STUDENTS' INFORMATION

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Questions From Senior Dental Students

The AACD is committed to reaching people at all levels of dentistry, especially our rising graduates in dental schools. We enjoy the opportunity to see early efforts in esthetic dentistry and a search for the knowledge required to achieve excellence. This section is dedicated to questions and clinical cases in early endeavors in esthetic dentistry.

QUESTION

There are different research directions concerning bioengineering of teeth. What are they, and how far has research come to date?

ANSWER

We all understand the steps in tooth formation, beginning with epithelial tissue thickening and ending in tooth eruption. Given this understanding and building upon it, two main research groups have emerged, both trying to find the ideal way of tooth regeneration, but with different approaches to tissue engineering in terms of tooth formation.[1]

The first group is the Forsyth team, led by Pamela C. Yelich and Jolin D. Bartlett (the Forsyth Institute, Boston, MA), in cooperation with Joseph P. Vacanti (the Harvard Medical School) and Robert S. Langer (the Massachusetts Institute of Technology). The second group is the Sharpe team, led by Paul T.

Sharpe (King's College, London) and Conan S. Young (the Harvard School of Dental Medicine).

The Forsyth team is researching tooth formation by conducting tissue engineering on biodegradable polymer scaffolds. They are attempting to build adult teeth from their constituent cells. The research uses pig teeth, which are prepared through an extraction process of a heterogeneous random mixture of dental, enamel epithelial, and pulp mesenchymal cells. These obtained cell mixtures are then seeded into biodegradable tooth-shaped polyester plastics, wrapped in omentum, and surgically implanted into rat hosts. Approximately 20 to 30 weeks later, tiny tooth-like structures are visible within the confines of the original scaffolds. Their shape and tissue organization resembles the crowns of natural teeth, and it includes enamel, dentin, pulp and beginning root structures.

The current conclusion in this ongoing study is that a mixture of dental cells apparently can reorganize themselves on scaffolds into arrangements that favor normal tooth-forming configurations. The research continues, and is searching for a more precise technique of finding a method to place different dental cell types within biodegradable scaffolds to achieve a more accurate tooth structure. This team is also conducting a parallel study, which investigates the use of hidden stem cells (potent progenitors of other cell types possibly found within the adult dentition in erupting wisdom teeth) for their responsibility in the formation of new tissues.[2]

The Sharpe team is trying to reproduce the natural tooth-forming process of embryonic tooth development, primarily testing the potential of various cell types to produce replacement teeth. This team's experiments are conducted with mouse cells—both stem and ordinary cells retrieved from embryonic and adult sources. The team uses tooth primordia (an aggregate of mesenchymal cells in the form of a solid mass) covered with epithelium cells that are closely monitored for several days for indications of tooth development. After this they are implanted into animal bodies (in vascular organs like kidneys), and allowed to grow for 20 days.

Clear tooth formation is obvious only when the used epithelium is derived from embryonic sources and the mesenchymal pellet contains at least some stem cells. Further, when the used stem cells are collected from adult bone marrow and used instead of oral mesenchymal cells, the transplanted constructs produce structurally correct teeth.

The first conclusion drawn is that embryonic mesenchyme[3] can be replaced with adult stem cells to generate desired growth. Yet more experiments proved that contained in the embryonic epithelium, there is a unique set of signals present that disappears from the oral environment after birth.

Although the findings of the Sharpe team to date are extremely encouraging, the ongoing challenge remains to find an effective population of substitute cells that can be derived from an adult source. To take the study further, the Sharpe team proved that extracted tooth buds from embryonic mice re-implanted in adult mice mouths can develop correctly, and therefore that the adult oral environment can be a suitable host for proper tooth development.

To date, all avenues presented have generated tooth tissue within normal sizes and shapes, are surrounded by new bone and connective tissue, yet present without developed roots. Therefore, the "complete tooth" engineering method is not yet fully understood, neither in its full regeneration time sequence, nor in its avoidance of immune rejection or easy obtainment of all needed cells.

This new research, however, opens a door to great hope in the possibility of tissue bioengineering from existing related cells, or even from unrelated cells. This immense step forward in the replication of variable organs could some day change the way we practice dentistry and medicine.

Special thanks are extended to Andre Fuetsch for providing the information pertinent to answering this question.

References

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3. Tucker AS, Sharpe PT. The cutting edge of mammalian development: How the embryo makes teeth. *Nature Reviews Genetics* 5(7):499–508, 2004.