RegendoGEL: A Bioinspired Hydrogel System for Endodontic Therapy



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

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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 cellladen 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 Pathwav:

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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DOCTRC

RegendoGEL – a bioinspired hydrogel for endodontic therapy

UNMET CLINICAL NEED

Dental caries is the most prevalent chronic infectious disease in humans. It has an estimated prevalence of over 90% of adults and 20% of children in western countries. If not treated, virtually all caries lesions will progress to affect the dental pulp, eventually requiring some form of endodontic treatment. The current gold standard of care for teeth with extensive caries or noncarious injury is direct pulp capping, or pulpotomy, which propose a partial amputation of dental pulp and replacement with either with a silicate cement (i.e. MTA) or the fixation of remaining pulp tissue using formocresol (Fig 1). Silicate cements are non-resorbable, and result in complete loss of pulp tissue responses. Formocresol contains 20% formaldehyde, and is officially classified as a potent carcinogenic as defined by the Center for Disease Control. There is an important need to develop improved materials for pulpotomy treatment that allow for regeneration (rather than amputation) of dental pulp and the lost dentin tissue.



Fig. 1. Comparison of outcomes from current treatment for pulpotomy with MTA or RegendoGEL

MARKET ANALYSIS

Avenues Interviews with clinical experts in Endodontics





Fig. 2. Answers to the question: 'Is there an unmet clinical need for this product in your practice?'

Fig. 3. Answers to the question: Is there a need for this product in 'high value' indications in your practice?

- Most respondents agreed that there is an unmet clinical need for root canal therapy because MTA and Biodentine are not permanent and will need to be replaced a few years down the line.
- For most endodontists, it was agreed that RegendoGEL would be a "high value" indication. They would not need it very often, but when they do this material would make their lives a lot easier
- Very positive feedback: *RegendoGEL is the first product that will regenerate the dentin* and keep the structure of the tooth intact. RegendoGEL is the ideal material for pulpotomy cases; if it is long lasting and has the ability to regenerate the original tooth dentin, tooth structure is never lost.

INTELLECTUAL PROPERTY

- OHSU/Tufts Tech Transfer office have been supporting our work since the beginning of this grant resulting in the submission of **3 IP patents/disclosures** (pending or issued).
- Additionally, our group have the support from the Oregon Clinical and Translational Research Institute (OCTRI), via its biomedical innovation program (BIP) in developing and implementing commercialization strategies for RegendoGEL.
- We have partnered up with Research Bridge Partners, a business development firm, that is advising on all issues related to IP and commercial development in the PI's laboratory and particularly on RegenedoGEL commercial development.

Luiz Eduardo Bertassoni¹, Pamela Yelick² ¹ Oregon Health & Science University, ² Tufts University

Dental Pulp

Dental Pulp

RESPONSES	
0.00%	0
0.00%	0
0.00%	0
0.00%	0
25.00%	1
75.00%	3
	4



Fig. 4. Composition of RegendoGEL

4. Cell migration Microgel size effect



Fig. 7. Larger microgels promote higher cell migration (Transwell assay). ANOVA, Tukey post-hoc

7. Orthotopic study in rats



MTA group (gold standard).



Consulted with Mayo Clinic GMP facility to begin manufacturing in 2021 if approved by advisory team and consortium leadership

RESULTS







- medical device
- clearance by the FDA
- stacked predicate approach
- - (experiments ongoing)

	1 st Funded proje 2019/ 2020
	USDA Sourcing
	Isolation of active ingre
	Hydrogel Optimizati
	Microgel developme
Research/ Technical	In-vitro validation of ingredient Determination of: > 50% more cell m activity than MTA > 50% more cell migration MTA > 50% more cell invasion MTA
	In-vivo validation – subcu model - rats
	In-vivo validation – o model- rats
	Regulatory Pathway S
Regulatory	Finalized Regulatory Bas to be sent to the FDA is o – Kay Fuller
Business ITP	3 patents – pending or Market assessment – A (Francine) – very pos feedback

- completion by early/mid 2022





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REGULATORY PATHWAY

• MDRS LLC. determined RegendoGEL to be regulated by the FDA as a class II

It will require a pending premarket notification (PMN) or 510k submission for

• MDRS anticipates a substantial equivalence to known predicate devices via a

• RegendoGEL is currently completing milestones to <u>freeze formulation</u>:

A. Determination of size variation of microgels (completed)

B. Ensuring ability to scale up manufacturing per GMP requirements (completed) C. Determination of reproducibility of active compound isolation from tooth matrix

• Next GMP plans will be discussed and reviewed with Regulatory & QAQC Core to ensure that the CRO is pre-qualified to do the proposed work.

TIMELINE & FUTURE DIRECTIONS



GMP manufacturing (Mayo Clinic) and GLP testing (Charles River) planned for

REFERENCES

• Horsophonphong S, Sercia A, Franca CM, et al. Equivalence of human and bovine dentin matrix molecules for dental pulp regeneration: proteomics analysis and biological function. Archives of Oral Biology

Subbiah R, Hipfinger C, Tahayeri A, Athirasala A, Horsophongphong S, Thrivikraman G, Franca CM, Cunha DA, Manssorifar A, Zahariev A, Jones JM, Coelho PG, Witek L, Xie H, Guldberg RE, Bertassoni LE. 3D printing of microgelloaded modular mirocages as instructive scaffolds for tissue engineering. Adv Materials. 2020