AT THE FOREFRONT

Illustrated Topics in Dental Research and Clinical Practice

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Preface

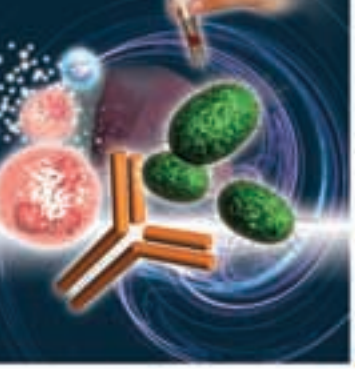
This book is divided into two distinct sections: The first half is designed as an introduction to advanced periodontology and tissue engineering, and the second half focuses on emerging clinical science in operative dentistry.

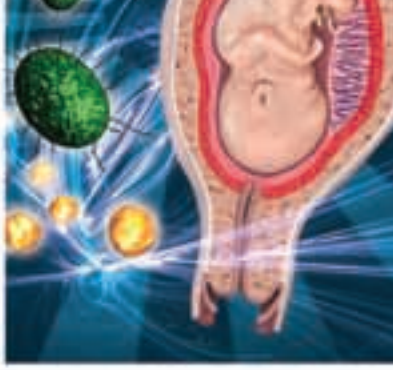
We are in a truly exciting period in the field of periodontology with understanding available to us about the science of molecular-based diagnosis, the vital link between periodontal diseases and systemic diseases, and the possibilities of biologic tissue regeneration in dental medicine. These developments in periodontal medicine and regenerative technologies have tremendous potential for application in dental science and will contribute to fundamental paradigm shifts in the approach to many clinical procedures.

We also have focused on clinical science, including innovation in operative dentistry and understanding problems secondary to tooth loss and implant placement. Events in our day-to-day clinical work can inspire us to open new lines of research. We have highlighted novel technologies in operative dentistry based on material and laser sciences. In addition, the scientific and biologic discussion of tooth loss and implant placement will be a useful contribution to many clinicians.

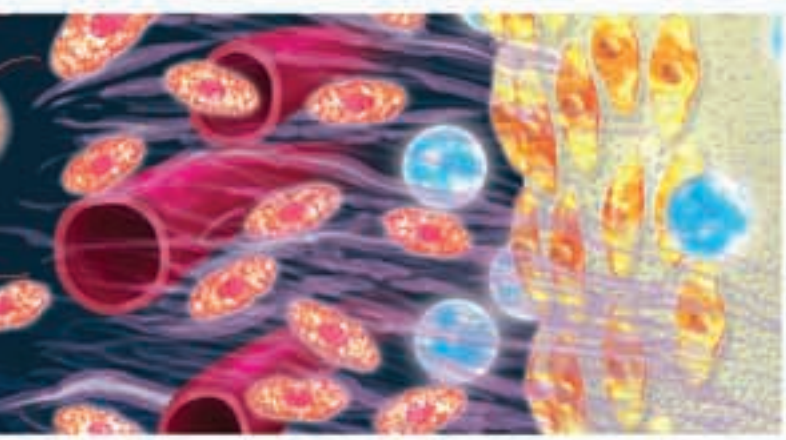
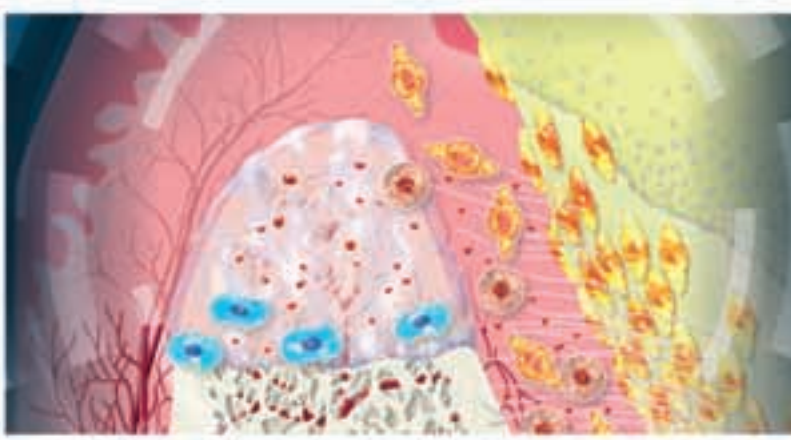
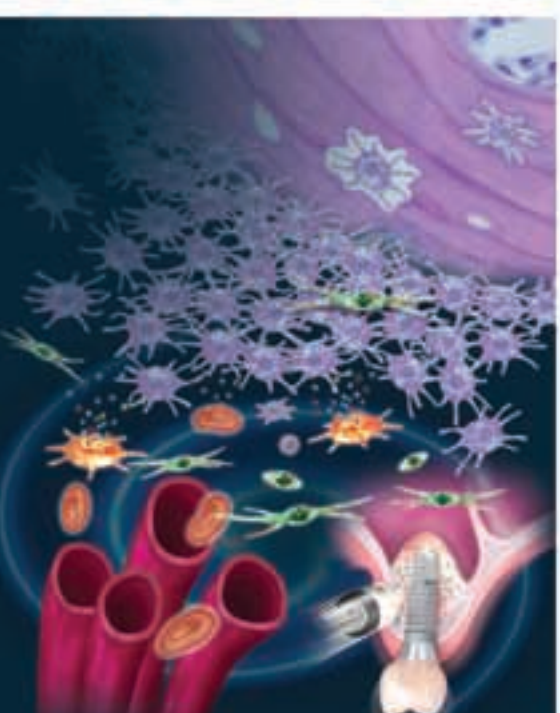
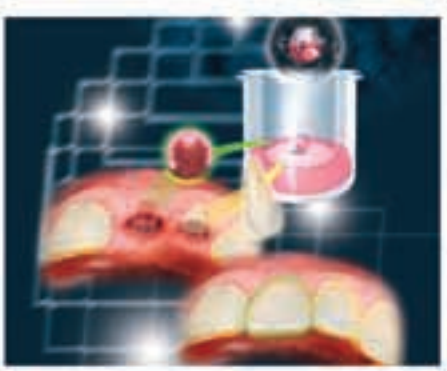
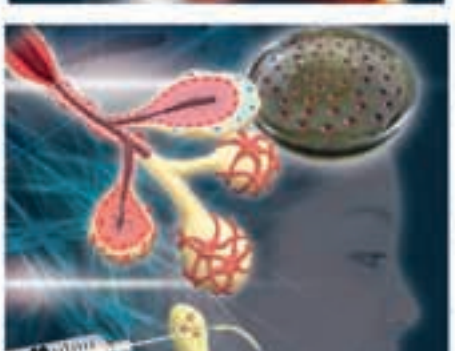
The chapters in this book are straightforward and clear and were written by clinicians and researchers. Each chapter touches on a specific topic in dental research or clinical practice with a scientific focus. In addition, chapters include amazing three-dimensional images to illustrate the salient points. It is hoped that this book will be useful to introduce these concepts to students, clinicians, and researchers.

I am grateful to all the chapter authors for their hard work and wish to acknowledge the excellent cooperation of the publisher.

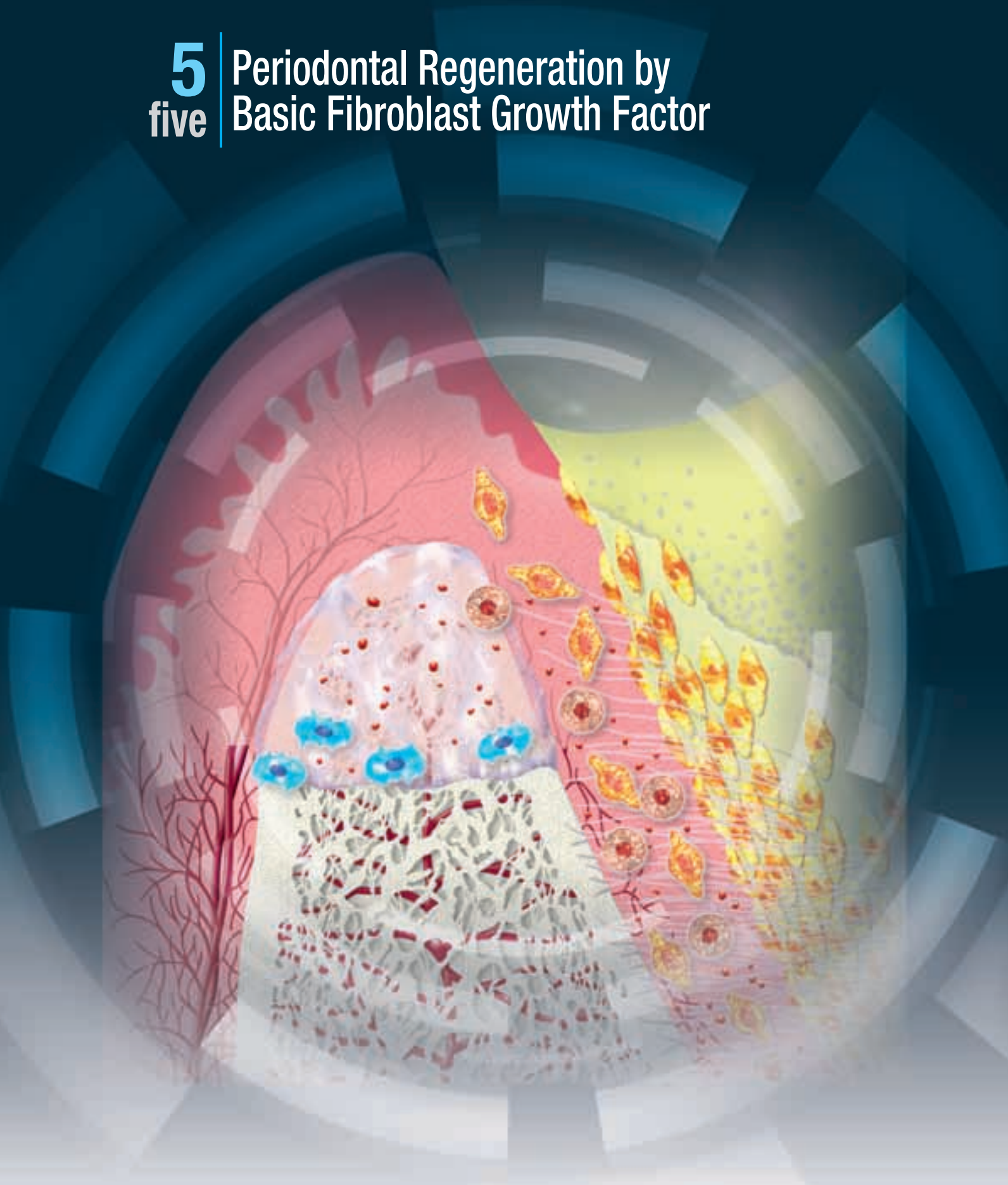




Part one | Illustrated Bioscience


5 five Periodontal Regeneration by Basic Fibroblast Growth Factor



Development of regenerative therapies is expected to create innovative medical therapeutic systems in the 21st century. Tooth development begins with the tooth germ, or *tooth bud*, which is generated by epithelial-mesenchymal interactions during the embryonic stage of development. It is a highly organized aggregation of cells comprising several cell types, forming the periodontium, mineralized tooth tissues, and dental pulp. Tooth regeneration has been developed as a model for organ replacement therapy that aims to replace a lost or damaged organ following disease or injury using bioengineered organs.

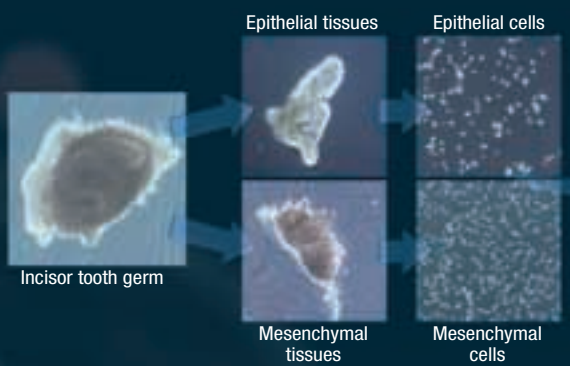
The current regenerative therapy approach is the transplantation of tissue-derived stem or progenitor cells into the site of the damaged tissue or organ. The ultimate goal of regenerative therapy is the development of a fully functioning bioengineered organ that can replace a lost or damaged organ after injury, disease, or aging.

A tooth is developed from a tooth germ, which is generated by epithelial-mesenchymal interactions at the embryonic stage of development. It is a highly organized organ comprising several kinds of cells, forming tooth and periodontium, mineralized tissues, and blood vessels. The current strategy for tooth regeneration is the production of a bioengineered tooth germ reconstituted from immature epithelial and mesenchymal cells isolated from the developing tooth germ. The realization of tooth regeneration therapy requires the development of a wide variety of technology, including cell processing technology for reconstituting the tooth germ, identification of cell seeds capable of reconstituting the bioengineered tooth germ, and technology for the regulation of tooth size and morphology.

Organ Germ Method: Development of a Novel Three-Dimensional Cell Processing Method for Bioengineered Tooth Germs

A three-dimensional single-cell processing method has been developed for the production of bioengineered tooth germs and is called the *organ germ method.* It is a first step in the evolution of tooth regenerative therapy (Figs 10-1 and 10-2). A bioengineered tooth germ was reconstituted using dissociated dental epithelial and mesenchymal cells with correct cell compartmentalization at high cell density in collagen gel. The bioengineered tooth germ could regenerate a structurally correct tooth at a high frequency when transplanted into the subrenal capsule (Fig 10-3). The structurally correct tooth could also be regenerated from the bioengineered germ in an in vitro organ culture (Fig 10-4).

Fig 10-1 Steps in the development of three-dimensional cell processing technology (the organ germ method) to regenerate a bioengineered tooth germ. Epithelial and mesenchymal tissues were isolated from the incisor tooth germ of ED14.5 mice and completely dissociated into epithelial and mesenchymal cells, respectively.



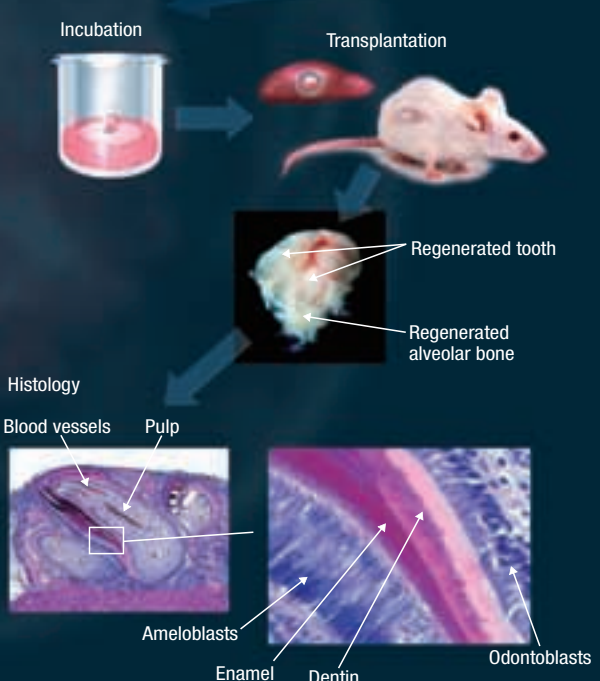


Fig 10-3 Development of a bioengineered tooth germ in vivo after subrenal capsule transplantation. The bioengineered tooth germ was incubated for several days with organ culture. The bioengineered tooth germ was transplanted into a subrenal capsule for 14 days. The bioengineered tooth and alveolar bone with correct tooth structure were observed 14 days after transplantation in the subrenal capsule.

Fig 10-2 Epithelial and mesenchymal cells at high cell density were successively injected into collagen gel. The bioengineered tooth germ was reconstituted using epithelial and mesenchymal cells with correct cell compartmentalization at high cell density.

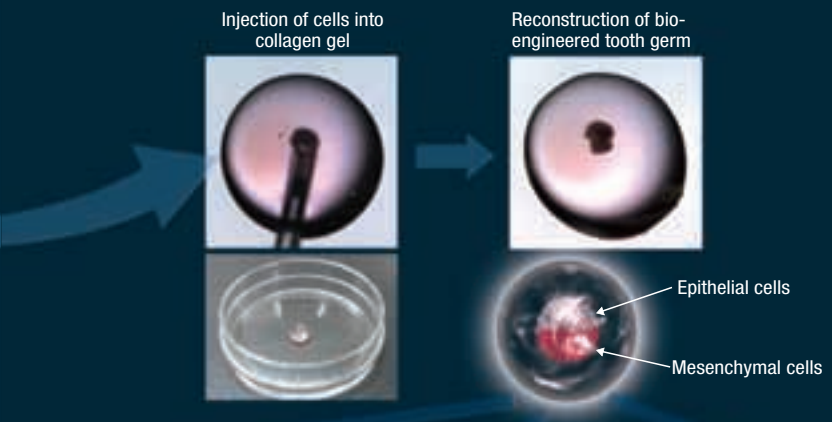
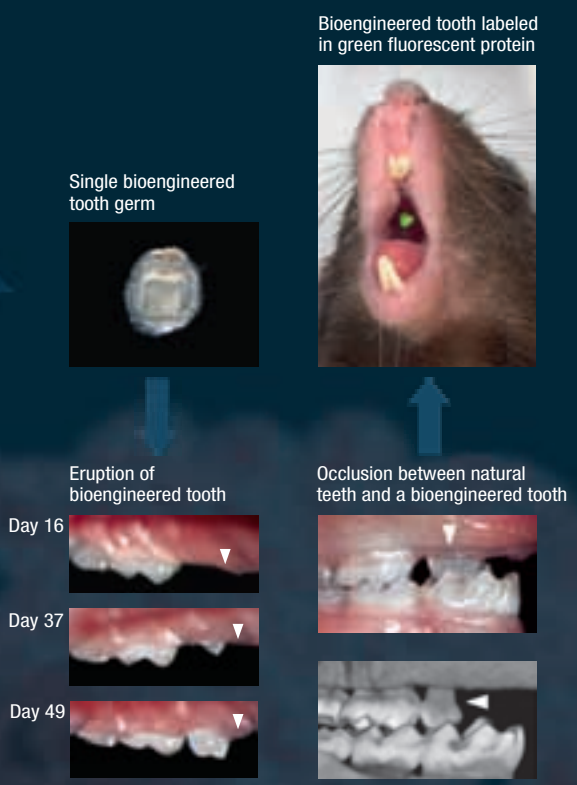


Fig 10-4 Development of the bioengineered incisor and molar tooth germ in vitro in organ culture. The bioengineered tooth germ was cultured in vitro for 14 days in organ culture. Incisor and molar teeth were formed from the respective bioengineered germs.

Fig 10-5 Eruption and occlusion of a bioengineered tooth. The reconstituted tooth germ was cultured for several days in an in vitro organ culture and formed into a bioengineered tooth germ. A single bioengineered tooth germ was isolated and transplanted into an edentulous space in the maxillary alveolar bone in an adult mouse. The bioengineered tooth erupted and reached the occlusal plane with the opposing mandibular first molar 49 days after transplantation.

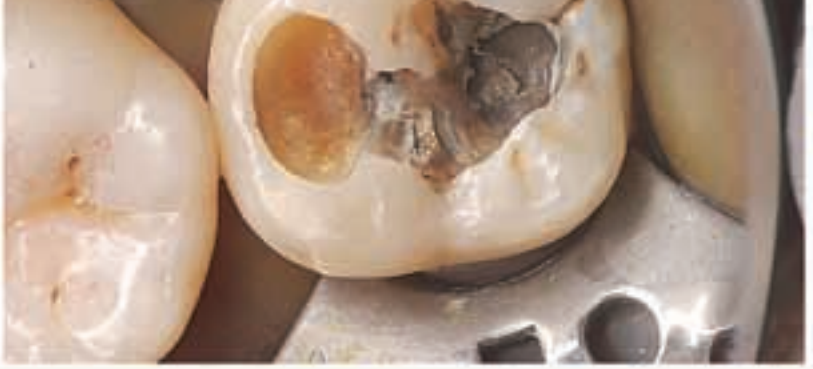
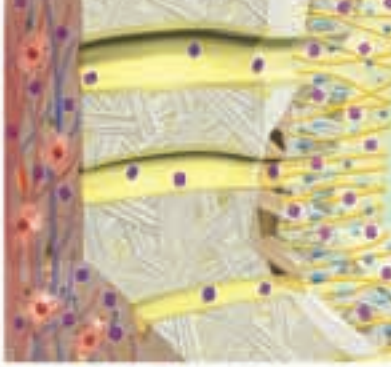


Analysis of the Regeneration of the Bioengineered Tooth Germ in an Adult Oral Environment

The bioengineered tooth germ was also incubated for several days in organ culture before being successfully transplanted into an endentulous gap in the maxillary alveolar bone. The bioengineered tooth germ erupted into occlusion with the opposing tooth in an adult oral environment (Fig 10-5).

This is a model for tooth replacement regenerative therapy. In addition, the bioengineered tooth had the correct structure and hardness of mineralized tissues for mastication, and it responded to stimulus such as mechanical stress and pain in sync with other oral and maxillofacial tissues. Our results demonstrate a substantial advance and emphasize the potential for bioengineered tooth replacement in future regenerative therapies.

Moreover, a feasibility study of the realization of tooth regeneration therapy has been performed in collaboration with dental research organizations. Further studies on the identification of adult tissue-derived cell seeds for the reconstitution of the bioengineered tooth germ, initiation signals for tooth development, and regeneration of periodontium and tooth root will help to achieve the realization of tooth regenerative therapy for missing teeth. These technical achievements will make substantial contributions to the development of bioengineering technology for future organ-replacement regenerative therapy and to an improved quality of life for many people.

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