# Stem cells in dentistry

Danica Izgarevic

Stem cells are undifferentiated, immature cells found in all multicellular organisms. They are characterized by the ability to self-renew and differentiate into any mature cell type (1). There are multiple forms of stem cells which can be distinguished from one another based on the type of cells they can differentiate into and where they are sourced in the body. Recent studies have shown that oral tissues are also a source of stem cells (2). Given their unique abilities, stem cells can be used for tissue engineering to regenerate or replace damaged, diseased, or missing tissues and even organs (3).

## Sources of stem cells in dentistry

There are 2 main types of stem cells – embryonic stem cells and adult stem cells – which are classified according to their origin and differentiation potential (4). The adult stem cells are hematopoietic stem cells (HSCs) and mesenchymal stromal cells (MSCs). HSCs can create every blood cell type, while MSCs create cartilage, bone, bone marrow, fat and muscle tissue cells. They are often harvested from bone marrow but can also be accessed through other sources such as liver, umbilical cord, placenta, adipose tissue, synovial membrane, amniotic fluid and even teeth (5).

## Bone Marrow-Derived MSCs (BMSCs)

BMSCs are multipotent progenitor cells present in the adult bone marrow. Due to their replicative capacity, they can also differentiate into numerous cells of the connective tissue. BMSCs can be isolated from the iliac crest, the largest of the three bones that make up the pelvis (6). A study by H. Eugusa confirmed that BMSCs from the iliac crest can differentiate into myogenic, osteogenic, adipogenic, chondrogenic and even non-mesenchymal neurogenic lineages (6). The process of collecting cells from the iliac crest is invasive for donors, but it has been used for many years in dental bone regeneration.

In regenerative medicine, it is the most documented cell source, possibly because it is routinely collected for bone marrow transplantation for leukemia treatment (7).
Studies have shown age-related decline in the osteogenic potential of BMSCs isolated from the human iliac crest and femur (8). One of the challenges associated with the use of such cells is that their in vitro capability for expansion is limited and they tend to lose their multi-differentiation potential (6). Functionally and phenotypically different from iliac crest BMSCs are orofacial BMSCs, owing to their distinct embryonic origins. Human BMSCs can be isolated from the maxilla and mandible, the bone marrow is suctioned during dental treatments as with dental implantation, third molar extraction, orthodontic osteotomy, or cyst extirpation (9). Unlike BMSCs from the iliac crest, they can be used from patients irrespective of their age (10). Orofacial BMSCs' however, have a lower adipogenic potential than those isolated from the iliac, so when clinical trials are conducted, knowledge of both cell types is crucial (11).

## Periodontal Ligament Stem Cells

20 years ago Melcher proposed that stem cells can be found in periodontal tissues (12). Studies indicated that the presence of PDLSCs could result in a beneficial outcome for the treatment of periodontal disease. Case reports by Yoichi Yamada indicated that using autologous PDLSs to treat intrabony defects did not improve the periodontal index (13). Randomised controlled trials also showed that the use of autologous PDLSCs did not result in significant differences in treatment outcomes for patients. Currently, there are only three clinical trials supporting the use of PDLSCs for treating gingival diseases. Further studies are needed to analyze their effectiveness.

In 2003, Pini Prato et al. stated that in numerous cases, sufferers' gingival fibroblasts had been cultivated on a hyaluronic acid scaffold and had then been implanted onto the uncovered periosteum of the teeth where gingival augmentation was required (14).
The tissue engineering technique of culturing gingival dermal alternative grafts, composed of gingival fibroblasts and numerous matrices, may contribute to a growth in root coverage and in keratinized and connected gingival tissue. Additionally, an injectable tissue engineering approach with MSCs, platelet-rich plasma, and hyaluronic acid can be used to address gingival recession (seen as black triangles). This approach is minimally invasive, and can be a long term solution to improve gingival aesthetics (15). Therefore, cellular-based regenerative techniques can be considered a new, predictable and effective management technique for gingival and soft tissue augmentation.

## Oral mucosa-derived stem cells

To date, two extraordinary varieties of human adult stem cells have been recognized in the oral mucosa. One is the oral epithelial progenitor stem cells, which are a subpopulation of small oral keratinocytes (smaller than forty μm) (16). Although these cells appear to be unipotent stem cells, they can differentiate into epithelial cells. This is due to their clonogenicity and ability to regenerate stratified and well-prepared oral mucosal graft ex vivo, which suggests their potential usefulness in intra-oral grafting (17,18).
Other stem cells in the oral mucosa were found within the lamina propria of the gingiva, which attaches without delay, to the periosteum of the underlying bone with no intervening submucosa (19).
In 2010. study Marynka-Kalmani et al. showed that a multipotent neural crest stem cell-like population, termed oral mucosa stem cells (OMSCs), can be reproducibly generated from the lamina propria of the adult human gingiva and in vitro may differentiate into lineages of the 3 germ layers (20). Gingival stem cells may therefore, partially explain the excessive reprogramming efficiency of gingiva-derived fibroblastic cell populations during iPS cell generation (21).

## Salivary gland-derived stem cells

Stem cells inside the adult salivary gland are anticipated to be beneficial for autologous transplantation in the context of tissue engineered-salivary glands or direct cellular therapy. The salivary glands originate from the endoderm and consist of acinar and ductal epithelial cells with exocrine function. After ligation of the salivary gland duct, the acinar cells undergo apoptosis, and the duct epithelium eventually proliferates. The isolation of stem cells within the salivary glands has been attempted through the mobile subculture of dissociated tissue.

## Conclusion

Regenerative dentistry is an upcoming area of interest amongst dental researchers and clinicians, with many promising avenues for future research. Dental teaching should therefore pay more regard to this field. Through further research and teaching, regenerative dentistry has the potential to revolutionise dental treatment.