New stem cell delivery approach regenerates dental pulp-like tissue in a rodent model

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When a tooth is damaged, either by severe decay or trauma, the living tissues that comprise the sensitive inner dental pulp become exposed and vulnerable to harmful bacteria. Once infection takes hold, few treatment options—primarily root canals or tooth extraction—are available to alleviate the painful symptoms.

Researchers at Tufts University School of Dental Medicine (TUSDM) now show that using a collagen-based biomaterial to deliver stem cells inside damaged teeth can regenerate dental pulp-like tissues in animal model experiments. The study, published online in the *Journal of Dental Research* on Dec. 15, supports the potential of this approach as part of a strategy for restoring natural tooth functionality.

"Endodontic treatment, such as a root canal, essentially kills a once living tooth. It dries out over time, becomes brittle and can crack, and eventually might have to be replaced with a prosthesis," said senior study author Pamela Yelick, PhD, professor at TUSDM and director of its Division of Craniofacial and Molecular Genetics. "Our findings validate the potential of an alternative approach to endodontic treatment, with the goal of regenerating a damaged tooth so that it remains living and functions like any other normal tooth."

Yelick and her colleagues, including lead study author Arwa Khayat, former graduate student in dental research at TUSDM, examined the safety and efficacy of gelatin methacrylate (GelMA)—a low-cost hydrogel derived from naturally occurring collagen—as a scaffold to support the growth of new dental pulp tissue. Using GelMA, the team encapsulated a mix of human dental pulp stem cells—obtained from extracted wisdom teeth—and endothelial cells, which accelerate cell growth. This mix was delivered into isolated, previously damaged human tooth roots, which were extracted from patients as part of unrelated clinical treatment and sterilized of remaining living tissue. The roots were then implanted and allowed to grow in a rodent animal model for up to eight weeks.

The researchers observed pulp-like tissue inside the once empty tooth roots after two weeks. Increased cell growth and the formation of blood vessels occurred after four weeks. At the eight-week mark, pulp-like tissue filled the entire dental pulp space, complete with highly organized blood vessels populated with red blood cells. The team also observed the formation of cellular extensions and strong adhesion into dentin—the hard, bony tissue that forms the bulk of a tooth. The team saw no inflammation at the site of implantation, and found no inflammatory cells inside implanted tooth roots, which verified the biocompatibility of GelMA.

Control experiments, which involved empty tooth roots or tooth roots with only GelMA and no encapsulated cells, showed significantly less growth, unorganized blood vessel formation, and poor or nonexistent dentin attachment.

The results support GelMA-encapsulated human dental stem cells and umbilical vein endothelial cells as part of a promising strategy to restore normal tooth function, according to the study authors. However, they note that the current study was limited to partial tooth roots and did not examine nerve formation in regenerated dental pulp tissue. They emphasize the need for additional safety and efficacy studies in larger animal models before human clinical trials can be considered.

"A significant amount of work remains to be done, but if we can extend and validate our findings in additional experimental models, this approach could become a clinically relevant therapy in the

future," said Yelick, who is also a member of the Cell, Molecular & Developmental Biology; Genetics; and Pharmacology & Experimental Therapeutics programs at the Sackler School of Graduate Biomedical Sciences at Tufts. "Our work is early stage, but we are excited for the possibility of someday giving patients the option of regenerating their own teeth."

More information: Khayat et al. "GelMA Encapsulated hDPSCs and HUVECs for Dental Pulp Regeneration." *Journal of Dental Research* (2016). DOI: 10.1177/0022034516682005

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