

## Is Oro Dental Induced Pluripotent Stem Cells (Ips) an Alternate for Dental Stem Cell Banking?

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### Abstract

Dental stem cells, a new area of stem cell research is gaining popularity due to its easy accessibility and plasticity. On other hand iPSc (induced pluripotent stem cells) which can be generated from many tissues in the body has attracted many researchers towards it. This brief communication comparatively reviews the advantages and disadvantages of Dental Stem Cell Banking (DSCB) with iPSc. Similar to cord cell banking DSCB can also serve as source for stem cells. Reprogramming the cells by transfecting with specific transcriptional factors helps in deriving the iPSc cells. Recent studies have shown dental pulp cells can be efficiently reprogrammed than dermal fibroblasts in generating iPSc. Other than dental pulp, IPS cells were also made from other tissues of oro-dental region which includes gingival, buccal mucosa and periodontal ligament. The disadvantages of iPSc cells like, tumor and teratoma formation can be avoided by newer non integration techniques. It can be concluded that though iPSc cannot replace DSCB in the present scenario but, in future it has paramount role in regeneration after prospective research.

### Introduction

Ever since Gronthos et al first isolated Dental Stem Cells (DSCs) in 2001, its role in stem cell therapy is tenable [1]. It was also harvested from deciduous teeth (stem cells from exfoliated deciduous teeth [SHED]), periodontal ligament, apical papilla and dental follicle. Mesenchymal stem cells were predominately seen in the oral and maxillofacial area. These DSCs after expansion were characterized into osteoblasts, chondroblasts, adipoblasts, neural and muscular components. Numerous studies have proven DSCs were clinically used in various applications in experimental animals and humans.

Dental pulp stem cells (DPSCs) originate from neural crests cells embryologically. In dentistry dentin and pulp regeneration have been successfully attempted in animal models. New treatment modalities are currently in progress in which endodontically involved tooth can be regenerated using DPSCs [2]. DSC were also used in periodontal regeneration and closing small bone defects when used alone or in combination with bone marrow stem cells [3,4]. SHED (Stem cells from Human Exfoliated Deciduous teeth) were found to accentuate healing of wounds in nude mice [5]. Tissue engineered teeth were developed using porcine tooth bud cells which prove tooth regeneration is possible in future [6]. Apart from dentistry, dental stem cells were also used to improve left ventricular function in rats by reducing the infarct size [7]. Dental pulp cells regenerated peripheral nerve in rats and DPSC along with tissue engineered sheet have shown regeneration of cornea in rabbits after induced chemical injury [8].

With this background, it is clear that DSCs have a paramount role in stem cell therapy, and hence Dental Stem Cell Banking gained momentum recent days. The discovery of iPSc in 2006 by reprogramming human cells using transcriptional factors has revolutionized stem cell research [9]. The main advantage of this technique is reprogramming of terminally differentiated cells into pluripotent stem cells. Group of transcriptional factors like OCT3/4, SOX2, KLF4 and C-MYC were used for reprogramming. iPSc research is growing leaps and bounds, its pitfalls like teratoma formation, can be overcome by newer modifications like protein induced pluripotent stem cells (PiPSC) [10]. Many dental researches have showed their attention towards IPSCs which has got great potential for wider clinical applications. It was also generated from dental pulp, gingiva and buccal mucosa. Extracted teeth

which is considered as a biological waste is shown to be an excellent candidate for IPSC generation from the pulp.

A paradigm shift within the field of stem cell biology has geared up, which paved way for various arenas of applications. The advantages and disadvantages of dental stem cell banking and iPSc were discussed with the available English literature.

### Dental Stem Cell Banking (DSCB)

DSCB is getting popularized recent days due to its advantage over Cord Stem Cell Banking as it can be stored at various stages of life (deciduous teeth exfoliate at different stages of life). Discovery of SHED, which behaves like embryonic stem cell has paved way for concept of dental stem cell banking [11]. Adult teeth extracted for therapeutic purposes can also be used for banking. The protocols for harvesting and isolation of the stem cells were much simpler than cord stem cell banking. For DSCB posterior vital teeth is preferred than the anteriors. Dental stem cells after cryopreservation will not lost its ability for differentiation [12]. On the other hands, long-term studies have not been done on DSCB and their clinical applications. The expansion and clinical application of these DSCs need more detailed prospective study. The volume of tissue obtained from pulp and its microbial contamination may hinder the potential clinical application. The cost of banking is very expensive and needs to be renewed depending up on the contract with the firm for storing the tooth. Stem cells stored for longer years might not show good results

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warranted at the time of usage. Following up of the samples is a difficult task.

## Induced Pluripotent Stem Cells (iPSCs)

The somatic cells can be successfully transferred to pluripotent state, which was confirmed by nuclear transfer experiments [13]. iPSCs were based on the concept in which terminally differentiated somatic cells can be successfully reverted to pluripotent state. iPSCs were first discovered at 2006 using defined factors like OCT3/4, SOX2, KLF4 and C-MYC on mouse fibroblast. In 2007 human iPSCs were generated successfully using similar technique [14]. iPSCs can be generated from many tissues of the body at any time. Oro-maxillofacial region is one of the potential areas from which iPSCs cells can be harvested, which include tooth pulp, gingiva, buccal mucosa and periodontal ligament. iPSCs have limitations like viral gene transfection, low efficacy, teratoma formation. Teratoma or tumour formation is due to insertion of tumorigenic genes like C-myc which can be avoided by new factors like L-myc (reprogramming enhancer) in which human tumors are less reported [15] and also using new gene introduction technique with the safer virus like adeno virus. Newer integration free human iPSC cell generation has got remarkable lower risk comparing conventional techniques but with lesser efficacy. Recent animal studies have shown Protein Induced Pluripotent Cells (PiPSCs) have given a new dimension in iPSC production, where genetic modification is not involved. This new innovative technique will allow direct introduction of reprogrammed proteins into the cell rather than transcription of delivered gene thereby eliminating the risk of modification of the same by exogenous material [10]. This technique is simple and fast when compared with the conventional technique. New advancement of research may increase its potential and make non-integration technique more reliable.

The advancement of iPSC research will have broad perspective of clinical application in medicine and dentistry. The main advantage of iPSC is, it is autologous, can be generated from many tissues in the body as against banking which can be stored only at specified times. The viability of the dental stem cells after long term storage has not been well documented. Long term maintenance and follow up is needed in banking. As of now very few clinical application were done using dental stem cells after banking it. Disease specific iPSC lines can be very useful in treating various conditions including neural, muscular, and cardiac and hematological disorders. In dentistry, craniofacial regeneration and tooth regeneration can be achieved with iPSC in future.

## Conclusion

Dental stem cell banking has an advantage of storing tissues at different stages of life and easier harvesting. Long-term studies for therapeutic clinical application of DSCs need to be addressed. On other hand iPSCs, can be procured at any time from many tissues throughout the body. Studies have shown pluripotent stem cells can also be made from dental pulp stem cells of discarded teeth. At present iPSC cannot replace Dental Stem Cell Banking as it needs more research and clinical translation. However, with new advancement it will be beyond our imagination, definitely iPSC cell will have a promising place in therapeutic application of humanly diseases.

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