CLINICAL NEED
Periodontitis affects nearly half of adults over 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.

CLINICAL TRANSLATION PATHWAY

**Publications:**

**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

**Product Launch Strategy:**
- In development with the MPWRM

*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

Ashlee Greene, Mostafa Shehabeldin, Jin Gao, Julie Kobyra, Patrick Donnelly, Steven R. Little, Charles Sfeir

UNMET CLINICAL NEED

- Periodontitis, one of the most pressing oral health care concerns. In 2010—65 million Americans were found to have periodontitis. Current treatment options focus on physical removal in combination with systemic administration of antibiotics. WHO has noted the need to switch away from the use of antibiotics in general because of antibiotic resistance. Current treatment approaches fail to address the uncontrolled host immune response that is responsible for most of periodontal damage and disease progression.

MARKET ANALYSIS

- ~15 to 20% of patients do not respond to traditional antibiotics or physical removal.
- 25% of 2.8M procedures done on mild/moderate patients fail (refractory periodontitis). With a treatment cost of $150 per use, we could reach an entry target market size of $105M.
- Potential to reach an estimated full market of $450 M/year.

INTELLECTUAL PROPERTY

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RESULTS

- cGMP grade manufacturing of CCL22 PLGA microspheres by CRO (University of Tennessee-Plough)
- Aseptic manufacturing to avoid loss due to terminal sterilization
- Production of rCCL2 by CRO (ProteinOne)

REGULATORY PATHWAY

- CCL22/CCL2 microspheres as an adjunct therapy to scaling and root planning
- Considered by FDA to be a biologic therapeutic (if recombinant version of API selected vs. considered as drug if solid state version of API selected)
- Division of Dermatology and Dental Products (DDDP) would hold oversight for Biologics License Application (BLA) or New Drug Application (NDA)

TIMELINE & FUTURE DIRECTIONS

ITP Cycle 4 Goals

- Months 1-3: Assessment of CCL22/CCL2 clinical applications
- Months 4-6: Selection of CCL22 API
- Months 7-9: cGMP manufacturing of pre-clinical grade CCL22 microspheres
- Months 10-12: Evaluation of cGMP manufacturing of pre-clinical grade CCL22 microspheres

Upcoming Years:
- Preparing for Pharmacokinetic and IND-directed toxicology studies for API: CCL22/ CCL2
- cGMP Manufacturing of CCL2 Microspheres

REFERENCES


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