Invite to Innovate

AMBER are investing in the development of **Next-Generation Regenerative Dental Restorative Solutions** and we're looking for industry partner(s) to **collaborate and co-fund** this exciting initiative.

AMBER
Advancing Materials for Impact

Contact denise.carthy@tcd.ie with your expression of interest

What is the clinical problem?

Dental decay continues to rank as one of the most prevalent global conditions, with toothache persisting as the leading cause for dental visits among both children and adults. This emphasizes the significance of effective endodontic treatment in preserving tooth substance, reinstating functionality, and enhancing overall quality of life.

An emerging clinical need in endodontics is the desire for more biologically-based treatment options that not only manage the infection but also promote the regeneration of healthy pulp tissue. Regenerative endodontic procedures aim to achieve this by utilizing bioactive materials, signalling factors, and stem cells to stimulate the regeneration of dental pulp tissue and restore the tooth's function and vitality

What is the scale of the problem?

Estimates suggest that millions of root canal procedures are performed annually worldwide. In the United States alone, it is estimated that over 15 million root canal treatments are completed each year and these numbers are likely to continue increasing.

Root Canal treatments are complex procedures that are often poorly carried out and do not promote regeneration of natural tooth. Root canal treatment is invasive for patients, expensive and can lead to downstream problems such as tooth fracture and discolouration.

What is the clinical and market opportunity?

Research and development is required to promote minimally invasive workflows and new materials that will improve the preservation and regeneration of natural teeth and address the current limitations of calcium silicate materials and vital pulp treatment techniques (Careddu & Duncan 2021).

Regenerative techniques could be effective for approx 50% of all current root canal treatments.

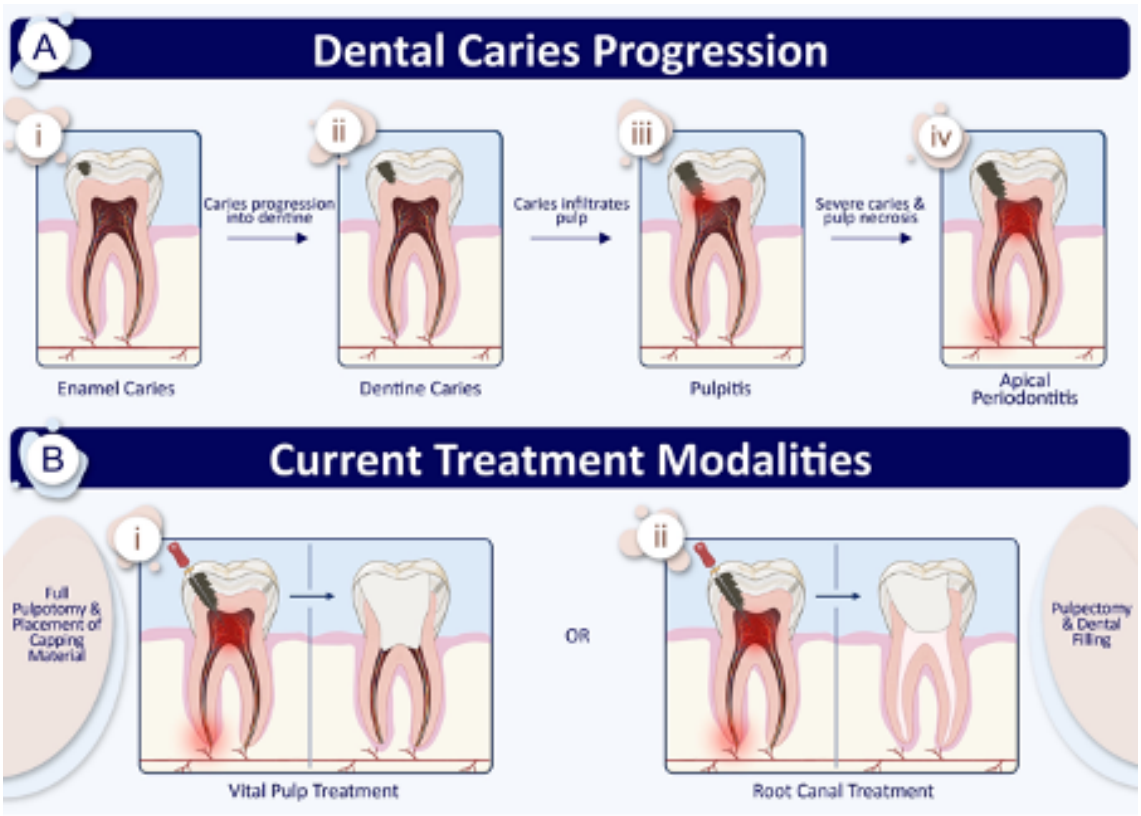

Figure 1. Dental caries progression & current treatments. *(A) Dental caries progression (i) Oral biofilm elicits enamel demineralisation (ii) Caries progresses into dentine, stimulating pulpitis (iii) Caries infiltrates the dental pulp, inducing severe pulpitis (iv) Caries left untreated results in pulp necrosis and subsequent apical periodontitis. (B) Reparative current treatment modalities (i) Vital pulp treatment of a full pulpotomy & capping material induces a reparative response (Jassal et al., 2023) (ii) Root canal treatment uses a pulpectomy followed by dental filling, which is destructive and costly.*

Translational research in endodontic regeneratioin conducted to date

Current minimally-invasive attempts to preserve pulp vitality have involved partial removal of the dental pulp, known as full/coronal pulpotomy, followed by the application of a hydraulic calcium silicate cement like MTA or Biodentine.

This approach primarily aims to maintain vitality rather than promote dentine-pulp regeneration. Drawbacks include replacing the entire coronal pulp with materials which impedes ongoing clinical assessment of the remaining pulp's health and complicates re-entry.

Therefore, approaches focusing on natural or approved materials, such as collagen-based biomaterials, to stimulate endogenous pulp regeneration driven by dental stem cells in the tooth offers considerable promise (Kearney et al., 2018).

A significant challenge in translating new concepts into clinical practice lies in the **extensive clinical and regulatory evaluation required.**

AMBER's Proposal

A central tenet of AMBER's proposal is the development of biomaterial platforms that are advantageous for pulp tissue regeneration, to design models for preclinical evaluation, and present new and innovative multifunctional strategies that hold promise for clinical translation.

AMBER's research on dental-pulp cells has revealed that optimised scaffold components, **with or without pharmacological inhibitors**, can enhance pulp tissue regeneration (Duncan et al., 2016).

These natural biomaterial scaffolds, enriched with extracellular matrix components and various properties like growth factors, angiogenic, antimicrobial, and anti-inflammatory agents, can transition from biological models to advanced clinical dental applications, as shown by AMBER in related fields (Early et al., 2021; Corciulo et al., 2020)

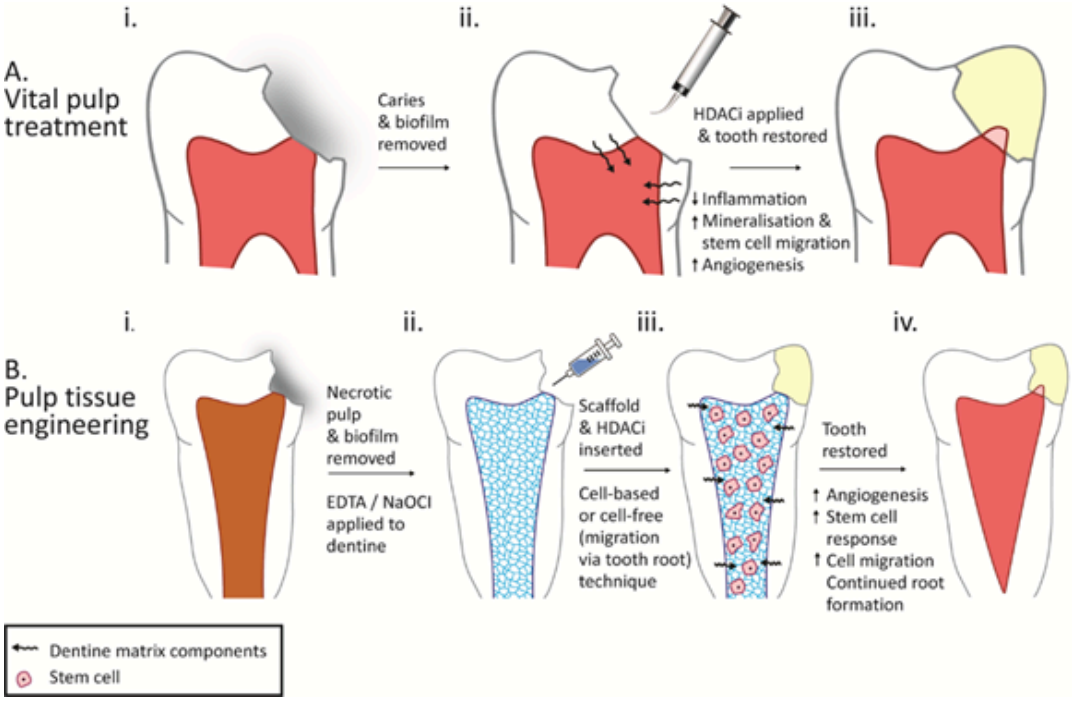

Figure 2. *Previous research in the group has focussed on the use of pharmacological epigenetic inhibitors to promote regenerative responses either within a vital pulp treatment or tissue engineering approach (Duncan et al., 2016).*

Successful translation of regenerative solutions from bench to chairside requires deep knowledge of, and practical experience dealing with, pulpal disease. This technology development will include expertly designed preclinical investigations, including immune reaction, biological response and toxicity studies.

We propose to develop a novel platform technology based on the use of new natural biomimetic scaffolds to regenerate damaged/diseased pulp tissue via the inclusion of carefully selected natural biologics and matrix products that can stimulate expansion and regeneration of pulp tissue within the tooth (**see Figure 3.**) this will also allow us to determine pulp health, perform re-entry (if required), while also reducing the size of tooth restoration. Our team has world-class proven experience in successfully developing these solutions for similar problems in related fields. (Early et al., 2021; Corciulo et al., 2020)

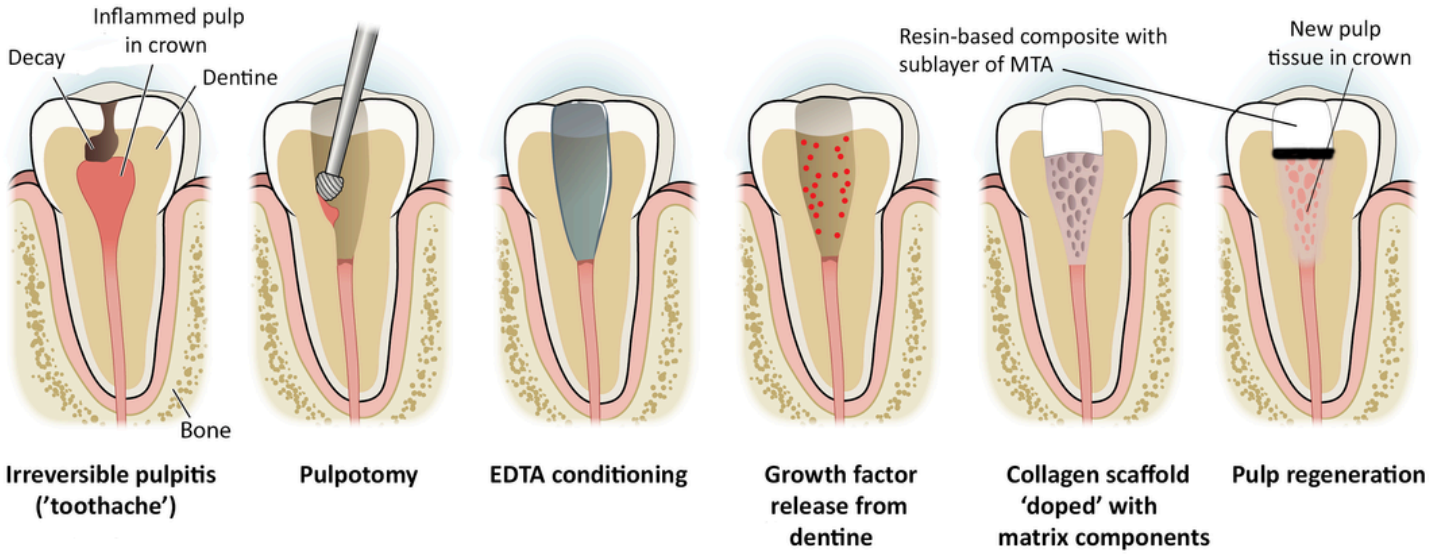

Figure 3. *Schematic showing common causes of pulpitis and current/future treatment pathways.*

One of AMBER's key focus areas is tissue engineering and regenerative medicine.

AMBER, the Advanced Materials and BioEngineering Research Centre based in Ireland, has made significant strides in the development of regenerative platform technologies for various tissue types. Here's a brief overview:

1. **Peripheral Nerve Regeneration**: AMBER in collaboration with Integra LifeSciences on peripheral nerve regeneration. Link to press release
2. **Bone Regeneration**: AMBER in collaboration with Johnson and Johnson researching materials for bone growth and repair in cases of fractures, defects and osteoarthritis. Link to press release.
3. **Cartilage Regeneration**: AMBER in collaboration with DePuy Synthesis on the use of biomaterials to facilitate cartilage repair in conditions like osteoarthritis. Link to press release
4. **Spinal Cord Repair**: AMBER in collaboration with the Irish Rugby Football Union charitable trust are leading a Spinal Cord Injury research project. Link to press release
5. **Vital Organ Tissue Engineering**: Tissue engineering of vital organs is an ambitious but potentially transformative area of research. Link

AMBER's contributions to these areas involve interdisciplinary collaborations combining expertise in materials science, biology, engineering, and medicine. Their work encompasses fundamental research, applied research, and translational efforts aimed at bringing promising technologies closer to clinical use.

Expression of Interest

If you are interested in collaborating with the AMBER Centre through a cost share model with leveraged funding available, please contact Denise Carthy (Business Manager) directly at denise.carthy@tcd.ie

Lead Investigators

Prof. Hal Duncan, Assistant Professor/Consultant in Endodontics in Dublin Dental University Hospital, Trinity College Dublin

Prof. Fergal O'Brien, Professor of Bioengineering & Regenerative Medicine, Deputy Vice Chancellor for Research & Innovation, and Head of the Tissue Engineering Research Group in the Royal college of Surgeons Ireland

Prof. Oran Kennedy, Associate Professor of Anatomy and Regenerative Medicine in the Royal College of Surgeons Ireland.

Prof. Daniel Kelly is a Principal Investigator in the Trinity Centre for Biomedical Engineering. His research focuses on developing novel approaches to regenerating damaged and diseased musculoskeletal tissues.

AMBER's expertise and capabilities

AMBER, The SFI Centre for Advanced Materials and BioEngineering Research, unites a multidisciplinary team across all Irish universities to conduct world-class research in material science and biomedical engineering. With cutting-edge material manufacturing and characterisation facilities, pre-clinical models, and access to patient-derived tissues and cell lines, we develop clinically relevant technologies to address common dental diseases and conditions

AMBER's expertise:

- Fabrication and characterisation of collagen-based scaffolds.
- Expertise in dental stem cell biology and epigenetics.
- Development of physiologically relevant 3D models.
- Chemistry for gene delivery system design.
- Immunological analysis in dental applications.
- Understanding regulatory pathways like Biosimilars and ATMPs. Utilizing regulatory science for CGT safety.
- Exploring non-viral gene therapy for scaffold functionalisation.

Processing & Characterisation Capabilities:

- Characterisation of nanomaterials
- Expertise in 3D printing and microCT imaging.
- Utilisation of confocal, multiphoton, and FRET microscopy.
- Experience in freeze-drying/lyophilization techniques.
- Design and evaluation of delivery systems for pharmacological applications.
- Physicochemical characterisation of regenerative scaffolds
- Microfluidic-based formulation of scaffold constituents.
- Bio-predictive in vitro and in vivo testing of scaffold systems.
- Design, synthesis, purification, and characterization of biomaterials and API (mRNA)

Link to digital brochure

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