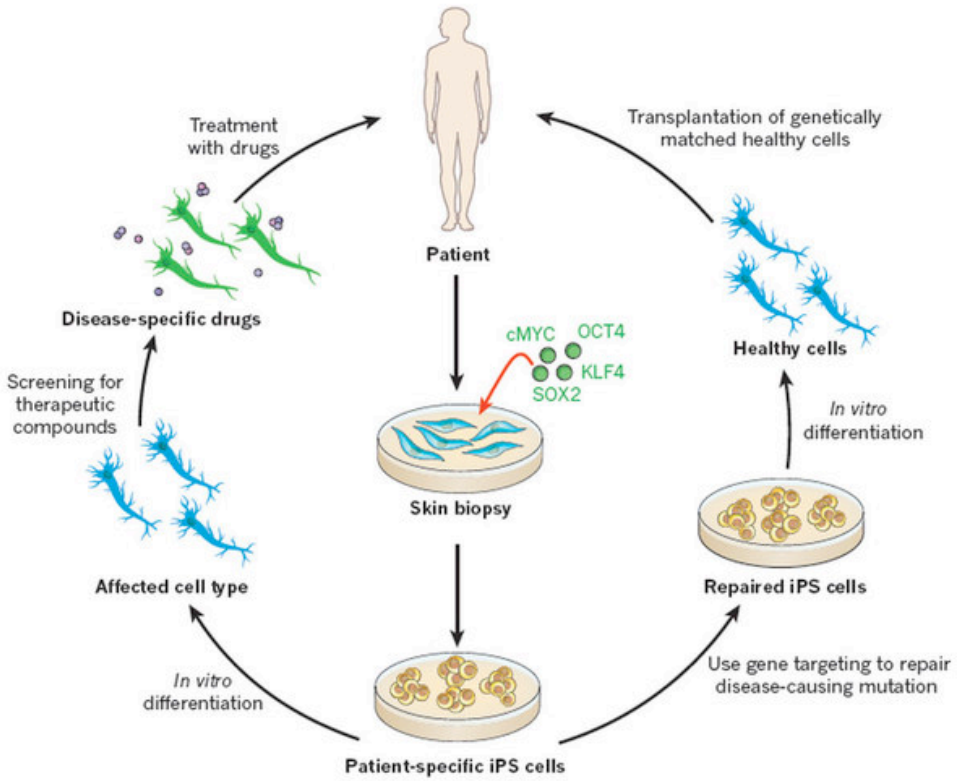
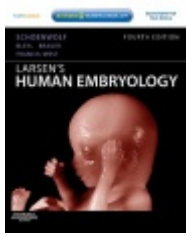
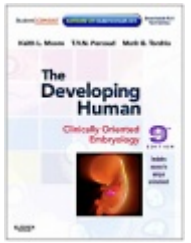
Stem Cell Biology and Technology





Resources:
http://php.med.unsw.edu.au/embryology/
Larsen's Human Embryology
The Developing Human: Clinically Oriented Embryology



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ANAT2341: lecture overview

Stem cell biology

- Stem cell niches
- Stem cell regulation
- Stem cells and cancer

Regenerative medicine

- Stem cell sources
- Stem cell differentiation
- Disease modelling
- Repair of genetic mutations

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Stem Cell Biology

Prenatal development

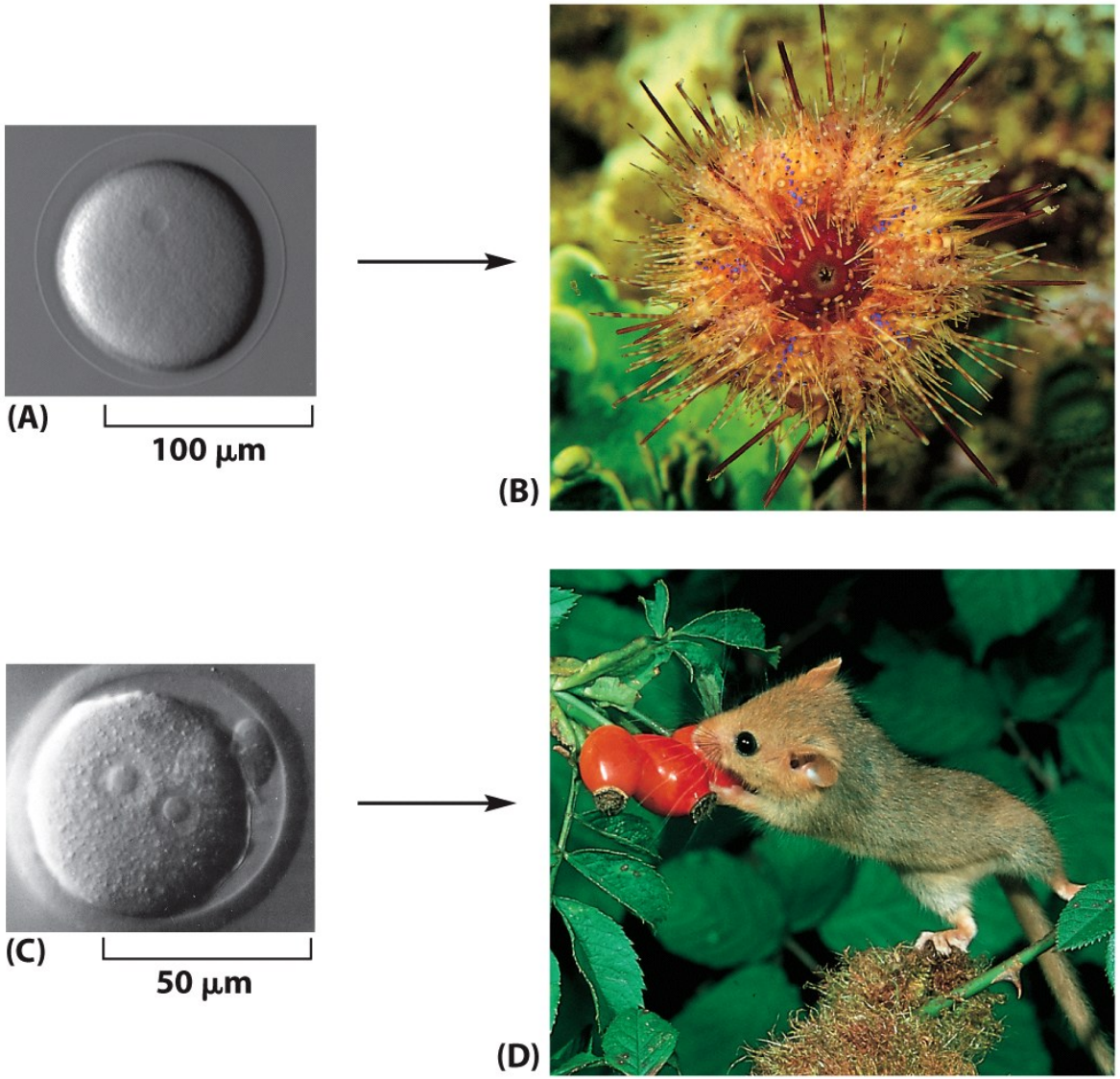


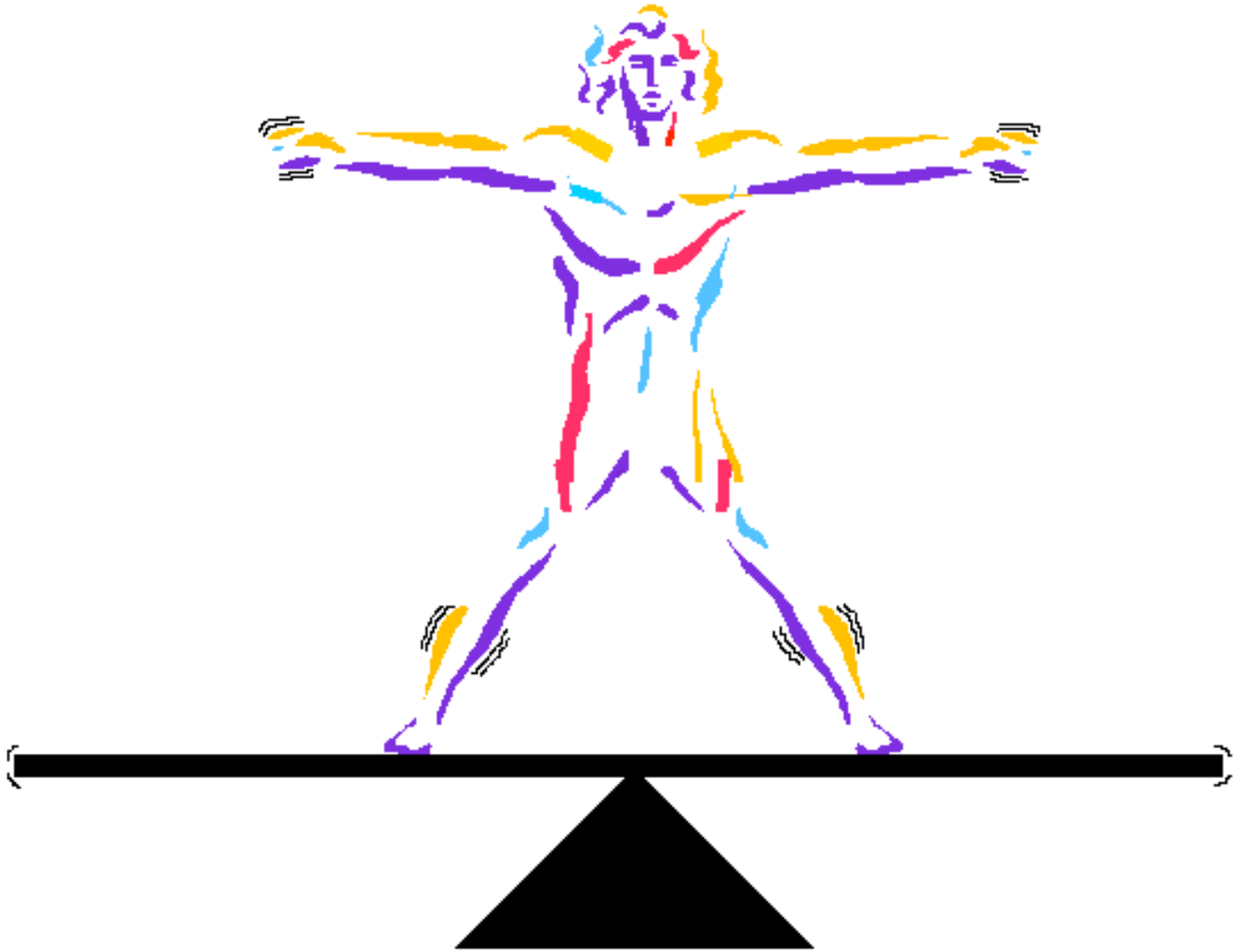
Figure 20-32 Essential Cell Biology 3/e (© Garland Science 2010)

Stem Cell Biology

Postnatal development

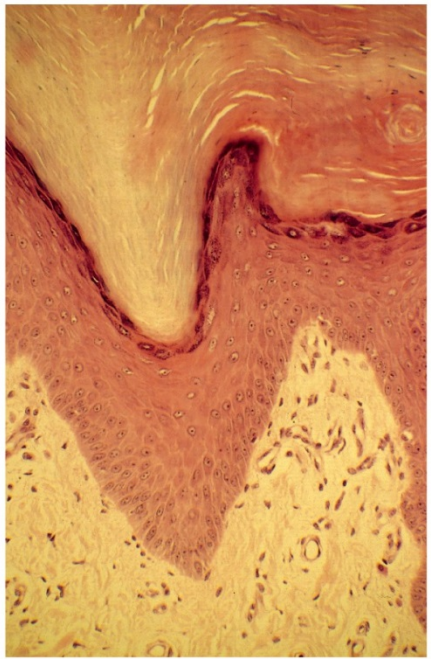
Homeostasis

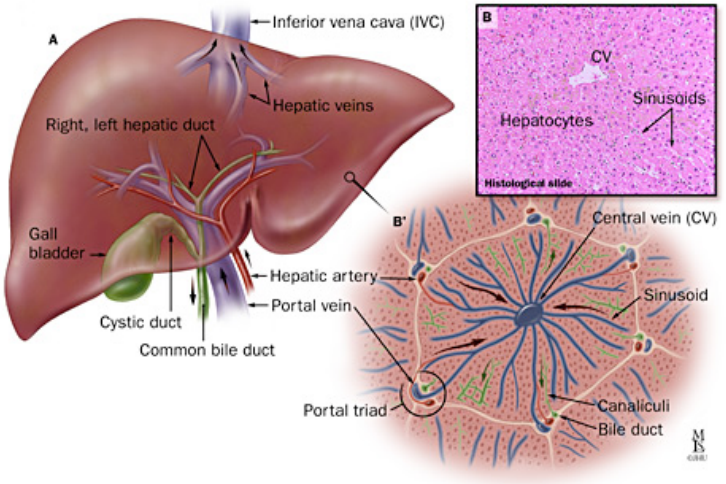
Maintenance of the organism's internal environment in response to internal and external conditions

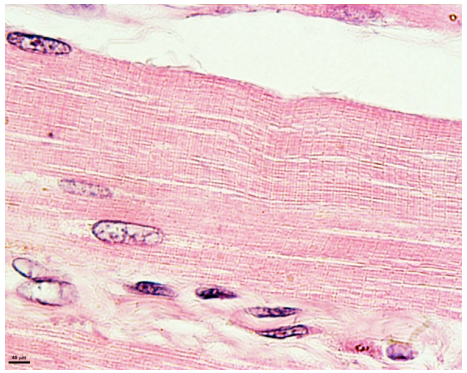


Stem Cell Biology

Tissue renewal in higher vertebrates







Stem Cell Biology

Stem cells divide asymmetrically

Mostly quiescent

High proliferation rates
No function

Limited proliferation
Highly functional cell

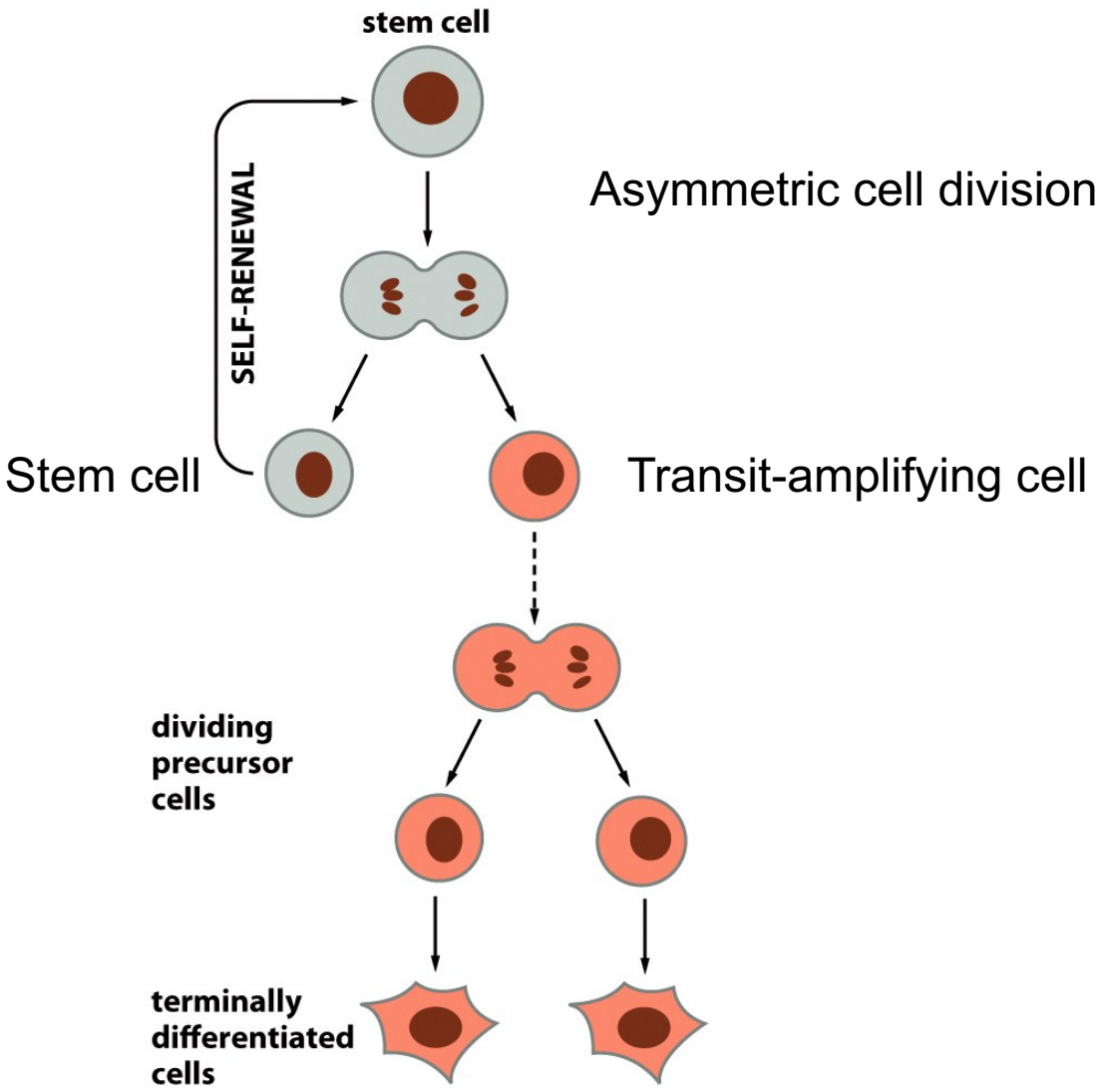
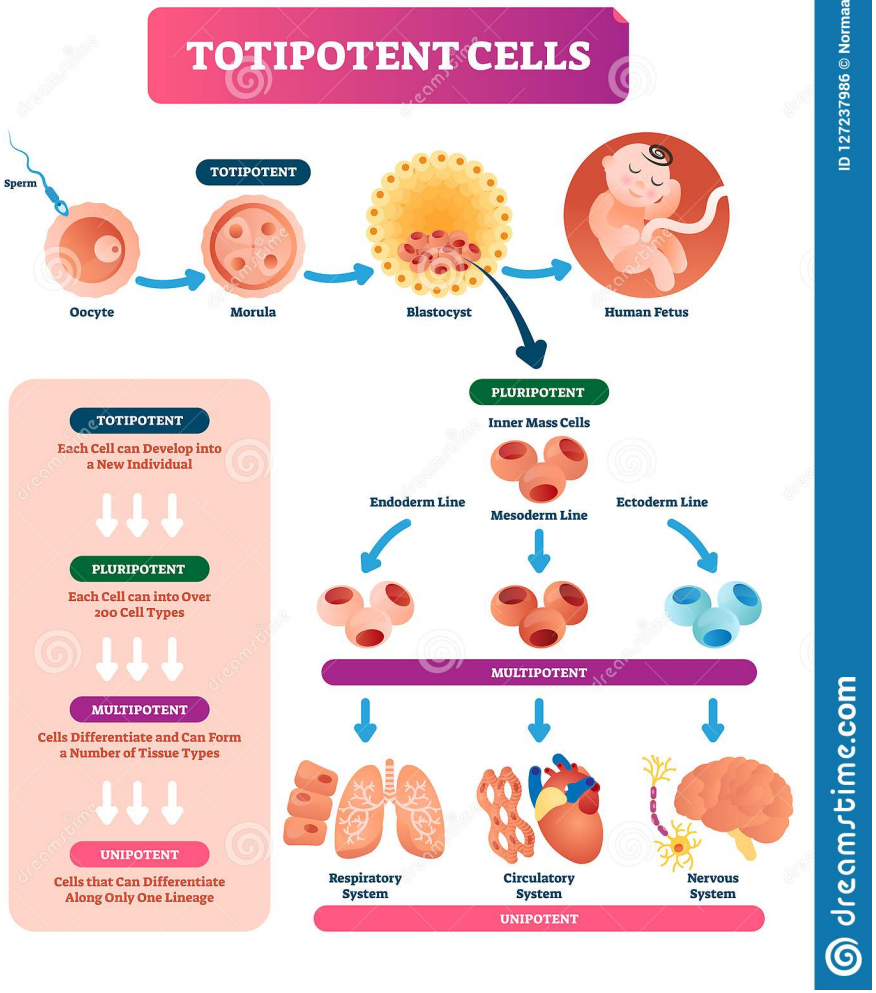


Figure 20-35 Essential Cell Biology 3/e (© Garland Science 2010)

Stem Cell Biology

Stem cell potential

- **Totipotent stem cells:** Capacity to generate all cell types within the body + extraembryonic tissue
- **Pluripotent stem cells:** Capacity to generate all cell types within the body
- **Multipotent stem cells:** Capacity to give rise to more than 1 cell type
- **Unipotent stem cell:** Tissue precursor cells, capacity to give rise to one cell type only



ANAT2341: lecture overview

Stem cell biology

- **Stem cell niches**
- **Stem cell regulation**
- Stem cells and cancer

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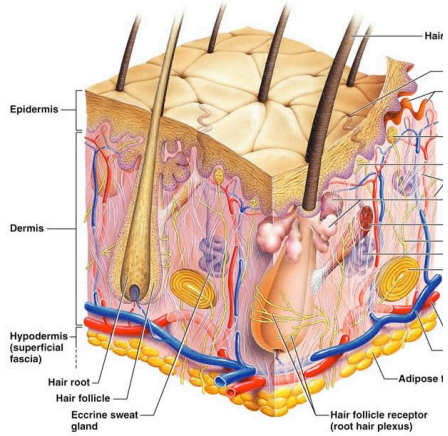
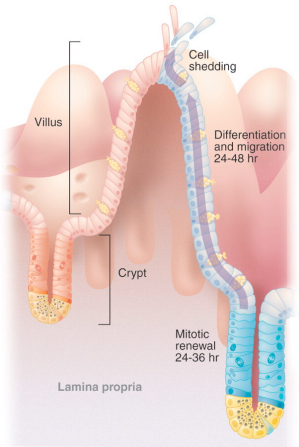
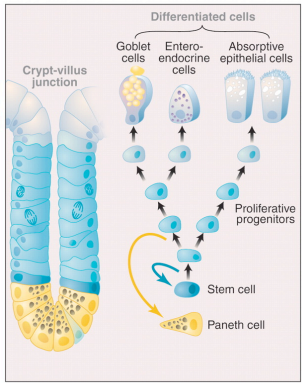
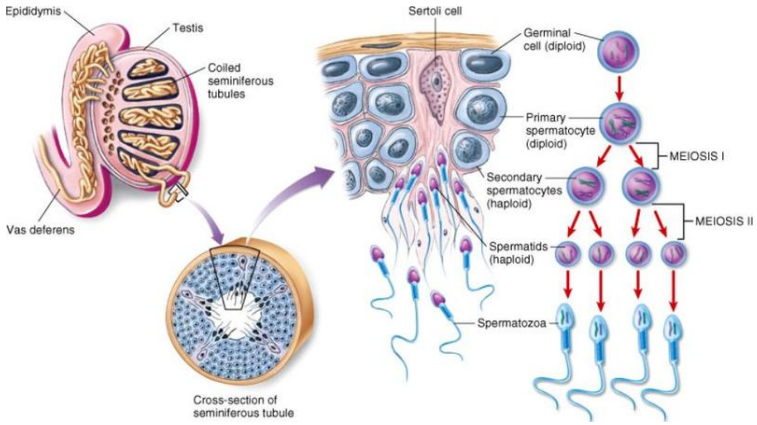
Stem Cell Biology

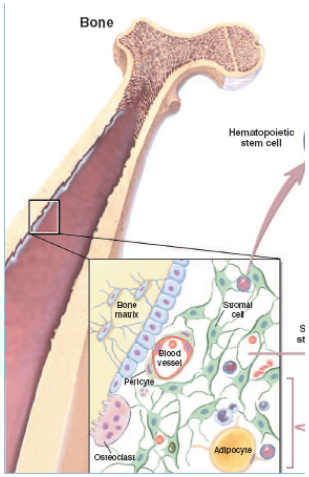
Stem cell niche: the home of the stem cells











Stem Cell Biology

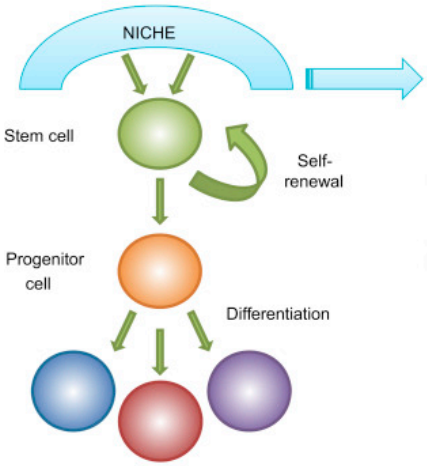
The stem cell niche controls stem cell behavior

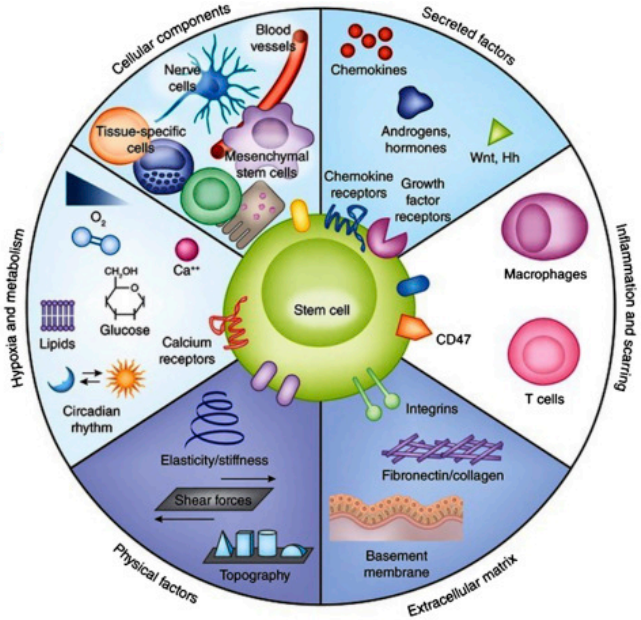
Signals from the stem cell niche instruct stem cells what to do:

- Divide
- Remain quiescent
- Differentiate
- Apoptose

Signals can be:

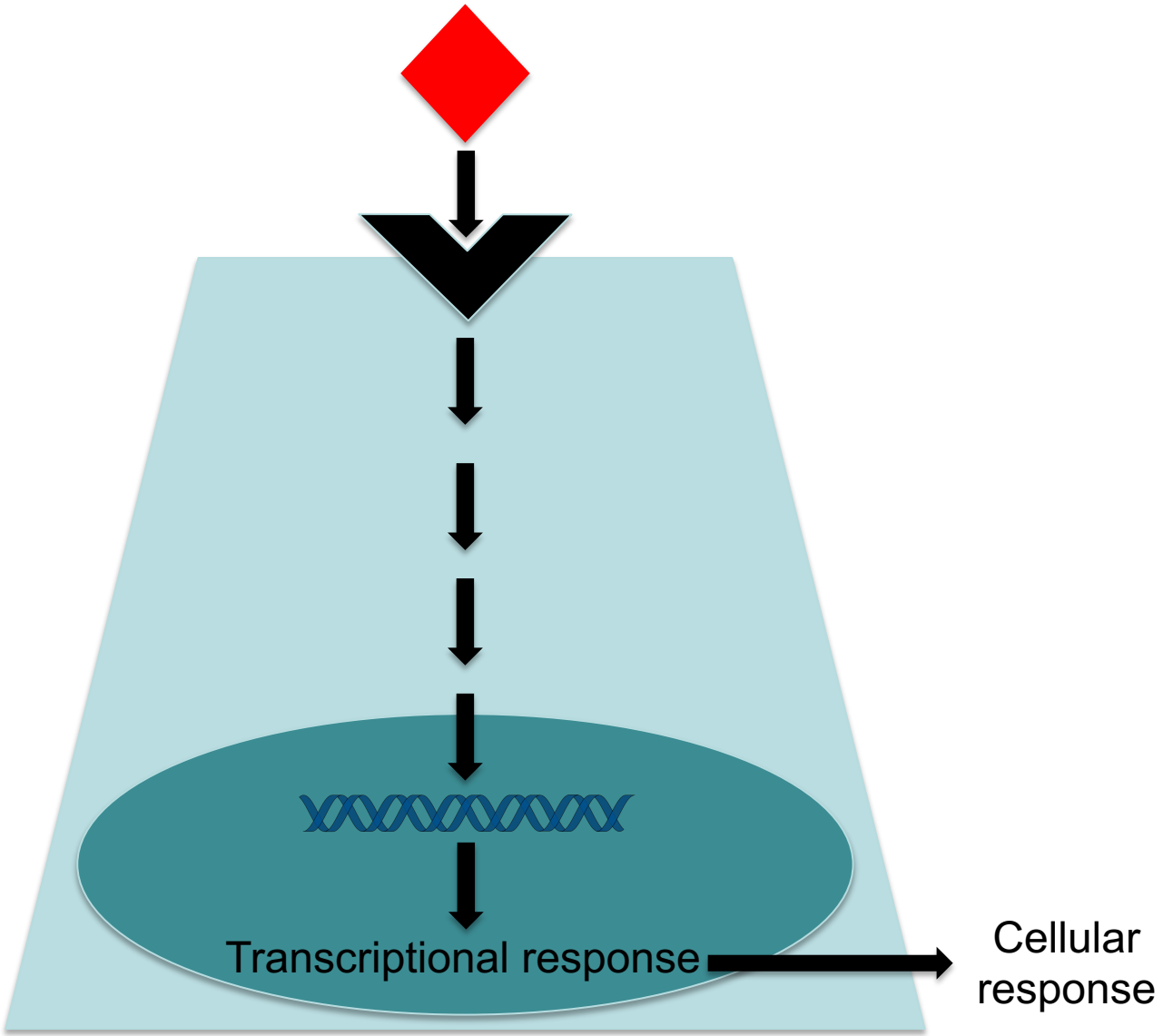
- Signalling factors
- Cell-cell adhesion
- Cell-matrix interactions
- Mechanical factors
- Environmental factors
- Inflammation





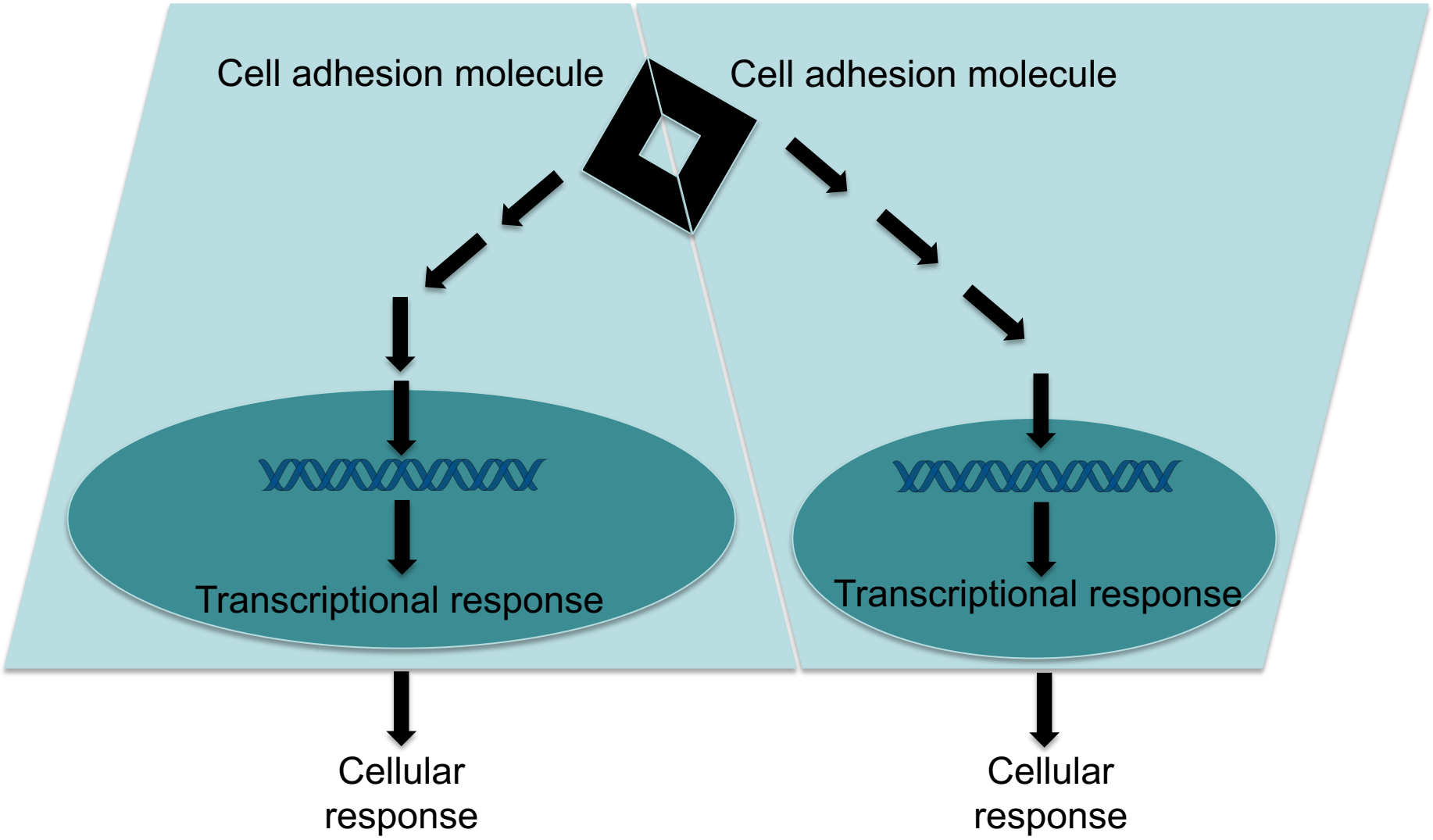
Stem Cell Biology

Signalling factors



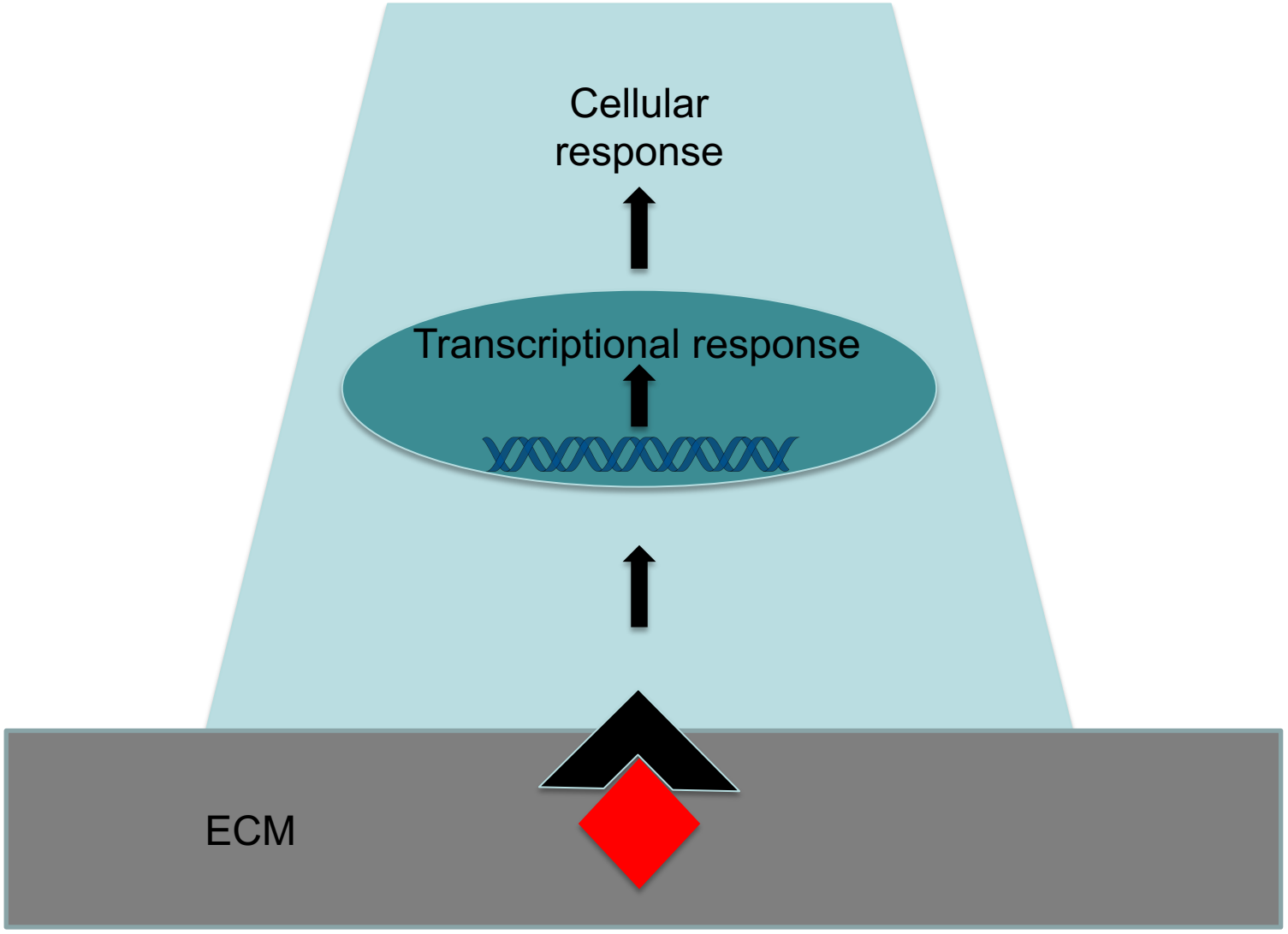
Stem Cell Biology

Cell-cell adhesion signals



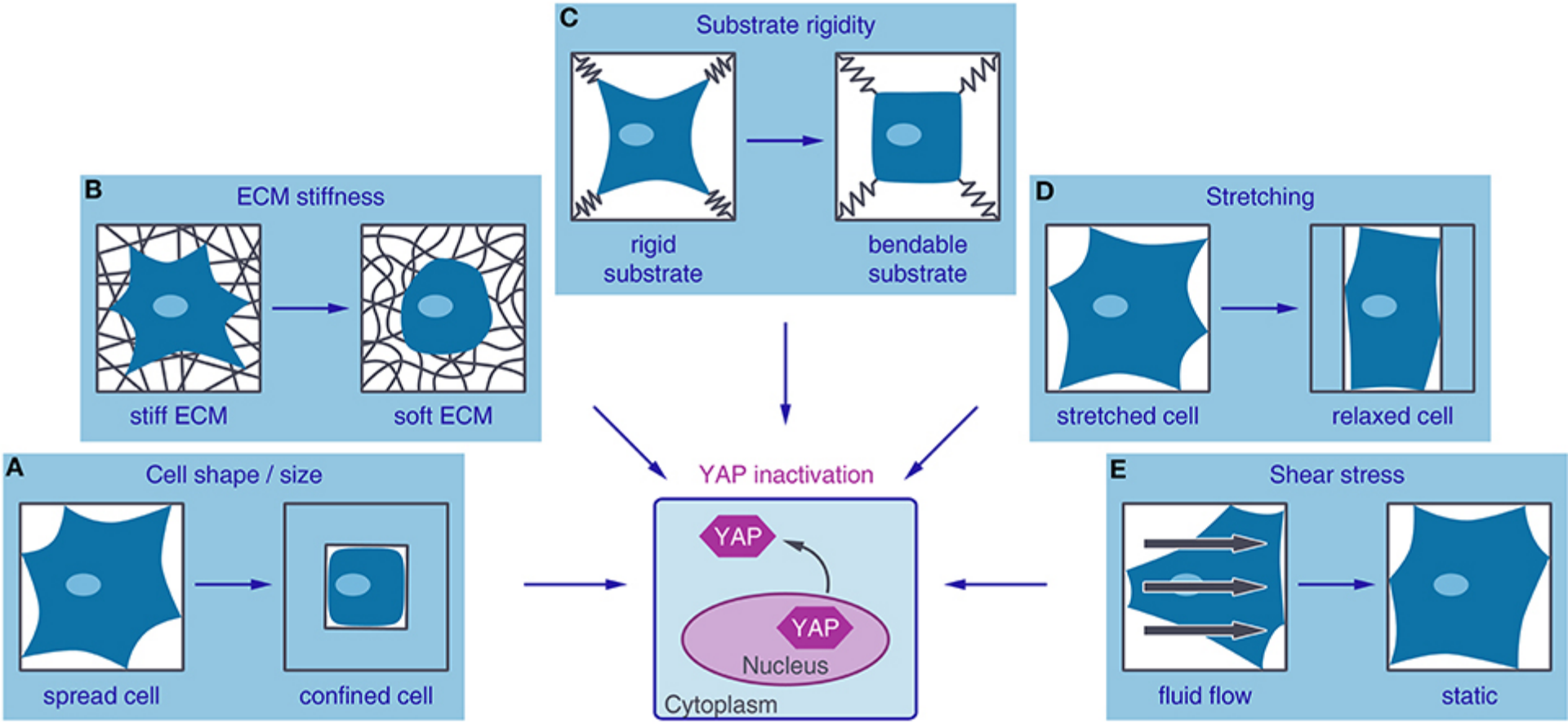
Stem Cell Biology

ECM signals



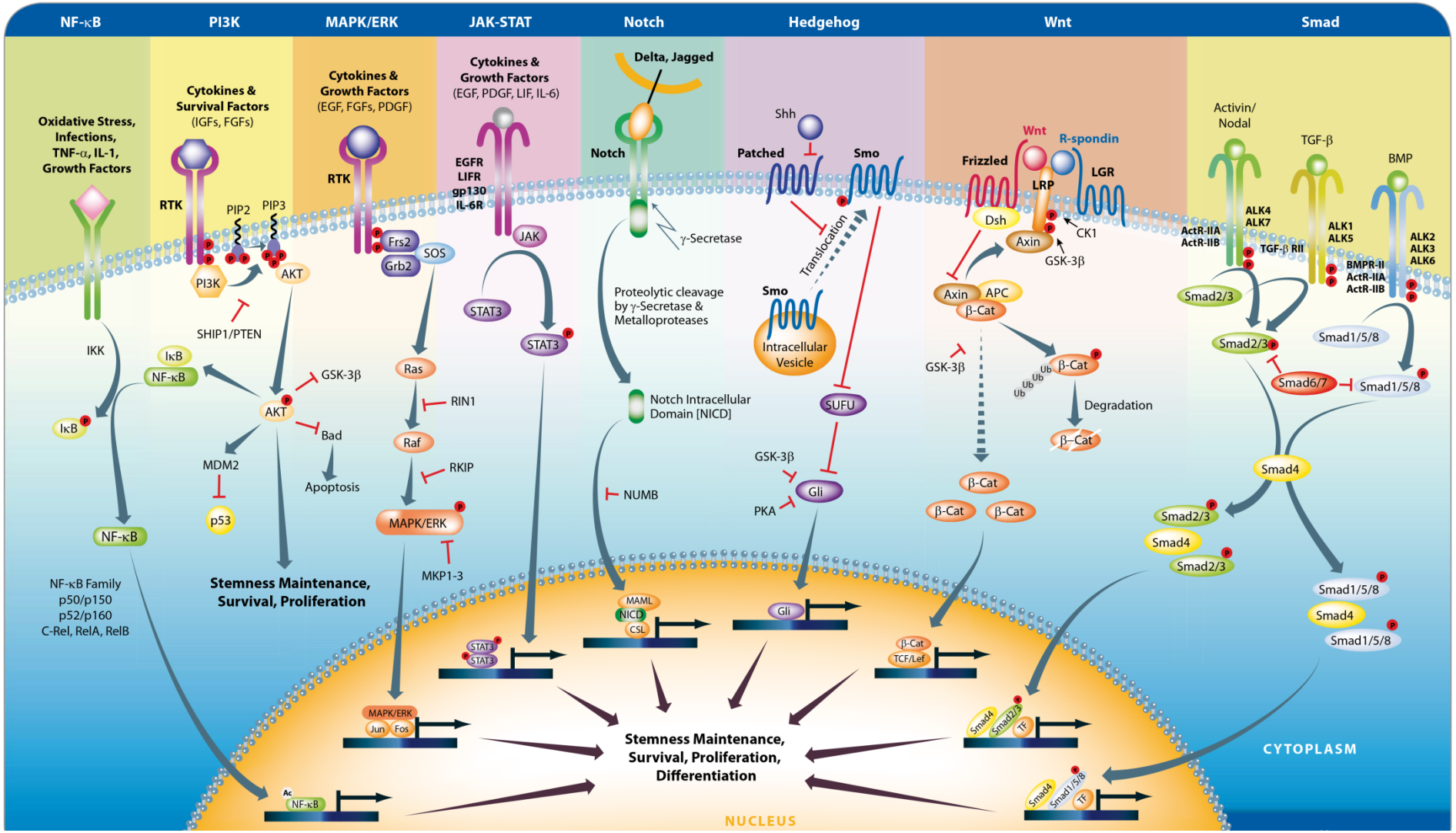
Stem Cell Biology

Mechanical factors



Stem Cell Biology

Signalling pathways



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Regenerative medicine

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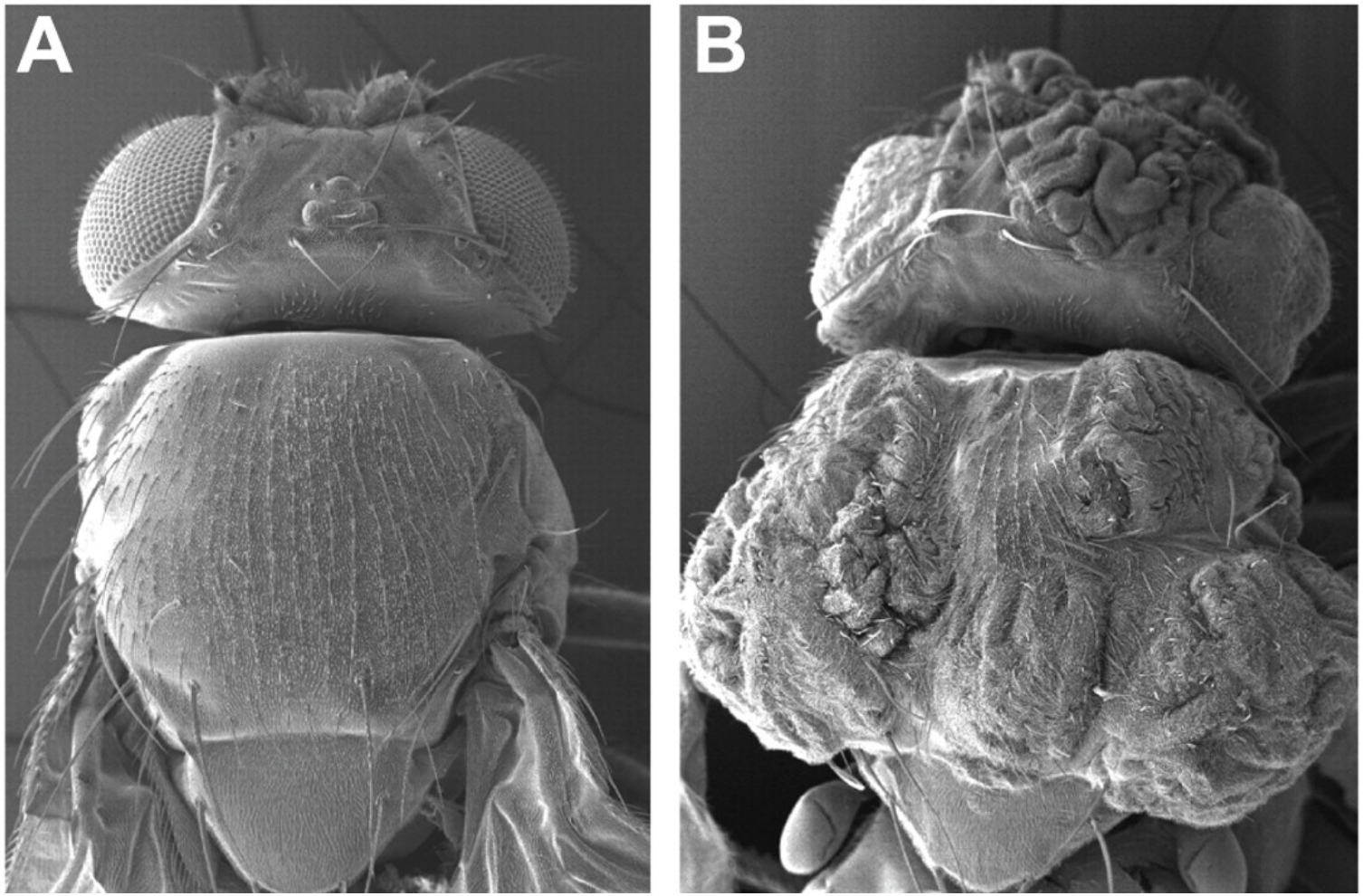
Stem Cell Biology

Cancer

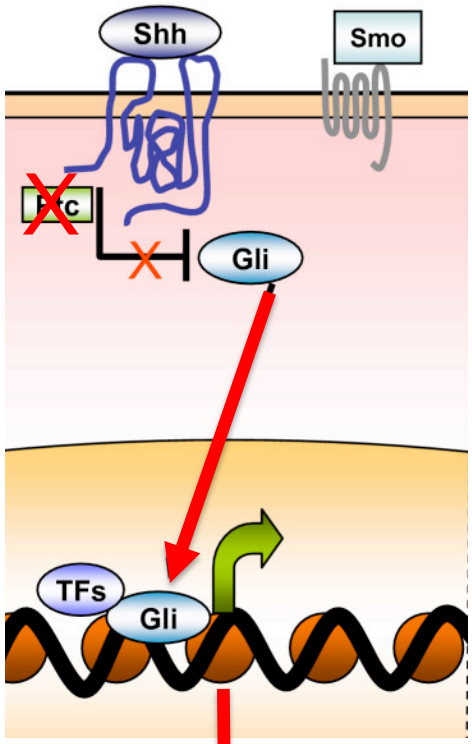
What happens if control of cell renewal is perturbed?



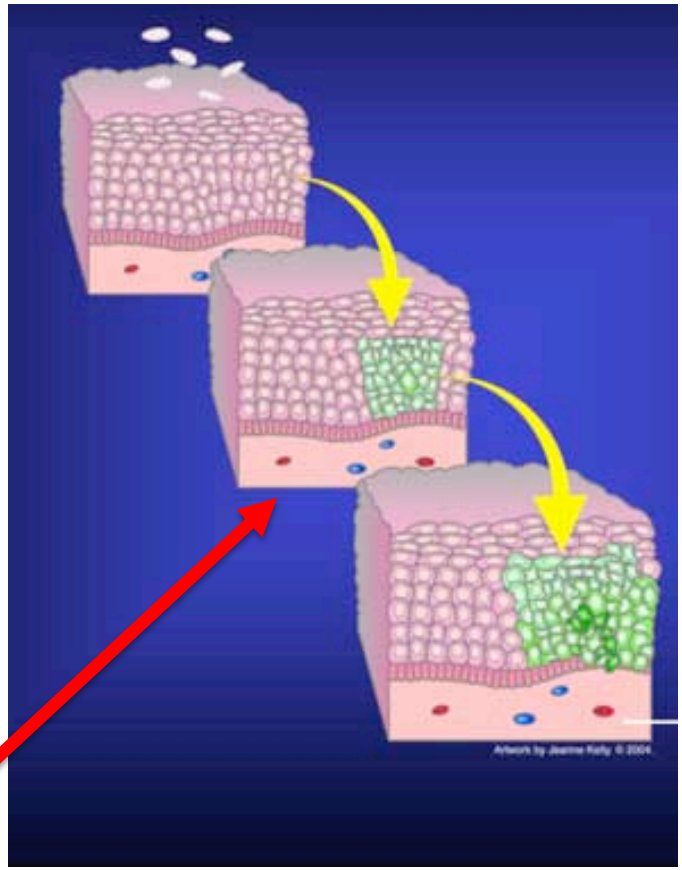
Stem Cell Biology

Cancer

Mutations in Hedgehog pathway in epidermal stem cells result in basal cell carcinoma



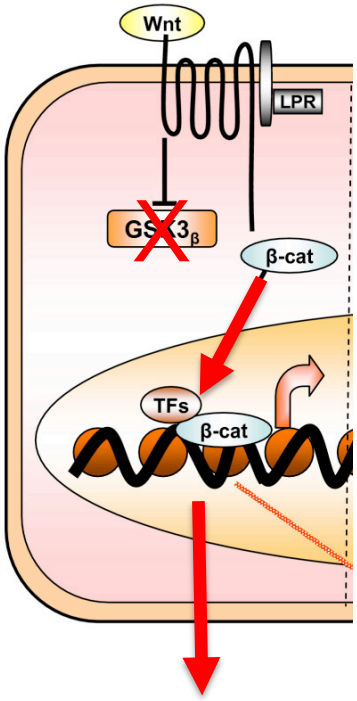
hyperproliferation

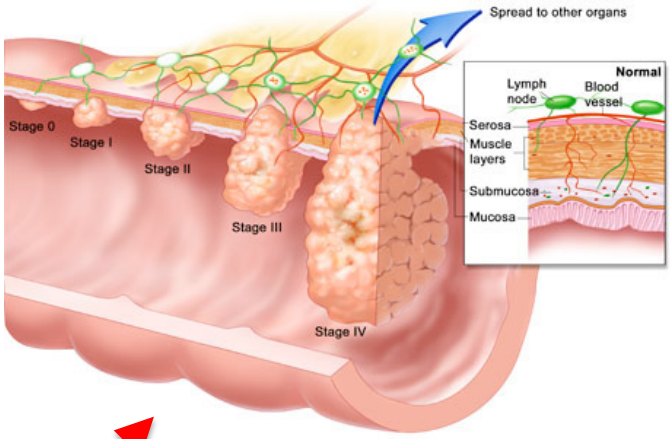


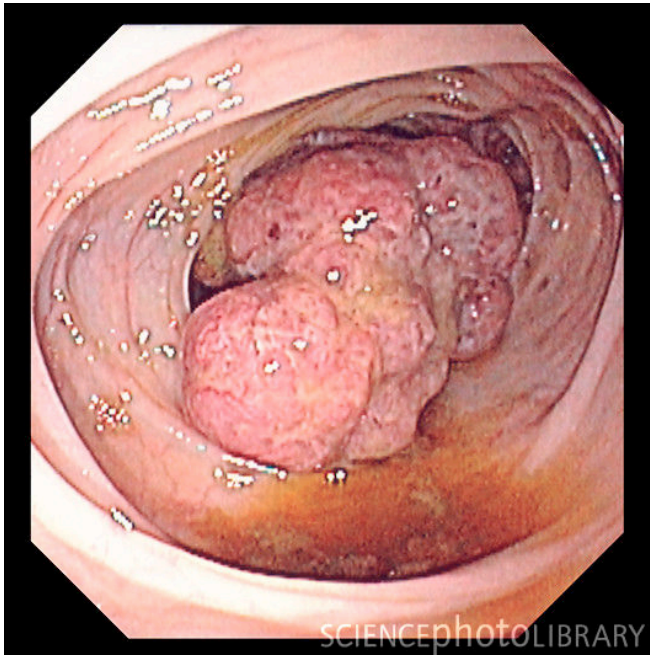
Stem Cell Biology

Cancer

Mutations in Wnt pathway in intestinal crypts stem cells result in colon cancer







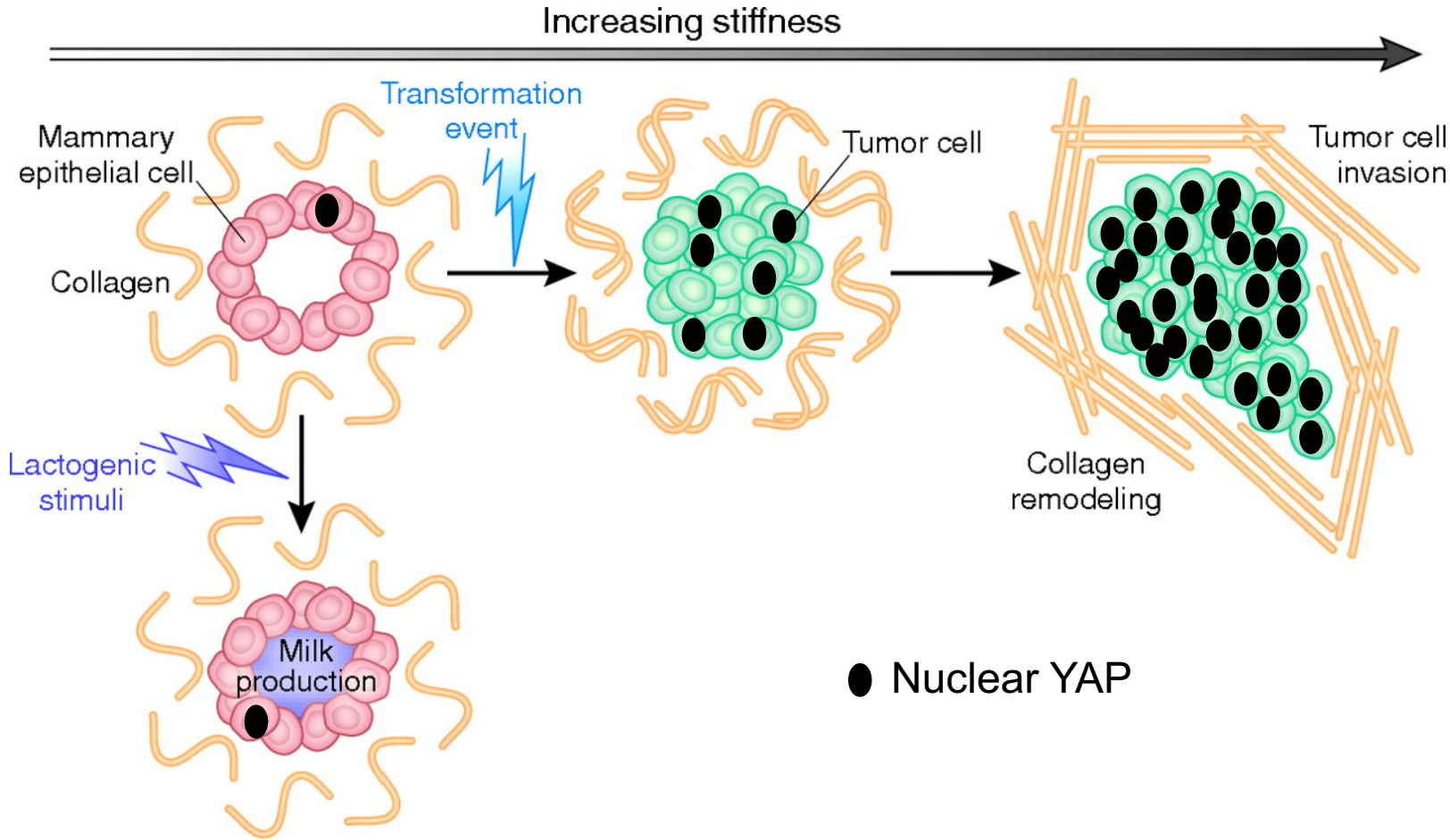
hyperproliferation

Stem Cell Biology

Cancer

Increasing stromal stiffness promotes cancer progression

activation of nuclear YAP -> increased stem cell proliferation -> tumor growth



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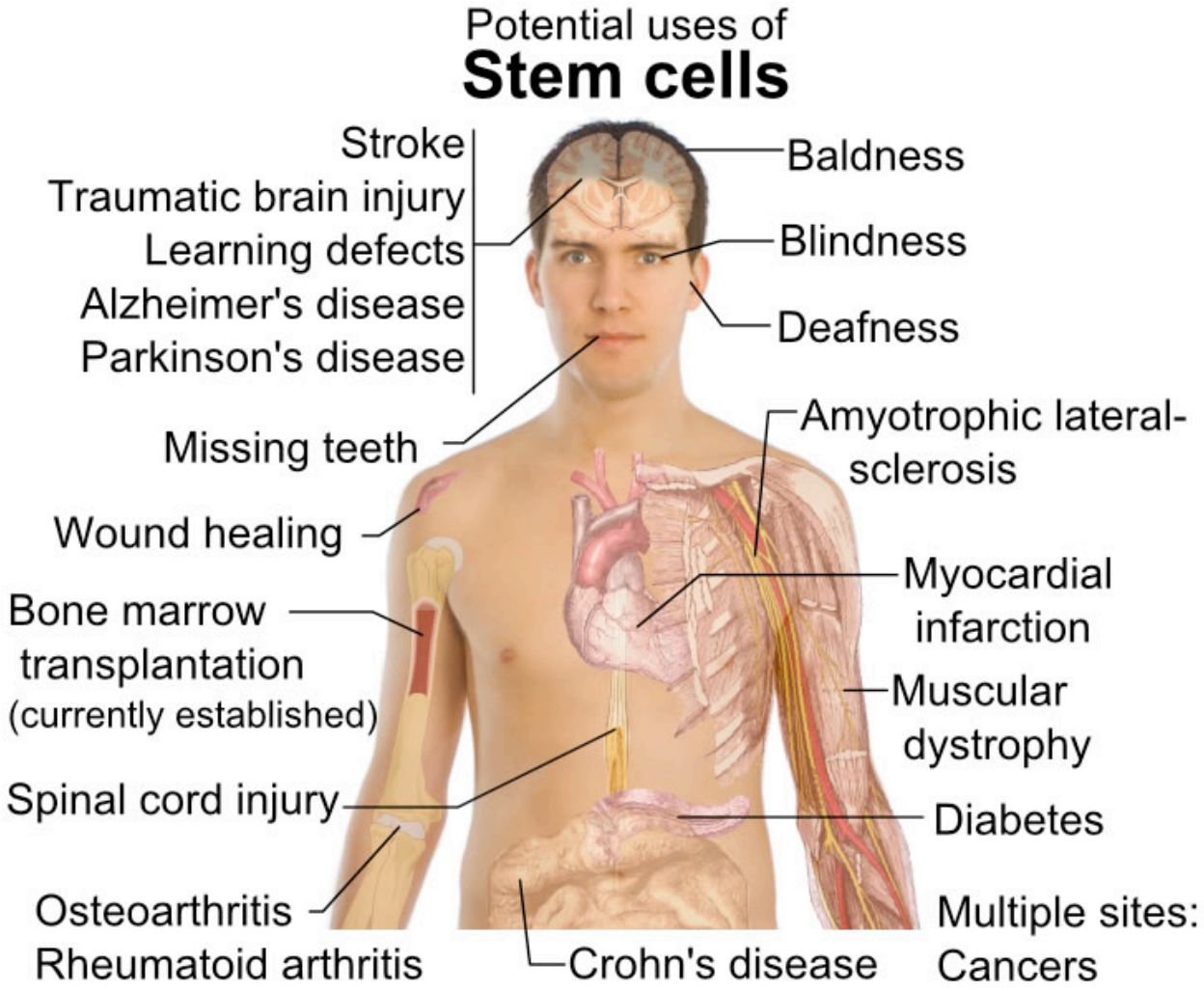
Regenerative medicine

the clinical application of stem cells

"process of replacing or regenerating human cells, tissues or organs to restore or establish normal function"



Regenerative Medicine

1- where can we find stem cells?

2- how we can direct differentiation?

3- how we can cure diseased cells?

4- how we can repair mutations in cells?

Regenerative Medicine

1- where can we find stem cells?

2- how we can direct differentiation?

3- how we can cure diseased cells?

4- how we can repair mutations in cells?

Where can we find stem cells?

1. Embryonal carcinoma cells
2. Embryonic stem cells
3. Adult stem cells
4. Induced pluripotent stem cells

1. Embryonal Carcinoma Cells

Isolated from teratocarcinomas (germ cell tumours)
1964 – Pierce and Kleinsmith

Pluripotent
In vitro culture and expansion
Genetic abnormalities

2. Embryonic Stem Cells

Isolated from inner cell mass

1981 – Martin Evans, Matthew Kaufman and Gail Martin

Pluripotent

No genetic abnormalities

In vitro culture and expansion

Ethical issues

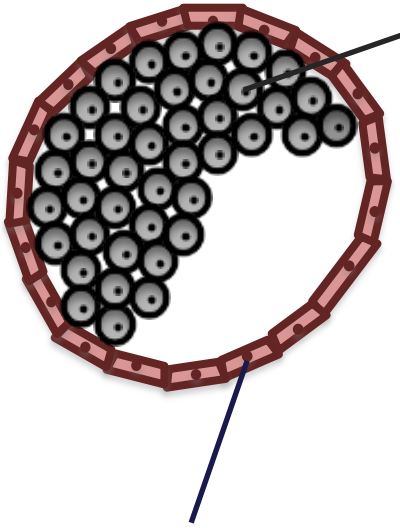
2. Embryonic Stem Cells

Isolated from inner cell mass

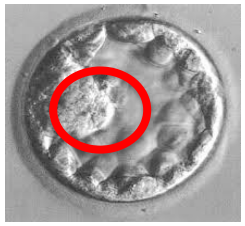
1981 – Martin Evans, Matthew Kaufman and Gail Martin

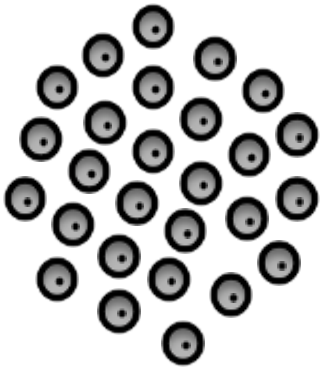
blastocyst

cells inside
= 'inner cell mass'



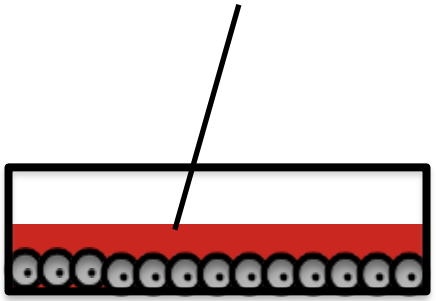
outer layer of cells
= 'trophectoderm'





embryonic stem cells taken from
the inner cell mass

fluid with nutrients

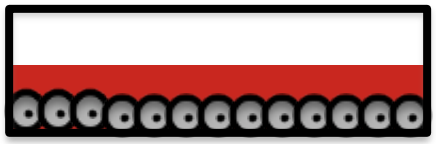


culture in the lab
to grow more cells

2. Embryonic Stem Cells

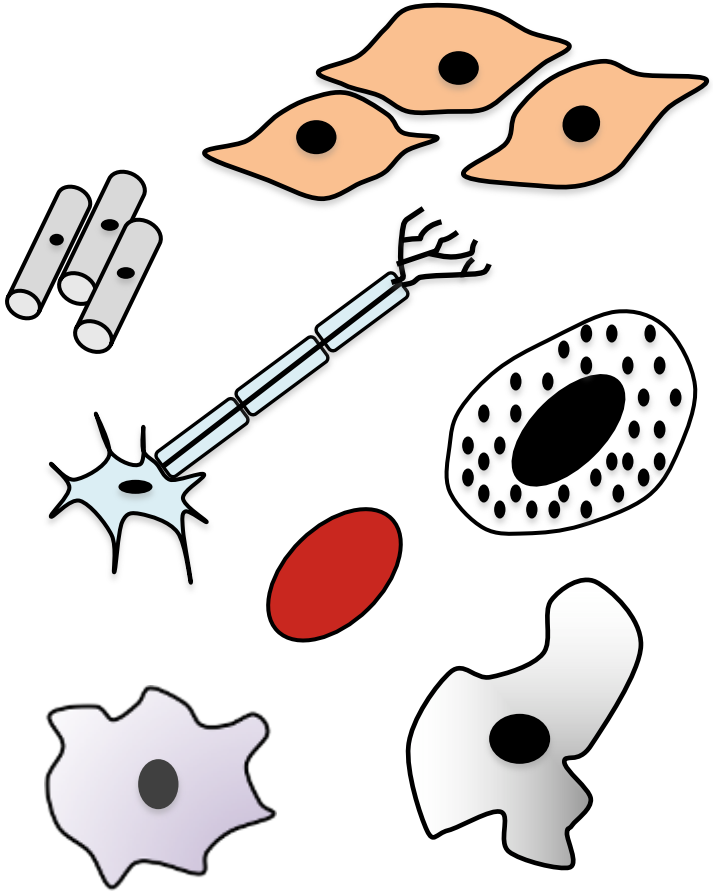
Isolated from inner cell mass

1981 – Martin Evans, Matthew Kaufman and Gail Martin



embryonic stem cells

Uncontrolled differentiation



all possible types of specialized cells

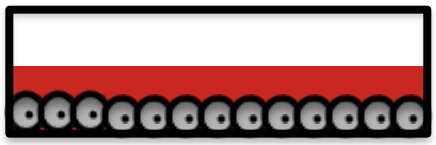
PLURIPOTENT

2. Embryonic Stem Cells

Isolated from inner cell mass

1981 – Martin Evans, Matthew Kaufman and Gail Martin

Directed differentiation:



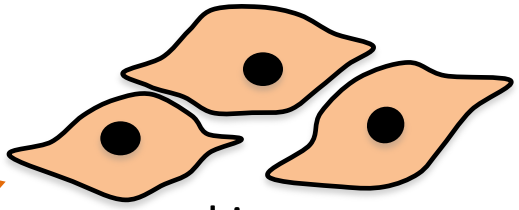
embryonic stem cells

grow under conditions A

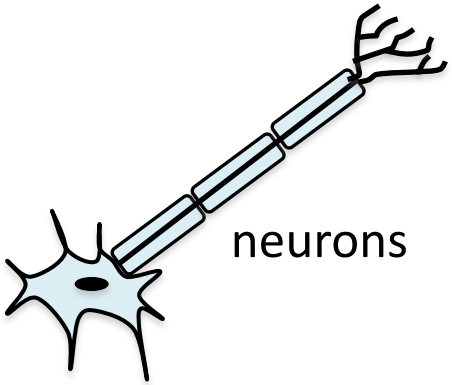
grow under conditions B

grow under conditions C

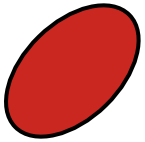
grow under conditions D



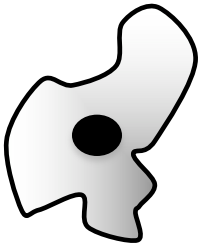
skin



neurons



blood



liver

Pluripotent

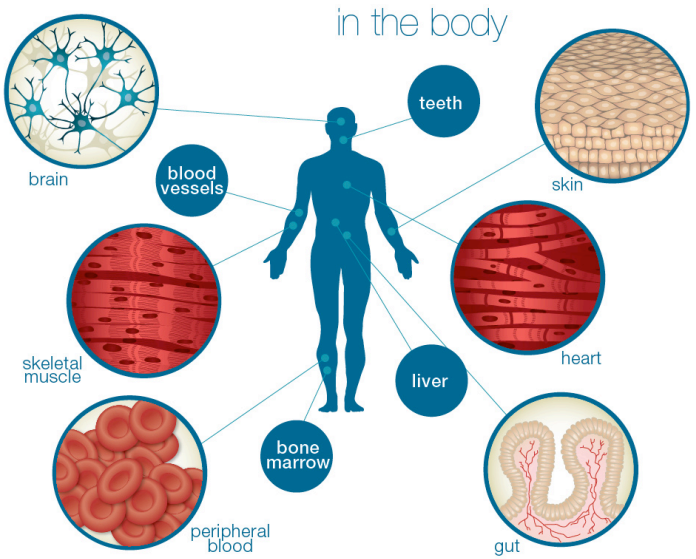
No genetic abnormalities

In vitro culture, expansion and differentiation

Ethical issues

3. Adult stem cells

“An undifferentiated cell, found among differentiated cells in a tissue or organ that can renew itself and can differentiate to yield some or all of the major specialized cell types of the tissue or organ”

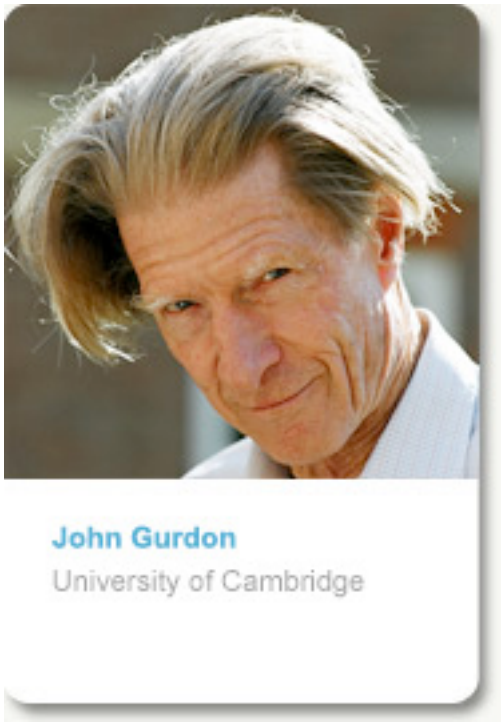


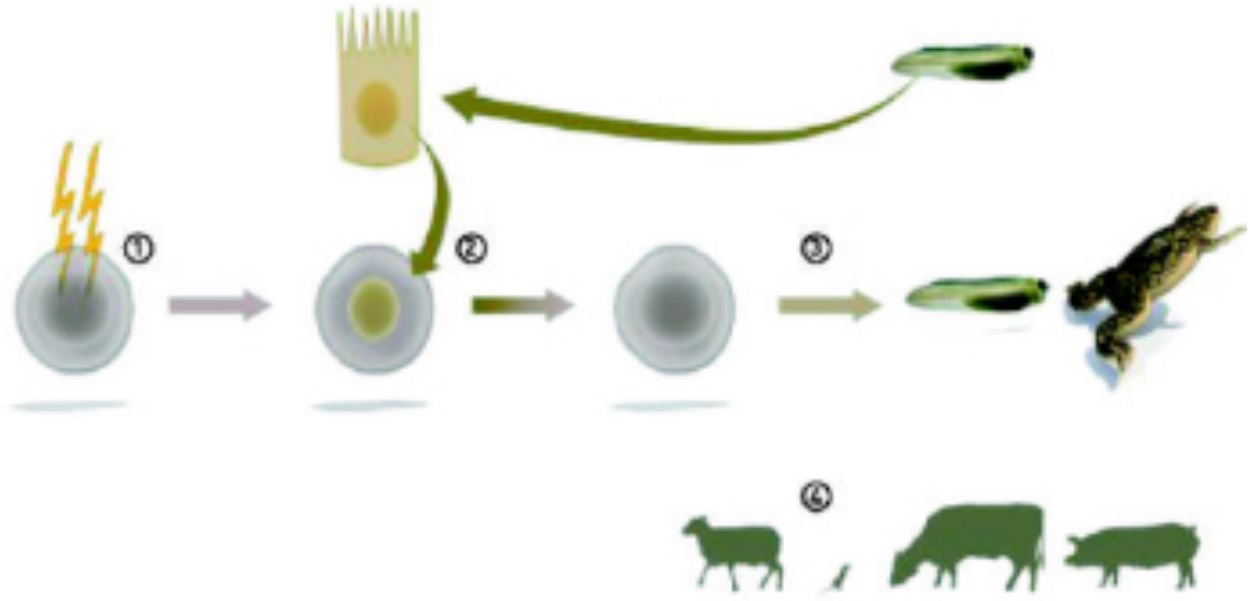
No ethical issues
Restricted plasticity
Limited quantities
Hard to identify

4. Induced Pluripotent Stem Cells

Somatic Cell Nuclear Transfer (John Gurdon, 1958)

The developmental potential of nuclei of differentiated cells





4. Induced Pluripotent Stem Cells

Somatic Cell Nuclear Transfer (John Gurdon, 1958)

“mature, differentiated cells can be reprogrammed to become pluripotent”

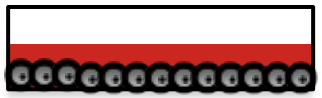
4. Induced Pluripotent Stem Cells

Nuclear Reprogramming
Induced pluripotency (iPS), Yamanaka, 2006

‘genetic reprogramming’
= add certain genes to the cell

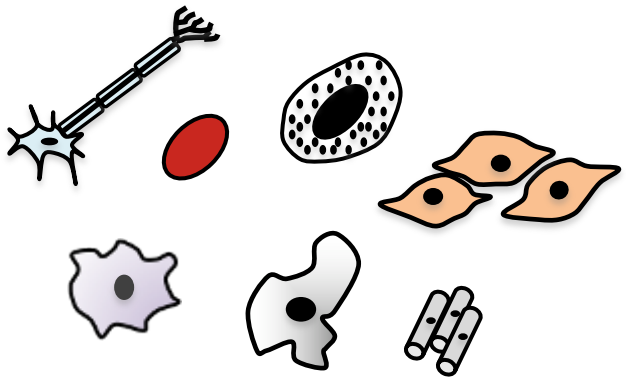
cell from the body

induced pluripotent stem (iPS) cell
behaves like an embryonic stem cell



culture iPS cells in the lab

differentiation



all possible types of specialized cells

Advantage: no need for embryos!

4. Induced Pluripotent Stem Cells

Nuclear Reprogramming
2012 Nobel Prize

Regenerative Medicine

1- where can we find stem cells?

2- how we can direct differentiation?

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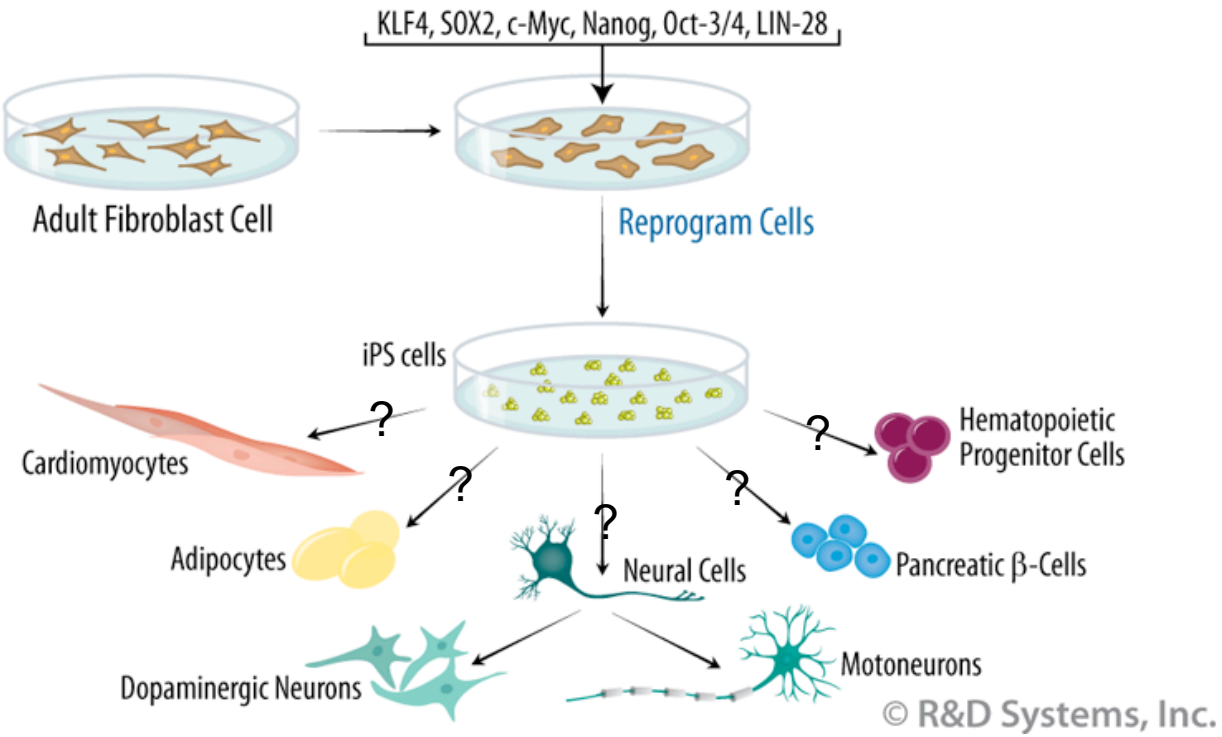
Future Stem Cell Technologies

How can we direct differentiation?

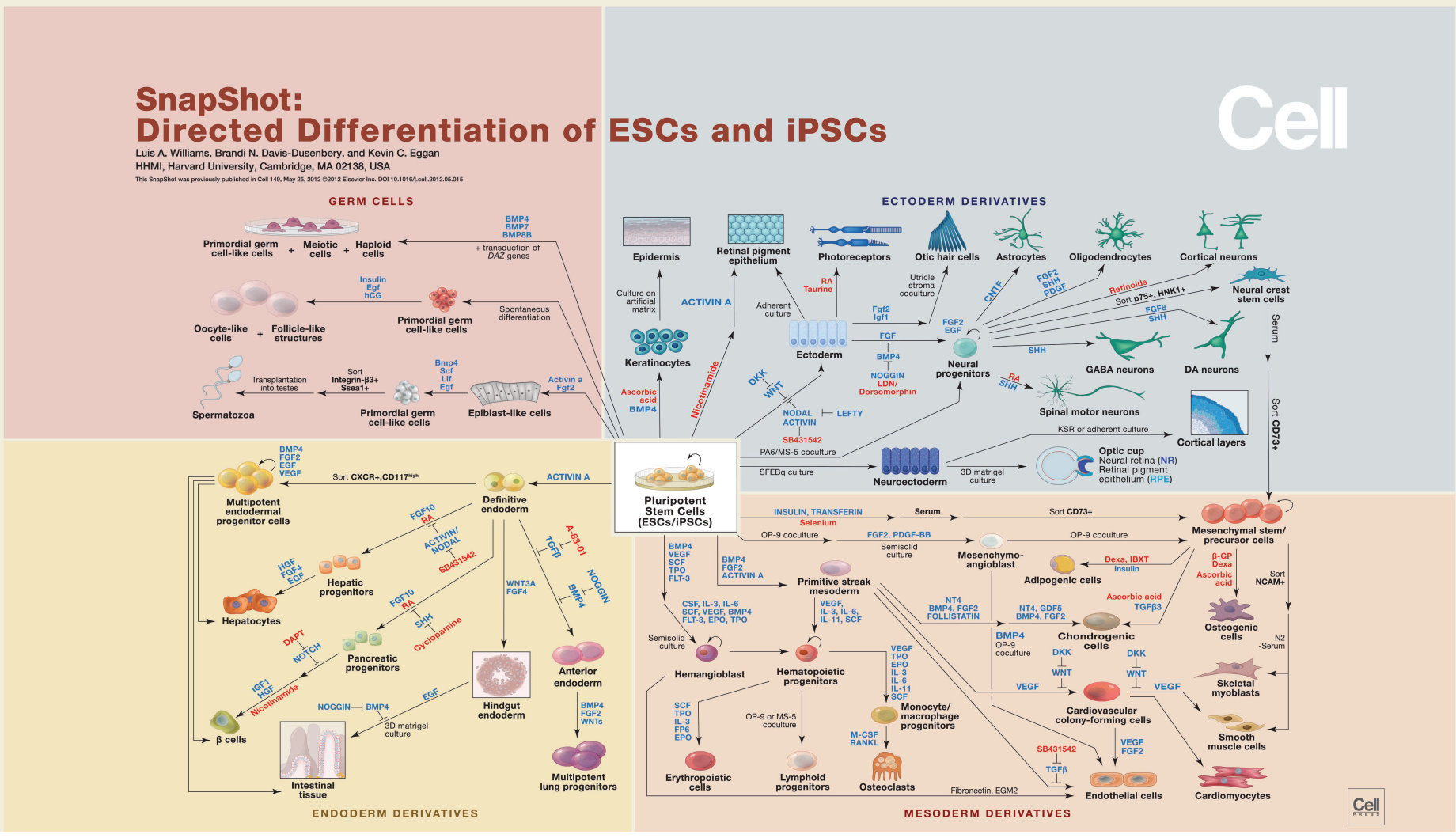
Uncontrolled differentiation

Directed differentiation



Future of Regenerative Medicine

Directed differentiation of pluripotent stem cells:
Mimic instructive signals from niche
Developmental biology



Regenerative Medicine

1- where can we find stem cells?

2- how we can direct differentiation?

3- how we can cure diseased cells?

4- how we can repair mutations in cells?

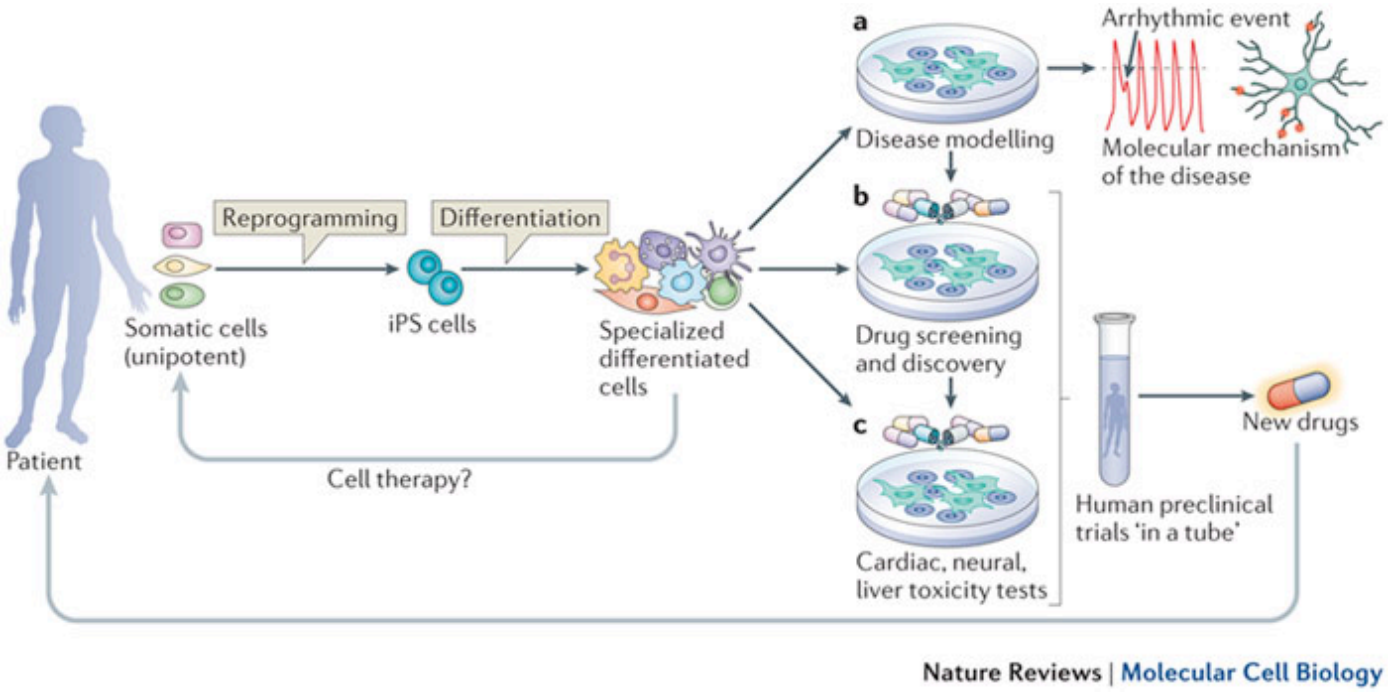
Regenerative Medicine

How can we cure disease?

Disease modeling using iPS cells derived from patients

Drug discovery using iPS cells derived from patients

(personalized medicine)



Regenerative Medicine

1- where can we find stem cells?

2- how we can direct differentiation?

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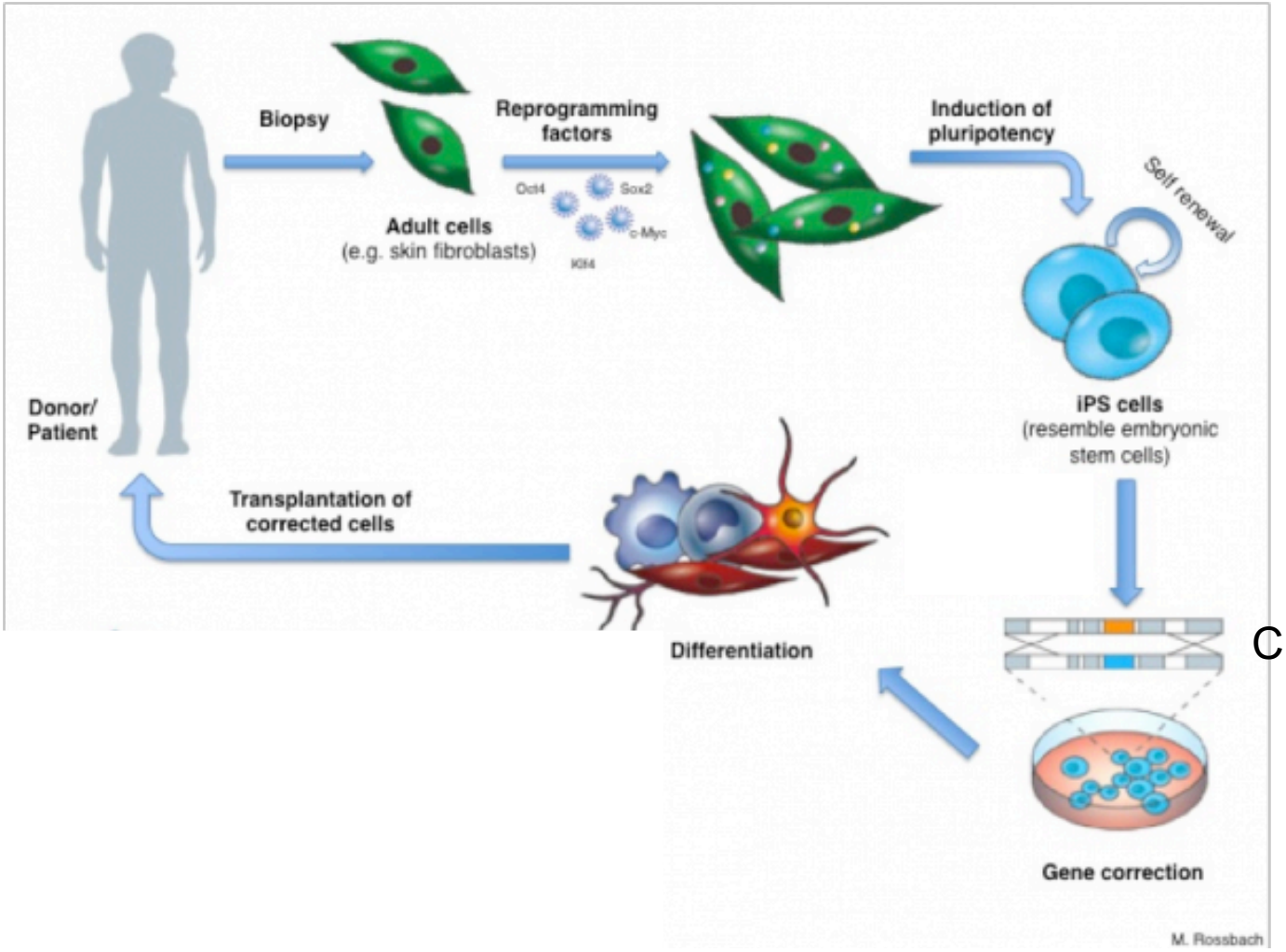
Regenerative Medicine

CRISPR/CAS9 Genome engineering of iPS cells



CRISPR/CAS9

Regenerative Medicine

Very hopeful and promising,

but are we there yet?

http://www.sbs.com.au/news/insight/tvepisode/stem-cells

http://iview.abc.net.au/programs/head-first/DO1333V001S00

ANAT2341: lecture overview

Stem cell biology

- Stem cell niches
- Stem cell regulation
- Stem cells and cancer

Regenerative medicine

- Stem cell sources
- Stem cell differentiation
- Disease modelling
- Repair of genetic mutations

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