Characterization of Coronal Pulp Cells and Radicular Pulp Cells in Human Teeth

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Abstract

Dental pulp has garnered much attention as an easily accessible postnatal tissue source of high-quality mesenchymal stem cells (MSCs). Since the discovery of dental pulp stem cells (DPSCs) in permanent third molars, stem cells from human exfoliated deciduous teeth and from supernumerary teeth (mesiodentes) have been identified as a population distinct from DPSCs. Dental pulp is divided into 2 parts based on the developing stage: the coronal pulp and the radicular pulp. Root formation begins after the crown part is completed. We performed a sequential study to examine the differences between the characteristics of coronal pulp cells (CPCs) and radicular pulp cells (RPCs) from permanent teeth, mesiodentes, and deciduous teeth. Interestingly, although we have not obtained any data on the difference between CPCs and RPCs in permanent teeth, there are some differences between the characteristics of CPCs and RPCs from mesiodentes and deciduous teeth. The MSC characteristics differed between the RPCs and CPCs, and the reprogramming efficiency for the generation of induced pluripotent stem cells was greater in RPCs than in CPCs from deciduous teeth. The proportion of $CD105^+$ cells in CPCs versus that in RPCs varied in mesiodentes but not in permanent teeth. The results indicate that the proportion of $CD105^+$ cells is an effective means of characterizing dental pulp cells in mesiodentes. Taken together, the stem cells in deciduous and supernumerary teeth share many characteristics, such as a high proliferation rate and an immunophenotype similar to that of DPSCs. Thus, mesiodentes accidentally encountered on radiographs by the general dental practitioner might be useful for stem cell therapy. *(J Endod 2017;■:1–5)*

Key Words

Coronal pulp, deciduous teeth, dental pulp stem cells, mesiodentes, radicular pulp

The use of stem cells in human regenerative medicine is rapidly advancing. Of these, dental pulp stem cells (DPSCs) have proved to be ideal candidates for the repair or regeneration of defective organs or tissues such as bone, cartilage, spinal cord, and heart.

Significance

We tested the characterization of dental pulp cells based on the developing stage from permanent teeth, mesiodentes, and deciduous teeth. The characterization of dental pulp stem cells in coronal pulp differ from those in radicular pulp from mesiodentes and deciduous teeth, but not permanent teeth. CD105 surface marker is an effective means of characterizing dental pulp cells. In addition, the reprogramming efficiency in coronal pulp cells differ from that of radicular pulp cells.

We previously showed that the expression of dentin sialophosphoprotein and the tissue-forming capacity of dental papilla cells differ between the horn and central parts of the porcine third molar at the late bell stage (1). Other groups have shown that the characteristics of dental papilla/pulp cells depend on whether the tooth is in the crown completed, root formative, or root completed stage (2–4). Therefore, dental papilla/pulp cells show different characteristics depending on the location and stage of development.

Dental pulp is divided into coronal and radicular parts. Although the histologic characteristics of the 2 parts are very similar, the developmental mechanisms are vastly different (5, 6). Formation of the crown is first completed before the entire epithelium switches to root formation. Nuclear factor I-C (NFI-C)/CAAT box transcription factor was shown to play a role in root formation in mice because disruption of this factor resulted in the absence of root formation (7).

Mesenchymal stem cells (MSCs) have previously been found in the coronal pulp of exfoliated deciduous teeth (8), but MSC characteristics have never been examined in the radicular pulp of deciduous teeth. The present proceeding focuses on dental pulp stem cells (DPSCs) and the comparison between coronal pulp cells (CPCs) and radicular pulp cells (RPCs) in completed human teeth (9). In addition, we investigated the usefulness of a surface marker, CD105, for the isolation of MSCs in dental pulp (10).

Tooth Development

The tooth is composed of the crown and root, the development of which is regulated by reciprocal inductive signals between ectoderm-derived epithelium and neural crest–derived ectomesenchyme (11, 12). Tooth development is divided into 4 stages: bud stage, cap stage, bell stage, and root formation stage, as shown in Figure 1*A–D*. As shown in Figure 1, the boundary between the dental papilla and the dental follicle is unclear at the bud stage and cap stage. At the bell stage, the boundary between the dental papilla and the dental follicle is almost visible on histologic examination (Fig. 1*C*).

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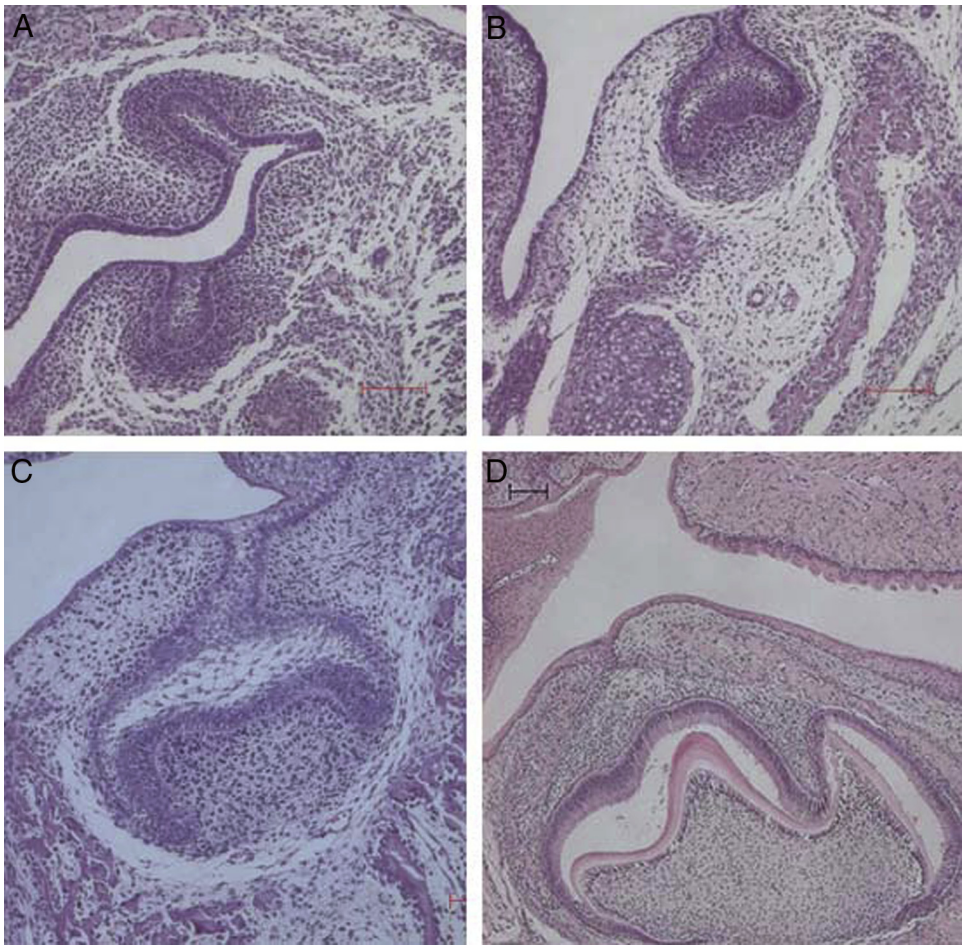

Figure 1. Tooth crown morphogenesis. (*A*) Mouse tooth bud in the dental lamina stage on embryonic day 13. Bar = 100 μm. (*B*) Mouse tooth bud displaying the cap stage on embryonic day 14. The enamel organ, dental papilla, and dental follicle together constitute the tooth bud. Bar = 100 μm. (*C*) Tooth bud displaying the early bell stage on embryonic postnatal day 0. (*D*) Tooth bud displaying the late bell stage on postnatal day 3. Two principal hard tissues, dentin and enamel, of the tooth are observed. Bar = 50 μm.

The dentin-secreting odontoblasts differentiate from ectomesenchymal stem cells in the dental papilla, and crown formation is finally completed (Fig. 1*D*). After crown formation is complete, the immature dental papilla in the coronal part of the tooth generates mature tissues such as dental pulp, which contains DPSCs (13, 14). At this stage, the apical papilla is located at the top of the root close to the dental pulp inside enamel-covered dentin, called the crown, and starts to generate radicular dentin when Hertwig's epithelial root sheath (HERS) develops (Fig. 2*A*). In addition, stem cells in the apical papilla (SCAPs) at the root apex are implicated in the development of radicular pulp (Fig. 2*B*) (2, 15).

The mechanism of development of the apical papilla is poorly understood. Here, we consider 2 theories about this mechanism. First, ectomesenchymal stem cells present in the dental papilla contribute to the development of the apical papilla at the same time as the extension of HERS. Second, ectomesenchymal stem cells in the dental follicle migrate into the apical papilla region and differentiate into odontoblasts at the root formation stage. Several reports suggested that dental follicle cells are able to differentiate into odontoblasts (16–18). In addition, primary dental follicle stem cells (DFSCs) appeared and migrated from dental follicle tissue fragments faster than DPSCs in an *in vitro* study (19).

There is a close relationship between the apical papilla and root formation because removal of the apical papilla from molars abrogated root development despite the remaining pulp tissue being intact (15). However, there is no histologic difference between the apical papilla and the dental follicle, and they appear to be a single entity; it is unclear which cells in the dental papilla or the dental follicle give rise to SCAPs. HERS plays a role in the induction and differentiation of SCAPs into odontoblasts. In addition, DFSCs are able to migrate on the dentin surface through the discontinuous regions of HERS and then differentiate into cementoblasts. The dental follicle may also participate in apical papilla development, and HERS may facilitate the migration of DFSCs into the apical papilla. Thus, HERS may regulate root formation *in toto* including the generation of dentin, pulp, and cementum.

Genetic Differences between Tooth Components

Crown and Root

Recently, it has been acknowledged that the crown is formed in the early embryonic stage, whereas the root is formed during the late embryonic and postnatal stages (20). This raises the possibility of differences in genetic traits and developmental phenotype between the crown and root. For instance, NFI-C has a unique function in determining radicular dentin formation but not coronal dentin formation. It has been demonstrated that the target molecule downstream of