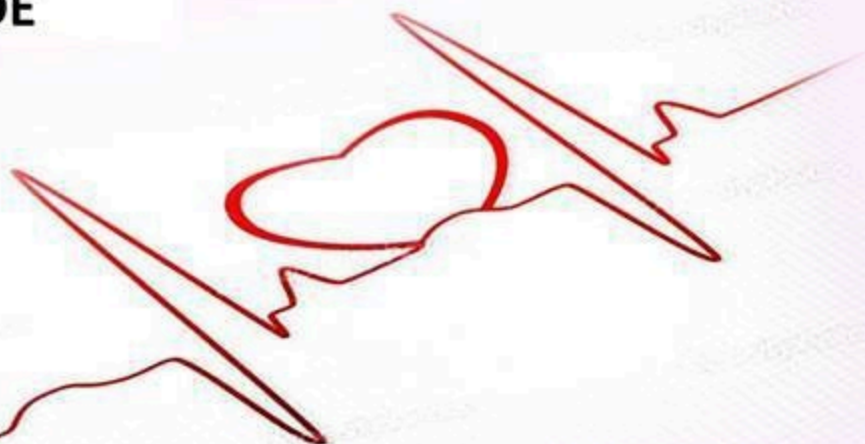


SHEET



SLIDE



Slide :

11



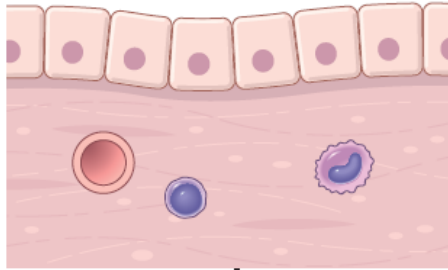
Doctor: Mazen Al-Salhi





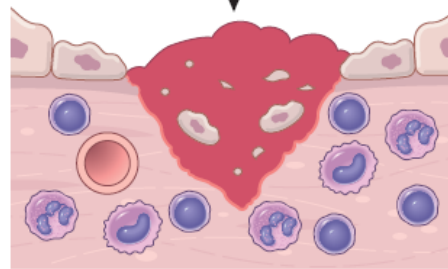
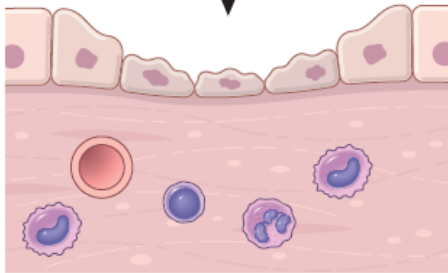
Tissue Repair

NORMAL



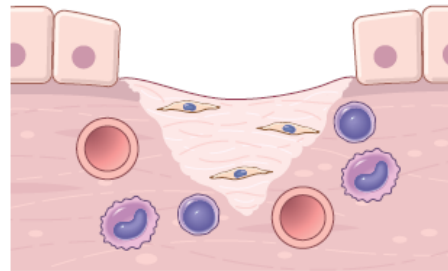
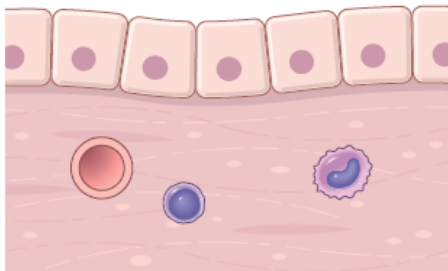
Mild, superficial injury

Severe injury



REGENERATION

SCAR FORMATION



Repair/Healing

Restoration of tissue architecture & function

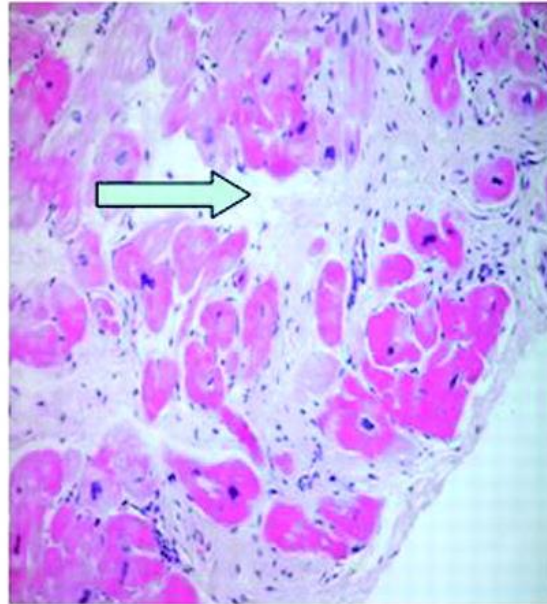
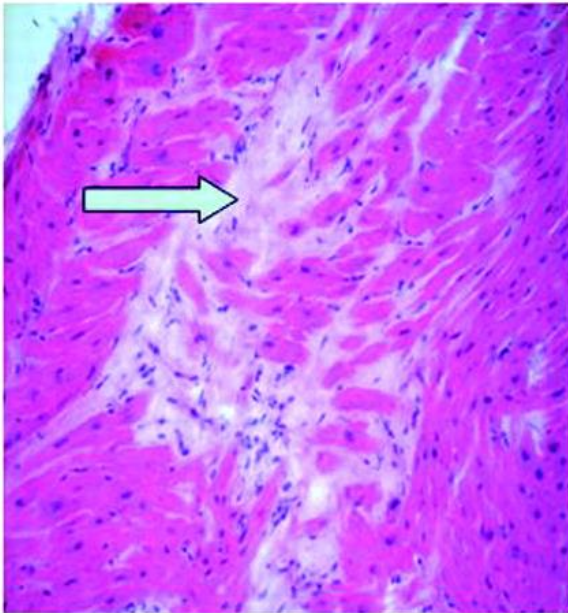
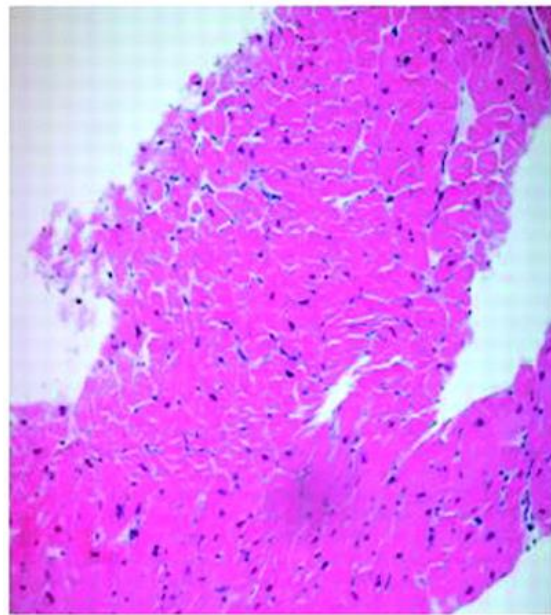
Regeneration:

- Same cell replacement
- Proliferative ability
- Function maintained
- Architecture restored

Scar formation:

- Fibrous tissue (CT) replacement
- Potential loss of function
- Architecture somewhat restored

Cardiac biopsies showing fibrosis



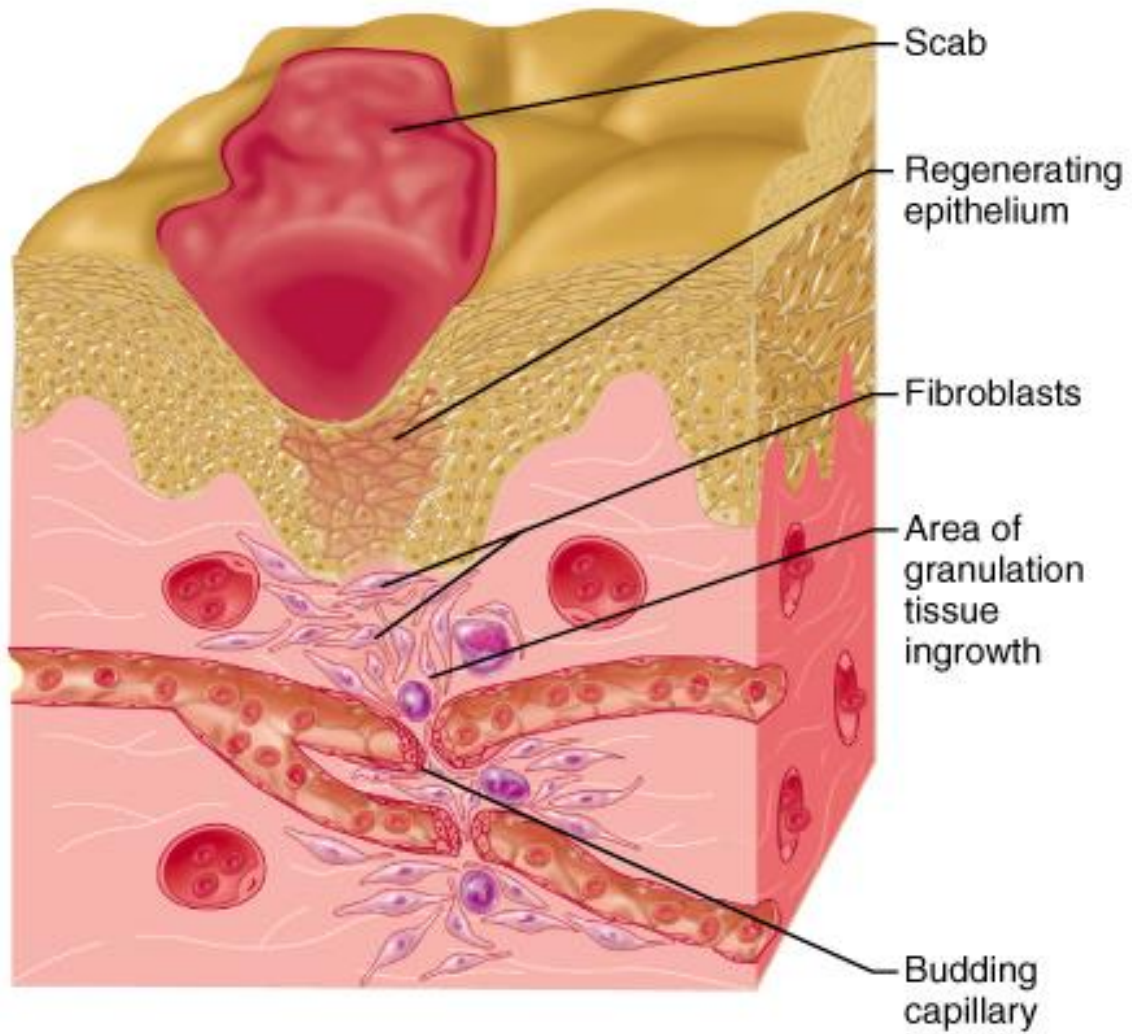
Fibrosis

Extensive deposition of collagen in organs (e.g. liver, lung, kidney, heart)

- Idiopathic
- Chronic inflammation
- MI

Deposition in a tissue space containing inflammatory exudate = organization



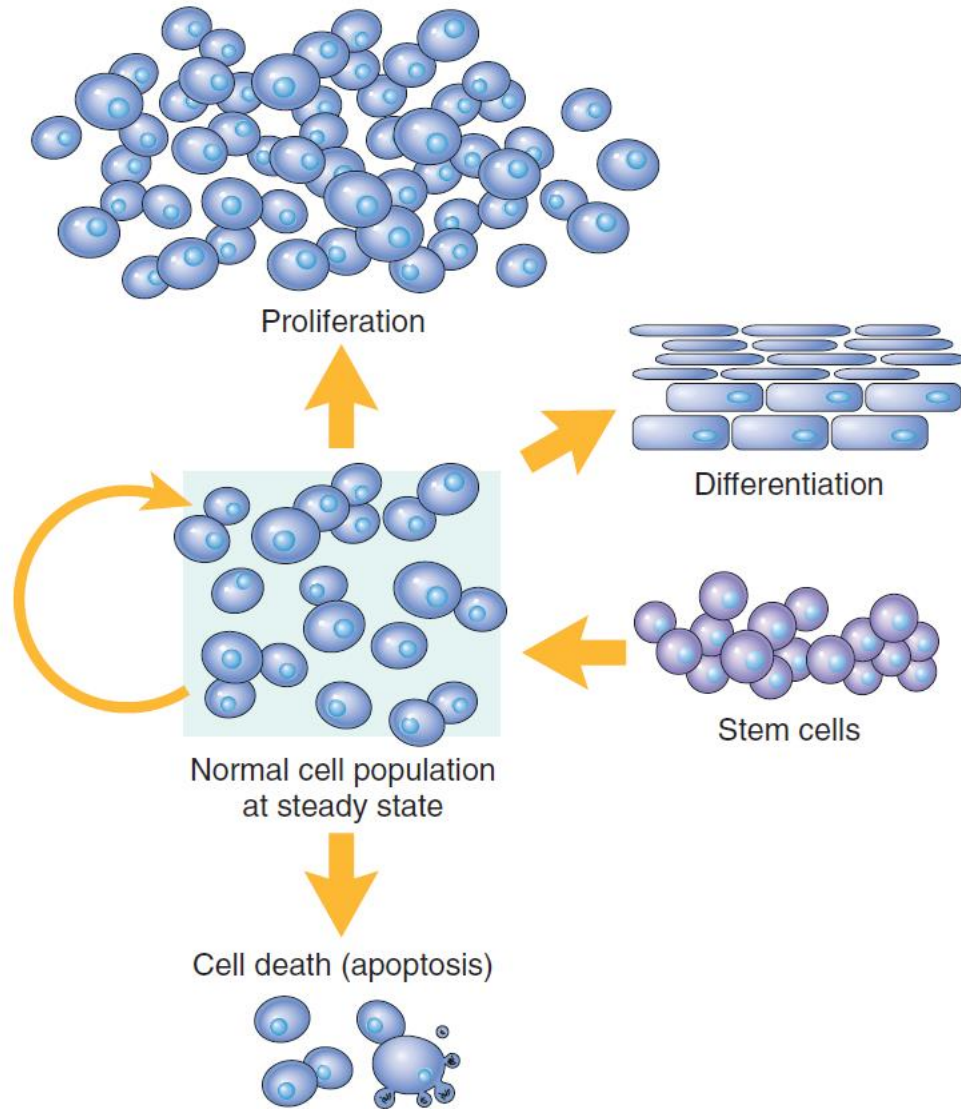


Requirements

1. Cell proliferation
2. Interaction with the ECM



Cell proliferation



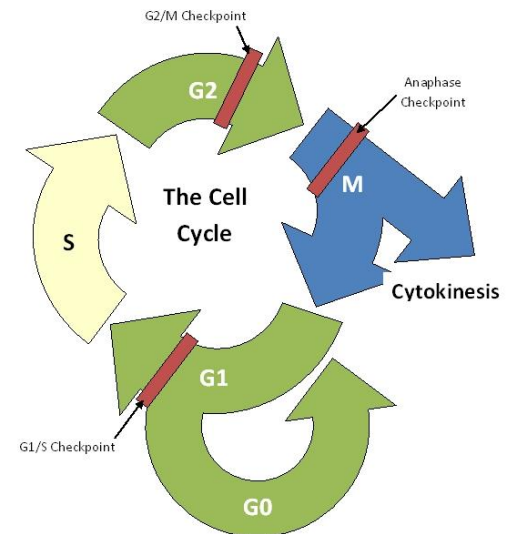
Proliferation control

Cell cycle control

Response to growth factors

Differentiation

Apoptosis



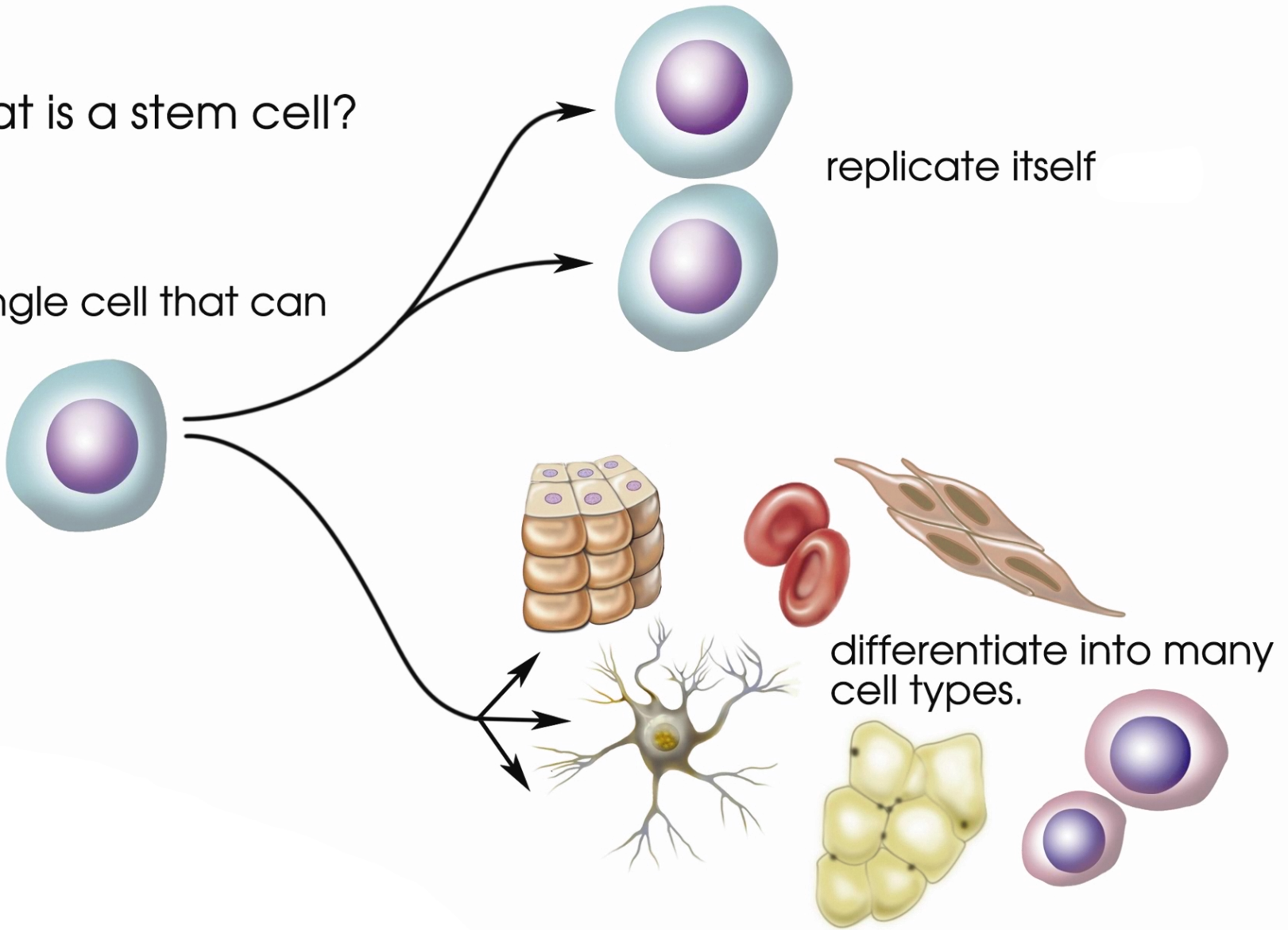
Proliferation capacity

Tissue	Characteristics	Examples	%distribution
Labile	<ul style="list-style-type: none"> Continuously dividing mature & stem cells Can regenerate if stem cells are intact 	<ul style="list-style-type: none"> BM Surface epithelia 	
Stable	<ul style="list-style-type: none"> Quiescent Minimal replicative activity normally Capable of proliferating if/when needed Limited regeneration capacity* 	<ul style="list-style-type: none"> Solid tissue parenchyma* Endothelium Fibroblasts Smooth Muscles 	
Permanent	<ul style="list-style-type: none"> Terminally differentiated and non-proliferative Limited stem cell replication and differentiation = no regeneration 	<ul style="list-style-type: none"> Neurons Cardiac & skeletal muscle 	



What is a stem cell?

A single cell that can

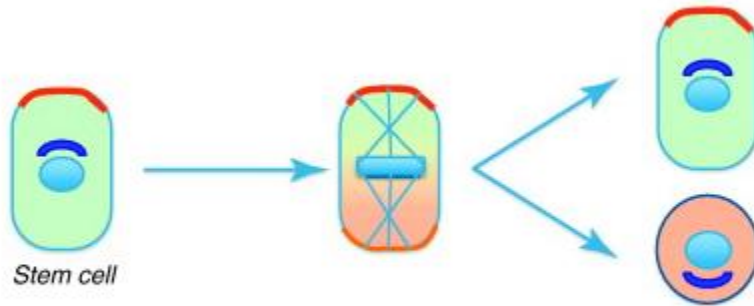


replicate itself

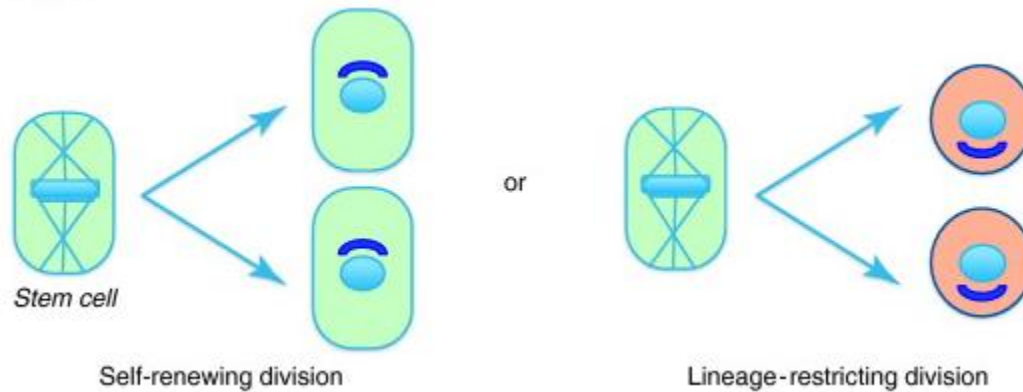
differentiate into many cell types.



(a) Asymmetric division



(b) Symmetric division



Stem cells

- Self Renewal
- Asymmetric replication

2 types:

Embryonic

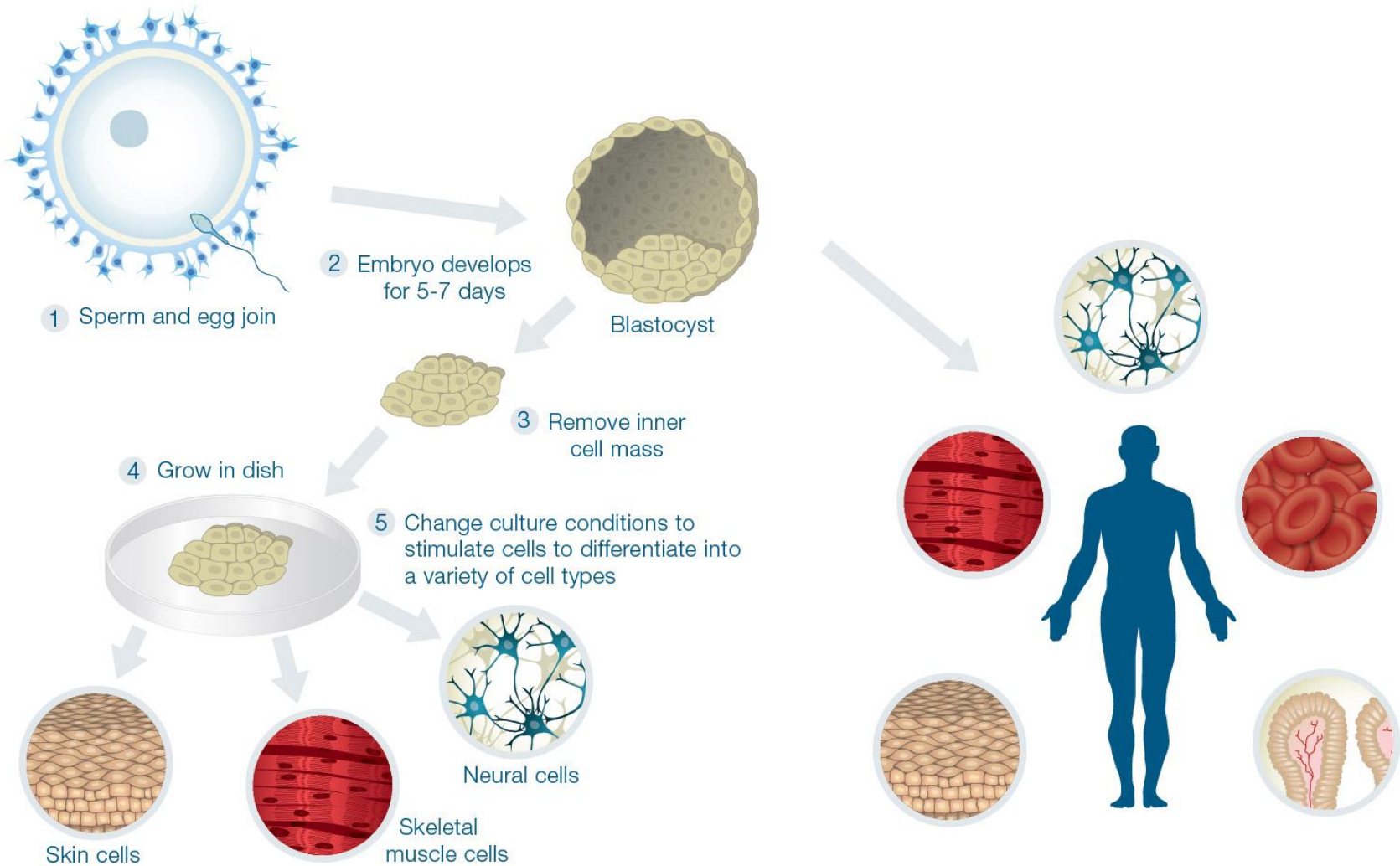
- Self renewal
- Unlimited differentiation
- Organism creation

Adult/Tissue

- Limited self renewal
- Limited differentiation
- Tissue homeostasis



Embryonic stem cells



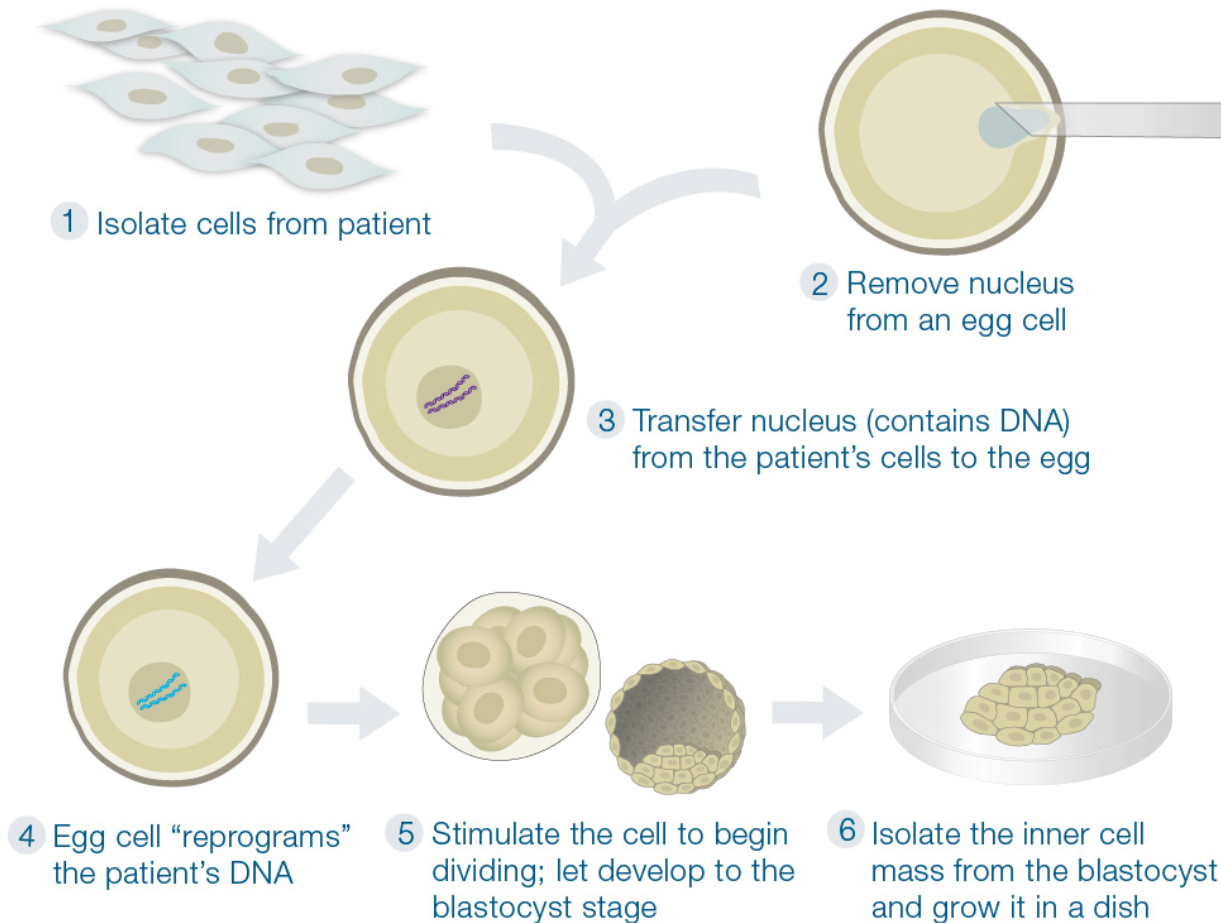
Pitfalls & Ethics of ES use

Graft rejection

Embryo destruction



Creating **ES cells** through therapeutic cloning (somatic cell nuclear transfer)



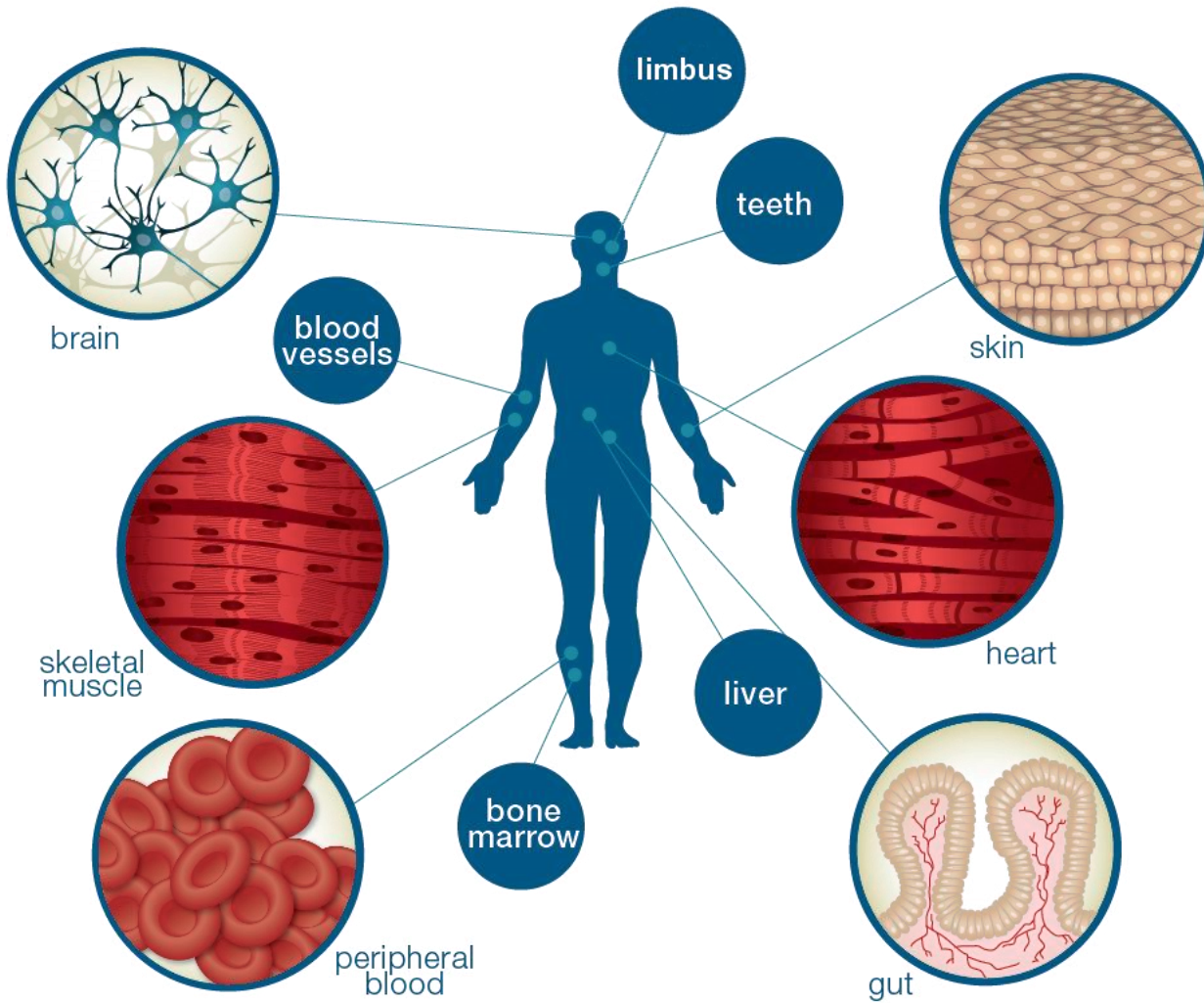
Therapeutic cloning

No graft rejection

Time consuming,
inefficient, and expensive

Achieved in 2013

Ethical considerations?



Tissue stem cells

Therapeutic potential without graft rejection

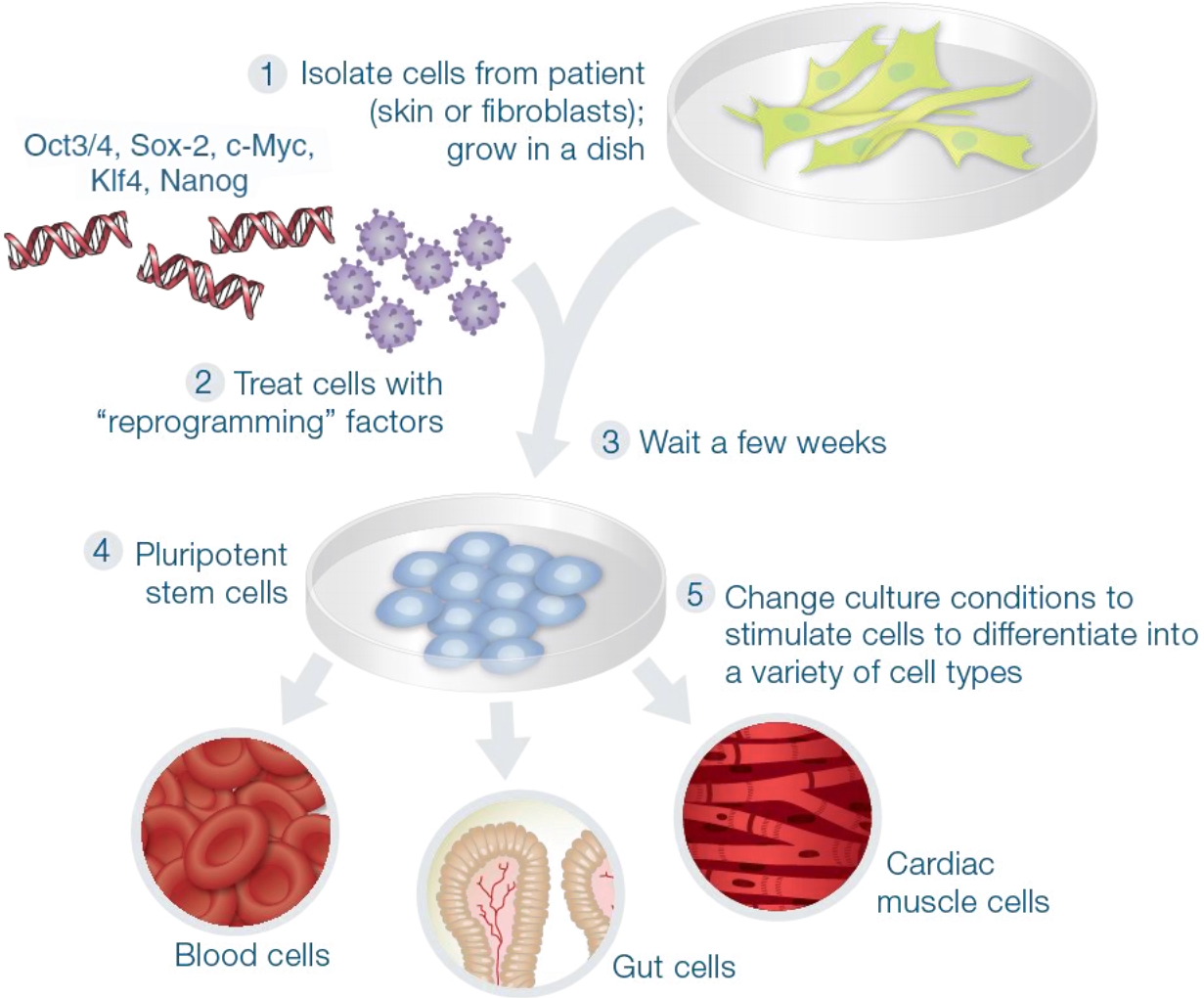
Rare and very difficult to isolate to purity

Bone marrow hematopoietic stem cells although rare can be purified and are used in certain leukemias, lymphomas

Bone marrow mesenchymal stem cells differentiate into chondroblasts, osteoblasts, and myoblasts



Creating **iPS** cells



Regenerative medicine

Reprogramming factors = genes critical for "stem-cell-ness"

No graft rejection

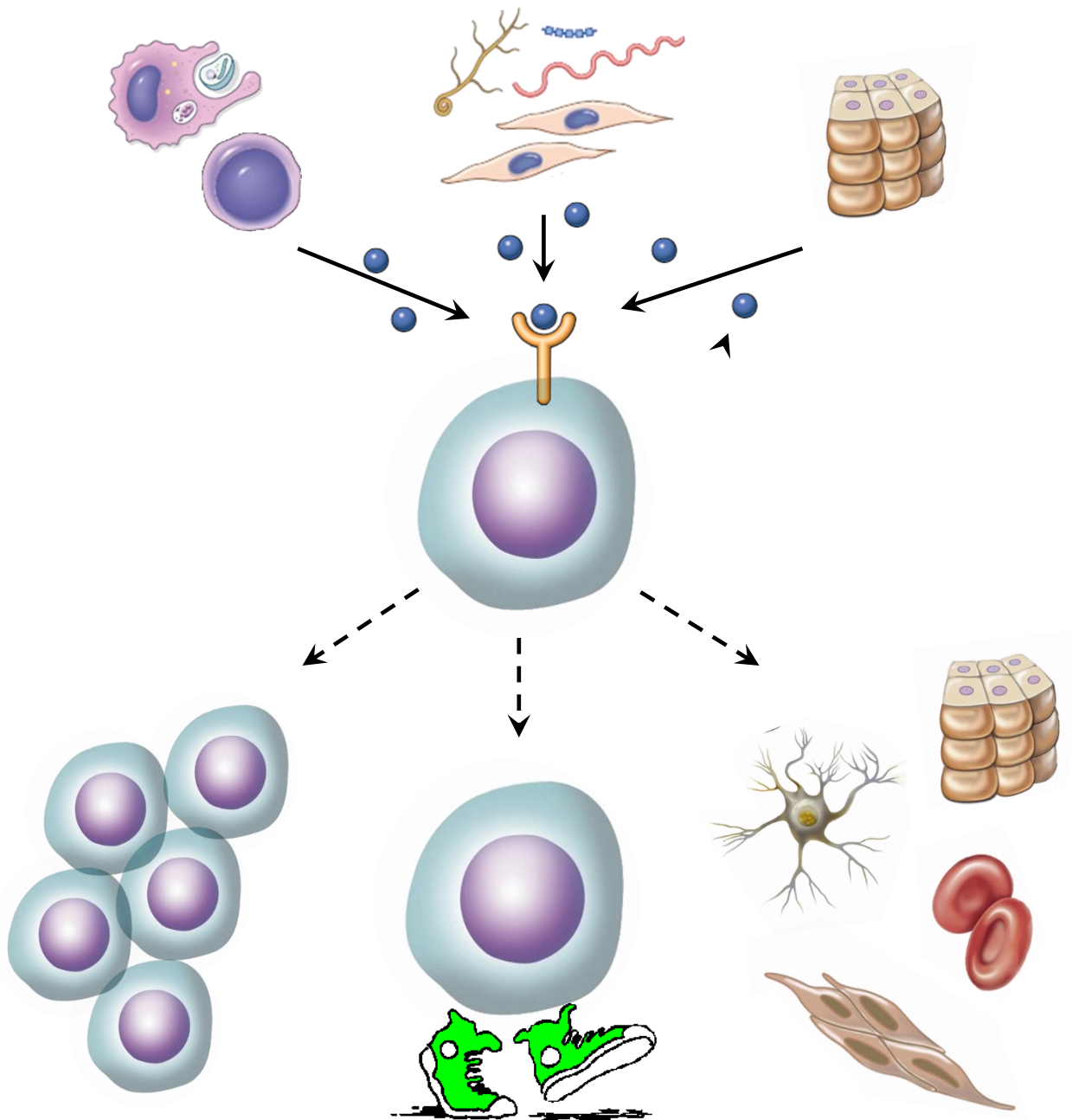
Cheaper and quicker than therapeutic cloning

Due to the genetic modifications during reprogramming the safety of using iPS cells in patients is uncertain

Still in research



Cell proliferation - Growth factors



Growth factors

Mostly proteins from:

- Lymphocytes
- Macrophage
- Stromal cells
- Parenchymal cells

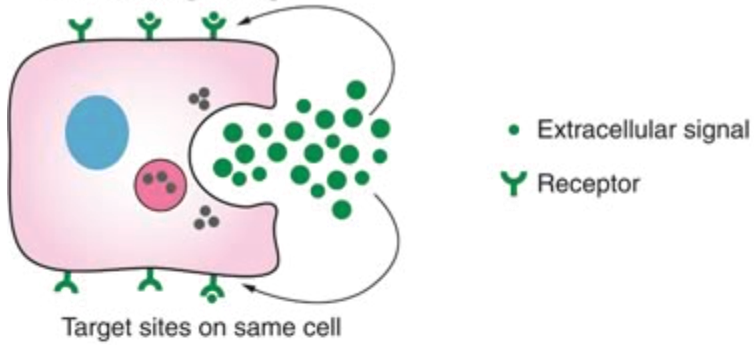
Induce cells to:

- Survive/Proliferate
- Migrate
- Differentiate

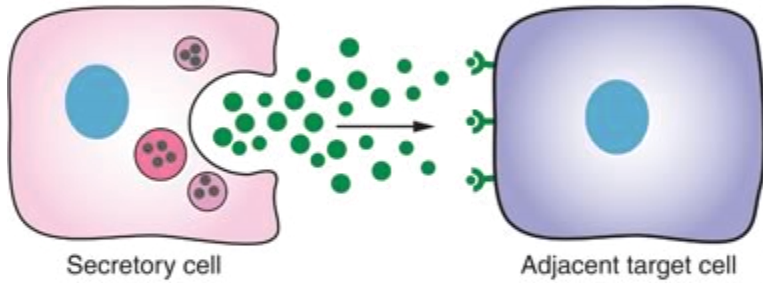
Induce proliferation through gene expression:

- Promote cell cycle entry
- Relieve cell cycle blocks
- Inhibit apoptosis
- Protein production ↑

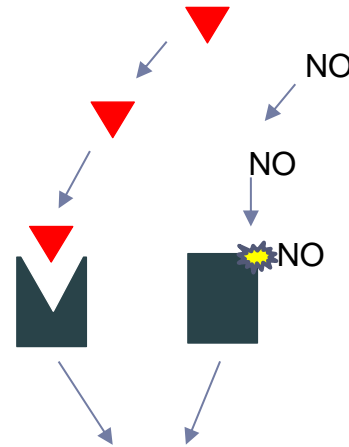
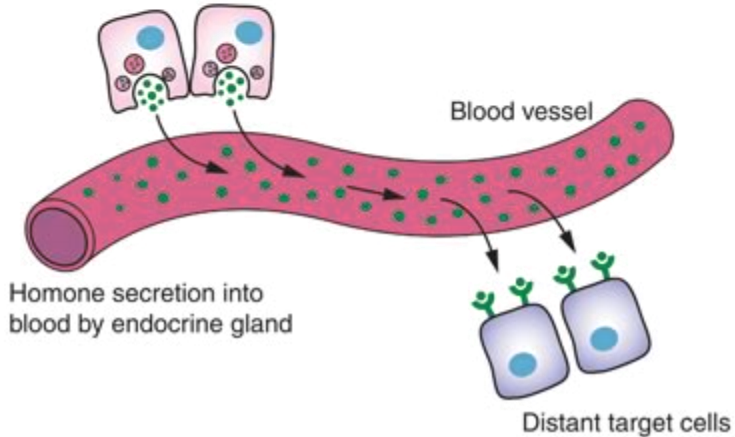
Autocrine signalling



Paracrine signalling



Endocrine signalling



Cell signalling types

Stimulation or repression of gene expression can occur

3 types based on origin and termination of signalling molecule

2 types based on location of receptor



EGF, VEGF,
FGF, HGF

Inflammatory
mediators,
hormones,
chemokines

Cytokines
including
interferons, GH,
CSFs, EPO

Plasma membrane receptors

3 types based on type of
signal transduction:

- Kinase receptors
- GPCR
- No intrinsic enzyme activity

