Does wisdom tooth provide tooth germs for tooth regeneration?
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Abstract

Introduction
Regenerating a tooth completely in human oral cavity is not achieved by current studies yet. Here, we have conceived a man-induced method to construct a tooth germ which might be used to regenerate a tooth in vivo. This idea was generated by traits of the development of the compound odontoma, a benign tumour of tooth malformation. This is a kind of developmental tooth malformation, characterised by several small teeth inside the entity. Those scattered denticles/daughter teeth germs, formed in the early stage of odontoma morphogenesis, show similar layers as in a normal tooth, and could grow into tooth-like shapes. In consideration with recent report that mouse tooth germ constructed in vitro could develop into a fully functioned tooth in adult mouse jaws. We hope this hypothesis helps generate tooth germs for in vivo implantation.

Hypothesis
Tooth germ of wisdom tooth might be separated into small daughter germs by bone trabecular using tissue-engineering method, to provide more than one tooth germ for tooth regeneration.

Evaluation of hypothesis
By reconstruction existing dental tissues during tooth organogenesis in the jaw, this hypothesis shows advantage than generating tooth from single stem cell or artificial tooth graft.

Conclusion
Proving this hypothesis not only facilitates the acquirement of numerous homologous and immunological rejection-free teeth germs to treat tooth loss and deficit, but also helps afford an alternative lesson that merits attention in other human organ regeneration fields.

Introduction

Tooth regeneration is a promising and challenging project of important part of human organ tissue engineering. It serves to find the best and most potential materials and methods to engineer an artificial whole tooth, and to biologically repair dental carries or cure the inherited or acquired tooth loss and deficiency.

During the 20th century, three methods—xenotransplantation, allotransplantation and autotransplantation—have been used not only under investigation but also in the clinics to study the tooth organogenesis and to attempt a better tooth replacement. Till now, various strategies on engineering teeth have been developed, and they can be sorted into two main streams: one is to recombine and coculture the dislocated epithelium (odontogenic or not) and kinds of mesenchyme cells to form tooth-like tissue. To attempt this, a variety of enriched or purified stem cells, such as dental pulp stem cells, periodontal ligament stem cells, dental follicle stem cells, dental epithelial stem cell, embryonic stem cells, pre-adipose cells and bone marrow stromal cells or even newly established dental cell lines, have been applied. Certain combinations have been proved to successfully generate well-calcified hard tooth tissues, such as enamel-dentin structures, tooth crown, root, periodontium and cementum. Those regenerated hard tissues show similar characteristics to that of a natural tooth. The other approach is to reproduce the developmental process of organogenesis to engineer a tooth germ, in which most cell types that have been used are dental epithelium and mesenchyme. Seeding them into in vitro biodegradable three-dimensions scaffold results in teeth germs and could be transplanted in vivo afterwards. This was achieved eventually in an adult mouse by Takashi Tsuji et al. in 2009, with a fully functional bioengineering tooth model. Hence, for the time being, the autogenic reconstructed tooth germ seems to be the most potential in the near future.

Wisdom tooth is common in most many, but most of them get it extracted due to abnormalities in eruption or difficulty in mastication. By traits of daughter teeth germs development in the compound odontoma, we have hypothesised a method to obtain more tooth germs from one wisdom tooth.

The compound odontoma is a subtype of the odontoma, formed in jaw bones, appears as a pile of several small tooth-like masses, and most of it contains normal enamel–dentin arrays and develops as packaged with loosely textured connective tissue with cords and islands of odontogenic epithelium. In series histopathological sections of immature compound odontomas, pind-sized tooth germs could be usually detected with a low-magnification microscope.
Hypothesis

All the evidences mentioned above and supplemented later point to the same direction as our hypothesis–tooth germ of wisdom tooth could be cut into small daughter germs by bone trabecular and continue to provide more than one tooth germ for clinical use. This is a most potential method in vitro to control and culture the body’s own tooth germs. Related evaluation and strategy are synoptically demonstrated in detail in further sections.

Evaluation of Hypothesis

Theoretically, it is possible to create a natural tooth from a single cell. But this faces a few unsolved problems, such as comprehensive reciprocal interaction between epithelium and mesenchyme, the source of stem cells (especially the embryo ones), the immunological rejection, let alone sequential gene joining at different stages during the organogenesis. Comparatively, the way of generating a natural tooth from a near-end-shape developing organ germ by reproducing organogenesis in the read-made microenvironment demonstrates more probability and operability, and steers clear comprehensive interactions amid the tooth development in some extent, although it still needs to regulate and control the detached germs development in vitro culture.

Evidences

In osteopetrotic (op/op) mice, incisor tooth germ could not erupt, but odontoma tissues are formed in the root apex instead due to the invasion of alveolar bone trabecular510. Owing to lack of some tooth eruption requirements, especially the osteoclastic induction factors56, one of the most intensively studied factors is macrophage colony-stimulating factor (M-CSF). By down regulating the osteoprotogerin in the dental follicle, M-CSF enabled the osteoclastogenesis and launched the alveolar bone resorption and remodelled during the tooth germ maturation process and the eventual eruption11-13. Impaired osteoclast function in src(-/-) mice demonstrated 100% presence of odontomas in the region of the unerupted incisors14.

When the eruption-inhibited germs detached from osteopetrotic (op/op) mice were cultured in vitro without the influence of osseous tissue constituents, they all developed without interruptions and formed a natural well-balanced tooth. But, once the in vitro culture environment was added with the alveolar osseous element, the germ development would be interrupted by bone trabecular invasion and several daughter germs are formed by segmentation16-18. Furthermore, the odontoma-derived mesenchymal cells could be differentiated to generate new dental structures like nerve, dentin and cementum in vivo, which proved to be the hold of post-natal stem cells in odontoma19.

Besides the evidence mentioned above, early studies also have confirmed the inner daughter teeth germ formation during the destruction and remodelled during the tooth germ maturation process and the eventual eruption11-13. Impaired osteoclast function in src(-/-) mice demonstrated 100% presence of odontomas in the region of the unerupted incisors14.

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Figure 1: Sketch of separation of wisdom tooth germ and construction of new tooth in ectopic socket. Tooth germ of wisdom tooth (a); bone trabecular invasion by bioscaffold (b); mature daughter tooth germs and transplant into tooth loss place (c); and regenerated tooth originated from daughter germs of wisdom tooth (d).

Discoveries of tooth regeneration imply that the process of tooth formation is not as strictly regulated as previously thought. The hypothesis suggests that even after bone trabecular invasion, the process of tooth formation could be continued and a self-agomphious region later to re-cover the masticatory function. A physiological functional position may be needed to adjust it into the jaw sites where ever they are needed. Third, after the tooth eruption, orthodontic treatment may be needed to adjust it into a physiological functional position (Figure 1).

Discussion

This hypothesis of tooth regeneration intends to apply a bio-derived scaffold of controlled-release osteoclastic inhibitors into early dental germs to fabricate the daughter germs formation in the wisdom tooth. These harvested germs could be cultured in vitro and transplanted back into a self agomphious region later to recover the masticatory function.

Conclusion

In general, there is still a need for more and further research on the odontogenesis and on how to reproduce the process to make a whole tooth from a single cell. Proving this hypothesis could not only facilitate the acquirement of numerous homologous and immunological rejection-free teeth germs to treat tooth loss and deficit, but may also afford an alternative lesson that merits attention in other human organ regeneration fields.

Abbreviations list

M-CSF, macrophage colony-stimulating factor.

References


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