The whole concept of Tissue engineering is built on researches that **mainly** done on **bone** and little bit one the **skin** (first definition 1993 )

**biotechnology** is summation of methods or techniques that use living organisms or their parts as tools.

**Tissue regeneration :** is restoring morphology and function of loss tissues in a way similar to that occurring during development .

Taking a stem cell and culture it in certain conditions ( and here is the complexity ) , then implant it in vivo to produce the regenerative tissue.

Types of tissue engineering : 1)ex vivo 2)in vivo

**in vivo :** directly without culturing , cells already present in tissue I do genetic manipulation to induce certain genes or inserting signaling factors to induce certain process directly

in **development** I have a migration of Neural crest cells then a cellular condensation then a spatial reorganization of cells then progenitor cells then differentiated cells so different types of tissues

In **regeneration** blood clot formation then inflammatory reaction then granulation tissue then a progenitor cells then a differentiated cells ( different turnover rates )

***In Tissue engineering*** we aim for regenerationin an approach that utilize **biodegradable** synthetic or natural scaffold , as well as advanced molecular techniques in order to replace tissue function.

the goal of tissue engineering is functional biological structure , to achieve this goal the cells must be instructed to differentiate , and to and to receive positional cues , and to synthesize the appropriate extracellular matrix molecule in overall shape and dimensions of a diseased or missed tissue or organs

* tissue engineering components: 1)stem cells 2)scaffold 3)signaling molecule

1. stem cells

embryonic stem cells and adult stem cells

types :

-Bone Marrow Stem Cells (BMSC)-

-Epithelial Stem Cells (ESC)-

-Dental Pulp Stem Cells (DPSC)-

-Stem Cells from Exfoliated Deciduous Teeth (SHED )-

-Periodontal Ligament Stem Cells (PDLSC)

Embryonic stem cell could be totipotent or pluripotent

**-Totipotent**: a cell that can give a complete organism + placenta and supporting tissue (similar to morula) (very primitive)

**-Pluripotent:** a cell that can give a complete organism without placenta or supporting tissues (more differentiated than totipotent)

**\*** More plastic cells totipotent or pluripotent difficult to control and less stable and might induce carcinogenesis ( it has less number of genes and its only activity is proliferation)

**-Multipotent**: usually an adult stem cell , can give multiple tissue types according to the designed pathway

easier to manipulate ex : from a bone marrow stem cell , it can give bone , adipocyte , myocardial cell , cartilage … depend on the genes that is activated

**-Unipotent**: give only one tissue type like precursors of keratinocytes that found in the basal cell layer of epithelium

its recently (2009-2010) known that most of the unipotent are inducible pluripotent

\*by activating certain genes ( 4 genes mainly )we can retune a fully differentiated cell to its origin ( undifferentiated stem cell )

so we know now that cells are **plastic** and it has the ability to accommodate and withstand different conditions

**Mesenchymal stem cells** :

Undifferentiated cells -

High proliferation rate over long time-

- Can differentiate into different cell types

- They have Asymmetrical mitosis

Gronthos at 2000 : take tissues from the centre of the pulp and culture it then implanted it in mice subcutaneously for 3 weeks

Result was the formation odontome like tissue so he conclude that there is a capacity of regeneration from an adult stem cells

**Dental Stem Cells**

Dental pulp stem cells (DPSCs) ( Gronthos et al, 2000) -

-Stem cells from exfoliated deciduous teeth (SHED) (Miura et al, 2003)

exfoliated NOT extracted because with extraction there will be contamination and it affects the stem cells

Periodontal ligament stem cells (PDLSCs) ( Seo et al, 2004) -

-Stem cells from apical papilla (SCAP) ( Sonoyama et al, 2006 , 2008)

Specifically third molars

Dental follicle precursor cells (DFPCs) ( Morsczeck et al, 2005 ) -

Ex : from third molars or any other tooth in its early development

**Chrastaristics of dental stem cells :**

In comparing to BMSC ( classical examples , first discovered )

1-Higher proliferation rate than BMSC under same conditions

2-Expression of STRO-1, VCAM-1, α-sma more than BMSC so :

3-High plasticity, Can give : Osteoblasts, Chondroblasts, Adipocytes

1. scaffold

types:

1)autogenous graft 2)allograft 3)xenograft 4) synthetic materials

Role of scaffold :   
1 - Provide physical support Barrier   
2- restrict cell migration in a selective manner   
3-Scaffold for cell migration & proliferation   
4 -Serve as time-release mechanism for signaling molecules

Why not to use scaffold alone

1)fibrous inclusion 2)problems with resorption: especially the bovine origin 3)cell adhesion

4)porosity:control is very critical

5)oxygen passage 6)vascularization

1. signaling molecules : 1)rhPDGF 2)BMPs 3)FGF-2 4)EMD 5)PRP

WHY NOT TO USE SIGNALING MOLCULES ALNOE?

1)short biological half life 2)receptor binding problems

3)stability of carrier system 4)cell adhesion : the necessity of having a surface where cells adhere to , because these molecules in order to function it needs cells that already attached

**Akizukietal,2005 :**

A study done on dog's teeth ,They did a periodontal defect with specific dimensions so it exceeds the regenerative potential of the tissue ( can't regenerate by itself ) , then they insert periodontal ligament stem cells in a shield (PDLSCs) , after certain period they took histological sections and found periodontal tissue regeneration full and functioning .

**WHY we do tissue engineering ?**

1-Dentine repair mainly 2-Tooth tissue engineering

3-Tissue engineering:A) Bone B)Cartilage C) Nerve D) Muscles

**Challenges :**

**Biological challenges :**

1-Growth factors 2-Signaling pathways

3- Root development >> very difficult and still there is areas of uncertainty about cementum and PDL formation

**Technical challenges :**

1-Culture conditions

2-Xenogenic products >> usually they use ([Fetal Bovine Serum)](https://www.google.be/url?sa=t&rct=j&q=&esrc=s&source=web&cd=6&cad=rja&uact=8&ved=0ahUKEwjX0vvlipLRAhVEiRoKHXZjCV4QFghJMAU&url=https%3A%2F%2Fwww.labome.com%2Fmethod%2FFetal-Bovine-Serum.html&usg=AFQjCNEnu79bRV3sMAuFVvdwadROpdbIBQ&bvm=bv.142059868,d.d2s)  a material from the fetus of bovine because its rich in growth factors and nutrients help to culture cells

3-Timing 4- Ideal scaffold 5-Delivery system

**Clinical challenges:**

1- Immunogenic rejection 2- Oncogenic properties

3-Functional integration >> still there is no long term studies to know its functional integration.