under the soft tissue, without any external components protruding through the skin. The distraction is actuated through a magnetically driven external controller that can implement physician-defined distraction protocols.

COMPETITIVE ADVANTAGE

As the device has no parts protruding the skin, it is expected to decrease morbidity such as soft tissue infection and scarring associated with the current device form factor. In addition, as the manipulation will be remotely-controlled and software-driven, patient non-compliance and inaccuracies are also expected to be decreased.

ITP SUPPORT

With support from the ITP program, Ostiio will be developing device prototypes and performing mechanical and biocompatibility testing.



ARI M WES, MD, MSC

Ostiio LLC

"Ostiio is trying to alleviate the stress felt by parents of children undergoing CMF distraction, while giving control back to the surgeon."

http://pennhealthx.com/ostiio

CLINICAL TRANSLATION PATHWAY

Publications:
Complications in Posterior Cranial Vault Distraction. Ann Plast Surg. 2016.

Precision of the PRECICE internal bone lengthening nail. Clin Orthop Relat Res. 2014.

Intellectual Property:
PCT/US2018/021269 Systems and Methods for Contactless Cranio-maxillo-facial distraction

Regulatory Pathway:
Anticipated:
Device, 510(k)

Commercialization Strategy:
Ostiio plans on bringing their device through the FDA. After clearance, the team will assess the different options for driving adoption by hospitals and patients.

Product Launch Strategy:
Following FDA clearance, Ostiio will explore partnerships with prominent players already in the CMF space to drive adoption.

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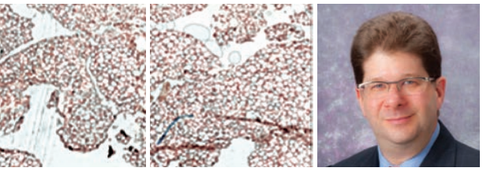
A Device to Preserve Adipose Tissue Grafts for Soft Tissue Reconstruction



J. PETER RUBIN, MD, FACS
University of Pittsburgh

"The ability to easily and inexpensively store tissue on-site will result in significant decrease in patient discomfort and risk, as well as significant decrease in surgeon time spent on the repeat procedure."

https://plasticsurgery.pitt.edu/research/research-labs/adipose-stem-cell-center-ascc

CLINICAL NEED

Soft tissue deformities and volume/ contour deformities from craniofacial trauma, congenital anomalies, and cancer treatment are difficult to correct. Current standard of care includes injectable fillers, implants, and soft tissue flap procedures, which have limitations and often involve operations with significant risk. As such, autologous fat transfer is being explored as a lower risk alternative. However, as optimal results with fat transfer often require at least two treatments, there is a need for an on-site preservation of harvested tissue for subsequent procedures to minimize donor site morbidity and encourage fast recovery.

SOLUTION

A team of researchers at the University of Pittsburgh led by Dr. Peter Rubin has previously validated the use of autologous fat transfer as a minimally invasive therapy for the restoration of craniofacial form. In order to facilitate fat transfer with minimal donor site morbidity, the team has developed a novel device to cryopreserve adipose for storage at the treatment facility, which can directly be used for the subsequent fat transfer(s).

COMPETITIVE ADVANTAGE

With the on-site cryopreservation and storage of the fat tissue, the device is envisioned to reduce patient and clinician burden for tissue harvest. The utilization of the device obviates the need for repeat tissue grafting procedures, and is anticipated to lead to reduction in treatment costs as the fat transfer injections may be performed outside of an operating room in a less acute setting.

ITP SUPPORT

The work supported by the ITP program is focused on the generation of a prototype cryopreservation/storage device that can be used for clinical trials. Towards that end, project plans include prototype development and validation, as well as the development of a regulatory strategy and commercialization plan.

CLINICAL TRANSLATION PATHWAY

Publications:
Optimization and Standardization of the Immunodeficient Mouse Model for Assessing at Grafting Outcomes. Plast Reconstr Surg 2017.

Intellectual Property:
PCT/US2018/049083 Method and Kit for Preservation of Adipose Tissue Grafts

Regulatory Pathway:
Anticipated: Device, 510(k)

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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Tissue Engineering Functional Human Lips

CLINICAL NEED

Tissue engineering and regenerative medicine face several barriers preventing translation of *in vitro* technology to the clinical arena: (1) the inability to create composite soft tissue structures that contain striated muscle, skin, and mucosa with a mucocutaneous junction (lip) and (2) difficulty in developing an *in vivo* perfusion system (blood vessels) to supply nutrition for large segments of tissue created in vitro. Lack of tissue perfusion is a major limitation of survival of implanted *in vitro* produced complex composite soft tissue implants.

SOLUTION

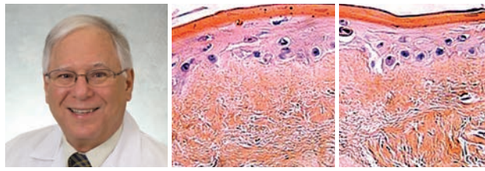
A team of researchers at the University of Michigan led by Dr. Stephen E. Feinberg has developed a tissue engineering approach in conjunction with the surgical technique of prelamination, to create an innervated pre-vascularized prelaminated composite soft tissue microvascular free flap based on the latissimus dorsi muscle for use in functional reconstruction of human lips.

COMPETITIVE ADVANTAGE

This approach addresses the issues of creating autogenous complex composite soft tissue structures with an adequate perfusion system. In addition, this approach provides a platform technology for fabrication of autogenous mucocutaneous junctions in the body such as the anus, vagina, and eyelid that circumvents the need for immunosuppression required from allotransplants.

ITP SUPPORT

With the overall objective of using mucocutaneous constructs to restore soft tissue, support from the ITP program will be used for preparatory and follow-through events surrounding IND discussions with the FDA for initiation of a first-in-human clinical trial.



STEPHEN E. FEINBERG, DDS, MS, PHD
University of Michigan

"The success gained from the proposed first-in-human Phase I multicenter clinical trial to tissue engineer functional human lips will establish a platform technology that will create a paradigm shift on how the surgeon may reconstruct composite soft tissues that have a mucocutaneous junction, i.e., lips, vagina, eyelids, and anal sphincter. It will also validate a method to fabricate autogenous composite soft tissue grafts that will supplant procedures requiring lifetime immunosuppression."

CLINICAL TRANSLATION PATHWAY

Publications:
In Vitro Development of a Mucocutaneous Junction for Lip Reconstruction. J Oral Maxillofac Surg. 2016.

Tissue engineering of lips and muco-cutaneous junctions: *in vitro* development of tissue engineered constructs of oral mucosa and skin for lip reconstruction. Tissue Eng Part C. 2012.

Intellectual Property:
US 7,887,829 Mucosal cell composites and methods

US 8,835,169 Compositions, methods and systems for preparation of a stem cell-enriched cell population

Regulatory Pathway:
Anticipated: Biologic, IND to enable BLA

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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AxoMax®: A Novel Conduit for Enhanced Nerve Repair

KACEY MARRA, PHD
University of Pittsburgh

"This technology has the potential to revolutionize treatment of long gap nerve repair."

https://www.mirm.pitt.edu/our-people/faculty-staff-bios/kacey-g-marra-phd

CLINICAL NEED

Injuries resulting in facial paralysis significantly affect a patient both physiologically and psychosocially. The standard of care for nerve injury requiring surgical repair is nerve autograft, which is suboptimal for various reasons. While several nerve guides are commercially available for regeneration of nerve gaps <3cm, those for use in large nerve gaps (>3cm) are not. Furthermore, despite the available interventions, current cases of nerve autografting or allografting result in insufficient functional recovery, where ~50% of patients are unable to return to pre-injury employment 1 year post-operation.

SOLUTION

Kacey Marra, PhD, and her team at the University of Pittsburgh have developed a novel conduit for long-gap nerve repair, named AxoMax®. AxoMax® consists of a degradable poly(caprolactone) nerve guide capable of controlled local delivery of drugs for nerve regeneration. Evaluation of the AxoMax® in a 5cm median nerve defect model showed ~80% return to function after one year.

COMPETITIVE ADVANTAGE

Unlike decellularized technologies, AxoMax® elutes factors essential to nerve growth for several months, rendering it biologically similar to an autograft, the standard of care, without the need for a surgery to harvest the graft, thereby avoiding comorbidities associated with such procedures. The elimination of the harvesting procedure spares the patient from lifelong loss of sensation, as well as operating room time, saving an excess of 60 minutes per case.

ITP SUPPORT

With the ultimate goal of commercialization of AxoMax® for bridging craniofacial nerve defects, the work supported by the ITP program includes continued market validation and biocompatibility testing in support of a Q-submission to the FDA.

CLINICAL TRANSLATION PATHWAY

Publications:
Incorporation of double-walled microspheres into polymer nerve guides for the sustained delivery of glial cell line-derived neurotrophic factor. Biomaterials, 2010.

Sustained Growth Factor Delivery Promotes Axonal Regeneration in Long Gap Peripheral Nerve Repair. Tissue Eng Part A. 2011.

Intellectual Property:
US 9,498,221
Implantable medical devices having double walled microspheres.

Regulatory Pathway:
Anticipated: Device, 510(k), then IDE to enable PMA

Commercialization Strategy:
Technology licensed by AxoMax Technologies, Inc., a start-up company founded to advance AxoMax®

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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Non-Viral Aquaporin-1 Gene Therapy to Restore Salivary Flow in Patients Suffering from Radiation-Induced Xerostomia

CLINICAL NEED

In the treatment of head and neck cancers, radiotherapy is commonly prescribed in conjunction with other modalities such as surgery and/or chemotherapy. Because of the anatomical proximity, salivary glands receive secondary damage, where xerostomia is one of the common effects of this damage. While intensity-modulated radiotherapy has significantly reduced the incidence of radiation-induced xerostomia, a pressing need exists for the remaining patients, especially for those in whom amifostine leads to significant side effects.

SOLUTION

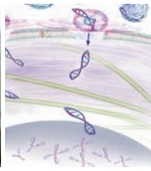
A team of researchers at the Allegheny Health Network led by Michael Passineau, PhD, has developed an ultrasound-assisted gene transfer technique (UAGT), to deliver AQP1 gene for the amelioration of radiation-induced xerostomia. This non-viral gene delivery is based on sonoporation generated by the ultrasound, enabling gene transfer as cell membrane permeability is altered. The delivery of AQP1 to the parotid glands in a mini-swine model has restored salivary flow to pre-treatment levels, demonstrating the efficacy of non-viral AQP1 gene transfer.

COMPETITIVE ADVANTAGE

While a recent clinical trial using AQP1 gene delivery demonstrated increase in saliva production, this approach has not advanced beyond a successful Phase I/II trial to regulatory approval due to the utilization of the adenovirus vector for gene delivery. With the preclusion of a virus for gene transfer, this approach is anticipated to provide enhanced safety and enable serial dosing to provide patients with the benefit of the AQP1 gene transfer throughout their lifetime.

ITP SUPPORT

The long-term objective of this research program is to improve the quality of life in patients who have suffered from radiation-induced xerostomia. In collaboration with Dr. Isabelle Lombaert at the University of Michigan, the ITP program will support the continued validation and characterization of UAGT for the delivery of AQP1 gene towards enabling FDA submission.



MICHAEL PASSINEAU, PHD
Allegheny Health Network

ISABELLE LOMBAERT, PHD
University of Michigan

"We are working to develop a safe gene therapy to provide lifelong relief from dry mouth in patients whose salivary function has been damaged by radiotherapy for head and neck cancers."

http://media.dent.umich.edu/labs/lombaert

CLINICAL TRANSLATION PATHWAY

Publications:
Ultrasound-assisted nonviral gene transfer of AQP1 to the irradiated minipig parotid gland restores fluid secretion. Gene Ther 2015.

Intellectual Property:
In development with MPWRM Core

Regulatory Pathway:
Anticipated: Biologic, IND to enable PMA

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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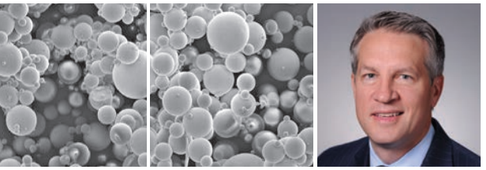
Romosozumab to Treat Alveolar Bone Loss for Dental Implant Reconstruction



WILLIAM GIANNOBILE, DDS, DMEDSC

University of Michigan

"This novel technology offers systemic bone anabolic drug delivery to promote the regeneration of bone defects around teeth affected by periodontal disease or dental implants needing bone reconstruction."

media.dent.umich.edu/labs/giannobile/

CLINICAL NEED

Periodontitis is known to affect approximately 50% of the U.S. adult population, with approximately 10% of patients afflicted with severe form of the disease leading to tooth loss. Although various procedures have been explored for the regeneration of the periodontium and bone, predictable treatments to arrest and rebuild lost tissues around teeth and/or tooth-replacing dental implants are limited, and to date, there are no FDA-approved bone anabolic agents available to treat periodontal or peri-implant bone loss.

SOLUTION

A team of researchers led by Dr. William Giannobile at the University of Michigan, is developing a systemic delivery of sclerostin monoclonal antibody to restore lost periodontium or implant-supporting alveolar bone. The approach offers the potential for easy dosing of sclerostin antibody to regenerate lost periodontium or improve peri-implant bone density.

COMPETITIVE ADVANTAGE

By taking advantage of easy delivery of sclerostin monoclonal antibody, which is already clinically approved for improvement of bone density in other indications such as osteoporosis, this approach may represent an improved access to drug therapies for periodontal and dental implant-related diseases that might otherwise not be as available due to limited reimbursement through typical dental insurance.

ITP SUPPORT

The work supported by the ITP program is focused on the IND submission for the design of a phase I/II human clinical trial to use systemic sclerostin antibody delivery to treat periodontal disease.

CLINICAL TRANSLATION PATHWAY

Publications:
Sclerostin neutralizing antibody enhance bone regeneration around oral implants. Tissue Eng Part A. 2018.

Sclerostin antibody stimulates bone regeneration after experimental periodontitis. J Bone Miner Res 2013.

Intellectual Property:
US 9,657,090 Method of treating alveolar bone loss through the use of anti-sclerostin antibodies

Regulatory Pathway:
Anticipated: Biologic, IND to enable BLA or NDA

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Michigan-Pittsburgh-Wyss Regenerative Medicine Resource Center is supported in part by the National Institute of Dental & Craniofacial Research of the National Institutes of Health under Award Number U24DE026915. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Immunomodulatory Strategies to Treat Periodontal Disease

CLINICAL NEED

Periodontitis affects nearly half of adults over of 30 in the U.S. If left untreated, dental implants and bone grafting procedures may be required. Antibiotics are currently used as an adjunct therapy to scaling and root planing, which remains the standard of care. With a shift away from antibiotics overuse, new treatment modalities that address the host immune response are needed.

SOLUTION

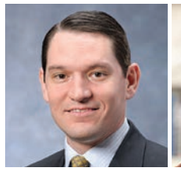
A team at the University of Pittsburgh led by Drs. Steven Little and Charles Sfeir has developed controlled release systems that repair the underlying immunomodulation dysfunction responsible for tissue degeneration in periodontitis. Both systems induce homeostasis and thereby reduce inflammation and destruction to promote tissue regeneration, either through recruiting regulatory T cells or polarizing M0-M1 to M2 macrophages.

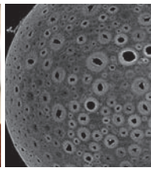
COMPETITIVE ADVANTAGE

While bacterial removal has shown clinical benefit, it does not directly address the chronic inflammatory response. By targeting the underlying immunoregulatory discourse, these controlled release systems are thought to overcome the current limitation in the treatment of periodontal diseases.

ITP SUPPORT

With the goal of FDA submissions, the ITP program is supporting the GMP-grade manufacturing and development of sterilization protocols, and establishing the effectiveness in a larger animal model for the regulatory T cell recruitment and macrophage polarization systems, respectively.





STEVEN LITTLE, PHD

University of Pittsburgh

CHARLES SFEIR, DDS, PHD

University of Pittsburgh

"This new class of treatments is extremely exciting in that organizing extraordinarily tiny amounts of proteins that are already found in the body seems to be capable of influencing the body's own cells to repair the destructive inflammation that produces periodontal disease. To give perspective, it is possible to deliver millions of times less drug and achieve a better effect than the current gold standard."

www.littlelab.pitt.edu

www.dental.pitt.edu/person/charles-s-sfeir-0

CLINICAL TRANSLATION PATHWAY

Publications:
Prevention of Inflammation-Mediated Bone Loss in Murine and Canine Periodontal Disease via Recruitment of Regulatory Lymphocytes. PNAS 2014.

Restoring Host-Microbe Homeostasis via Selective Chemoattraction of Tregs. J Dent Res 2014.

Induction of M2 Macrophages Prevents Bone Loss in Murine Periodontitis Models. J Dent Res 2019.

Intellectual Property:
US 8,846,098 Artificial cell constructs for cellular manipulation

Provisional patent application filed

Regulatory Pathway:
Anticipated: Biologic, IND to enable BLA or NDA

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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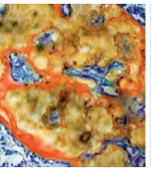
Optimization of a Novel Organic-Mineral Bone Adhesive



GEORGE KAY, DMD, MMSC
Harvard School of Dental Medicine

JOSEPH FIORELLINI, DMD, DMSC
Penn Dental Medicine

LaunchPad Medical

"The ITP program has been an innovative partnership between NIDCR, academia and a corporate entity. This partnership is ideally suited for a product such as Tetranite. With multiple resources available to all parties, the development process has been streamlined and made more efficient."

www.launchpadmedical.com

CLINICAL NEED

Although over 50% of adults over the age of 45 in the US have one or more missing teeth, only 2% of the eligible population receives a prosthetic tooth due to factors including time involved in multi-stage bone grafting procedures and associated costs. While most bones grafting materials demonstrate osteoconductivity to regenerate bone, many suffer from poor mechanical properties, necessitating the use of ancillary fixation or containment devices to prevent graft migration and ingrowth of fibrous tissue that impedes bone regeneration and remodeling.

SOLUTION

Researchers at LaunchPad Medical are exploring a novel technology, Tetranite®, for bone grafting applications. Tetranite is an injectable, synthetic, wet-field bioresorbable biomaterial which can create a strong load-bearing bond between wet bone tissue and metals. The material is chemically and structurally stable in a neutral pH aqueous environment and is degraded and resorbed in vivo without the loss of bond to bone, resulting in continuous bone deposition to exposed surfaces.

COMPETITIVE ADVANTAGE

The unique hard-setting and adhesive properties of Tetranite enable it to conform and fixate to complex, open-walled, horizontal, and vertical defect sites. Given these unique properties, the material is predicted to eliminate the need for ancillary or graft containment devices currently required to support the existing bone graft. In addition, Tetranite enables immediate placement of implants simultaneous to the bone augmentation procedure, simplifying the bone grafting procedure. The reduction in surgical intervention and costs are expected to enable prosthetics to more widely benefit patients.

ITP SUPPORT

The work supported by the ITP program will prepare for the pivotal animal studies to assess the optimal Tetranite formulation for bone regeneration. The data from this investigation will better characterize the temporal formation of bone and resorption of the Tetranite graft material.

CLINICAL TRANSLATION PATHWAY

Publications:
Optimization of a Novel Organic-mineral Bone Adhesive for Dental Bone Grafting. Presented at IADR General Session 2019, Academy of Osseointegration Annual Meeting 2019

Intellectual Property:
US 8,232,327, US 8,273,803 Tetra calcium phosphate based organophosphorus compositions and methods

US 8,765,189 Organophosphorous and multivalent metal compound compositions and methods

Regulatory Pathway:
Anticipated: Device, 510(k)/de novo (clinical trial underway for dental implant stabilization)

Commercialization Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/ Market Needs Core

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AmpliMag Barrier Membrane and Membrane Fixation System

CLINICAL NEED

Over one million dental bone grafting procedures are performed annually in the US, most frequently before dental implant placement. In the most challenging grafting procedures, where there is a significant vertical deficit, even expert clinicians face revision rates reaching 25% due to the difficulty of reliably regenerating sufficient bone for implant placement. Currently used barrier membranes and fixation systems are unable to offer the form-stability needed to protect healing grafting sites from mechanical insults, while also offering resorbability and gingival tissue friendliness. The inability of regenerative products to offer these three features result in dental bone grafting procedures that are highly technique-sensitive, prone to adverse events, and require invasive removal procedures.

SOLUTION

The AmpliMag system provides the form-stability and gingival-tissue friendliness needed to minimize adverse events and maximize bone regeneration. The system is fully resorbable which eliminates the need to retrieve hardware following healing. The AmpliMag system is based on a patented magnesium alloy system developed by nanoMAG and patent-pending magnesium/polymer composites developed at the University of Pittsburgh.

COMPETITIVE ADVANTAGE

No other barrier membranes offer both form-stability and resorbability which, taken together, enable maximization of alveolar ridge augmentation while obviating the need for device removal.

ITP SUPPORT

The ITP program has provided financial support for design, manufacturing, and benchtop and pre-clinical testing activities for the AmpliMag barrier membrane. Additionally, the Resource Center has provided expert clinical, market, regulatory, and quality advice.



ANDREW BROWN, PHD
Emergence Dental, Inc.

STEPHEN LEBEAU, PHD
nanoMAG, LLC

"Emergence Dental was founded to combine biomaterial intellectual property from nanoMAG and University of Pittsburgh to address unmet needs in dental bone regeneration. The Resource Center has enabled us to accelerate the development of the AmpliMag barrier membrane and membrane fixation not just with funding, but with expertise that we have not been able to access elsewhere."

www.nanomag.us
www.emergencedental.com

CLINICAL TRANSLATION PATHWAY

Publications:
Porous magnesium/PLGA composite scaffolds for enhanced bone regeneration following tooth extraction. Acta Biomater 2015.

Intellectual Property:
US 10,022,470 High Strength and bio-absorbable magnesium alloys

PCT/US2019/018545 Improved Magnesium Alloy and Process for Making the Same

Regulatory Pathway:
Anticipated: Device, 510(k) as 2 separate products (membrane/ fixation system)

Commercialization Strategy:
Emergence Dental, Inc. was formed to focus on the commercialization of dental regenerative devices based on intellectual property developed at nanoMAG and University of Pittsburgh.

Product Launch Strategy:
In partnership with a large implant or dental regenerative company, performing a clinical adoption study and distributing through existing sales channels.

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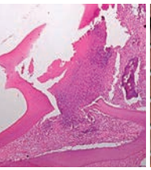
RegendoGEL: A Bioinspired Hydrogel System for Endodontic Therapy



PAMELA YELICK, PHD
Tufts University

LUIZ BERTASSONI, DDS, PHD
Oregon Health & Science University

"This technology will allow for much more predictable and successful outcomes in regenerative endodontics, and can be integrated into routine dental procedures with ease."

www.bertassonilab.com
dental.tufts.edu/people/faculty/pamela-yelick

CLINICAL NEED

Dental caries is the most prevalent chronic infectious disease in humans. If not treated, virtually all caries lesions will progress to affect the dental pulp, eventually requiring some form of root canal therapy. The current standard of care using polymeric/ceramic-like materials can elicit tertiary dentin formation in vital young teeth, but fail to mimic the composition, physical properties, and regenerative/biological capacity of the native pulp.

SOLUTION

A team led by Luiz Bertassoni, DDS, PhD and Pamela Yelick, PhD has developed a novel material for regenerative pulp treatment, intended to be the first-of-its-kind clinical product to promote vital pulp regeneration. RegendoGEL contains key stimulatory molecules found in healthy teeth that naturally promote pulp repair and regeneration, and may be used for direct pulp capping and pulpotomy.

COMPETITIVE ADVANTAGE

As compared to the existing synthetic rigid silicate or calcium hydroxide-based products currently used for endodontic treatments, RegendoGEL is a soft hydrogel system that more closely resembles the natural pulp tissue. Unlike traditional non-degradable cements, RegendoGEL stimulates cells to migrate into the defect site and regenerate living dental pulp tissue and dentin, thus revitalizing the tooth and regenerating tooth tissues in the target location. In addition, RegendoGEL is designed as a ready-to-use system that can be integrated into routine dental procedures in the clinic.

ITP SUPPORT

With a focus on direct pulp capping and pulpotomy, the support from the ITP program will be used to complete *in vivo* validation and optimization of the RegendoGEL system to enable FDA submission.

CLINICAL TRANSLATION PATHWAY

Publications:
A Novel Strategy to Engineer Pre-Vascularized Full-Length Dental Pulp-like Tissue Constructs. Sci Rep 2017.

Photopolymerization of cell-laden gelatin methacryloyl hydrogels using a dental curing light for regenerative dentistry. Dent Mater 2018.

Intellectual Property:
US 16/618,329 Dental pulp construct

US 15/777,304 Pulp regeneration compositions and methods of forming and using the same

Regulatory Pathway:
Anticipated: Device, IDE to enable 510(k)

Commercialization Strategy:
In development with the MPWRM Commercialization/Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/Market Needs Core

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Vital-Dent, A Revitalizing Root Canal Implant

CLINICAL NEED

Over 15 million root canal therapy (RCT) procedures are performed each year to treat carious infected teeth. Conventional RCT removes infected pulp tissue and fills the void with inert materials. The long-term survival of treated teeth is limited because the tooth is dead; it cannot mount an immune response to fight reinfection. On average, periapical infection is evident by 10 years, and the tooth is lost by 20 years.

SOLUTION

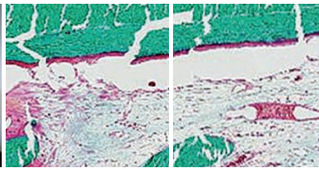
A team of researchers at the University of Pittsburgh, led by Drs. Juan Taboas and Herbert Ray, is developing a device to regenerate vital tissue within RCT-treated teeth. The two-part drug-free material system, termed Vital-Dent, is designed to be an off-the-shelf implantable device that replaces conventional sealers with a hydrogel and conventional obturating points with a sponge.

COMPETITIVE ADVANTAGE

Vital-Dent is anticipated to increase the long-term survival of the tooth by guiding ingrowth of cells and generating vascularized tissue capable of mounting an immune response. In a preliminary canine study, Vital-Dent showed regeneration of vital tissue within the RCT-treated roots, with mineralized tissue along the dentin walls, and vascularized fibrous tissue in the root canal proper, up to the crown sealer.

ITP SUPPORT

The ITP program will support the evaluation of Vital-Dent towards a design freeze of the device composition and delivery process, analyzing regenerated tissue composition and outcomes, as compared to revascularization procedure and conventional treatment with resin sealer and gutta-percha points.

JUAN TABOAS, PHD
University of Pittsburgh

"Vital-Dent is an off-the-shelf device that regenerates living tissue in root canal therapy treated teeth and prolongs tooth survival."

www.dental.pitt.edu/person/juan-m-taboas-1

CLINICAL TRANSLATION PATHWAY

Publications:
Acellular hydrogel regenerates a vascularized tissue producing organized mineral along the instrumented canal wall. Pulp Biology and Regeneration Group Satellite Meeting: Basic and Translational Research in Pulp Biology – Developing Technologies for Regenerating Vital Dental Tissues, 2019.

Intellectual Property:
PCT/US2019/023132 Regeneration of Vital Tooth Pulp

Regulatory Pathway:
Anticipated: Device, IDE

Commercialization Strategy:
In development with the MPWRM Commercialization/Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/Market Needs Core

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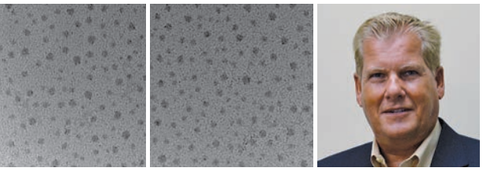
Targeted Remineralization Treatment Using Mineral Loaded Starch Nanoparticles



STEVEN BLOEMBERGEN, PHD

GreenMark Biomedical Inc.

"Targeted nanoparticle based regeneration of enamel will allow for more natural repair of dental caries using painless and non-invasive treatment, reducing discomfort during dental procedures, preserving dental tissue and improving long term oral health of patients."

http://greenmark.bio

CLINICAL NEED

Dental caries, caused by the demineralization of enamel, is the most common chronic disease worldwide. While caries is often treated surgically, recent treatment methods include the non-invasive approach of mineral ions and fluoride delivery using professionally applied fluoride varnishes, prescription and over-the-counter fluoride toothpastes, and calcium phosphate-based remineralization agents. However, these treatments are unable to regenerate enamel within the depth of subsurface carious lesions.

SOLUTION

GreenMark Biomedical Inc. has developed targeted biodegradable nanoparticles capable of delivering minerals and fluoride specifically to enamel, for in-office treatment of non-cavitated carious lesions ("pre-cavities"). The same technology platform is also being used in the development of a diagnostic product which illuminates carious lesions using a standard dental curing lamp to allow earlier detection of pre-cavities. The nanoparticles consist of starch, readily degraded by natural amylase enzymes in saliva, and their specific adhesion defines the interior lesion sub-surface morphology. While traditional fluoride treatments impact the surface of enamel lesions, this targeted delivery of minerals and fluoride to the dominant subsurface lesion is expected to enable a superior non-surgical dental treatment.

COMPETITIVE ADVANTAGE

High localized concentration of these minerals and fluoride is expected to facilitate tooth structure regeneration through nucleation and targeted formation of hydroxyapatite-like crystals to improve efficacy, lower the required therapeutic dose, and minimize reliance on patient compliance, yielding superior remineralization of lesions compared to other available treatments.

ITP SUPPORT

The support from the ITP program is expected to advance the technology with continued technical validation and development of regulatory and marketing strategies.

CLINICAL TRANSLATION PATHWAY

Publications:
Nanoparticle-Based Targeting and Detection of Microcavities. Adv Healthc Mater 2017.

Intellectual Property:
US15/331,408 Detection and treatment of caries and microcavities with nanoparticles

Regulatory Pathway:
Anticipated: Device, 510(k)

Commercialization Strategy:
In development with the MPWRM Commercialization/Market Needs Core and dental marketing partner firm

Product Launch Strategy:
In development with the MPWRM Commercialization/Market Needs Core and dental marketing partner firm

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Reversing Tooth Decay with Biomimetic Peptide Gel

CLINICAL NEED

Demineralization in tooth is often the cause of various dental concerns including dental cavities and hypersensitivity. The currently available commercial products with claims for remineralization properties aim to stabilize calcium and phosphate to deliver a high dosage of the ions to the oral cavity. Because this process is an indirect approach to mineralization, it cannot direct and catalyze mineral formation on the tooth surface, thereby limiting their clinical and long-term effectiveness.

SOLUTION

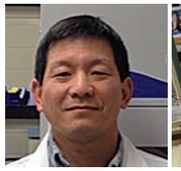
To address this need, a team of researchers at the University of Washington, led by Prof. Mehmet Sarikaya and Dr. Hanson Fong, has developed a peptide-containing gel to direct primary biomineralization of the lost dental tissues to treat tooth decay and other dental ailments caused by demineralization. The peptides have been demonstrated to form calcium phosphate minerals of controlled structural characteristics, forming stable layers of deposited mineral on extracted human and rat teeth, both on dentin and on enamel.

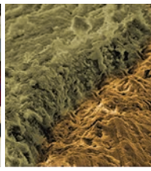
COMPETITIVE ADVANTAGE

This gel formulation is expected to be topically applied on the carious teeth with early stage tooth decay to restore mineral on the affected surface. As with the currently used fluoride varnish, this gel would also be applied in dentist's office. While the fluoride varnish does not actively add new mineral to the tooth surface, the active, mineralizing gel will serve as an effective procedure to reverse cavity progression.

ITP SUPPORT

With the overall objective to develop a user-friendly prototype product for the permanent treatment of demineralization-driven conditions including dental caries and hypersensitivities, the ITP program will be supporting the continued validation of the peptide-containing gel formulation for guided remineralization and exploration of FDA regulatory and OTC and clinical marketing strategies.





HANSON FONG, PHD

University of Washington

MEHMET SARIKAYA, PHD

University of Washington

"Novel remineralization therapies guided by naturally derived peptides will transform current dental health providing preventative and restorative oral care."

www.uwgemsec.com/principal-investigator

CLINICAL TRANSLATION PATHWAY

Publications:
Biomimetic Tooth Repair: Amelogenin-Derived Peptide Enables *in vitro* Remineralization of Human Enamel. ACS Biomater Sci Eng 2018.

Early caries in an *in vivo* Model: Structural and nanomechanical characterization. J Dent Res 2018.

Intellectual Property:
US 9,809,633 Reagents and Methods for Treating Dental Disease

PCT/US2017/013492 Reagents and Methods for Mineralization of Tooth Enamel

Regulatory Pathway:
In development with the MPWRM Regulatory Core

Commercialization Strategy:
In development with the MPWRM Commercialization/Market Needs Core

Product Launch Strategy:
In development with the MPWRM Commercialization/Market Needs Core

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Leadership: Operating Committee Members

Steven Goldstein, PhD *(U Michigan) – Chair*
Albert Donnenberg, PhD *(U Pittsburgh)*
William Giannobile, DDS, DMSc *(U Michigan)*
David Kohn, PhD *(U Michigan)*
Paul Kostenuik, PhD *(Phylon Pharma Services)*
Laurie McCauley, DDS, PhD *(U Michigan)*
Michael McGuire, DDS *(McGuire Institute)*
David Mooney, PhD *(Wyss Institute)*
J. Peter Rubin, MD *(U Pittsburgh)*
Charles Sfeir, DDS, PhD *(U Pittsburgh)*
Donald Taylor, PhD, MBA *(sciVelo/ U Pittsburgh)*
William Wagner, PhD *(U Pittsburgh)*

Core Services & Resources

IN VITRO/ IN VIVO VALIDATION

Microcomputed Tomography
Histology/Histomorphometry
Microscopy/Image Analysis
Biomechanics
Materials Fabrication & Characterization
Mechanical & Functional Assessment
Pre-Clinical Animal Models and Testing

TRAINING RESOURCES

Assist in the translation of DOC-related scientific discoveries into clinical practice; partnership with NIH-sponsored Clinical and Translational Science Award sites to foster research development, cultivate multidisciplinary collaborations, and train the next generation of researchers to improve health outcomes for patients in need.

STANDARDIZATION QUALITY CONTROLS

Provide inputs and tools/ templates as an approach to developing carefully planned studies, and serve as a resource to help interpret FDA requirements.

PROTYPING & MANUFACTURING

Cell/ Materials Manufacturing
Method and Process Development
Pre-Clinical Testing
Drug Release Profiling
Material Characterization

REGULATORY

Identify and navigate the regulatory pathway towards FDA submissions, in support of new DOC therapies.

INTELLECTUAL PROPERTY

Unearth, evaluate, analyze, and identify IP opportunities related to DOC technologies, to strengthen proprietary position.

MARKET ASSESSMENT

Supports the strategic decision making processes for new technology development by exploring market opportunities in the current DOC landscape.

COMMERCIALIZATION

Assist investigators to achieve successful business milestones and provide guidance on technology commercialization process.

About the Institutions

UNIVERSITY OF MICHIGAN, SCHOOL OF DENTISTRY

The University of Michigan School of Dentistry is one of the nation's leading dental schools engaged in oral health care education, research, patient care, and community service. The research mission promotes an integration of basic, translational, clinical and health services research along with associated educational programs to stimulate discoveries and their diffusion into practice. The school has an extensive history in the merger of engineering and life science technologies to solve problems in the dental, oral, and craniofacial space. Through partnership and collaborations with the School of Medicine and College of Engineering at Michigan, investigators and research cores have expertise in many technologies central to advancing tissue engineering/ regenerative medicine, including: biomaterials and drug delivery; biomechanics, imaging, and functional analyses; stem cells and cell sourcing, and gene therapy. Michigan also has significant expertise in the clinical trials arena and from bench to proof-of-concept (bed-side or chair-side), and bench to start-up for clinical application. Furthermore, the School of Dentistry has been a leading center for early stage (Phase1) clinical trials as well as pivotal clinical trials that have led to the Food and Drug Administration (FDA) approval of new dental drugs and regenerative devices. For more information about the School of Dentistry, please visit **www.dent.umich.edu**.

UNIVERSITY OF PITTSBURGH MCGOWAN INSTITUTE FOR REGENERATIVE MEDICINE

The McGowan Institute for Regenerative Medicine is a translational research enterprise focused on the development and delivery of technology to address tissue and organ insufficiency. McGowan Institute serves as a single base of operations for the University of Pittsburgh's leading scientists and clinical faculty working to develop tissue engineering, cellular therapies, and artificial and biohybrid organ devices. McGowan Institute integrates an ambitious regenerative medicine technology portfolio, coupling biology, clinical science and engineering. Success in our mission will impact patients' lives, bring economic benefit, serve to train the next generation of researchers, and advance the expertise of our faculty in the basic sciences, engineering and clinical sciences. For more information about the McGowan Institute, please visit **www.mcgowan.pitt.edu**.

UNIVERSITY OF PITTSBURGH CENTER FOR CRANIOFACIAL REGENERATION

Rooted in ground-breaking tissue regeneration and biomaterial advances made at the University of Pittsburgh, the Center for Craniofacial Regeneration (CCR) develops treatments for wounds and defects of the face and skull that restore function and appearance. Representing many scientific disciplines and interests, our team is dedicated to exploring all aspects of the varied and complex craniofacial region.

The CCR's dynamic approach draws upon the expertise of scientists, from cell and molecular biologists, polymer chemists and material scientists to bioengineers, imaging experts and clinicians. The CCR encourages the transfer of developed technologies and treatments to enable new biotechnology ventures. Recently awarded funding from the National Institutes of Health (NIH) to support a translational resource center bears this out, demonstrating how the work of centers, such as the CCR, ultimately can improve the lives of patients by bridging the gap between basic science and clinical treatments. For more information about CCR, please visit **www.dental.pitt.edu/center-craniofacial-regeneration**.

WYSS INSTITUTE FOR BIOLOGICALLY INSPIRED ENGINEERING

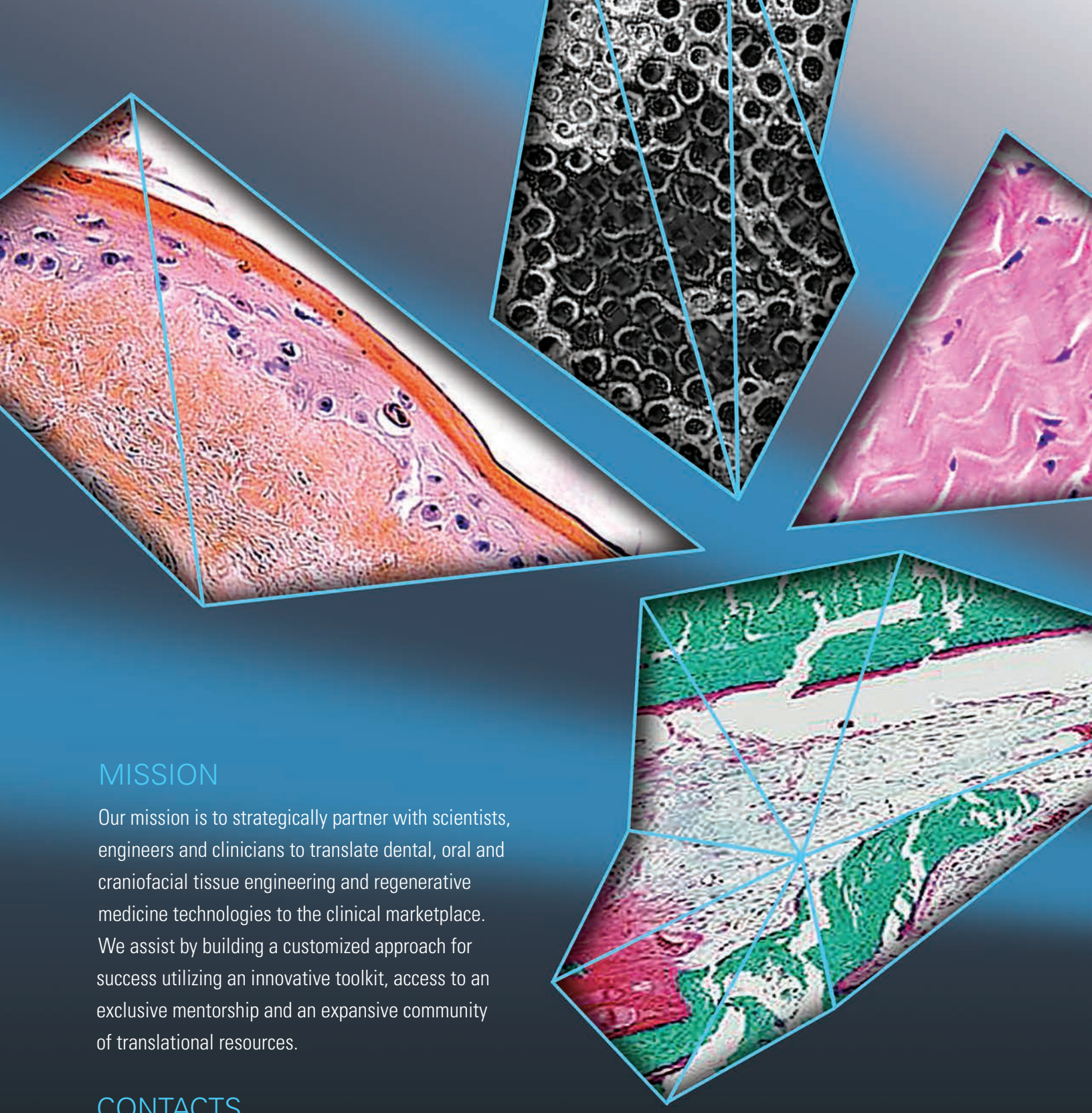
The Wyss Institute for Biologically Inspired Engineering uses biological design principles to develop new engineering innovations that will transform medicine and create a more sustainable world. They leverage recent insights into how Nature builds, controls and manufactures to develop new engineering innovations - a new field of research we call Biologically Inspired Engineering. Biologically Inspired Engineering combines synthetic biology, nanobiotechnology and other approaches that leverage biological design principles to develop new engineering Solutions for medicine and non-medical fields never before touched by the biology revolution. By emulating biological principles of self-assembly, organization and regulation, we are developing disruptive technology solutions for healthcare, energy, architecture, robotics, and manufacturing, which are translated into commercial products and therapies through formation of new startups and corporate alliances. For more information about the Wyss Institute, please visit **www.wyss.harvard.edu**.

NATIONAL INSTITUTE OF DENTAL AND CRANIOFACIAL RESEARCH

The mission of the National Institute of Dental and Craniofacial Research (NIDCR) is to improve dental, oral, and craniofacial health. We accomplish our mission by:

- Performing and supporting basic, translational, and clinical research;
- Conducting and funding research training and career development programs to ensure an adequate number of talented, well-prepared, and diverse investigators;
- Coordinating and assisting relevant research and research-related activities among all sectors of the research community;
- Promoting the timely transfer of knowledge gained from research and its implications for health to the public, health professionals, researchers, and policy-makers.

For more information about NIDCR, please visit **www.nidcr.nih.gov**.



MISSION

Our mission is to strategically partner with scientists, engineers and clinicians to translate dental, oral and craniofacial tissue engineering and regenerative medicine technologies to the clinical marketplace. We assist by building a customized approach for success utilizing an innovative toolkit, access to an exclusive mentorship and an expansive community of translational resources.

CONTACTS

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