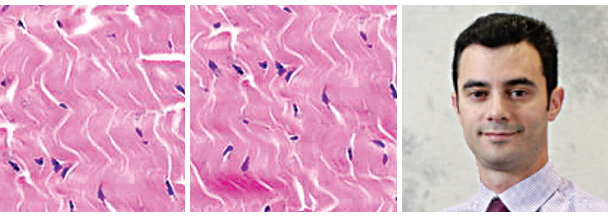
Extracellular Matrix Scaffold for TMJ Disc Repair



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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ECM Scaffolds for TMJ Disc Repair

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University of Pittsburgh

DOCTRC DENTAL, ORAL, & CRANIOFACIAL TISSUE REGENERATION CONSORTIUM

Michigan · Pittsburgh · Wyss Regenerative Medicine Resource Center

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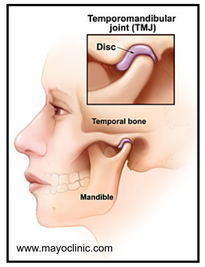
UNMET CLINICAL NEED

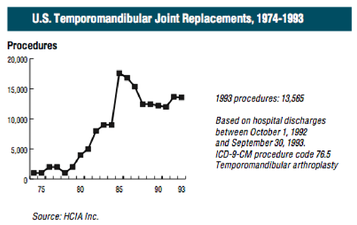
Temporomandibular Joint (TMJ)

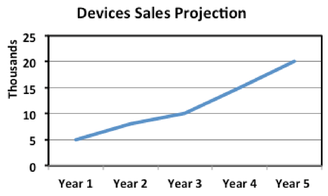
- Temporomandibular joint disorders (TMDs) affect between 10 and 36 million Americans
- For a percentage of these patients removal of the TMJ disc is the only option which relieves pain and restores motion of the jaw
- However, disc removal leads to bone-on-bone articulation, which predisposes the patient to condyle erosion and the eventual need for total joint replacement
- Some surgeons replace disc with autografts, but radiographic evidence shows resorption of autograft by 9-12 months
- Thus, an off-the-shelf solution is needed to prevent degenerative changes to the bone, which will not require autograft harvest, and remain in the joint space for at least 12 months



MARKET ANALYSIS

- Can expect to capture as much as 30% of this market
- Initially 5,000+ implanted patients
- Market expected to increase with an available solution
- Oral and maxillofacial surgeons would place a high value on this product





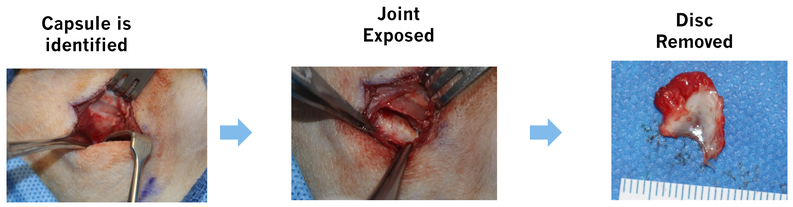
INTELLECTUAL PROPERTY

- Intellectual Property secured
  - Patent No.: US 9,314,340 B2
  - Date of Patent: April 19,2016
- The IP protects the formulation, size, shape, etc., of the device and its use to reconstruct the disc in temporomandibular joints
- IP already has been licensed by ECM Therapeutics
  - Interested in commercialization after results of first-in-man study

RESULTS

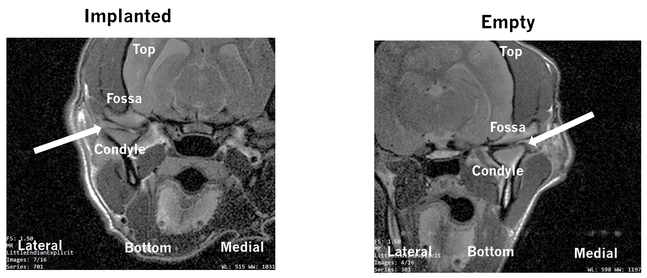
A Good Laboratory Practices (GLP) large animal study to assess the safety of TMJ Repair Graft manufactured in Good Manufacturing Practices (GMP) at 21 days

Device Placement:



21-Day Tissue Harvest:

21-Day Magnetic Resonance Imaging (MRI):



Gross Morphology and MRI both show new tissue formation as TMJ Repair Graft is remodeling, while no new tissue forms in joint after disc removal

MANUFACTURING

- Partnered with Cook Biotech to manufacture TMJ Repair Graft under GMP standards
- Device is composed of extracellular matrix (ECM) obtained from the small intestine submucosa of pig
- Device is manufactured as a pillow configuration with ECM powder encased by ECM sheets
- Cook will provide master file record to FDA

REGULATORY PATHWAY

- **Definitive Preclinical Trials**
- **First-in-man/IDE (5-10)**
- **Pilot Clinical Trial (10-20)**
- **Pivotal Clinical Trials (100-200)***
- **PMA Application**
- **Product to Market**

- Several communications with FDA
  - Main input is to show device is still in place after 12 months post-implantation

GMP device in GLP large animal preclinical trial will be last hurdle before first-in-man

- FDA will require PMA application

TIMELINE & FUTURE DIRECTIONS

- Still processing samples from 21-day study for histology and pathological evaluation
- Perform a 12-month study in GLP with GMP device
  - In addition to MRI and histology, FDA suggests to perform dynamic mechanical evaluation of the tissue
- Then FDA clearance is expected to perform first-in-man IDE study

Funding

Funding for the 21-day study was provided by Michigan-Pittsburgh-Wyss Resource Center: Advancing Dental, Oral, and Craniofacial Regeneration to Clinical Trial Initiation 1U24 DE029462-01