BHARATHIDASAN UNIVERSITY

Tiruchirappalli- 620024,
Tamil Nadu, India

Programme: M.Sc., Biomedical science

Course Title : Stem Cell Biology & Tissue Engineering

Course Code : 18BMS48C14

Unit-I

TOPIC: STEM CELLS NICHE

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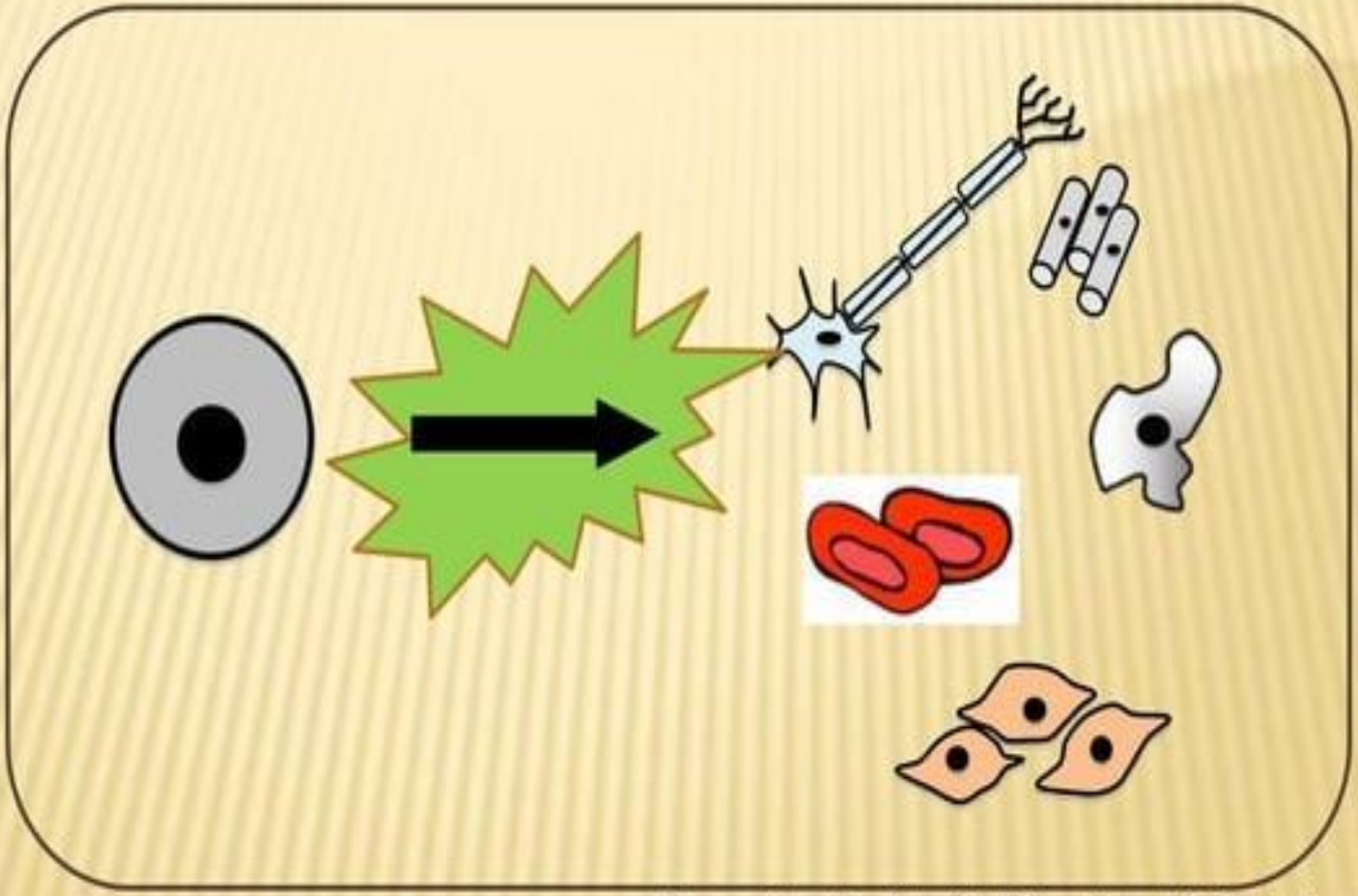
Guest lecturer
Department of Biomedical Science

OUTLINE

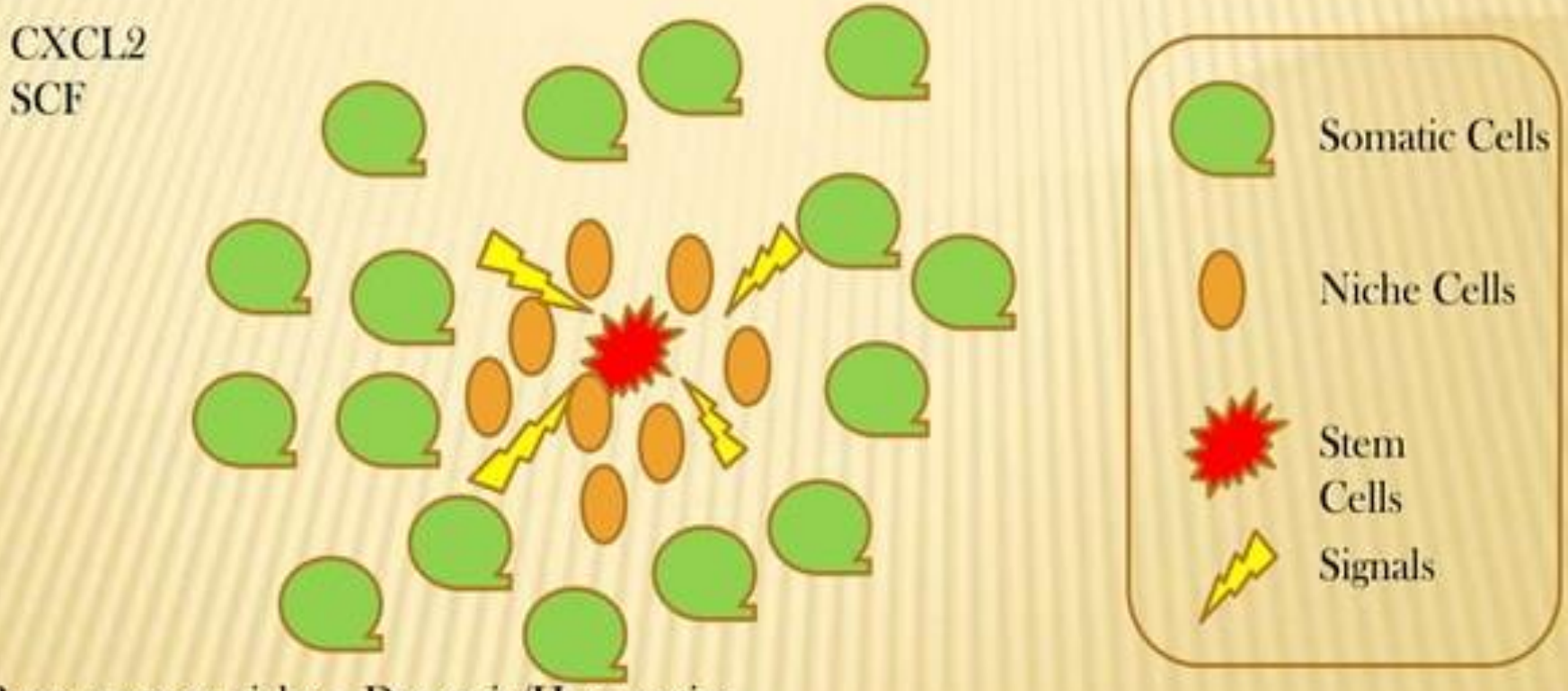
- Stem Cells
- What is Stem Cells Niche?
- Activation of Stem Cells
- Different types of niches
- Types of adhesions between stem cells and niche cells
- Signaling pathways
- Stem Cells and Therapeutic Applications



Source :What Are Stem Cells? Louisiana Life Federation

An Adult Human once a tiny cell, is a self assembling machine made of trillions of microscopic components…

WHAT IS STEM CELLS NICHE AND WHAT DOES IT CONSIST OF?



Bone marrow niche – Dynamic/Hyperactive
Neural niche – Slow reactive
Balance between quiescence and differentiation
Niche cells display a strong interaction in keeping this dynamic system functional. The communication and information play a major role in deciding the fate of the stem cells.

NICHE : WHERE STEM CELLS RESIDE, GET ACTIVATED TO DIFFERENTIATE AND PROLIFERATE?

Niches may be composed of cells, or cells together- extracellular matrix (ECM).

They may be sources of secreted or cell surface factors – including members of the Notch, Wnt, fibroblast growth factor (FGF), epidermal growth factor (EGF), transforming growth factor (TGF)-β, stem cell factor (SCF), and chemokine families – that control stem cell renewal, maintenance, and survival.

They may consist of just a single cell type, or a whole host of interacting cells.

They may derive from cells outside the stem cell's lineage, or they may derive primarily from the stem cell's own descendants.

Mof proteins
Cyclin Ds
Lamins

Components
niche cells, stem cells, differentiated cells, progenitor cells, CAM , ECM, physiochemical environment like pH, O2 tension , ionic strength (Ca^{2+} concentration), metabolite like ATP's are also important.

- Activation of stem cells

Niche Cells Activate Stem Cells

Extrinsic and Intrinsic signals

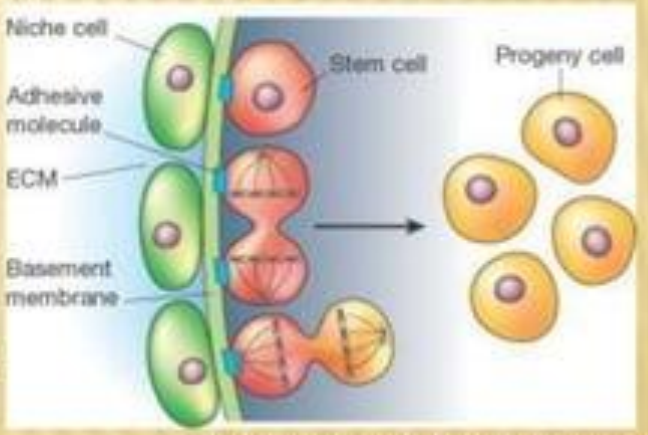
Differentiation

Apoptosis

Self Renewal

LTSC

STSC



Source: Nature, Niche structure

Self Renewal can be Symmetric or Asymmetric which is in the pool of quiescent stem cells.

in vivo studies of niche are difficult to perform in human beings

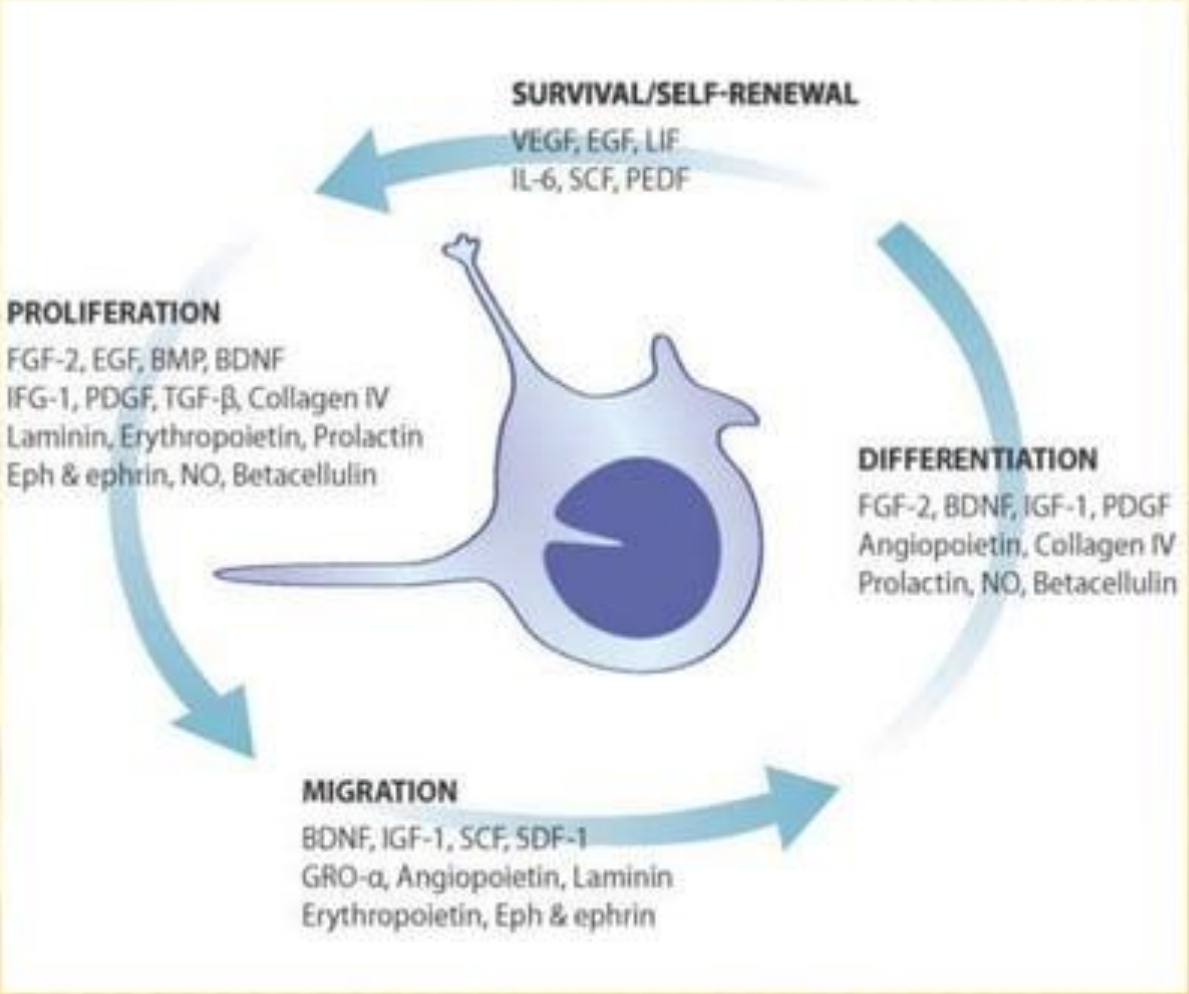
Activated stem cells go for. . .

SELF RENEWAL

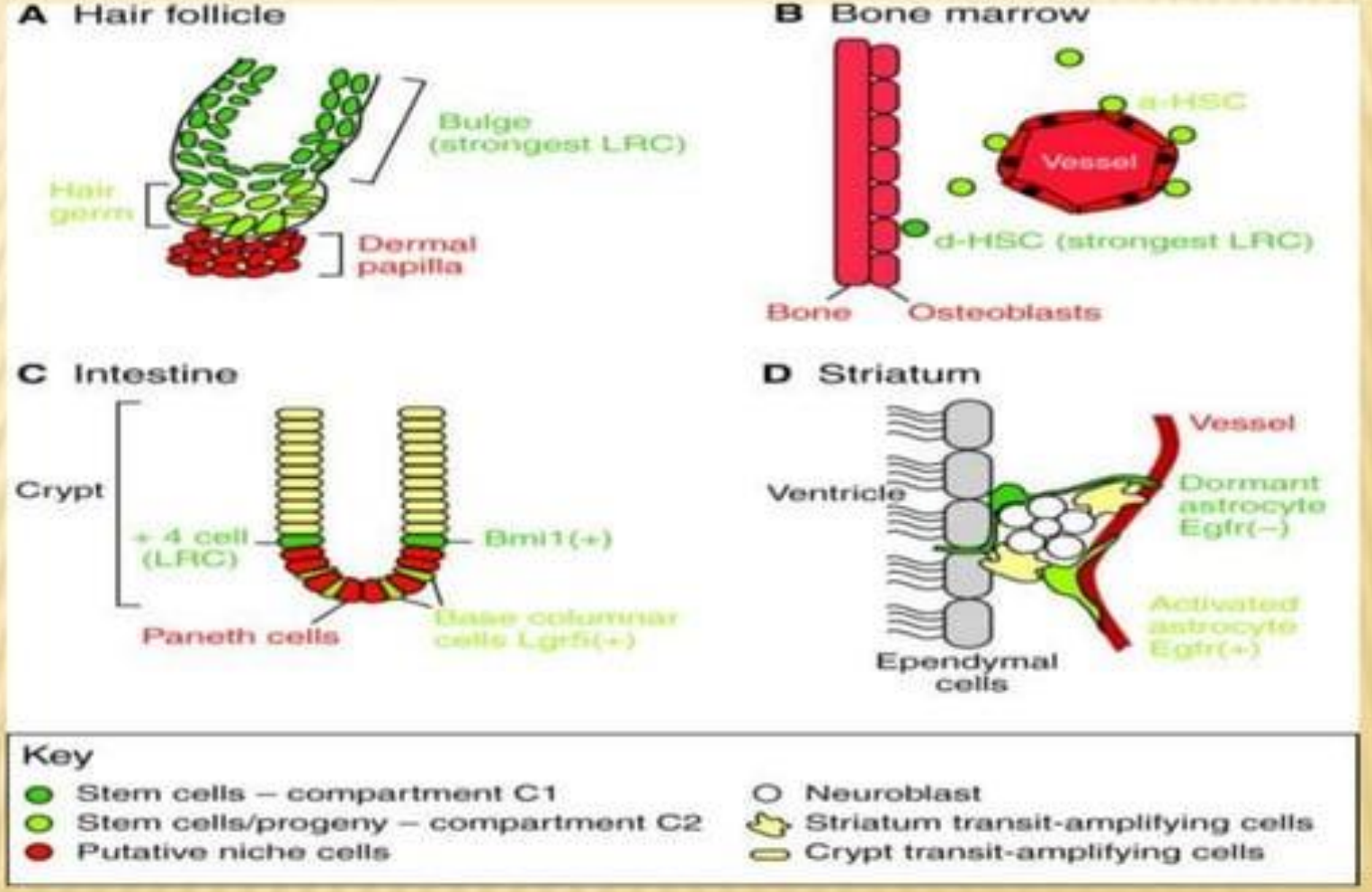
PROLIFERATION

MIGRATION

DIFFERENTIATION

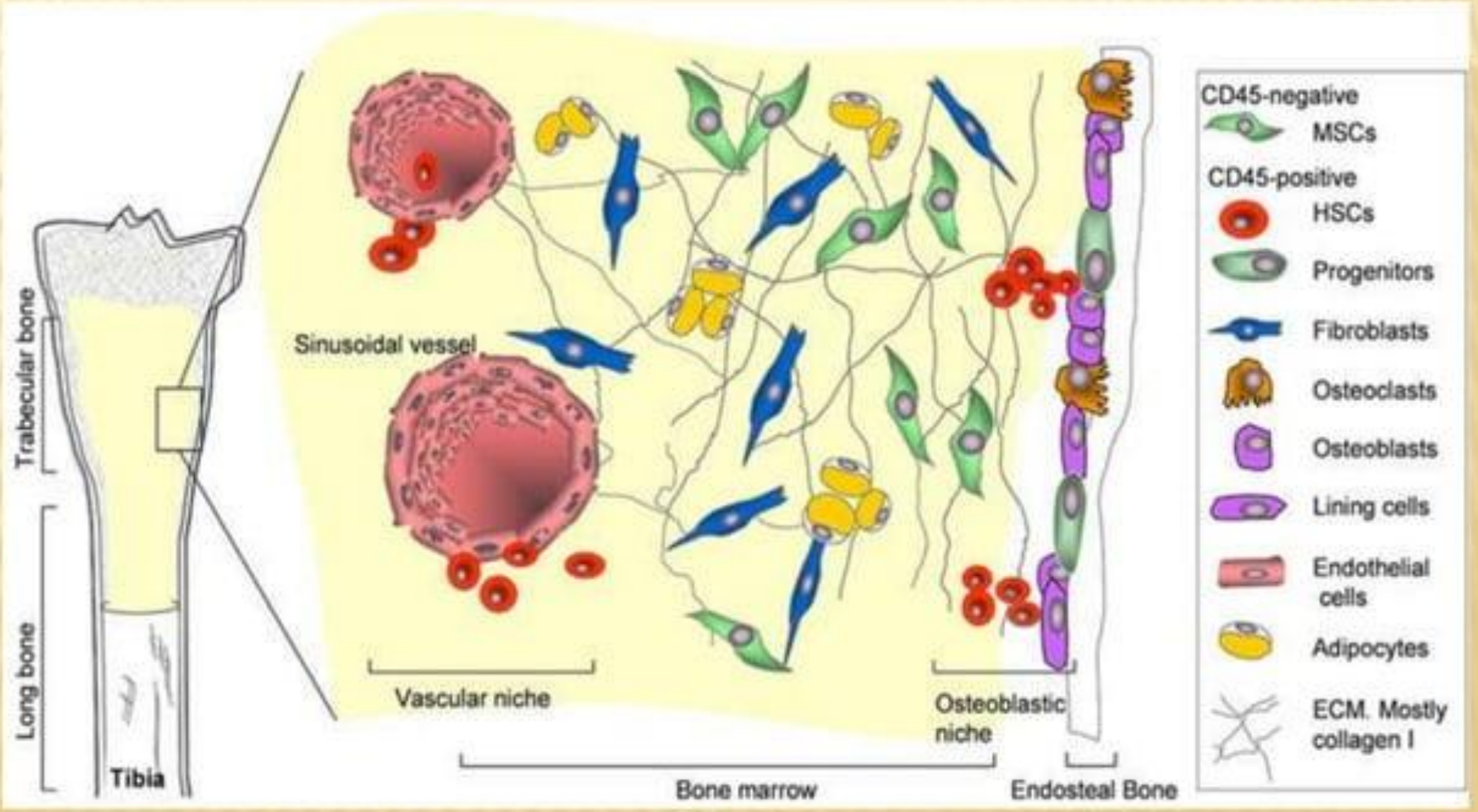


A Glance at Different Types of Niches



Source:Compartmentalized organization: a common and required feature of stem cell niches?- hypothesis by Valentina Greco Shanggin Guo

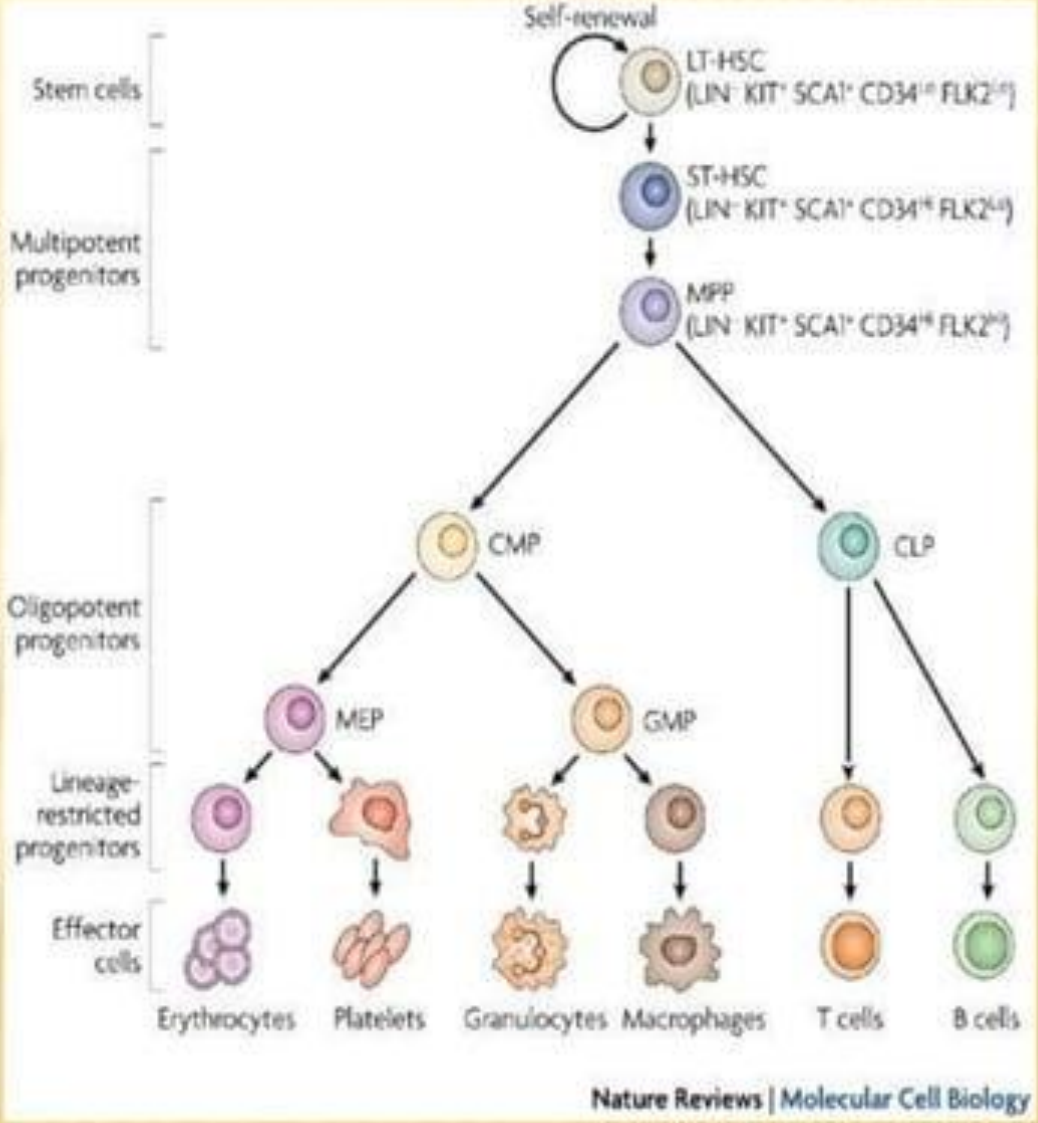
Blood Cell Niche



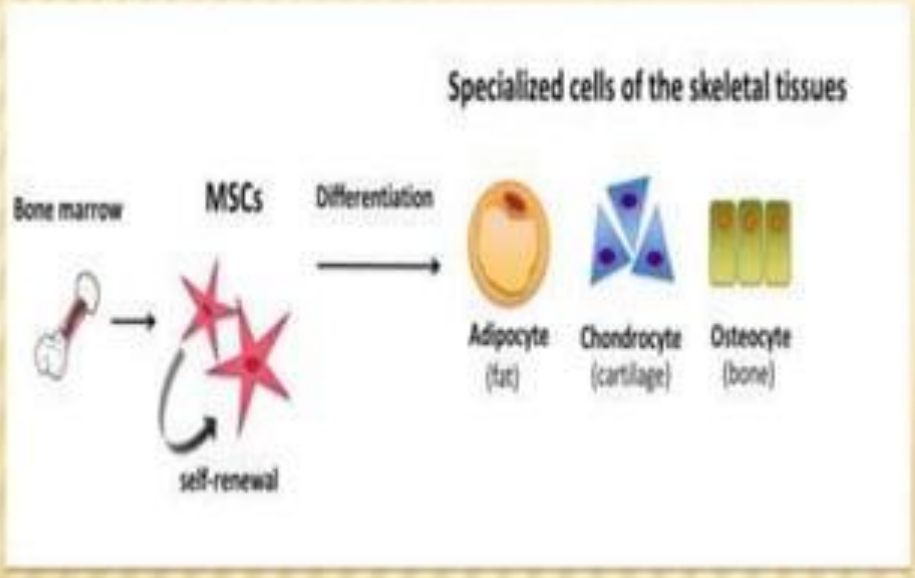
Source ; Stem cell niches,Beyond the dish

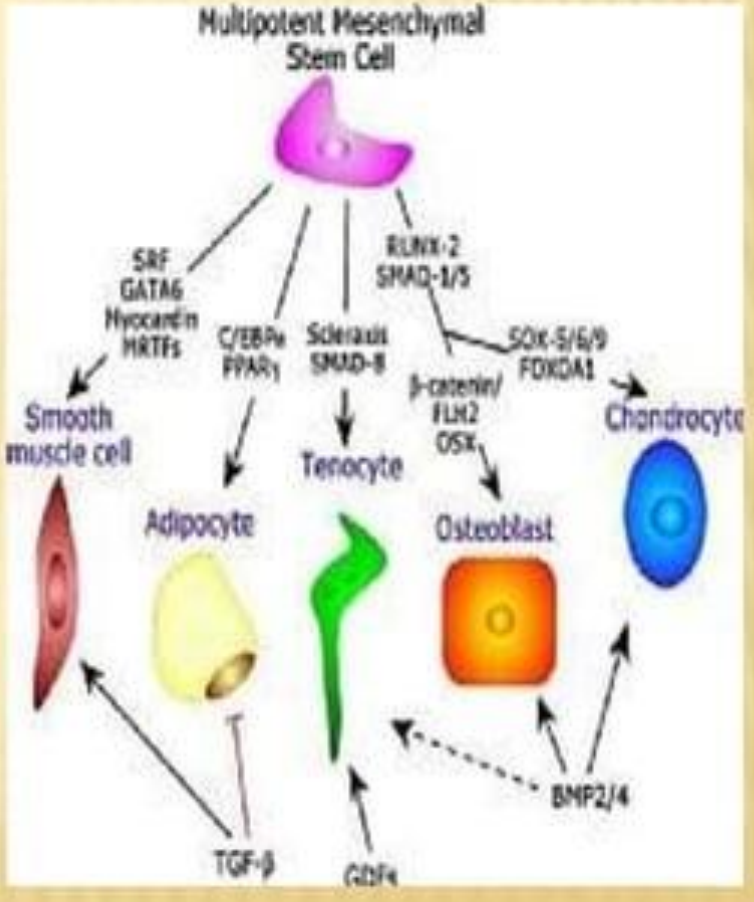
Therapeutic Applications of Hematopoietic Stem Cells

- Leukemia
- Sickle Cell Anemia
- Autoimmune disorders
- Severe aplastic disease
- Thalassemia
- Etc.



Cartilage and Bone niche





Source: Human Bone Marrow Mesenchymal Stem Cells: A Systematic Reappraisal Via the Genostem Experience

Stem Cell Treatment in Orthopedic Conditions

Stem cells to treat ;

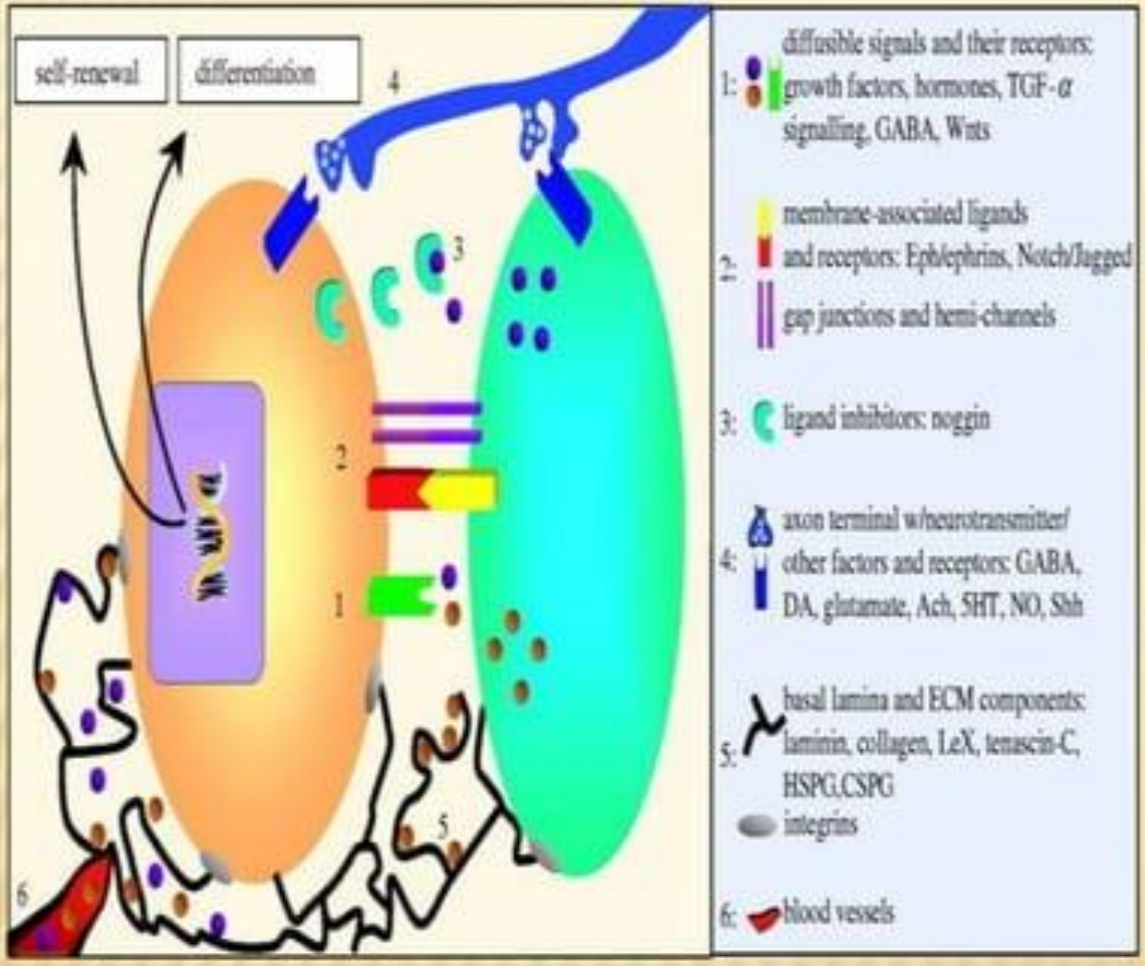
- AVN
- Osteoarthritis
- Ankylosing Spondylitis
- Bone fracture
- Sports injury
- Etc.

Fig: Case report of a 45 year old man, treated for AVN-

Radiological findings: Restoration of Joint space to near normalcy, articular surface was well defined, subarticular geodes had disappeared with signs of new cartilage formation.

Source: case study at StemRx Bioscience Solutions Pvt. Ltd

Neural Stem Cells Niche



Stem Cells can treat :

- Parkinson's disease
- Alzheimer's disease
- Neural disorder syndrome
- CVA
- Cord injuries
- Cerebral palsy
- And many more..

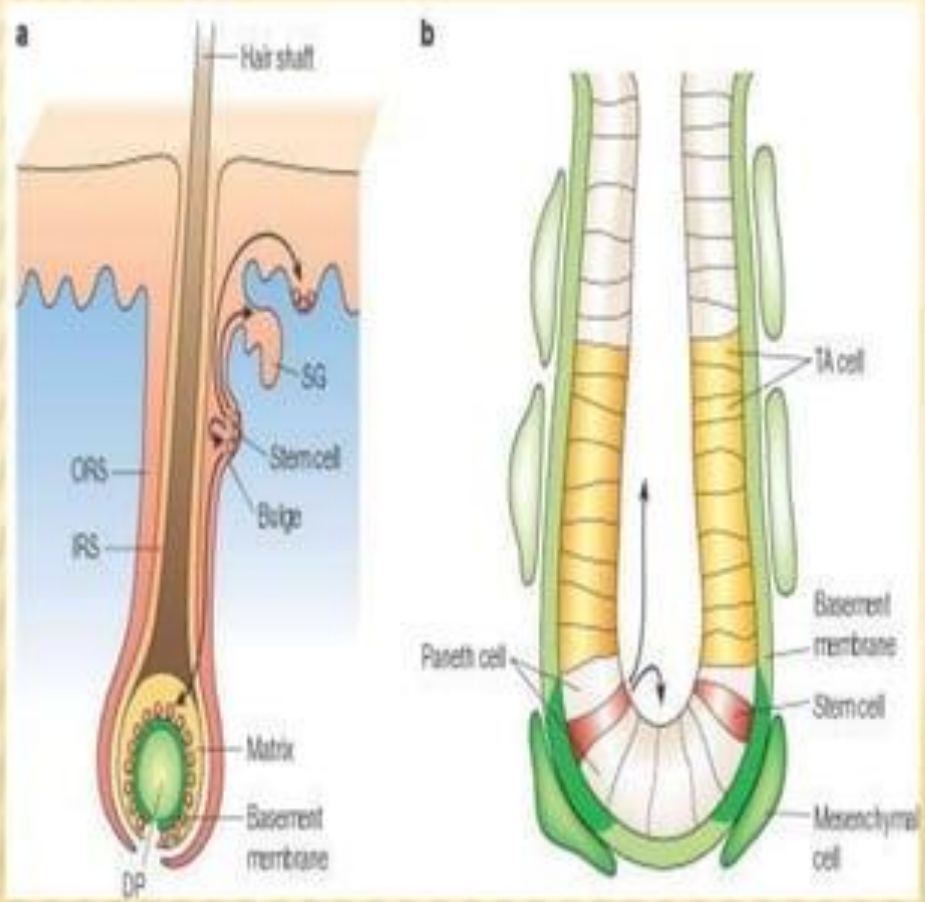
Traditional thought - Neurons cannot multiply,
Modern research – Neurons can be cultured and multiplied

Source;Human Bone Marrow Mesenchymal Stem Cells: A Systematic Reappraisal Via the Genostem Experience

CASE STUDY

TESTIMONIAL - AFTER TREATMENT

Skin and Hair niche



Stem Cells to treat :

- Alopecia Universalis
- Alopecia areta
- Hair fall
- Skin burns
- Leucoderma
- Vitiligo
- Antiaging

Source: Nature, epithelial stem cell niches

Stem Cells to cure blindness

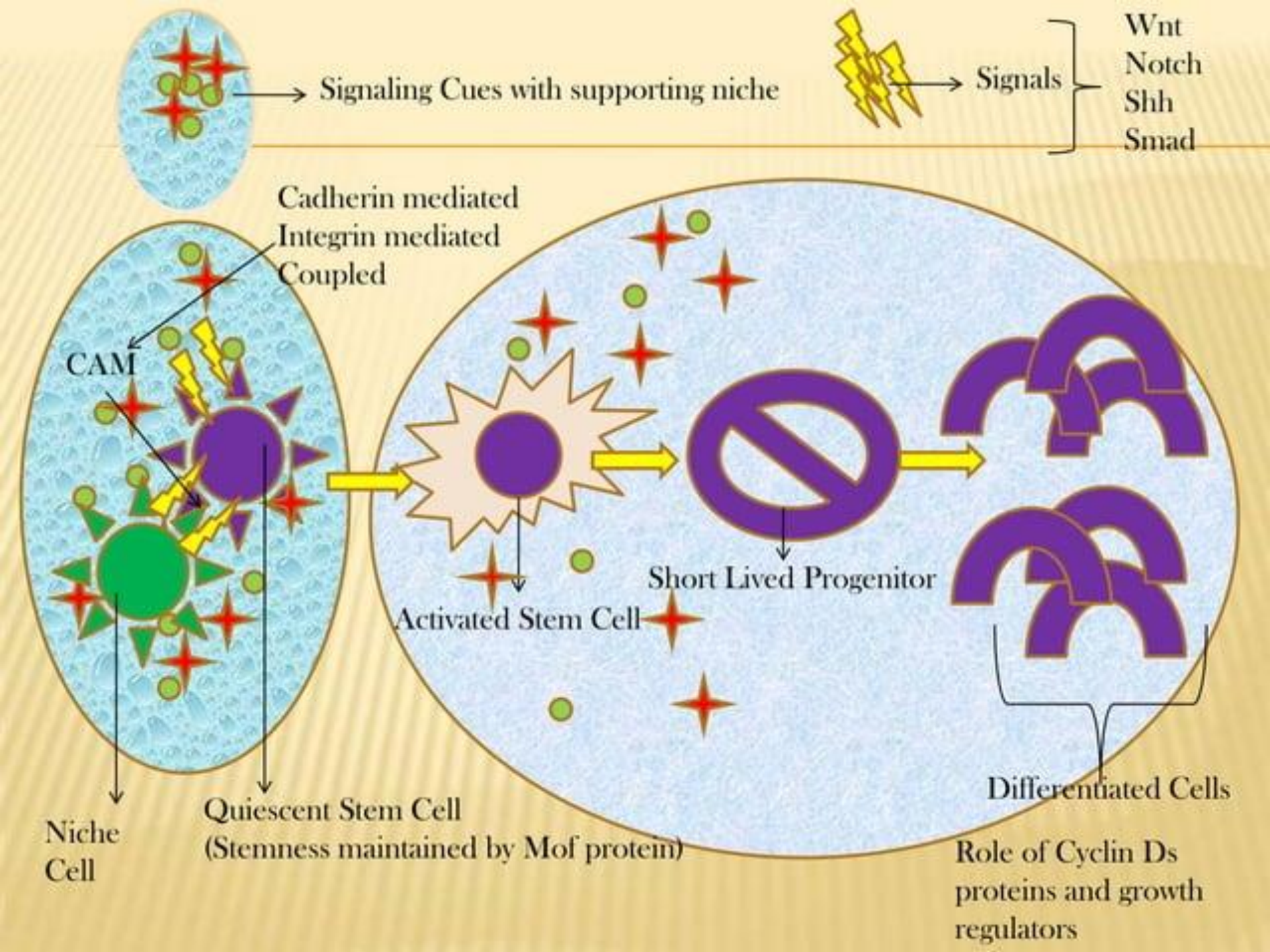
Stem cells can treat:

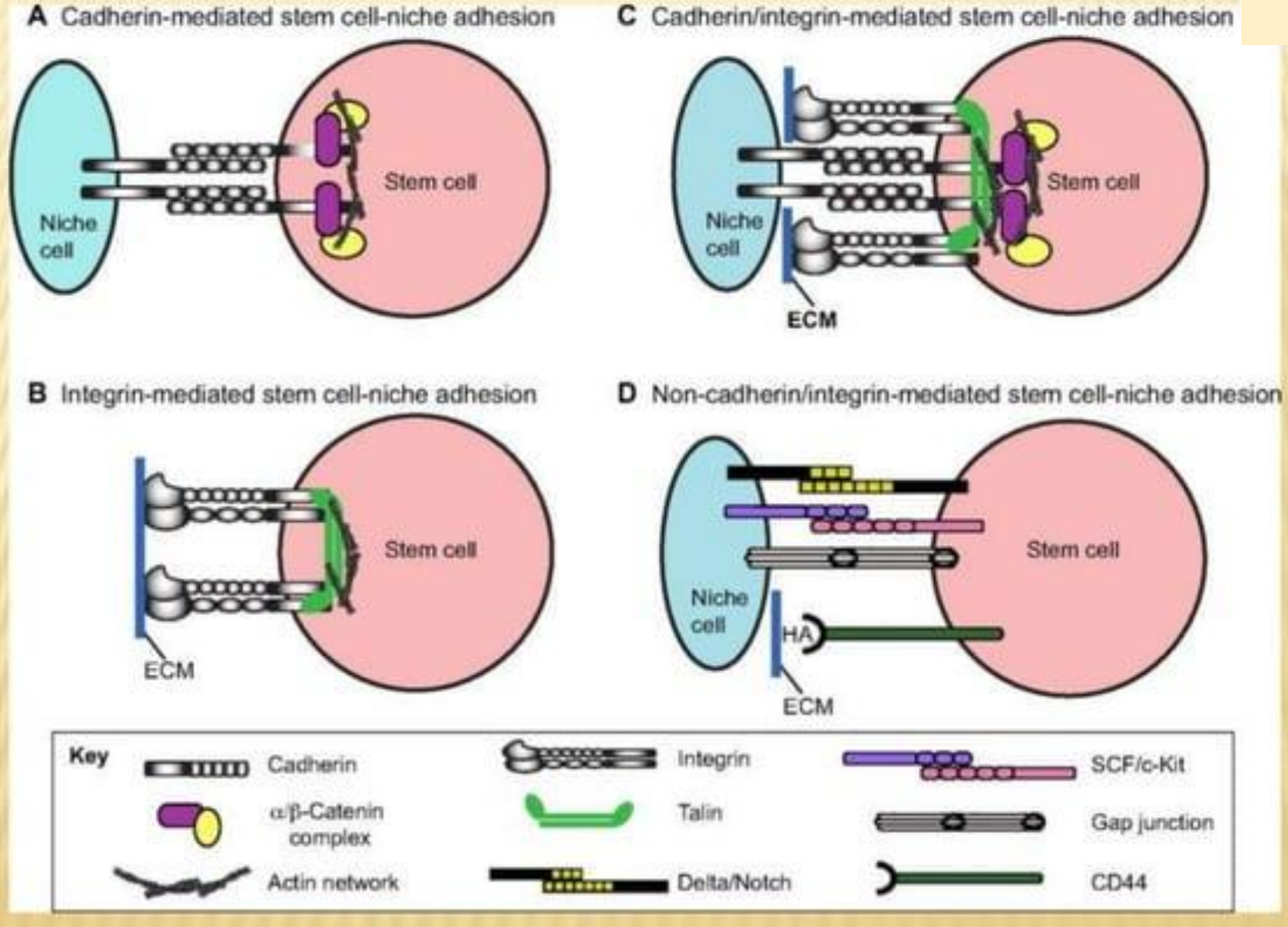
- Diabetic Retinopathy
- Ocular burns
- Optic nerve atrophy
- Corneal injuries
- Macular Degeneration
- Retinitis Pigmentosa
- Etc.

Stem cells were taken from the limbus in the patient's own eye, cultured, and then grafted back on the eye. The grafts had a success rate of 76.6% – leading to restored or improved vision.

Stem Cell Treatment in Many More as . . .

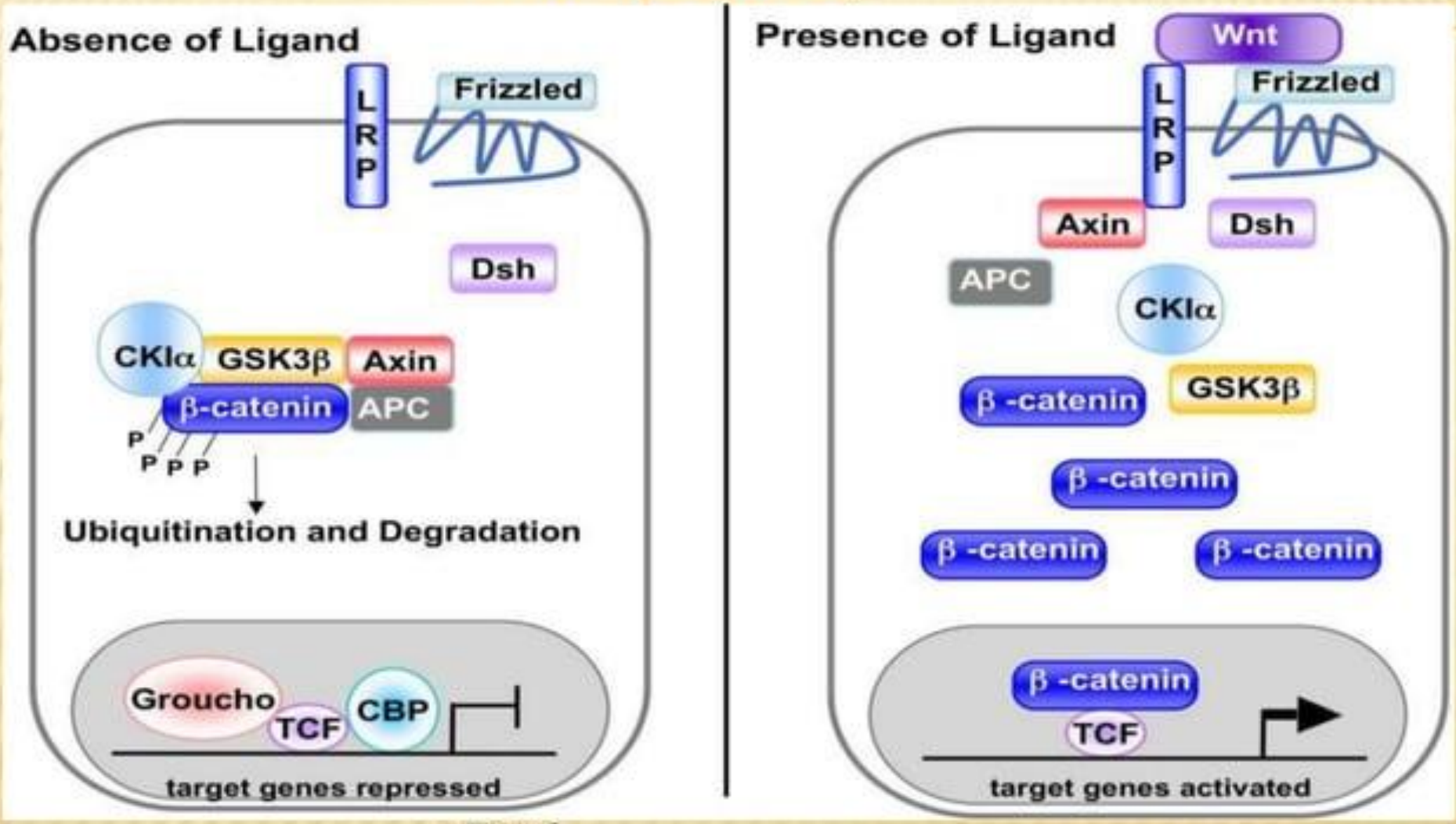
- Diabetes
- Erectile Dysfunction
- Cardiac disorders


Signaling Cues with supporting niche
Signals
Wnt
Notch
Shh
Smad
Cadherin mediated
Integrin mediated
Coupled
CAM
Short Lived Progenitor
Activated Stem Cell
Differentiated Cells
Niche
Cell
Quiescent Stem Cell
(Stemness maintained by Mof protein)
Role of Cyclin Ds
proteins and growth
regulators



Source ; Review Adhesion in the stem cell niche: biological roles and regulation

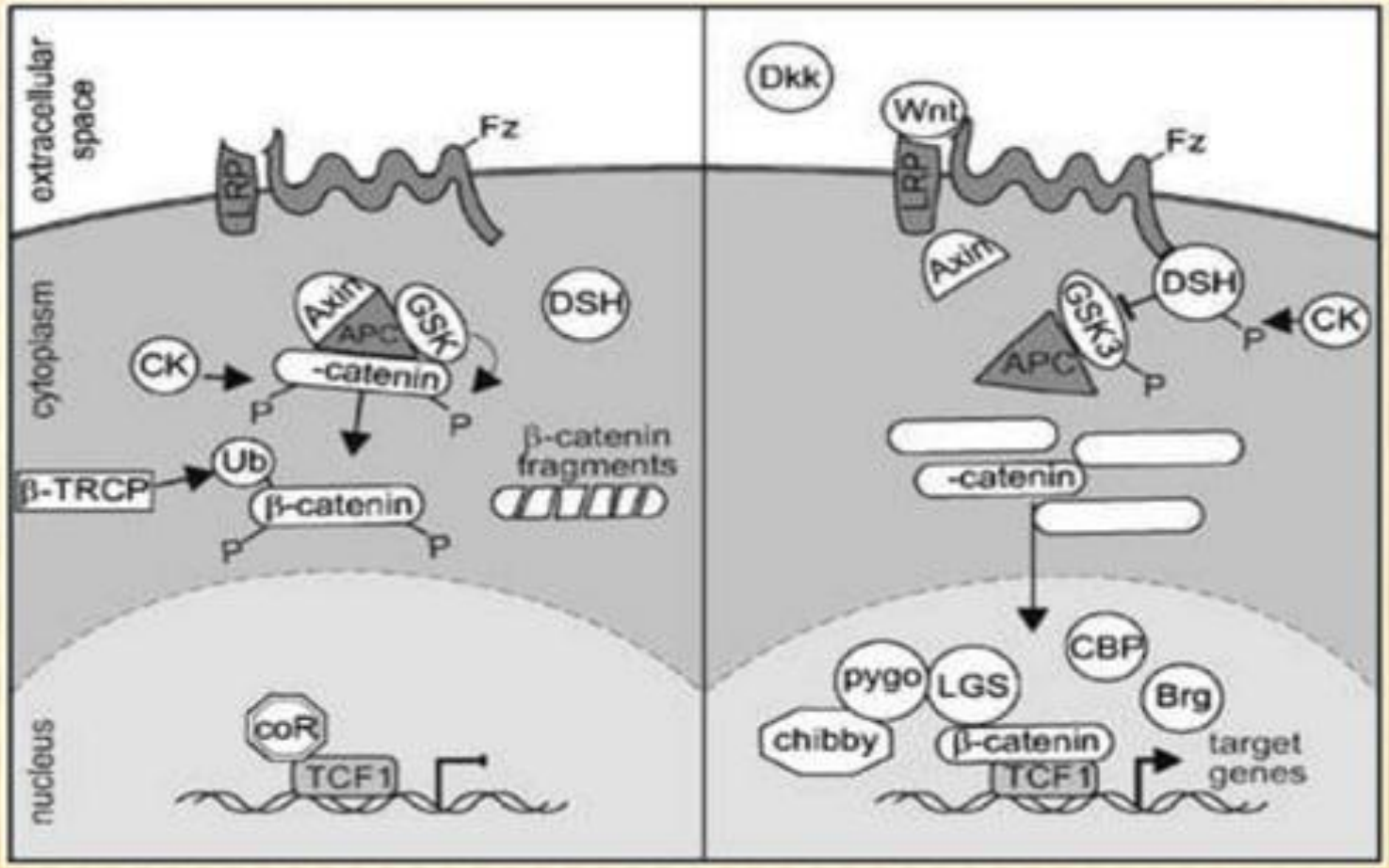
Wnt pathway



HSC-Self renewal → Foetal
HSC-Self renewal → Adult

Source : Wnt signaling-David M. Eisenmann-Department of Biological Sciences, University of Maryland Baltimore County

Notch Pathway



Differentiation
Into T cells

Delta/Jagged ligand ⟹ Haematopoietic progenitors

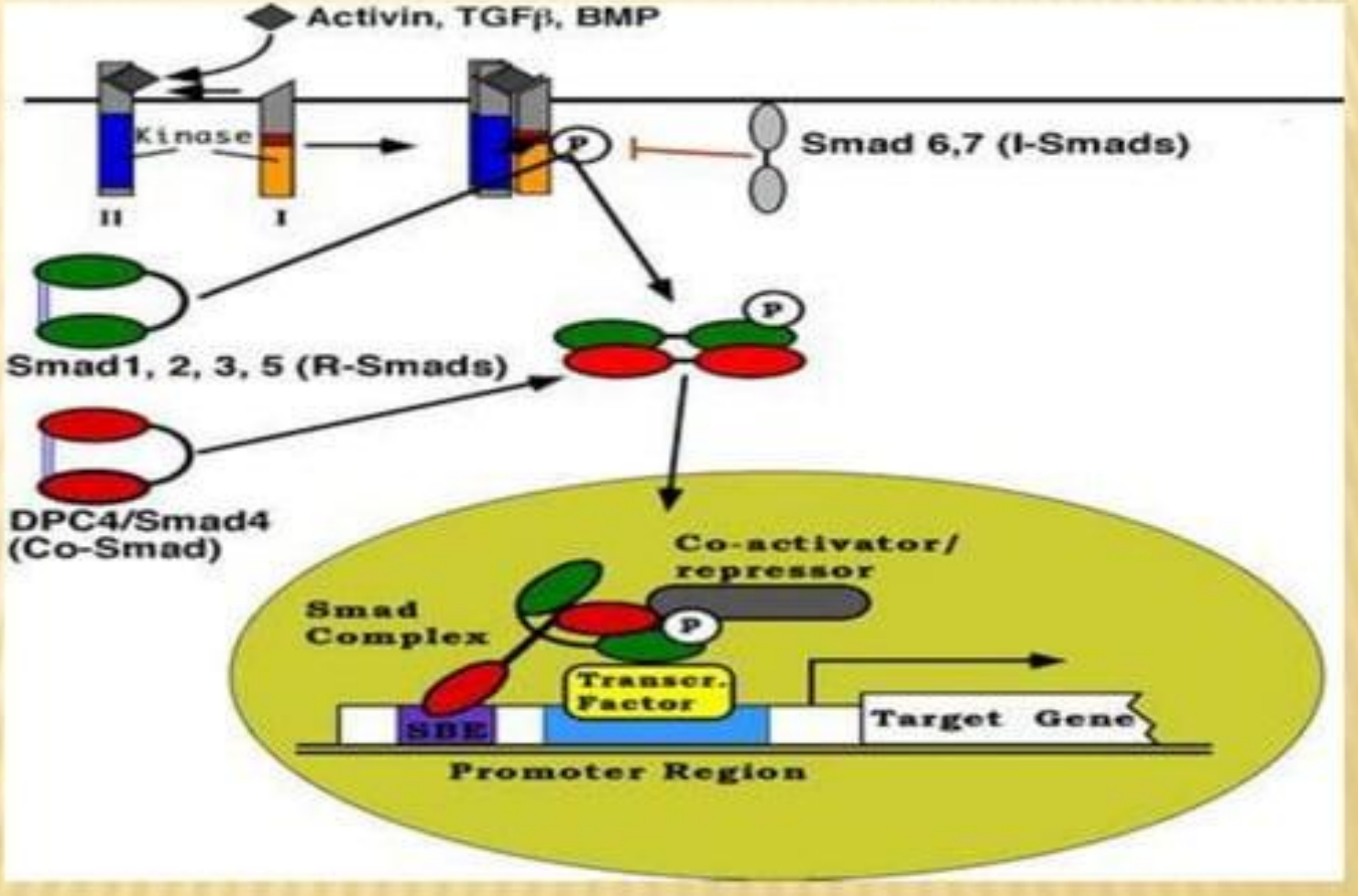
Osteoblasts and HSCs

Source ; Notch signaling: mediator and therapeutic target of bone metastasis byNilay Sethi & Yibin Kan

Smad Signaling Pathway

TGF-inhibitory
BMP-promoter

Regulation
of
HSC fate



All pathways participate in a cascade synergistically

Source; Ruhr-Universitat Bochum Department of Molecular Gi-oncology Stephan Hahn, M.D.

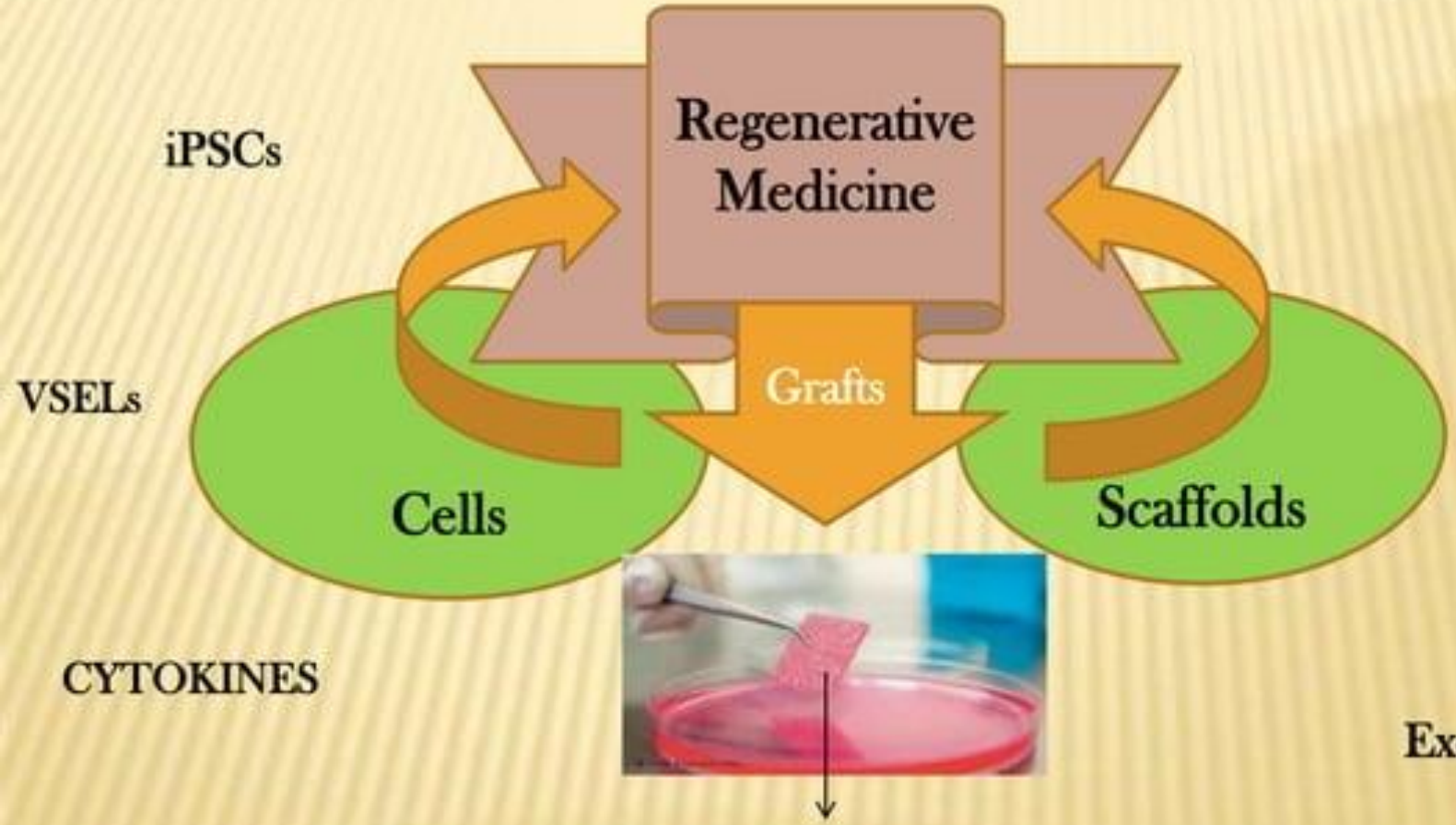
PARADIGM SHIFT FROM TRADITIONAL TO CELLULAR MEDICINE

Research

Traditional Medicine

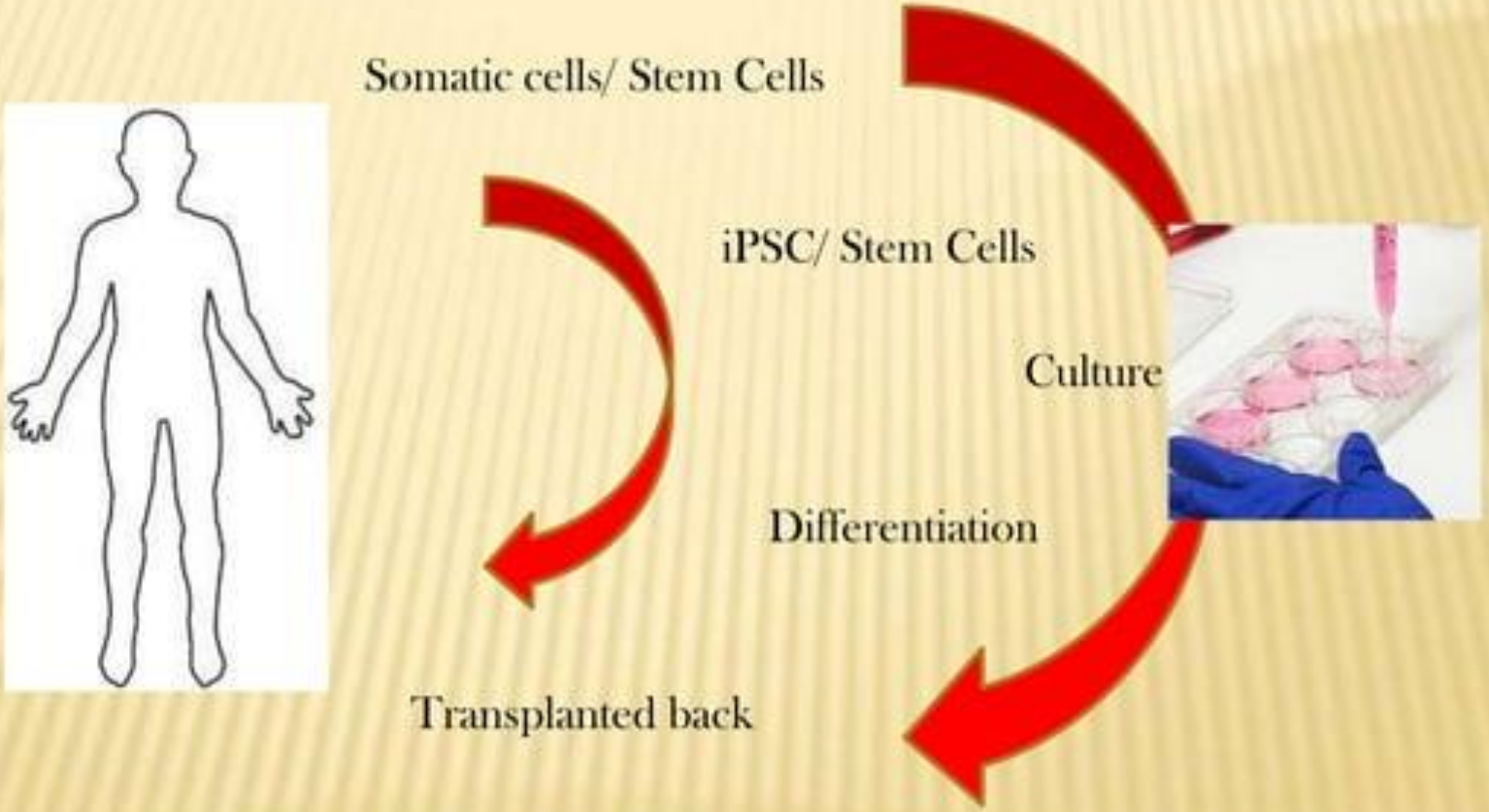
Cellular Medicine

FUTURE MEDICINE



Bioengineering and repair of the damaged tissue with the help of cells in scaffolds

DRUG DISCOVERY IN A DISH



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- **Linheng Li, Ting Xie. 2005. Stem cell niche: structure and function Annu Rev Cell Dev Biol. 21:605-31.**

- **Stem Cells in Regenerative Medicine, Science, Regulation and Business Strategies, Alain A. Vertes, Arnold I. Caplan, Lee E. Babiss, Nasib Qureshi, 2015. Wiley.**

THANK YOU