

Human Stem Cells and Tooth Regeneration

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Over the past decade, stem cell-based therapeutic approach is considered a powerful tool for the repair and/or regeneration of defective tissues and organs. Teeth are excellent targets for studying organ regeneration because they share developmental similarities with other organs (e.g. hair, lung and kidney), and are convenient for experimental research. Although using animal stem cells from embryo can rebuild a functional bioengineered tooth [1], it is unclear how to use human cell source to regenerate a tooth.

Human tooth germ results from interactions between epithelial stem cell mass and neural crest-derived mesenchymal stem cell mass during early embryonic development. Once embryonic oral epithelium and mesenchyme start interaction, the epithelial stem cells differentiate into ameloblasts; the mesenchymal stem cells differentiate into odontoblasts, fibroblasts and other cells; finally form functional teeth (Figure 1) [2]. Therefore, in order to regenerate a human tooth, two types of human stem cells are required: epithelial and mesenchymal stem cells. In animal, epithelial and mesenchymal stem cells from embryo showed the ability for tooth formation [1]. However, because of the ethical issue, in human's case, those stem cells have to be adult epithelial and mesenchymal stem cells. There are at least two types of human adult mesenchymal stem cells (HAMSCs) that can be used for tooth regeneration: dental mesenchymal stem cells and bone marrow derived mesenchymal stem cells [3,4]. Those two types of HAMSCs shared common features: the capacity of self-renew and multilineage differentiation potential. Because both of them have the capacity to give rise to osteo/odontogenic cell lineage, they have been assessed for tooth engineering purposes. Between dental mesenchymal stem cells and

bone marrow derived mesenchymal stem cells, dental mesenchymal stem cells, such as stem cells from the apical papilla (SCAP), dental pulp stem cells (DPSCs), stem cells from human exfoliated deciduous teeth (SHED), periodontal ligament stem cells (PDLSCs) and dental follicle precursor cells (DFPCs) received much more attention for tooth generation, as they appear to be more committed to odontogenic rather than osteogenic development. After immunocompromised animal transplantation, those dental mesenchymal stem cells can differentiate into almost all dental components, such as dentin, periodontal ligament, cement and dental pulp tissue except enamel [5].

In human embryo, dental epithelial stem cells are the only cell source for enamel generation. However, because human dental epithelial stem cells are limited in the embryo, a key question is where to find the replacement from adult. One potential candidate of the replacement is oral epithelial stem cells because of that they derived from embryonic epithelium as same as the dental epithelial stem cells. Oral epithelium is a stratified squamous tissue that renews itself rapidly due to the epithelial stem cells residing in the basal layers [6]. Epithelial stem cells infrequently divide, yet they can proliferate soon in response to injury and certain growth stimuli. Oral epithelial stem cells have been used for a variety of tissue-engineered reconstructions, such as oral cavity [7], epidermis [8], and especially ocular surface reconstruction [9,10]. In our recent work, using human normal oral epithelial cells (OECs) and dental pulp stem cells (DPSCs) we were able to build a three dimensional model to represent early tooth development due to some stem cells remaining in OECs [11]. The above-mentioned evidences suggest a possibility to use adult human oral epithelial stem cells for tooth regeneration. However, for tooth regeneration, although cell materials are the most important, the other environmental conditions, such as the scaffold, growth factor and culture medium, still need to be carefully tested. In the future, well designed systematic studies will hopefully soon clarify this question and lead to human teeth reconstruction.

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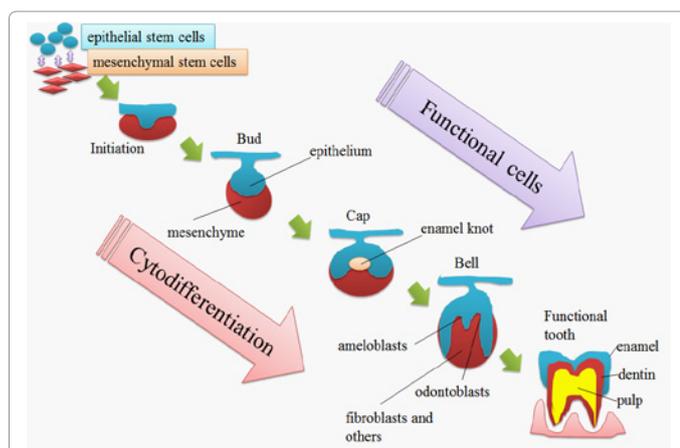


Figure 1: The journey from stem cells to teeth. Teeth develop from the interaction between epithelial stem cells and mesenchymal stem cells. Developing teeth undergo different stages: initiation, bud, cap and bell, and then become functional tooth. Through the molecular signaling network between epithelium and mesenchyme, epithelial and mesenchymal stem cells interact each other to differentiate into functional mature cells. The oral epithelial stem cells differentiate into ameloblasts and then form enamel. The mesenchymal stem cells differentiate into odontoblasts, fibroblasts and other cells; finally form dentin, dental pulp and other tissues. Therefore, the whole tooth acutely comes from those two types of stem cells.

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Received June 21, 2012; Accepted June 21, 2012; Published June 23, 2012

Citation: Xiao L (2012) Human Stem Cells and Tooth Regeneration. *J Stem Cell Res Ther* 2:e107. doi:10.4172/2157-7633.1000e107

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