Oral Biology
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Lecture - 08
Stem cells in the oro-dental region

Hi everyone, today we are going to deal an important topic and an interesting topic that is Stem cells in the oro-dental region.

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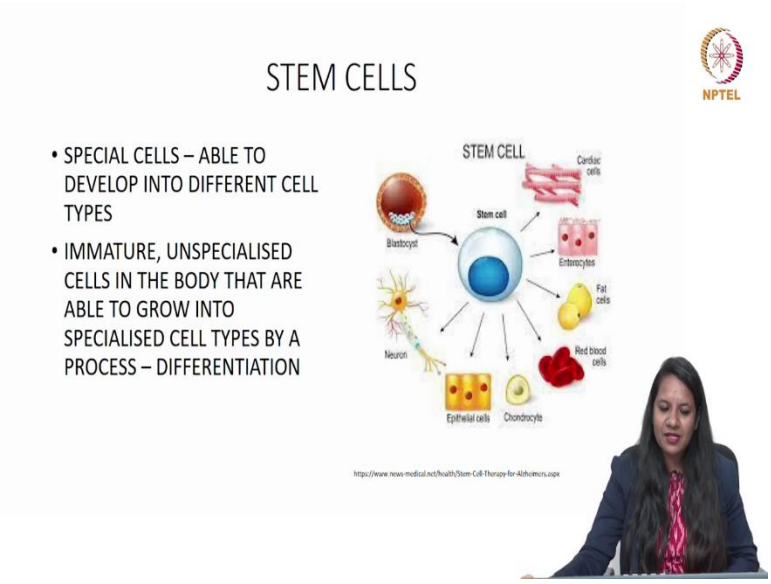

What are stem cells? Stem cells are special cells which are able to develop into different cell types. They are immature unspecialized cells in the body that are able to grow into specialized cell types by a process called differentiation. In simple words, we can say an undifferentiated cell getting converted to a differentiated cell according to our need.

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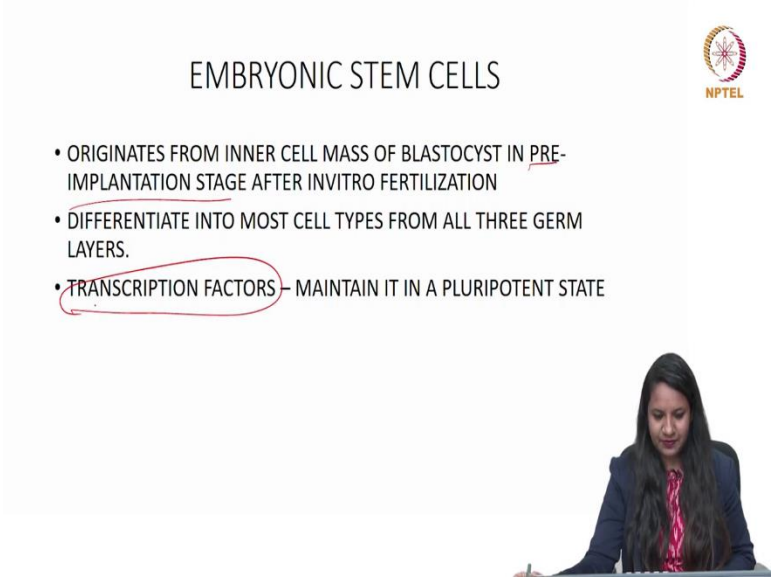

So, the type of stem cells involves embryonic stem cells and adult stem cells. Embryonic stem cells originate from inner cell mass of blastocyst in a pre-implantation stage after invitro fertilization. They can able to differentiate into most cell types from all three germ layers that is the ectoderm, endoderm and the mesoderm with the help of this transcription factors, it can able to maintain in a pluripotent state.

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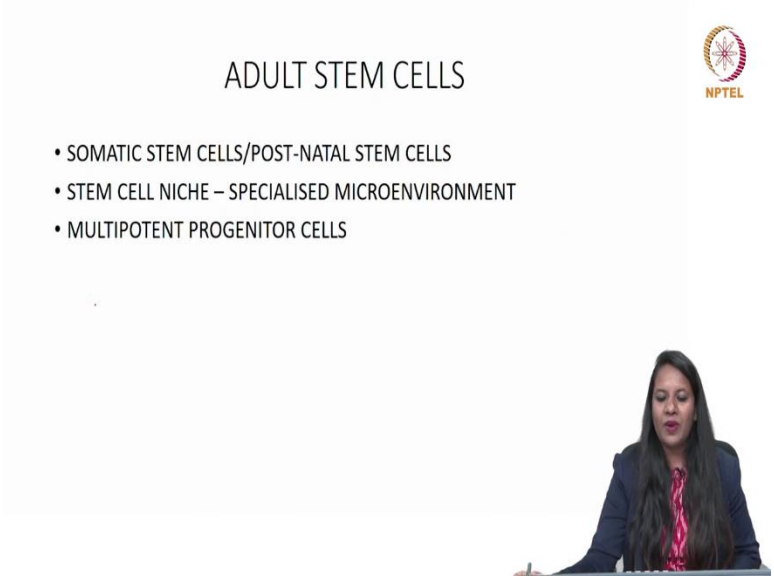

Adult stem cells are otherwise known as somatic stem cells or post-natal stem cells. They reside in a place called stem cell niche which is a specialized micro environment & these stem cells can reside there for a longer period. And they are multi potent progenitor cells, they are also capable of differentiating into many cell lineages of needs.

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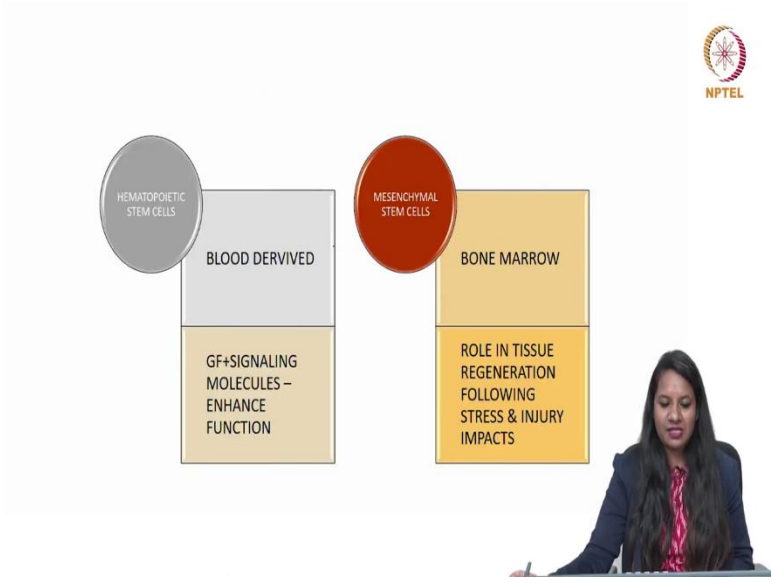

Now, moving to the types of adult stem cells that is one is hematopoietic and the other one is mesenchymal. As the name suggests hematopoietic stem cells derived from the blood and mesenchymal stem cells derived from the bone marrow. Blood derived that is the hematopoietic stem cells will have growth factors and a signaling molecules & they are responsible to enhance their function whereas, in bone marrow derived that is mesenchymal stem cells they have a role in tissue regeneration during any stress or injury impacts.

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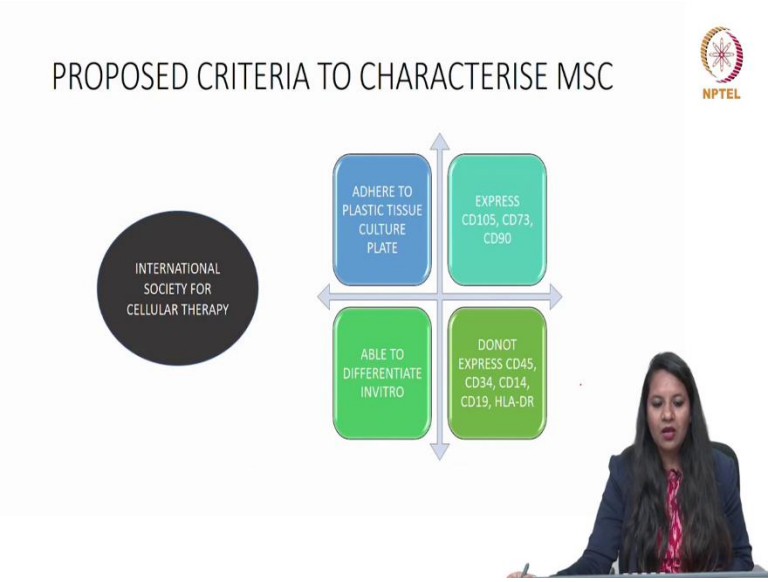

According to international society of cellular therapy, there are few criteria for a mesenchymal stem cell. So, a mesenchymal stem cell should adhere to the plastic tissue culture plate. It should express certain markers like CD105, CD73 and CD90 as well as they should not express few factors like CD45, CD34, CD14, CD19 and HLA-DR. And the last being able to differentiate invitro, these all are the proposed criteria to characterize a mesenchymal stem cell.

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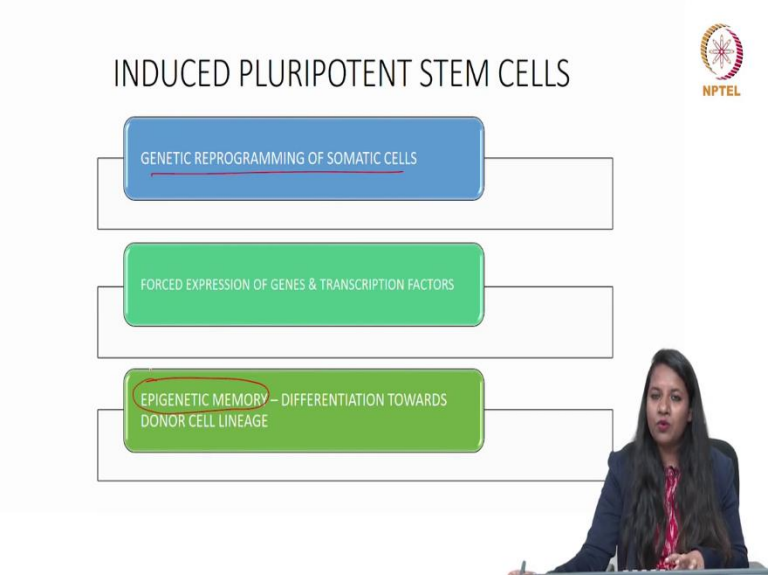

Induced pluripotent stem cells are nothing but genetic reprogramming of somatic cells by the forced expression of genetic factors and transcription factors. So, they have a peculiar future that is nothing but epigenetic memory which means that they can differentiate into donor cell lineage.

So, that is the speciality of induced pluripotent stem cells, lots of research have been going through in this where more gene and transcript factors were incorporated into the somatic cells to differentiate into donor cell lineage.

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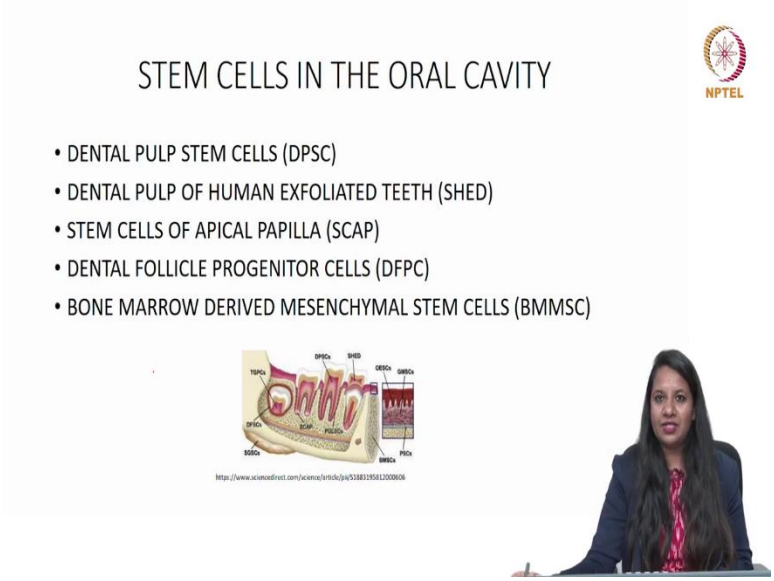

Now, moving to the stem cells in the oral cavity. Oral cavity has enormous amount of stem cell niche or stem cell population which can be utilized for various dental procedures. The first one being dental pulp stem cells, second from the periodontal ligament, third from the exfoliated deciduous teeth and fourth from the dental follicle or the apical papilla and the fifth one being bone marrow derived from the mesenchymal stem cells.

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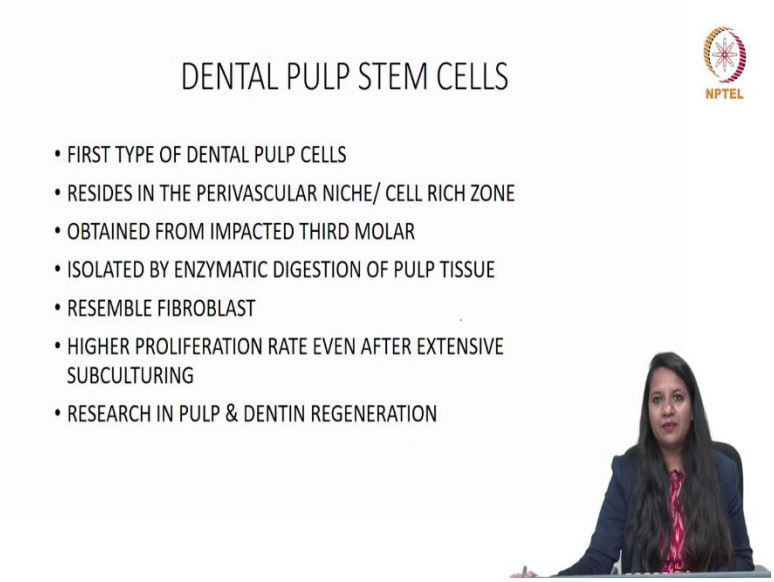

So, the first one being dental pulp stem cells which were derived from the dental pulp, that is the cell rich zone or the perivascular niche. The first type of dental stem cells is obtained from the impacted third molar. They are isolated by enzymatic digestion of pulp tissue and it resembles fibroblast which is the most common cell present in the dental pulp. It has the higher proliferation rate even after extensive sub culturing, the proliferation rate of dental pulp cells remains little higher than the other stem cells from the other parts of the oral cavity. Now, the research had been going on to develop a dentin-pulp complex.

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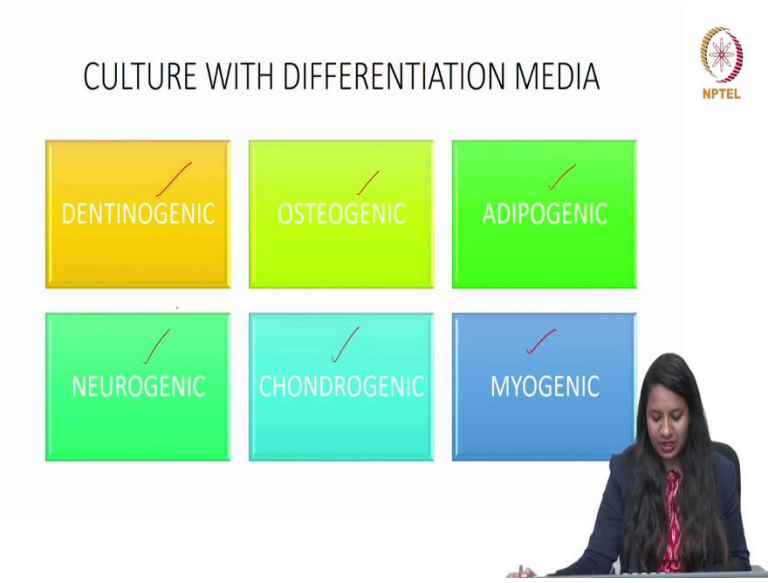

When it is cultured with different media, it can able to form a dentin, bone, adipose tissue, muscle chondroid bone and nerve. So, it has a capability of being dentinogenic, osteogenic, adipogenic, myogenic, chondrogenic and neurogenic.

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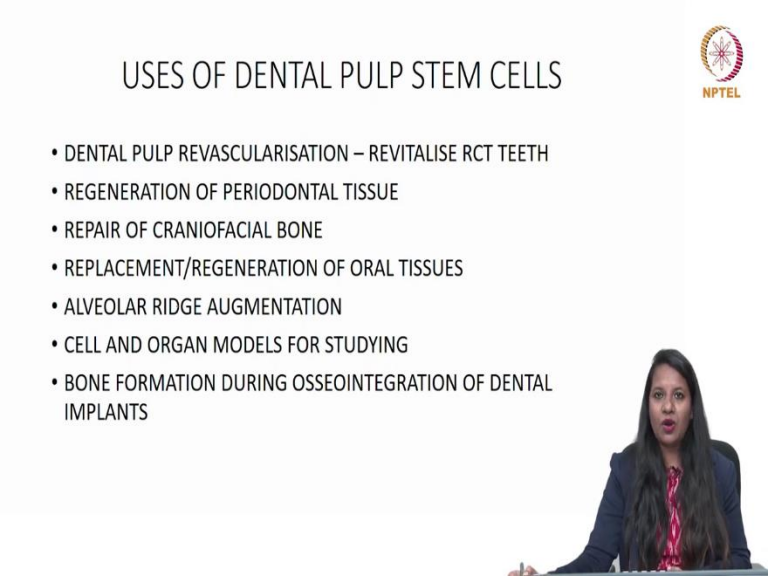

What are the uses of dental pulp stem cells? Not only the dental pulp stem cells, most of the stem cells from the oral cavity share the same uses. The first one being dental pulp revascularization which is nothing but the root canal treated tooth can be revitalized with the help of a regeneration from the dental pulp stem cells.

The second one is the regeneration of the periodontal ligament & then the third one is repair of craniofacial bone. So, it can be able to replace or regenerate the entire periodontium in vivo and the alveolar ridge augmentation, cell and organ models for studying. This is very interesting because nowadays organoid culture had been of great interest that is the stem cells have been used to mimic the miniature of organs. So, that it will be easy for the further study of tissue engineering or any drug intervention can be studied in that miniature model, then we can simulate the same with the normal organ.

It is also used for bone formation during intra osseointegration of dental implants. During dental implants if there is any bony defect that can be covered with the help of these stem cells which has an ability to form bone for the osseointegration of dental implant.

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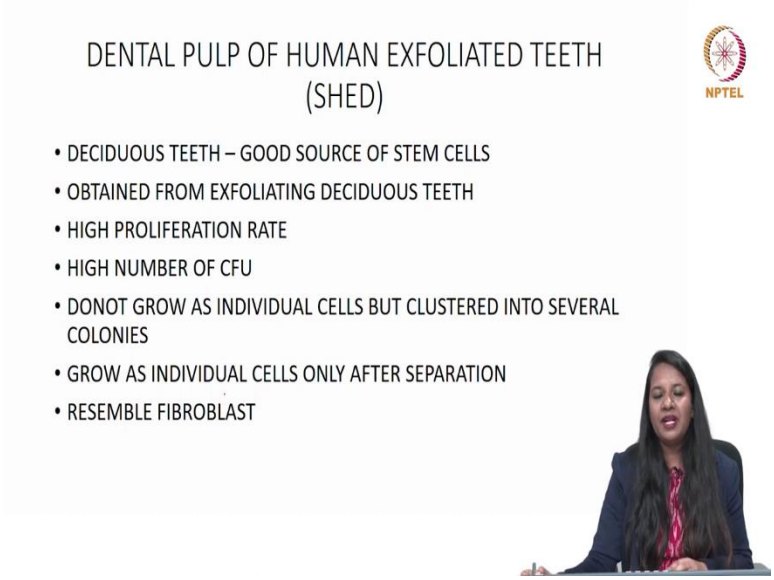

Next is dental pulp of human exfoliated teeth that is the deciduous teeth are the rich source of stem cells especially dental stem cells. So, they are obtained from exfoliating deciduous tooth and they also have a high proliferative index and high colony forming unit.

The stem cells derived from an exfoliated deciduous tooth is always in clusters, later only it can be separated and then it can be cultured. So, it grows as individual cells only after separation and just like dental pulp stem cells these also resemble a fibroblast.

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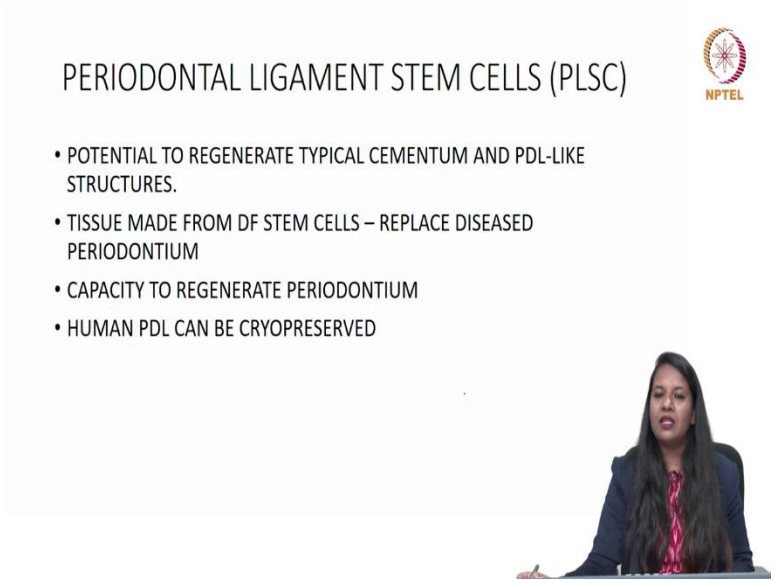

Then comes the periodontal ligament stem cell, as the name indicates it is derived from the periodontal ligament either from the extracted tooth or we can just scrape it from the alveolar bone surface. So, it has the potential to regenerate typical cementum and PDL like structures. It can able

to replace the deceased periodontium as it has the tendency to form a periodontium, human PDL is also cryopreserved.

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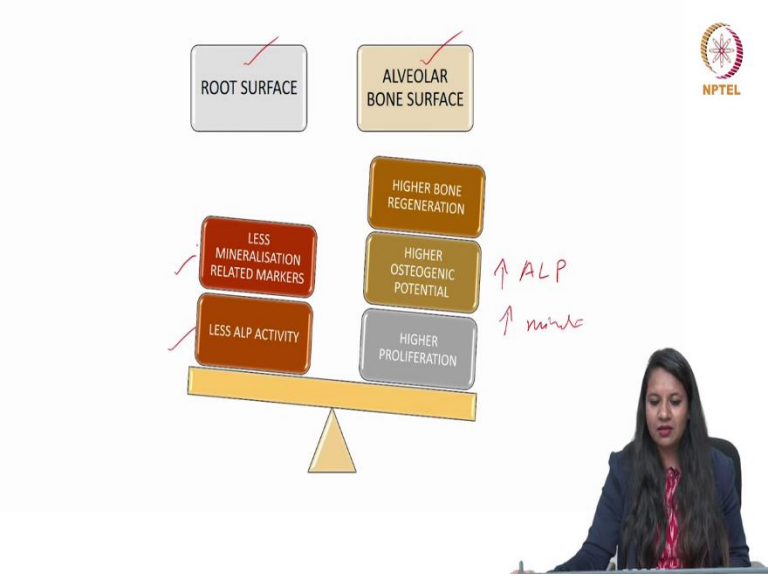

It is from derived from the root surface of the extractor teeth or from the alveolar bone surface. When compared to the one which is derived from the extracted root surface the one from the alveolar bone surface have higher osteogenic potential because it has the high ALP activity, it has higher bone regeneration and higher proliferation index, it also has a higher mineralization related markers whereas, in the root surface area it has less ALP and less mineralization related markers. And hence it is less osteogenic when compared to the one which is derived from the alveolar bone surface.

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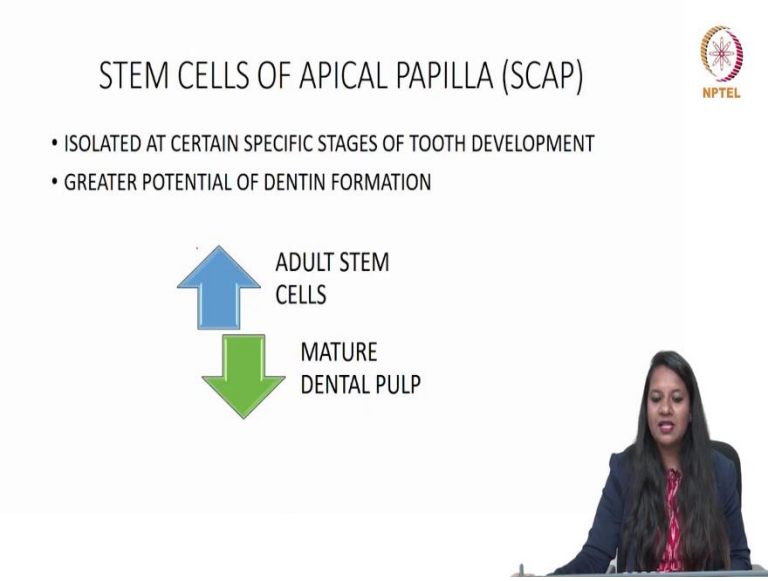

Stem cells of apical papilla is isolated at certain specific stages of tooth development and it has a greater potential of dentin formation more than mature dental pulp & it can have the ability to form more adult stem cells.

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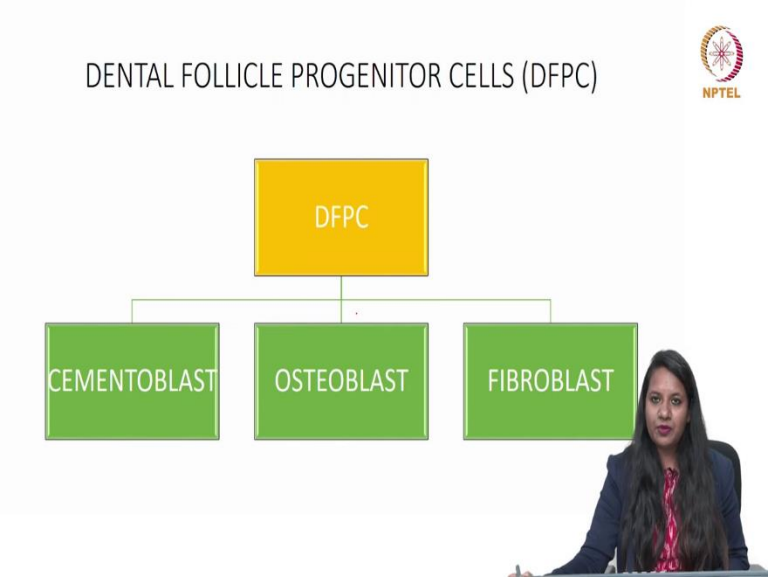

Moving to the dental follicle progenitor cells, which have an ability to differentiate into cementoblast, osteoblast and fibroblast just like other stem cells of the oral cavity.

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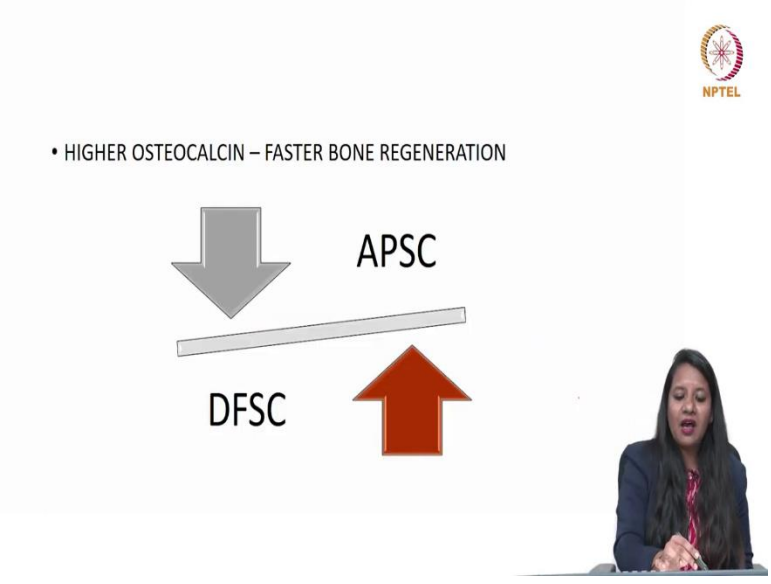

However, it has a higher osteocalcin and it has faster bone regeneration. So, when compared to dental follicle stem cell, apical papilla stem cell also has the greater bone regeneration capacity.

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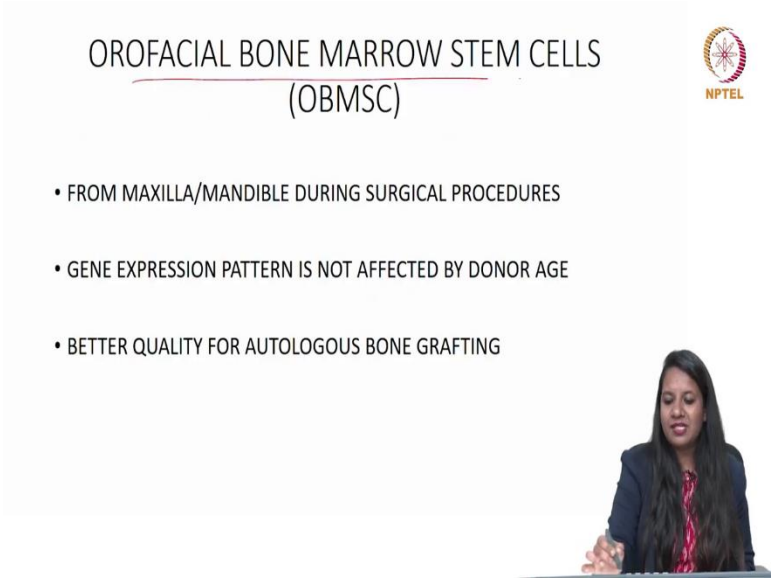

Orofacial bone marrow stem cells - As the name detects, it is derived from maxilla or mandible during surgical procedures of the oral cavity. Gene expression pattern is not affected by the donor age which is an important feature of an orofacial bone marrow stem cells, it has a better quality for autologous bone grafting which has been following till now.

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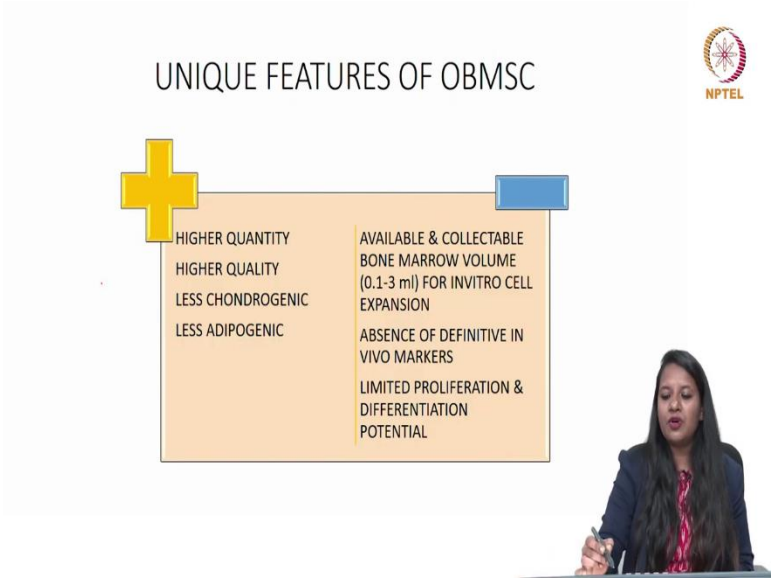

The unique features of bone marrow derived stem cell are its higher quantity, higher quality, less chondrogenic and less adipogenic. The disadvantages or the limitations is the available and collectable bone marrow volume is only 0.1 to 3 ml which is very minimal and absence of definitive in vivo markers and limited proliferation and differentiation potential when compared to other oral derived stem cells.

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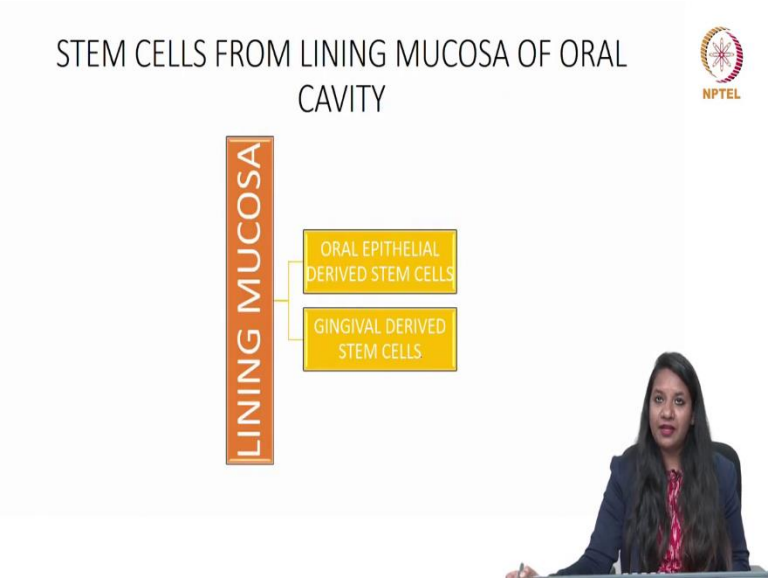

Stem cells from the lining mucosa of the oral cavity that is either from the oral epithelium derived or from the gingival derived either from the oral epithelium or from the gingiva.

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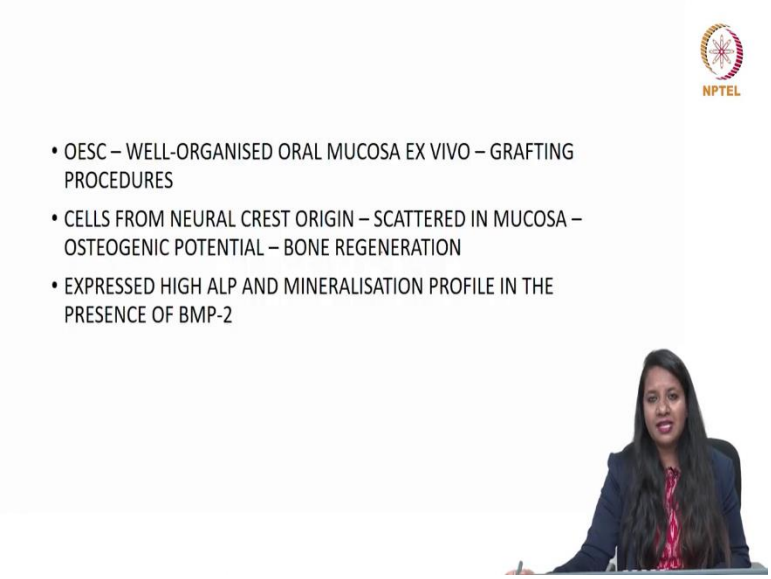

Oral epithelial derived stem cells can form into an organized oral mucosa ex vivo that is it is very well organized and very complex structure. Hence, it can be useful in the grafting procedures any gingivectomy or whatever the procedure involving the oral mucous membrane grafting can be done with the help of these type of stem cells.

Stem cell niche from neural crest origin can be scattered in the oral mucosa and can they can reside in any stem cell niche in the oral cavity. Those cells can be identified and cultured as they have an

osteogenic potential that is they have the capability of bone regeneration. It was found very recently and it expressed high ALP and mineralization profile in the presence of BMP-2 (Bone Matrix Protein 2).

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Gingival derived stem cells are very special because when they have been studied in an animal like rat in the cholangitis case & found that these gingival derived stem cells have the ability to minimize the inflammation ok. So, it is anti-inflammatory, immunosuppressive, immunomodulatory and the most important it is not tumorogenic.

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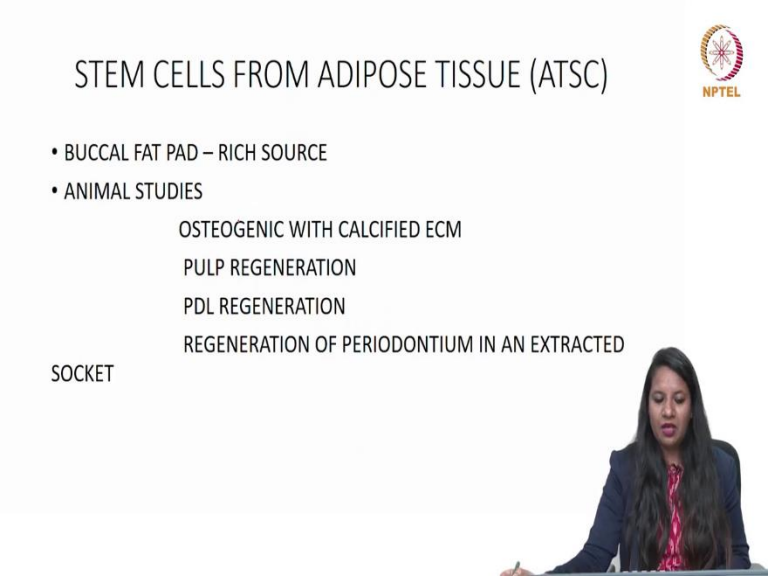

The source of adipose tissue in oral cavity is only buccal fat pad which is the rich source of adipose tissue and in the animal studies there are few revealing factors which they have been declared. It is osteogenic and calcified extracellular matrix had been formed in animals and they can able to regenerate the pulp as well as periodontal ligament and regenerate the entire periodontium in an extracted tooth of an animal model.

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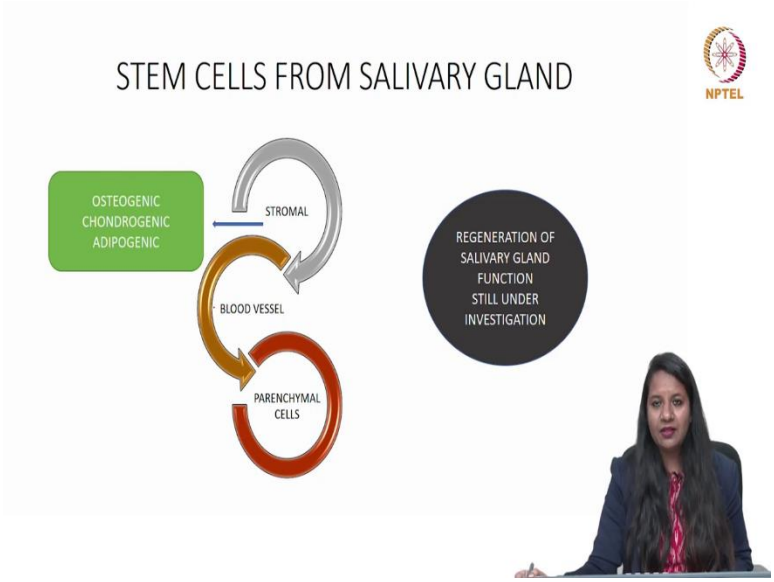

Stem cells from the salivary gland - whether it can able to regenerate the salivary gland function is still under investigation; however, the one from the stromal cells were osteogenic, chondrogenic and adipogenic as stem cells from the other parts of the oral cavity & research were going on from the blood vessel and the parenchymal cells of the salivary gland.

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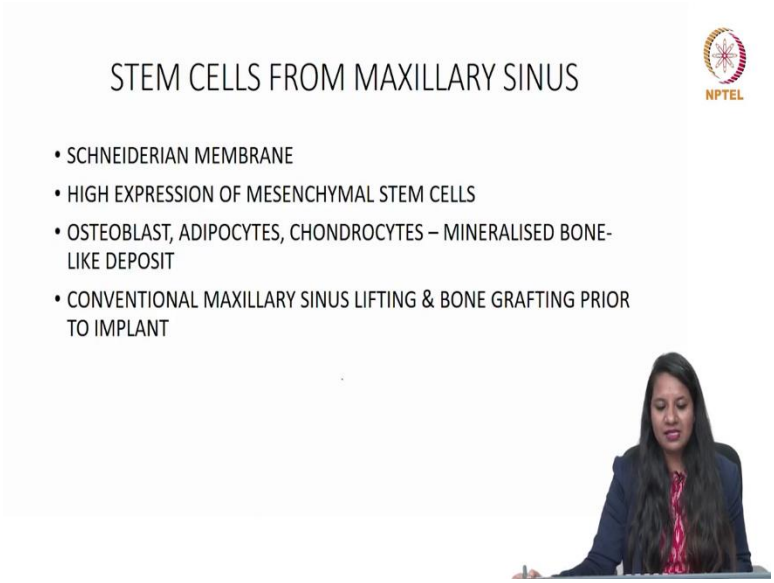

Then stem cells from the maxillary sinus - Schneiderian membrane which is present in the maxillary sinus is the source of the stem cells & cells from that part have an ability to form a differentiated type of cell lineages. So, they have higher expression of mesenchymal stem cells. So, they can able to differentiate into osteoblast, adipocyte & chondrocyte with mineralized bone like deposit. So, they can be used nowadays in a conventional maxillary sinus lifting and bone grafting prior to implant.

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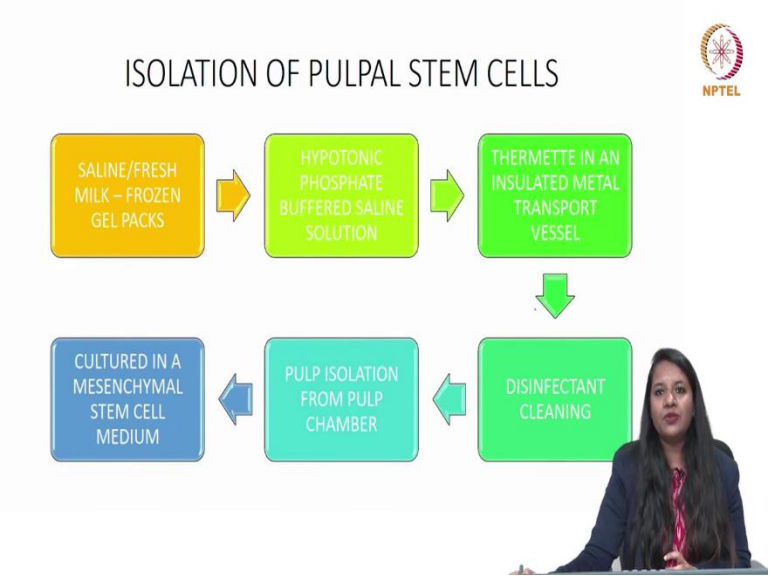

So, how do we isolate an stem cell from the oral cavity? First the tooth which is extracted has to be put it in saline or fresh milk with a frozen gel packs then it has to be placed in a hypotonic phosphate buffered saline solution, then it has to be transferred to thermette which is an insulated metal transport vessel, then passing the teeth to the disinfectant & the pulp is isolated from the pulp chamber and cultured in a mesenchymal stem cell medium.

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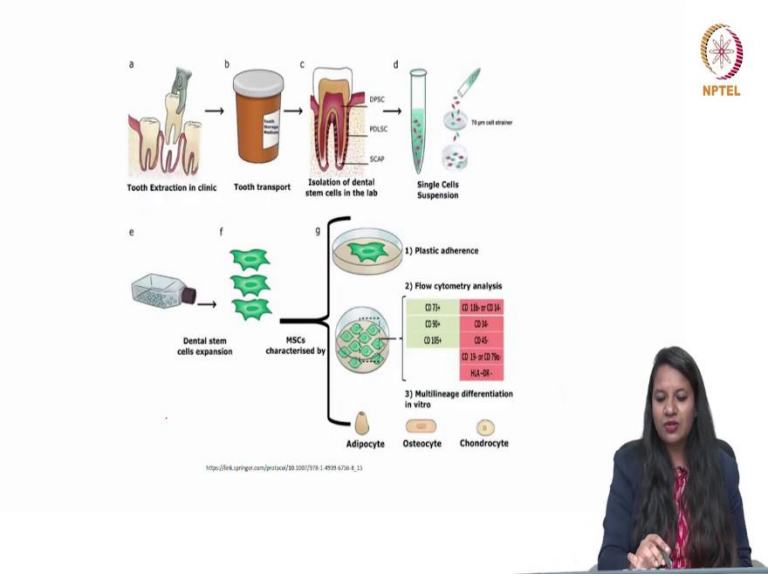

So, this is the picture where the tooth is extracted transported and, in the lab, it is isolated then one important feature of mesenchymal stem cell is plastic adherence and the evaluation of the markers, then multi lineage differentiation such as adipocyte, osteocyte and chondrocyte.

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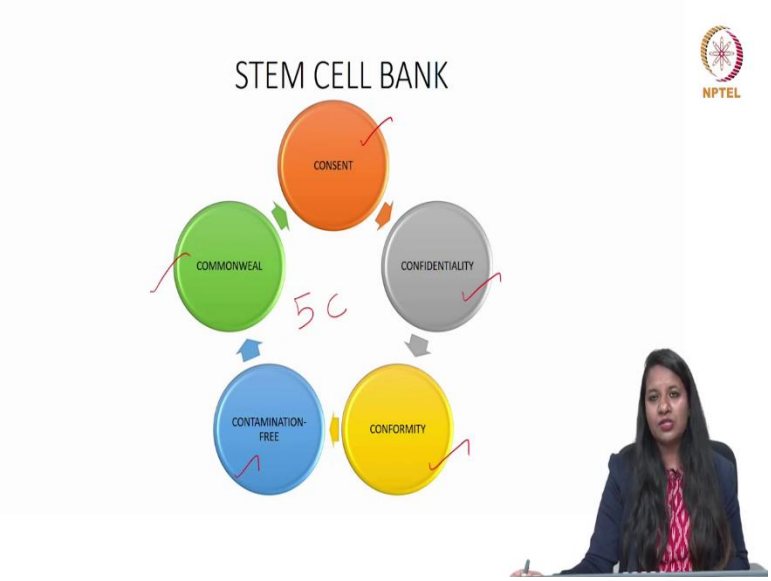

The stem cell bank is a place where the stem cells were preserved and stored for further processing and further tissue engineering. It includes 5 C - consent, confidentiality, conformity, contamination free and commonweal. Informed consent has to be got from the donor and he has to donate it by his own willingness. Second one is confidentiality - the name or any details of the donor should not be leaked to the any other external person even the family members of the donor.

The third one is conformity, the whole process of stem cell banking, processing and culturing everything has to be evaluated by the qualified person that is they must have knowledge about the

stem cell processing starting from the culture media, storage and contamination and the equipment's used for the processing of the stem cell has to be known by that qualified person to qualify the stem cell which is entering their bank.

The fourth one being contamination free; which is very important the stem cell has to be maintained maintain the sterile environment and it should be free of contamination from cell lineages and other bacterial contamination infection from mycoplasma has to be evaluated now and then. The last one being commonweal that is the donor should not be paid for his donation that is most important which is followed in many countries.

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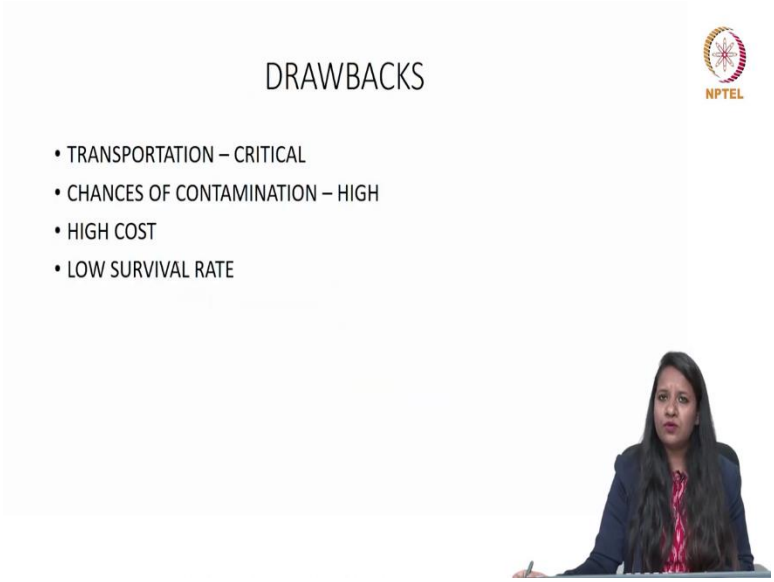

So, those stem cells have most of the advantages, there are few disadvantages the one being the transportation. Transportation of stem cells is really very critical & there is high chances of contamination throughout the transportation or contamination of different cell lineage is very common the third one being high cost and few of them have very slow survival rate.

These are my references.

Thank you.