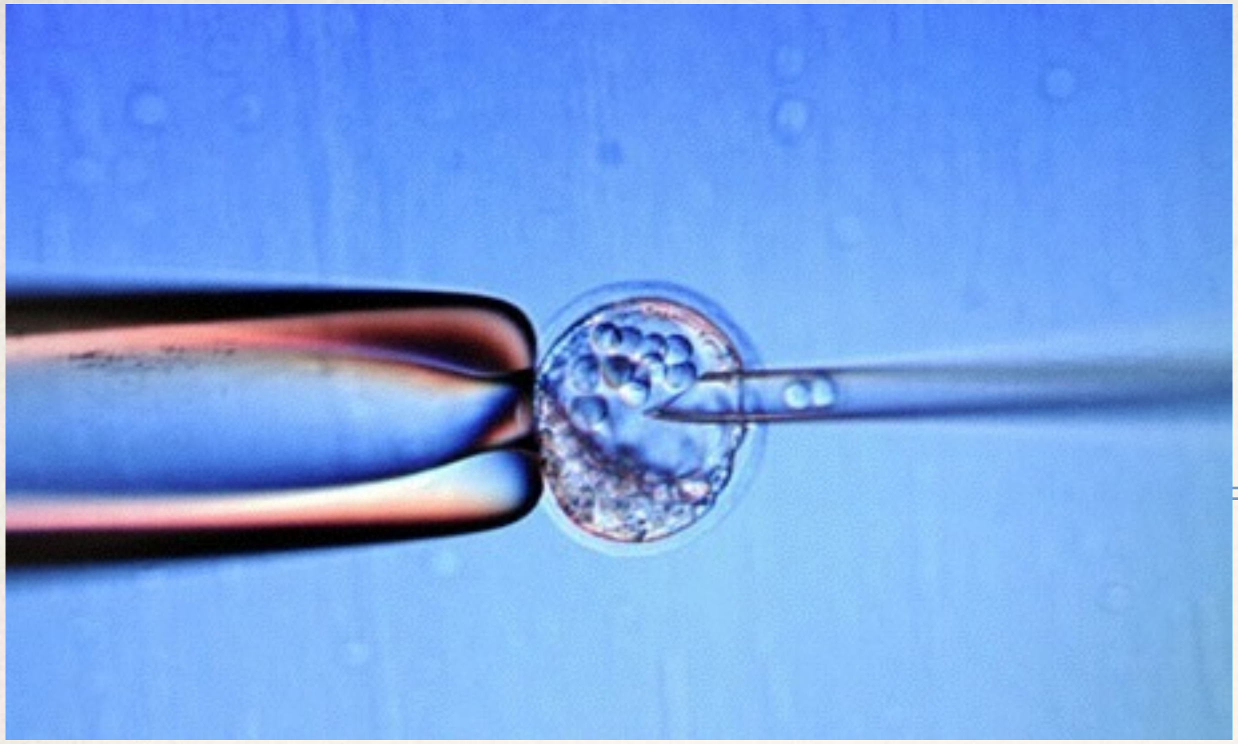
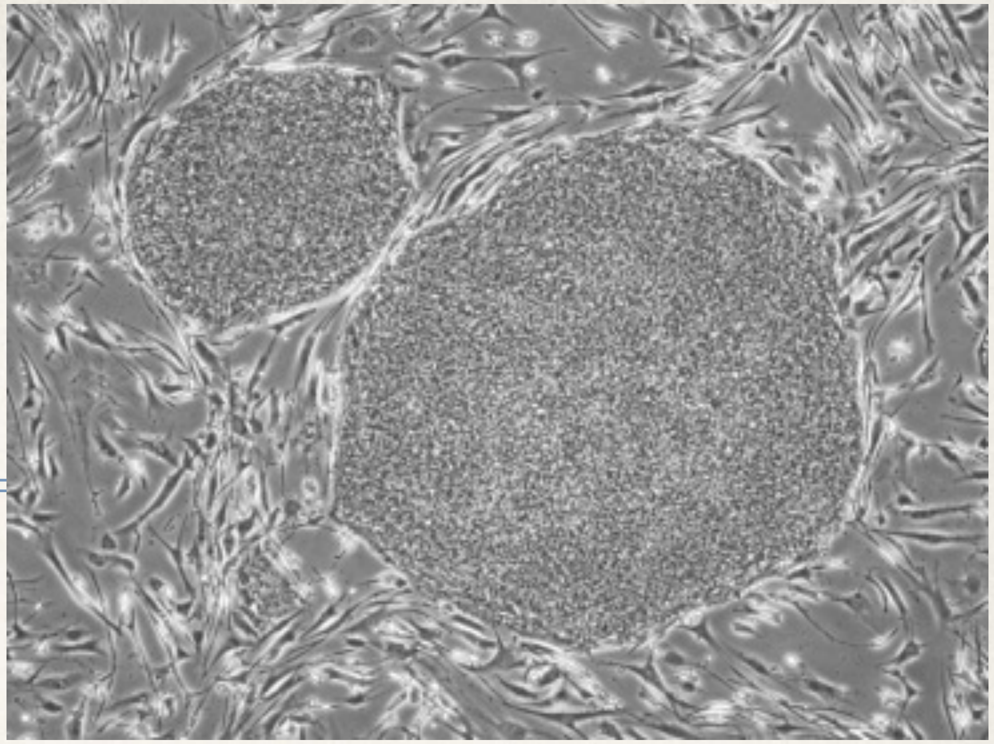
Cilmes šūnas - bioloģija un pielietojums

Dr.biol. Inese Čakstiņa



http://www.theguardian.com/science/2013/jul/01/nhs-drugs-watchdog-stem-cell

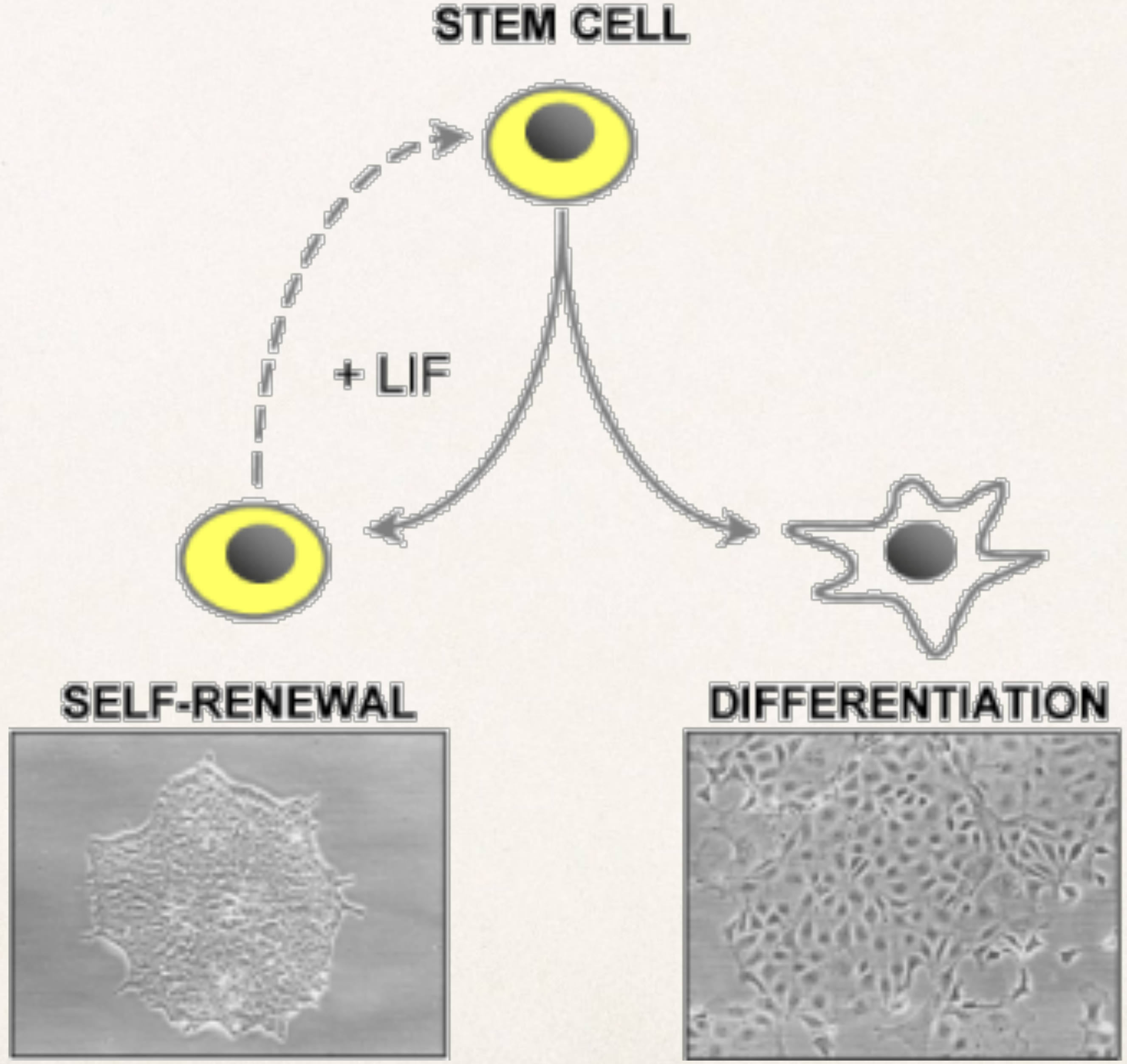


http://genetics.stanford.edu/research/stemcellcore/

Cilmes šūna - nespecializēta šūna ar spēju: pati sevi **atjaunot** (kopēt - *self-renewal*) un **diferencēties** par (jebkuru) specializētu šūnu

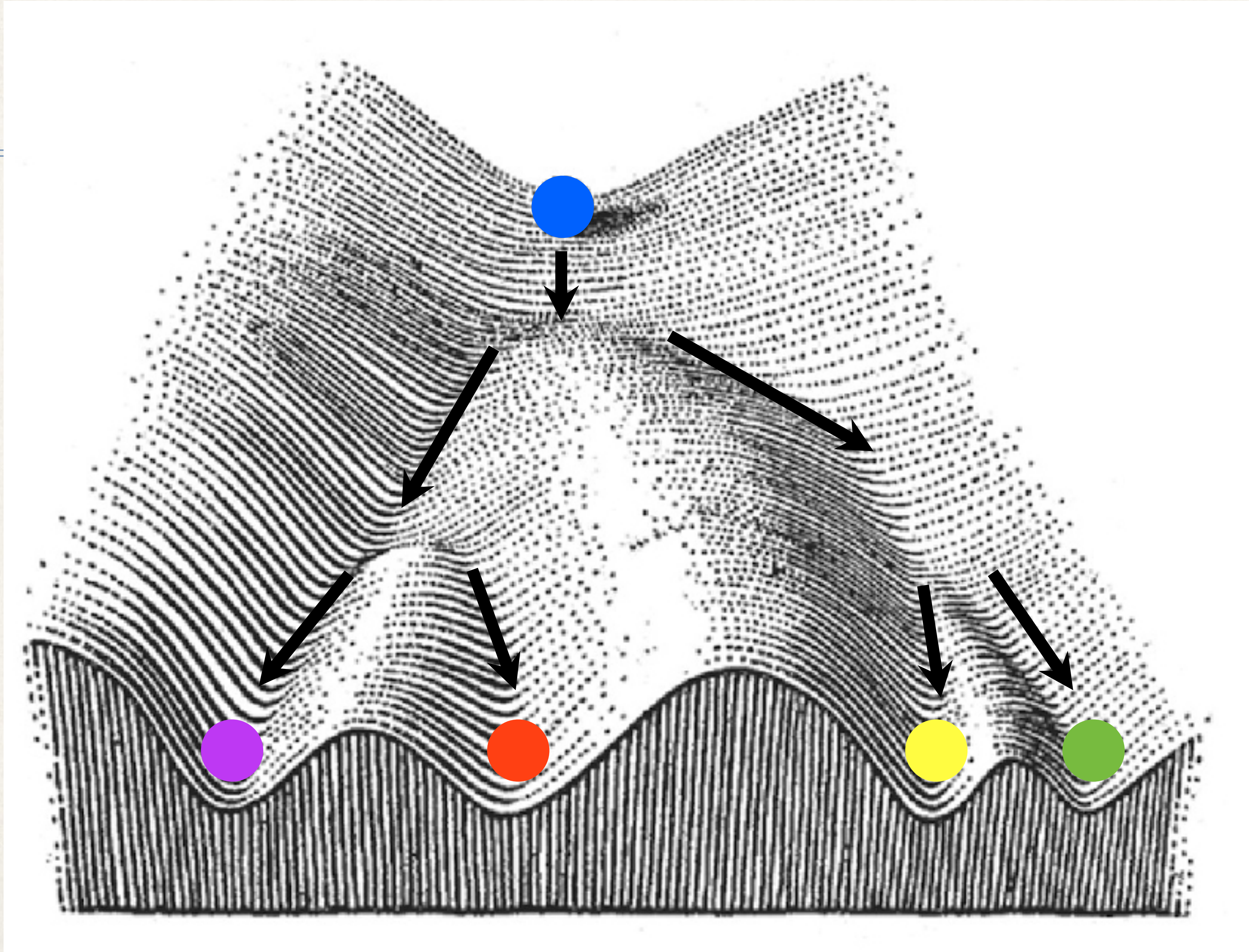
ik vienas mūsu organisma šūnas sākums

Pašatjaunošanās

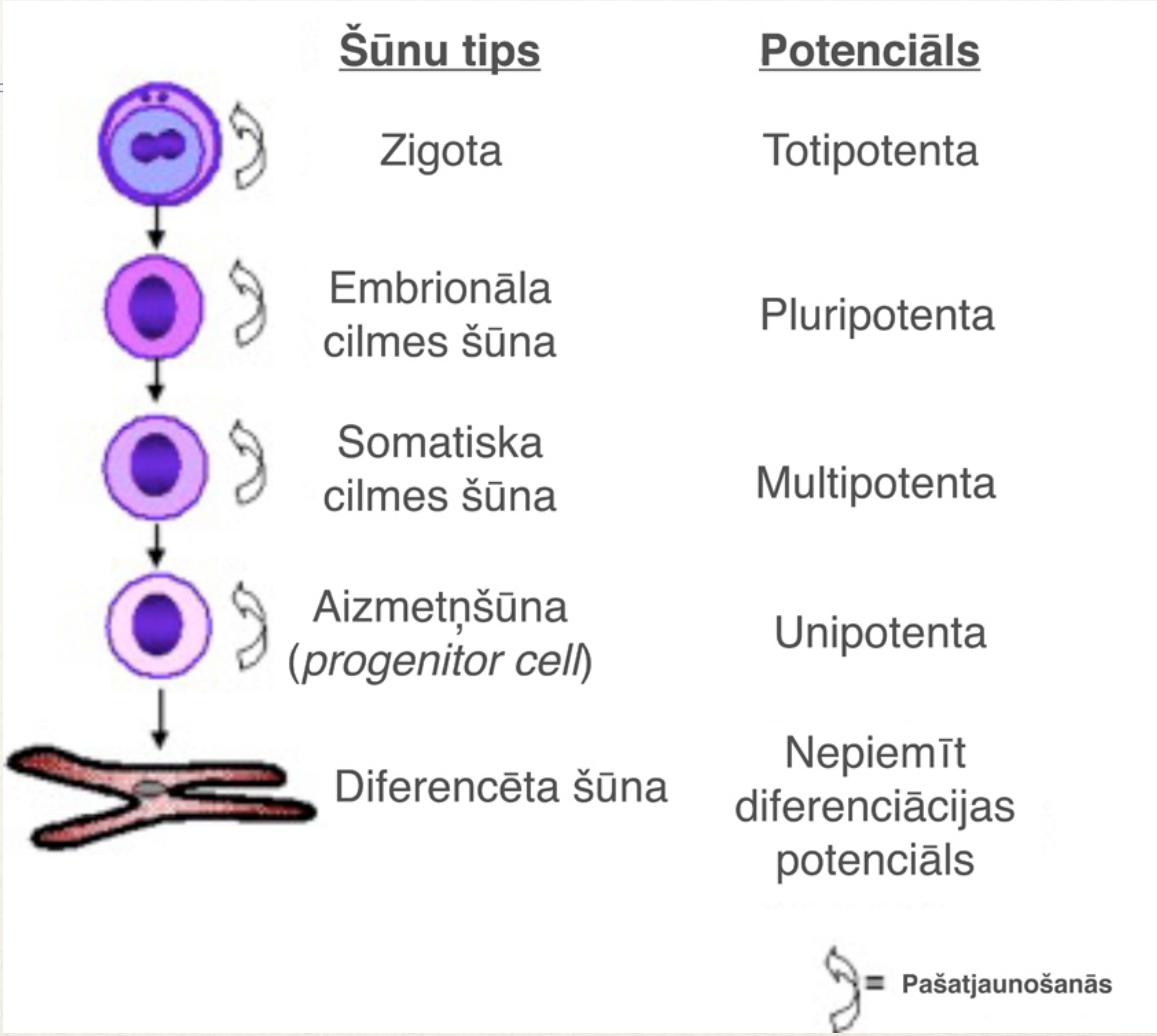


http://archive.eurostemcell.org/Outreach/outreach_about_stem_cells.htm

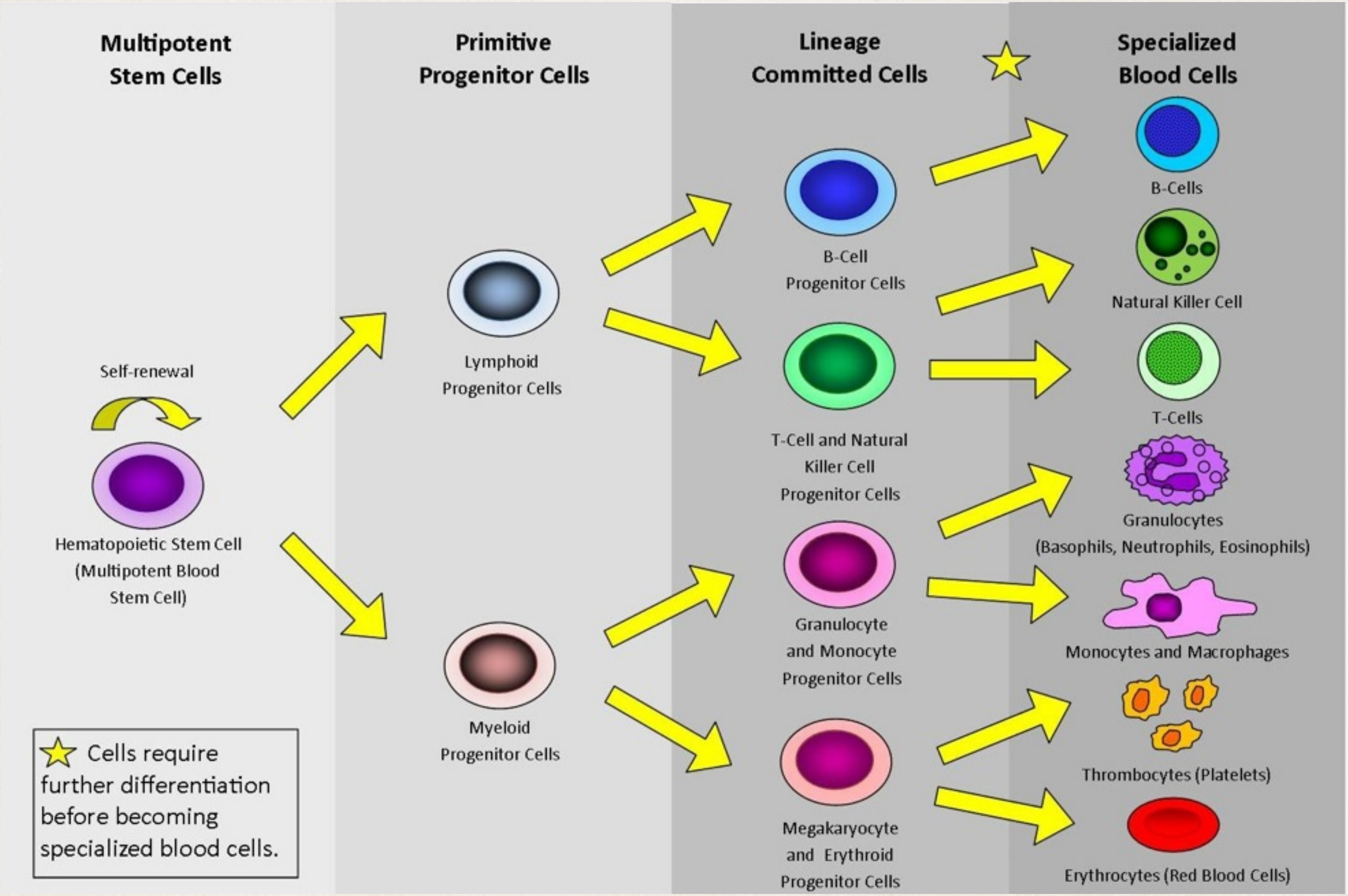
Diferenciācijas potenciāls



Diferenciācijas potenciāls



www.sciencedirect.com

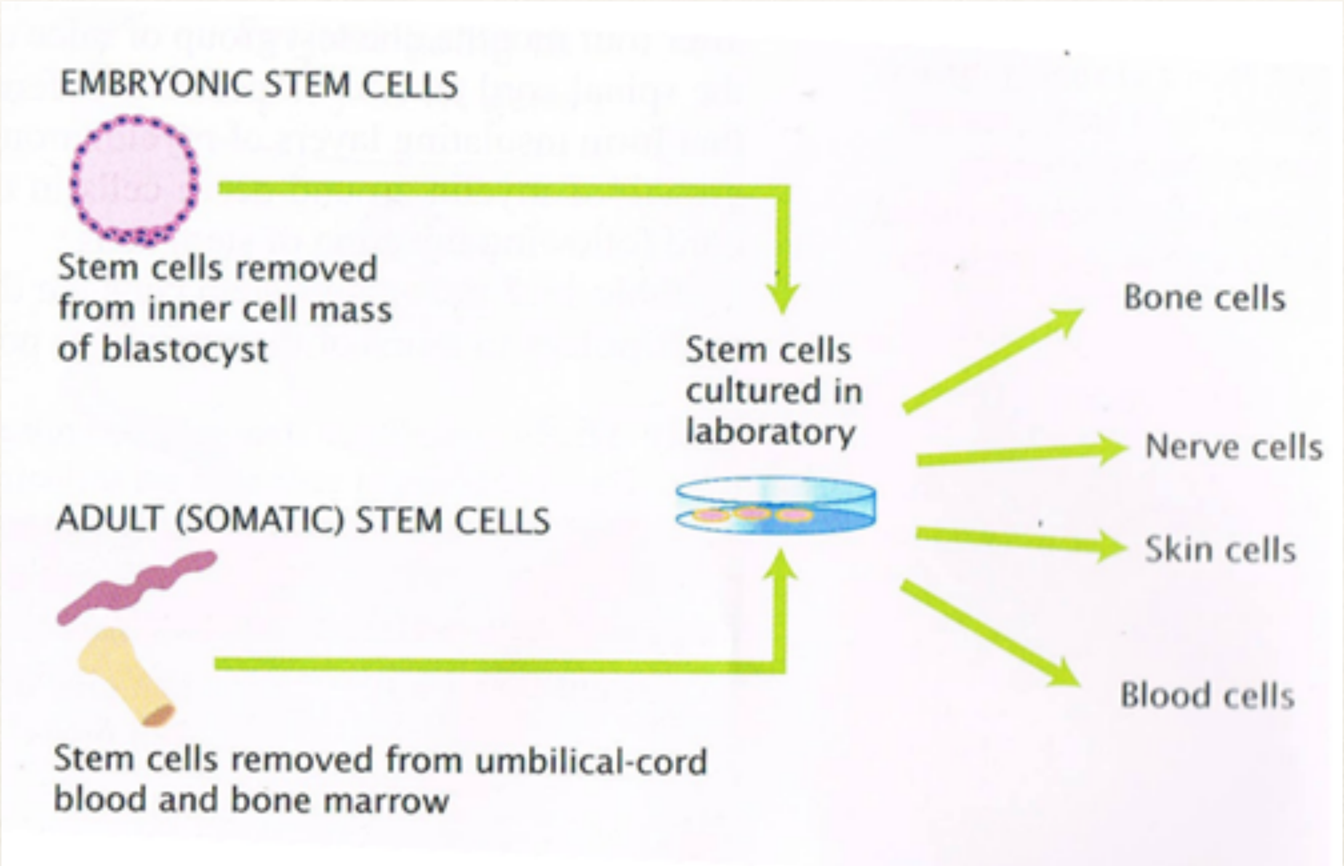


http://www.explorecuriocity.org/DesktopModules/CC_VideoPlayer/wfrm/wfrmPrintDocument.aspx?contentid=2439

Iedalījums

- Embrionālas Cilmes Šūnas (ECŠ) un inducētas Pluripotentas Cilmes Šūnas (iPCŠ)

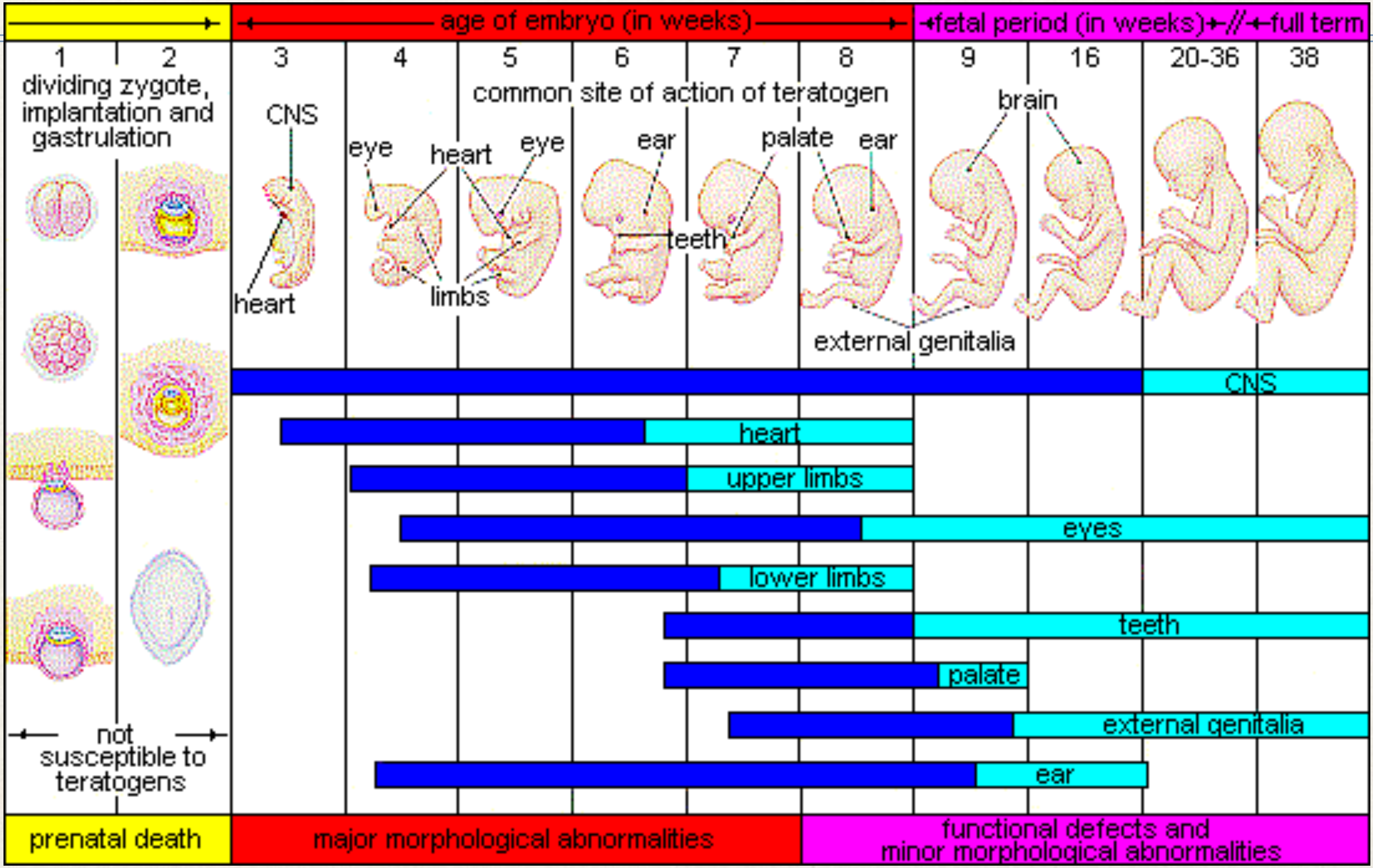
- Somatiskās Cilmes Šūnas (SCŠ)



http://biologysac4mj.wordpress.com/about/

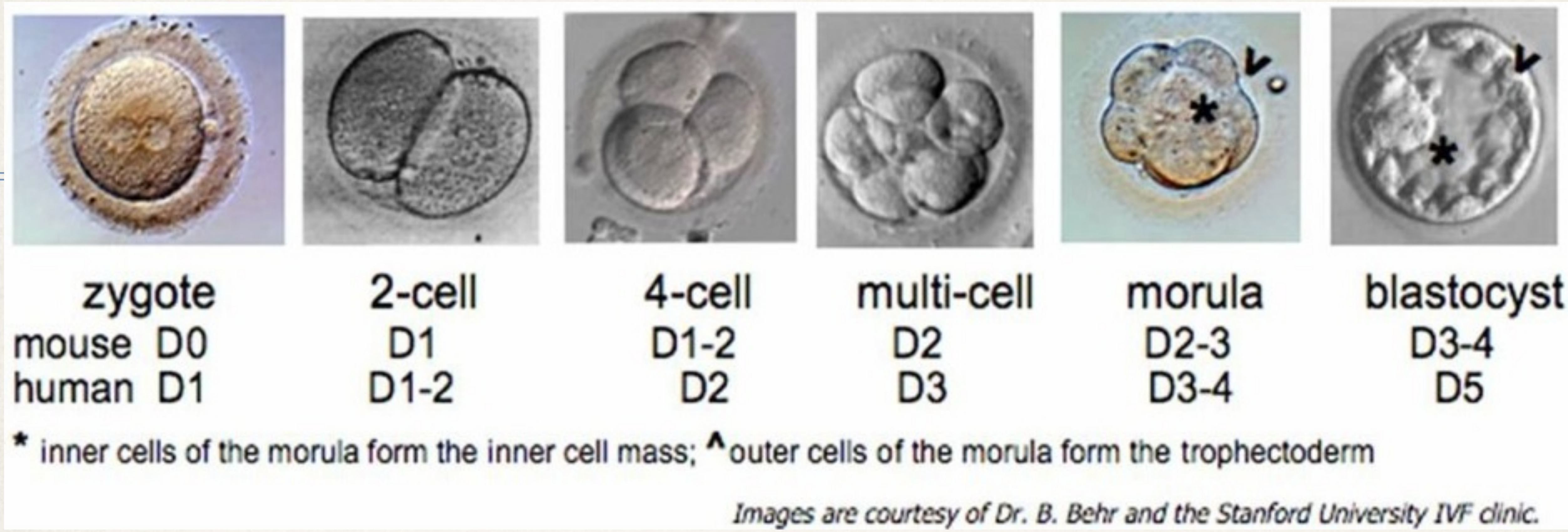
Embrionālās Cilmes Šūnas

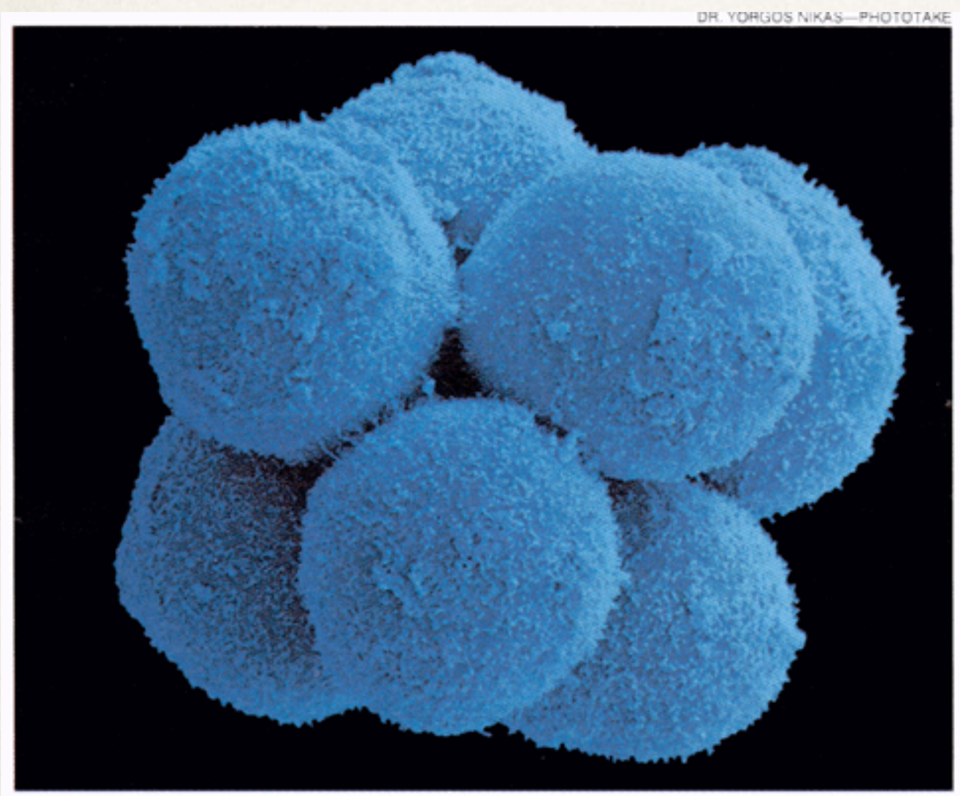
ECŠ iegūšana - cilvēka embrionālā attīstība



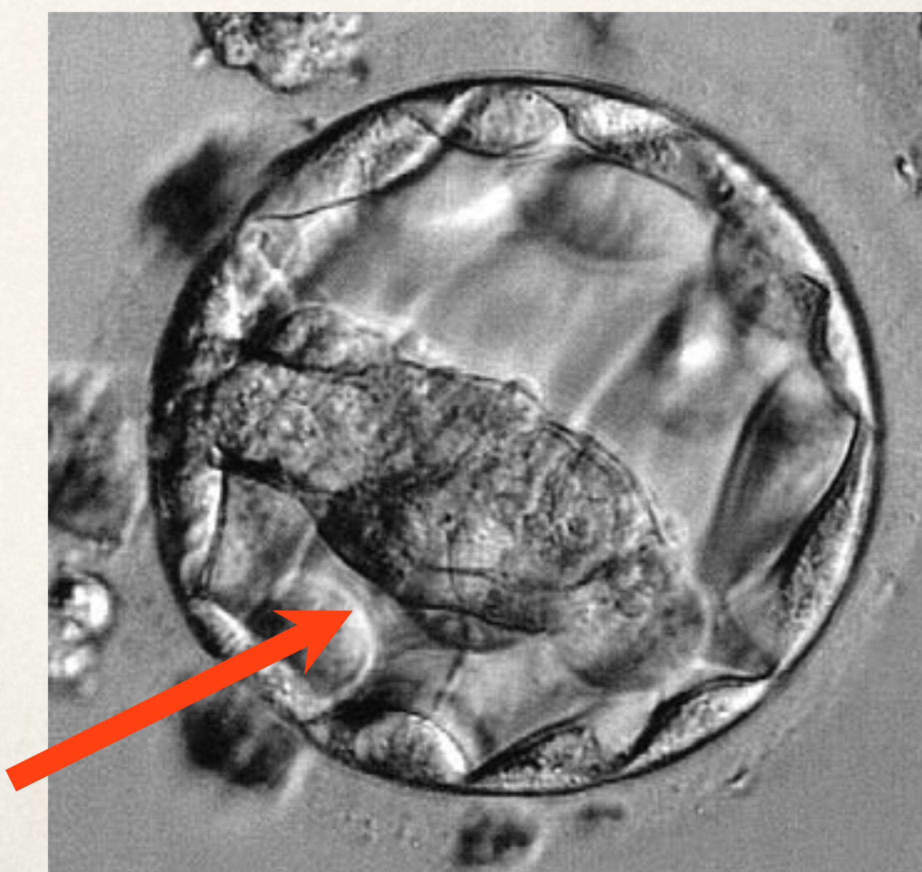
http://www-rohan.sdsu.edu/dept/phil/fetal.htm

ECŠ iegūšana



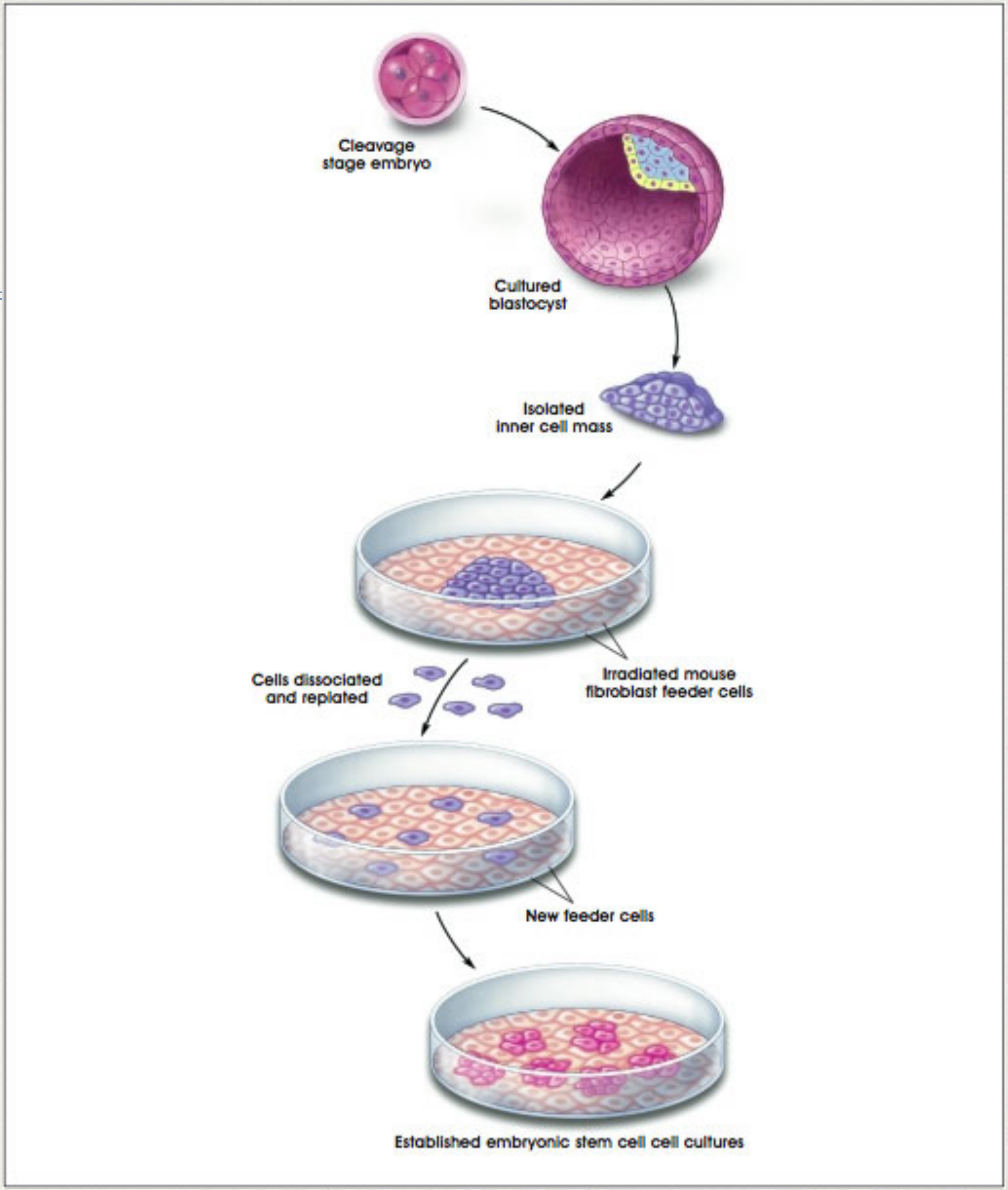

A magnified image of a 3-day-old human embryo

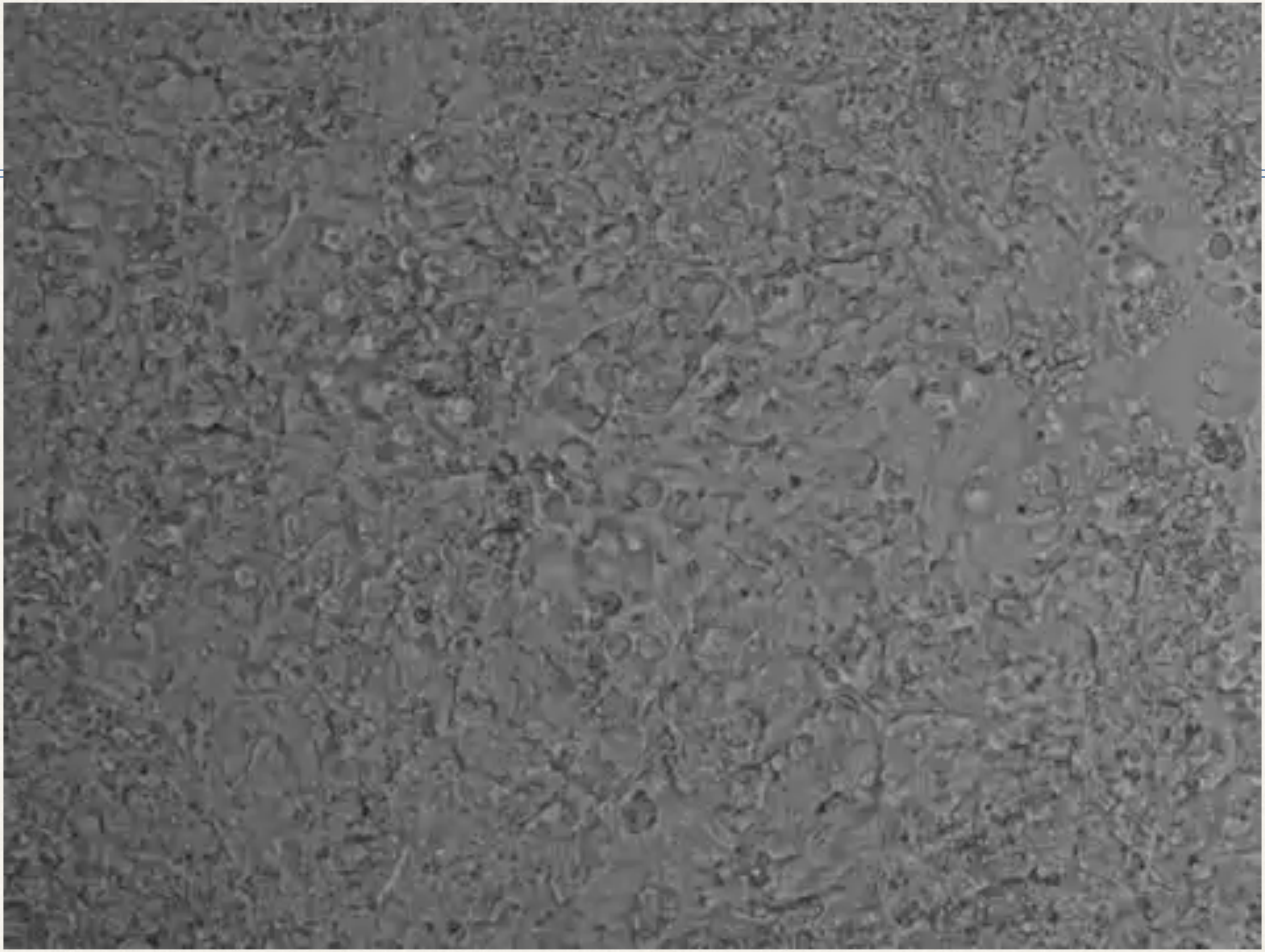
Iekšējā šūnu masa
(inner cell mass)



Sers Martins Evans un Metjū Kaufmans (1981.g.) - izdala un kultivē peles ECŠ

1998.g. - Džeims Tompsons cilvēka ECŠ

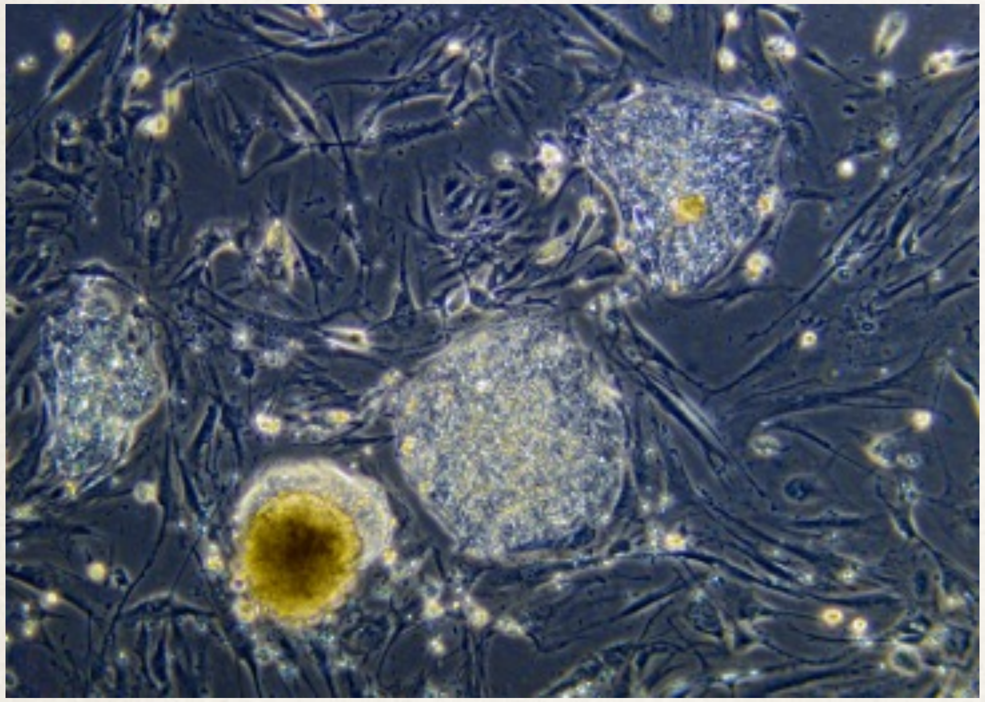




ECŠ

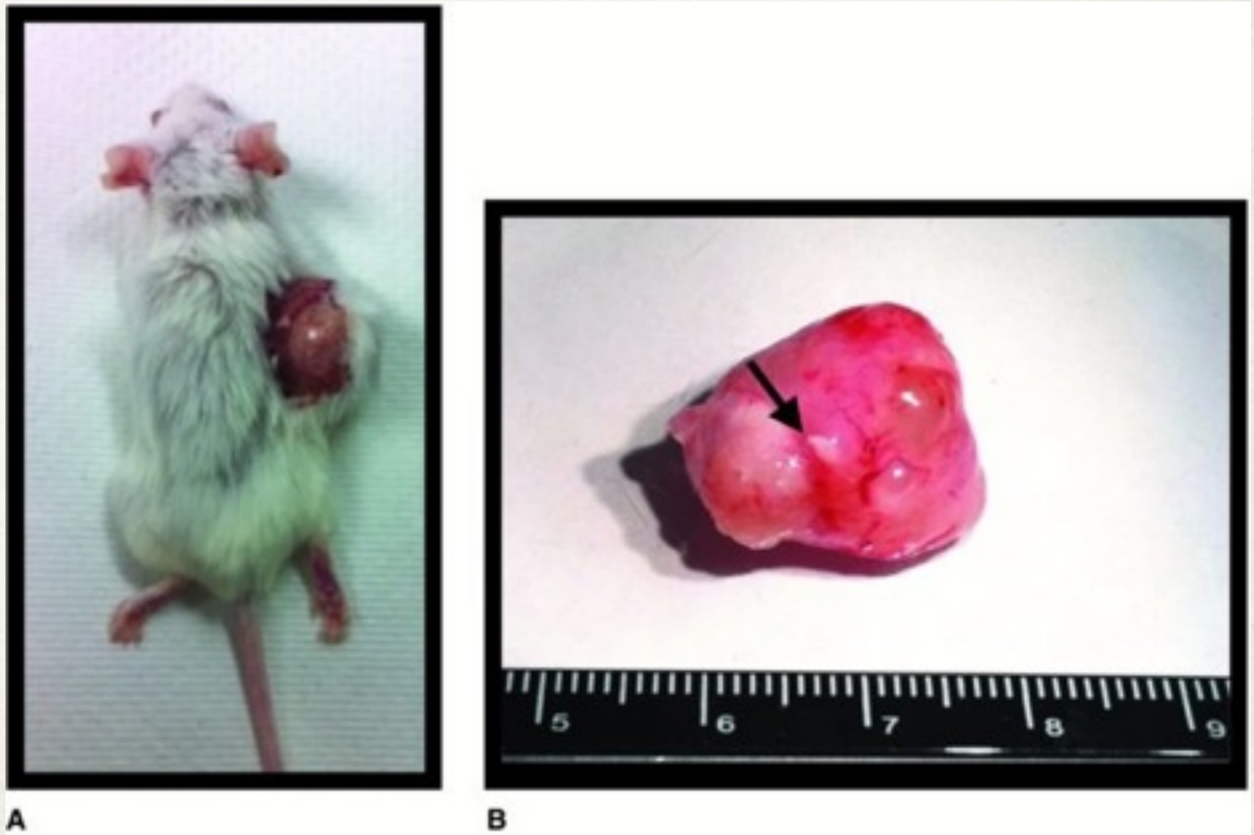
+	**-**

Augsts diferencēšanās potenciāls



http://stemcellmed.yolasite.com/the-basics-of-stem-cells.php

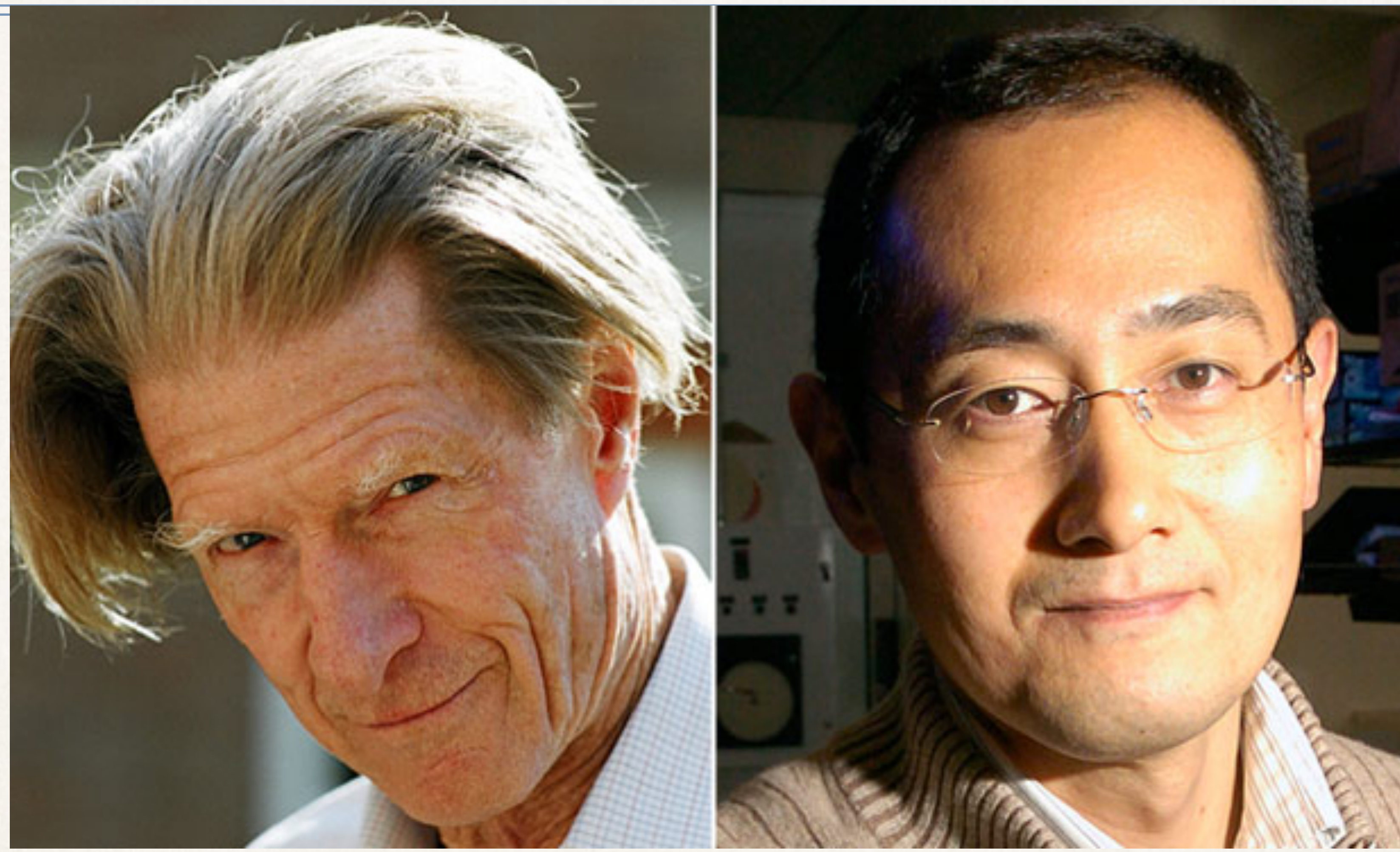
Augsts diferencēšanās potenciāls



Zhang et al., 2012, http://www.stembook.org

iPCŠ - inducētas Pluripotentas Cilmes Šūnas

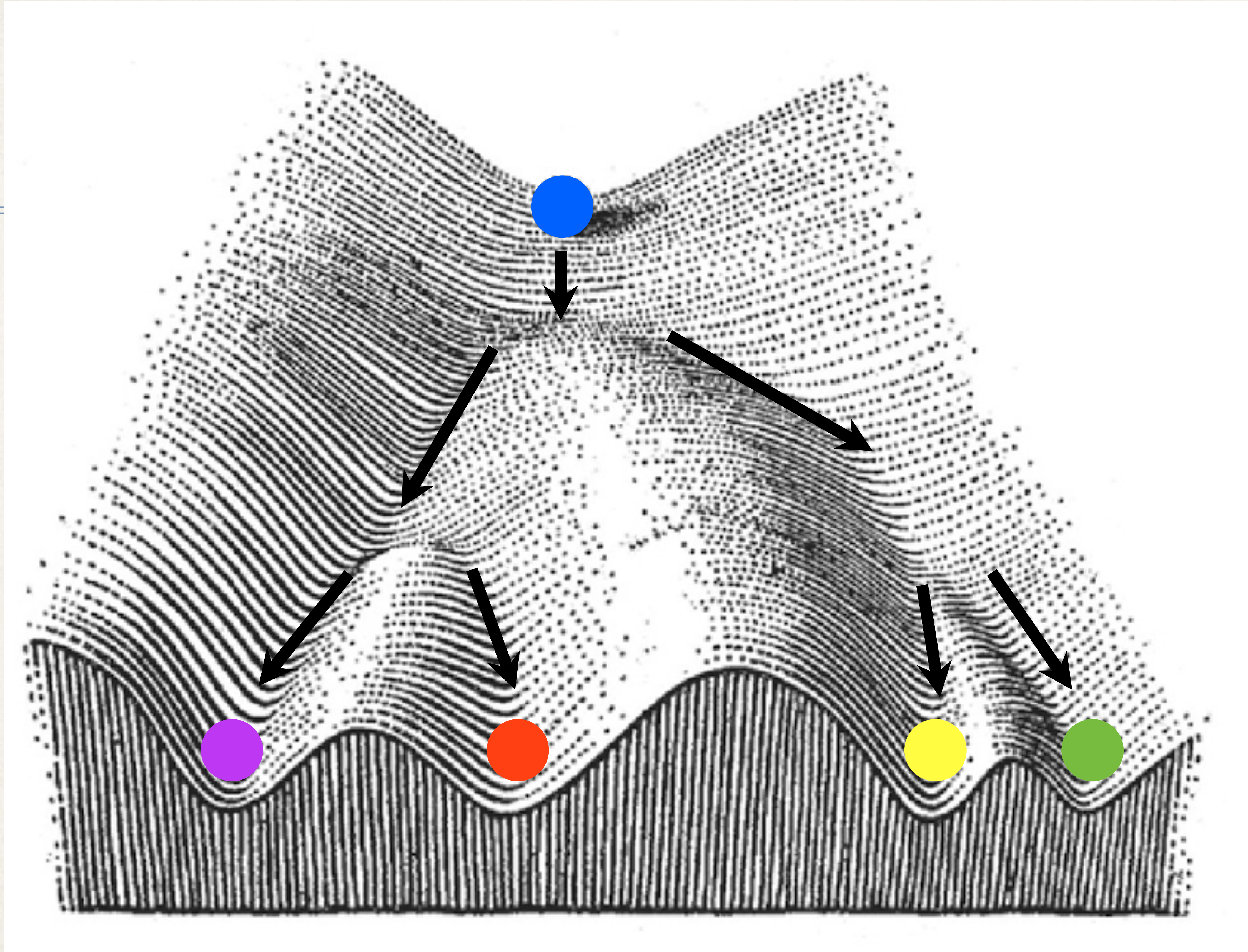
2012.g. Nobela prēmija Medicīna un fizioloģija



Sers Džons Gurdons
(Sir John Gurdon)

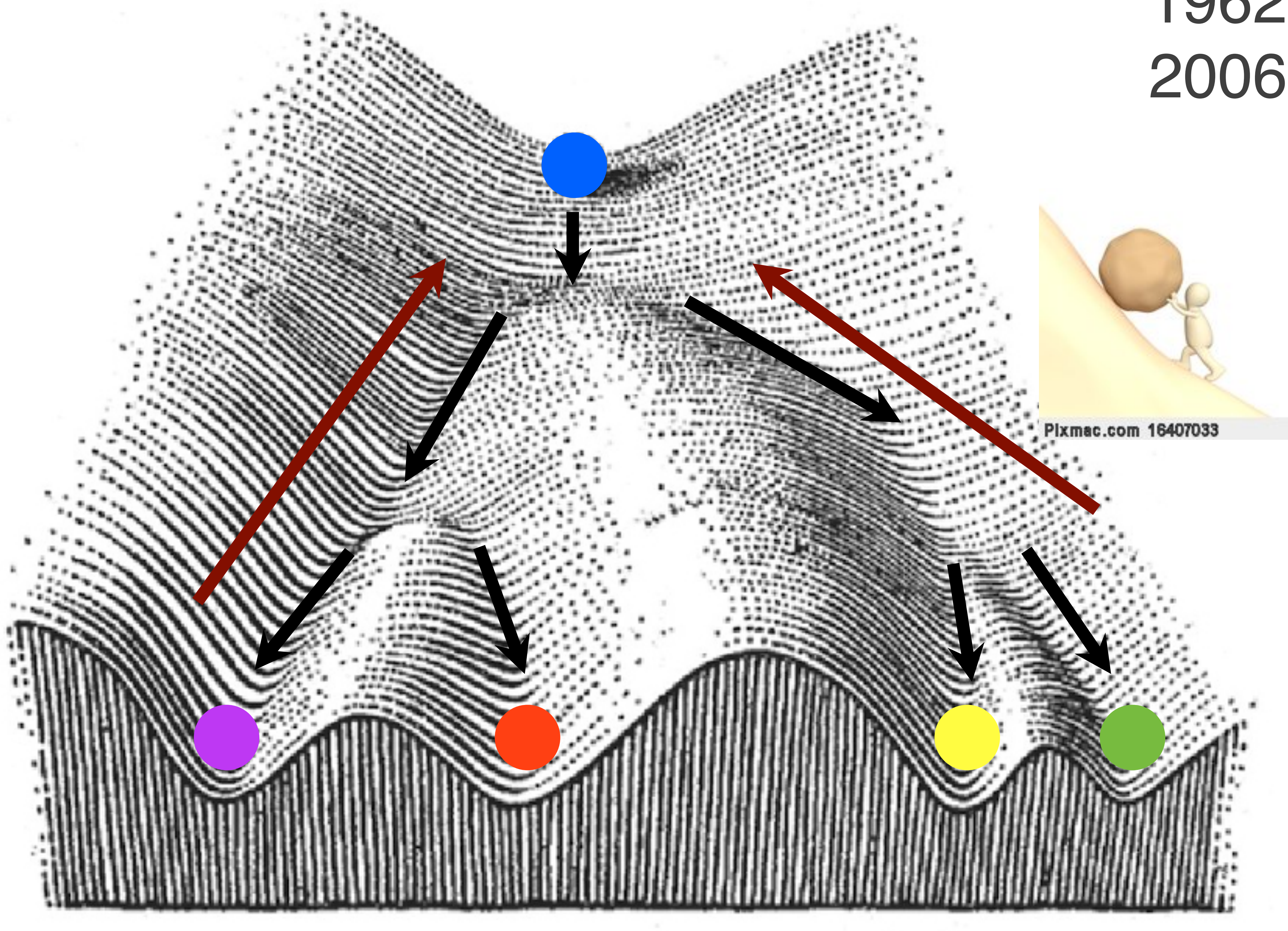
Šinaja Jamanaka
(Shinya Yamanaka)

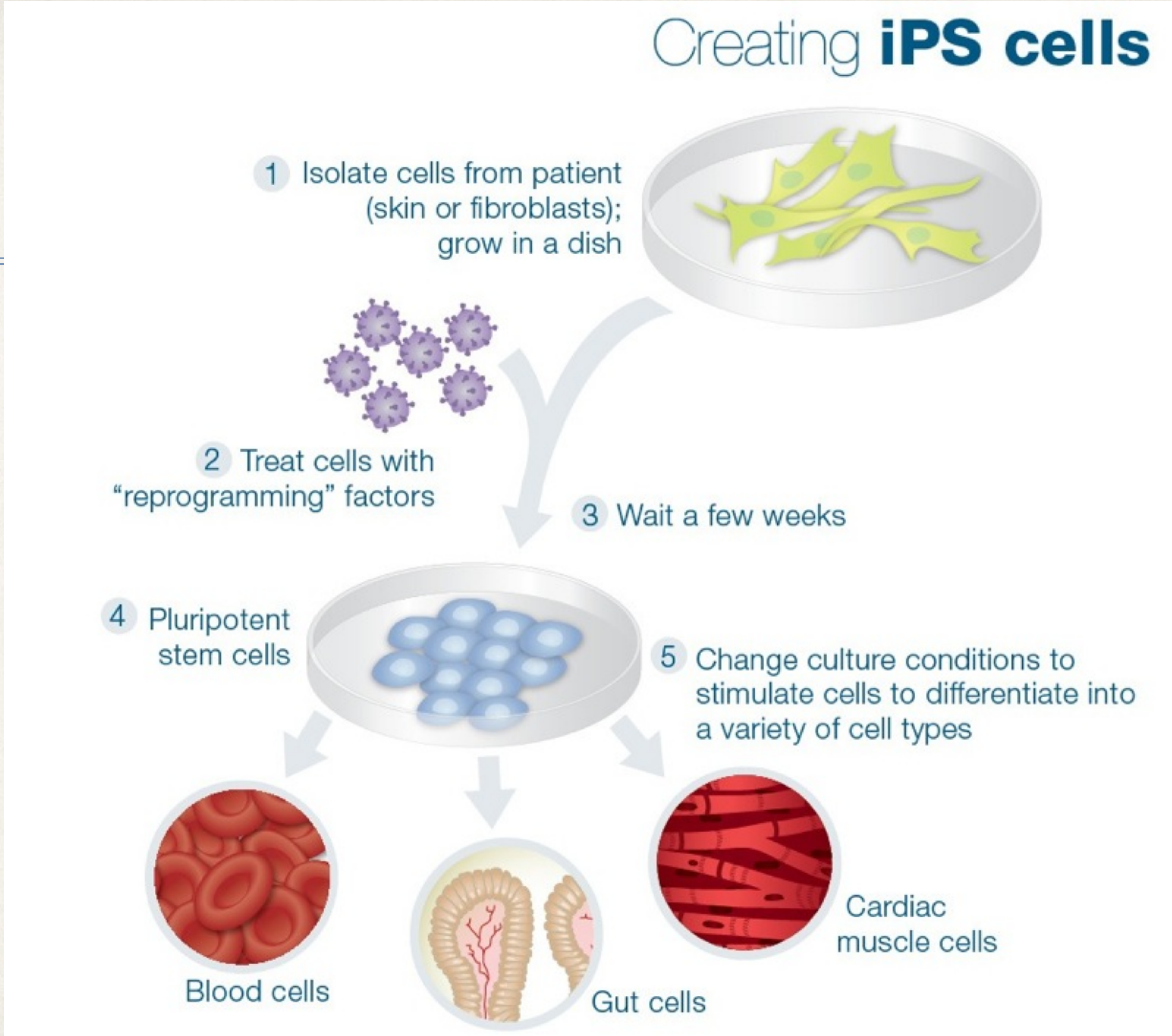
http://www.nobelprize.org/nobel_prizes/medicine/laureates/



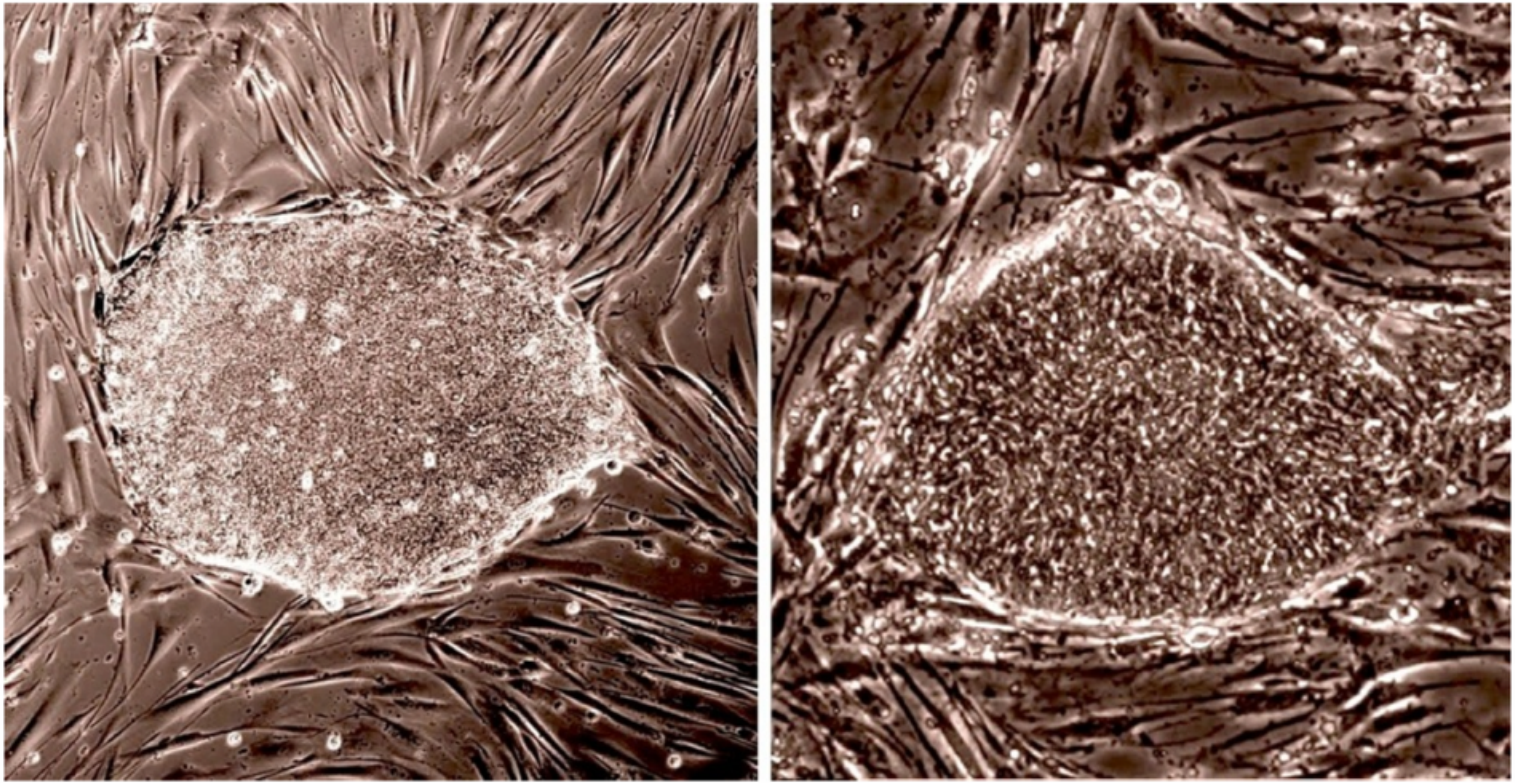
Sers Džons B.Gurdons un Šinaja Jamanaka

1962
2006

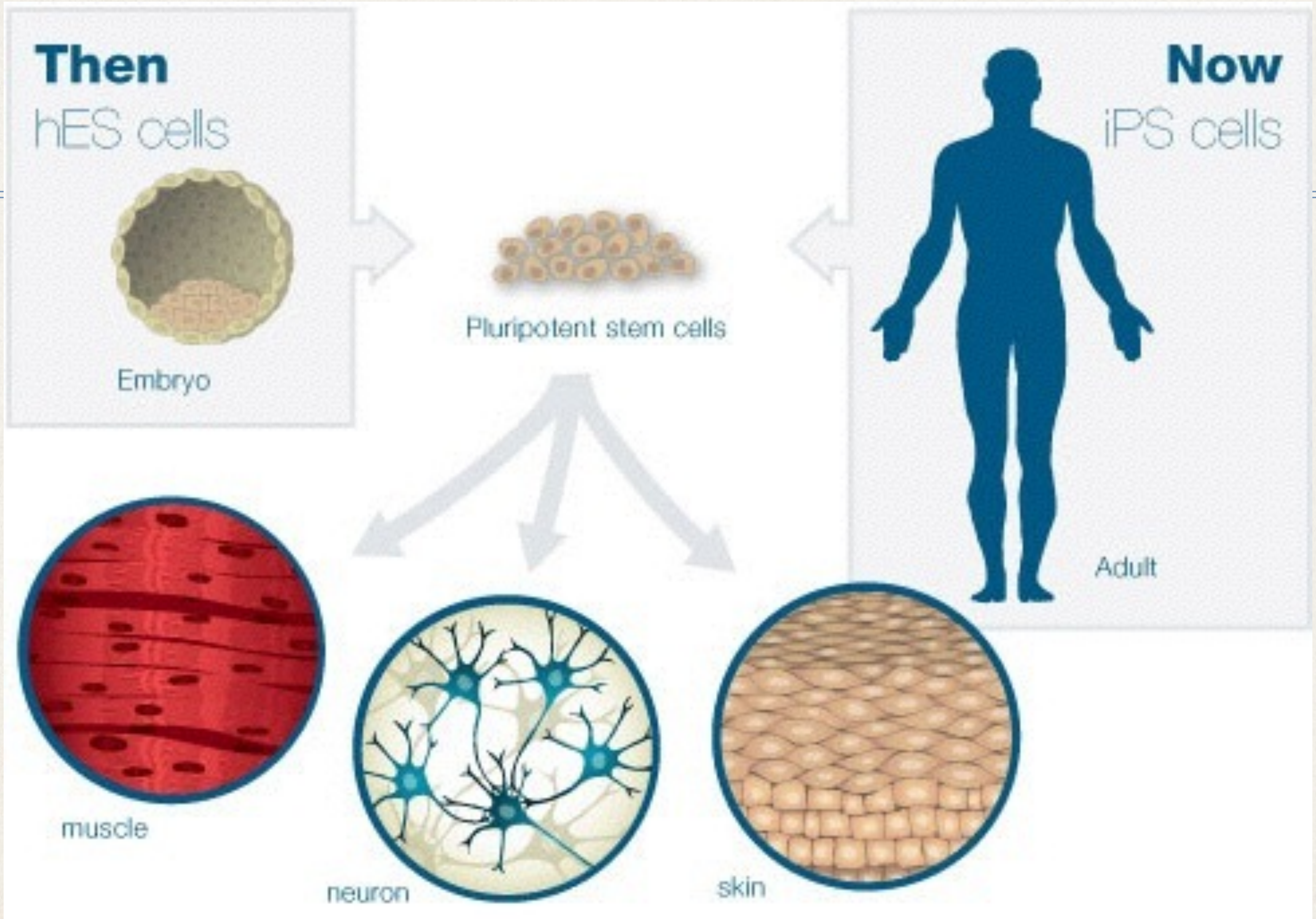




http://learn.genetics.utah.edu/content/stemcells/quickref/



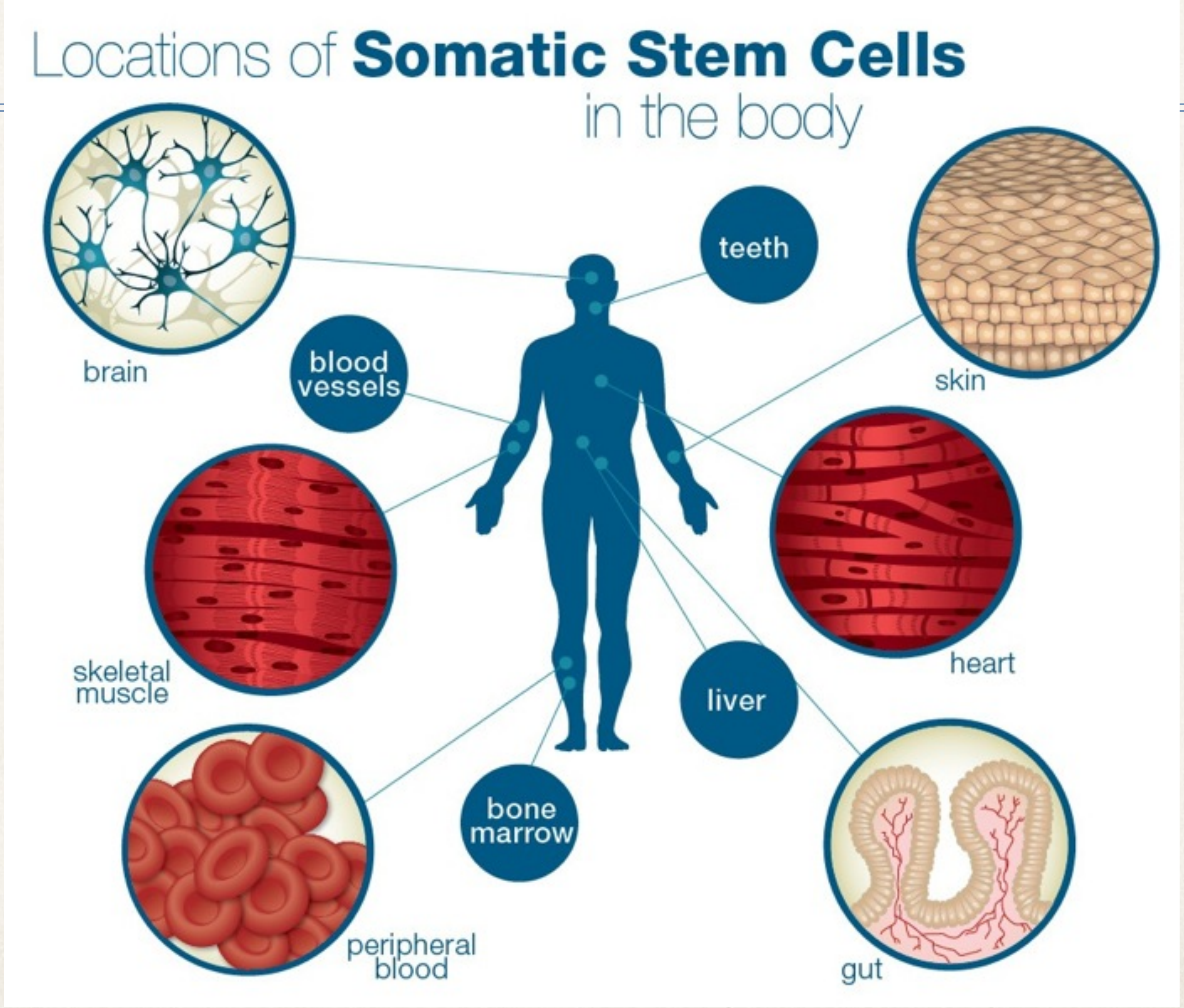
http://cirmresearch.blogspot.com/



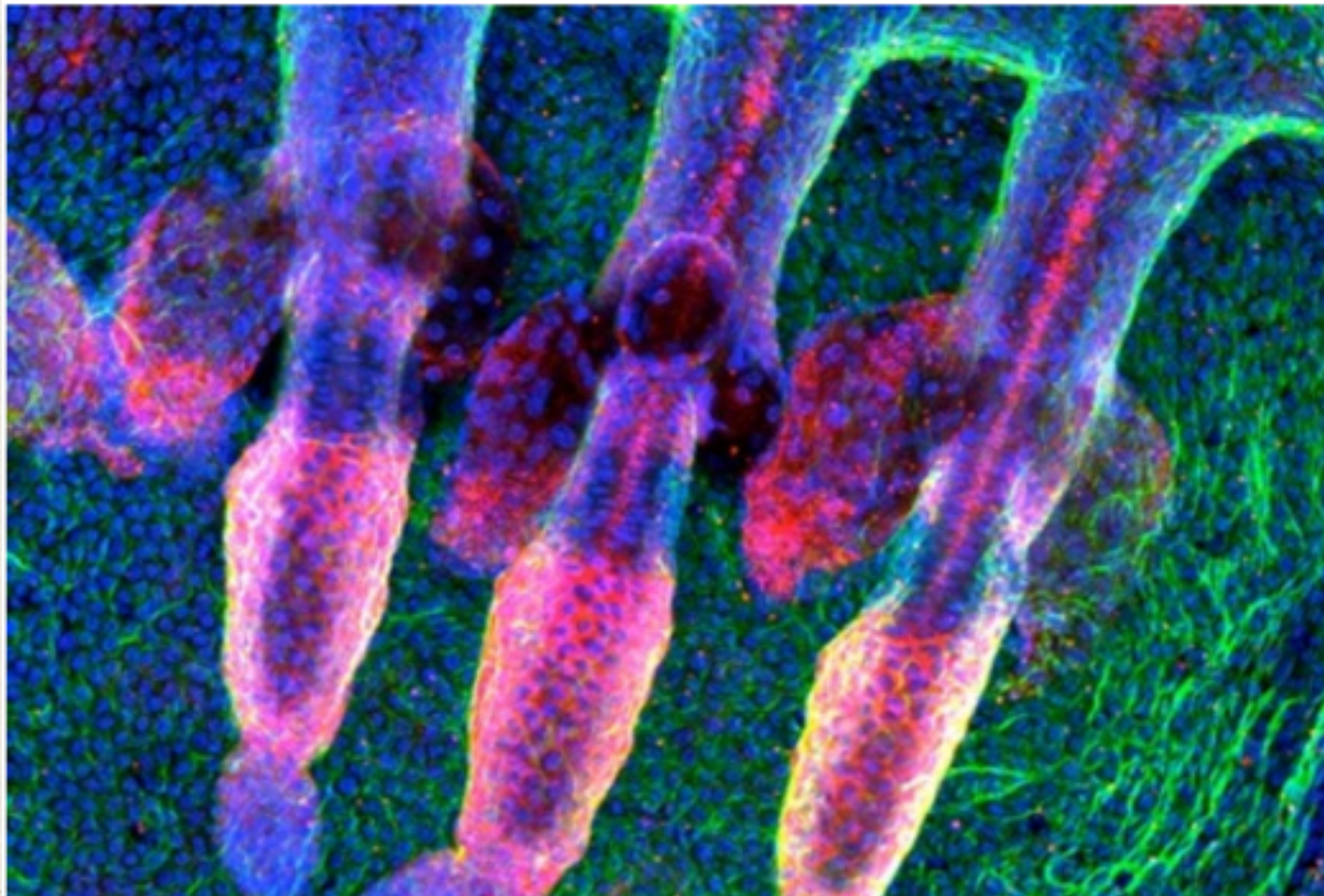
http://learn.genetics.utah.edu/content/stemcells/scissues/

SCŠ - Somatiskās Cilmes Šūnas

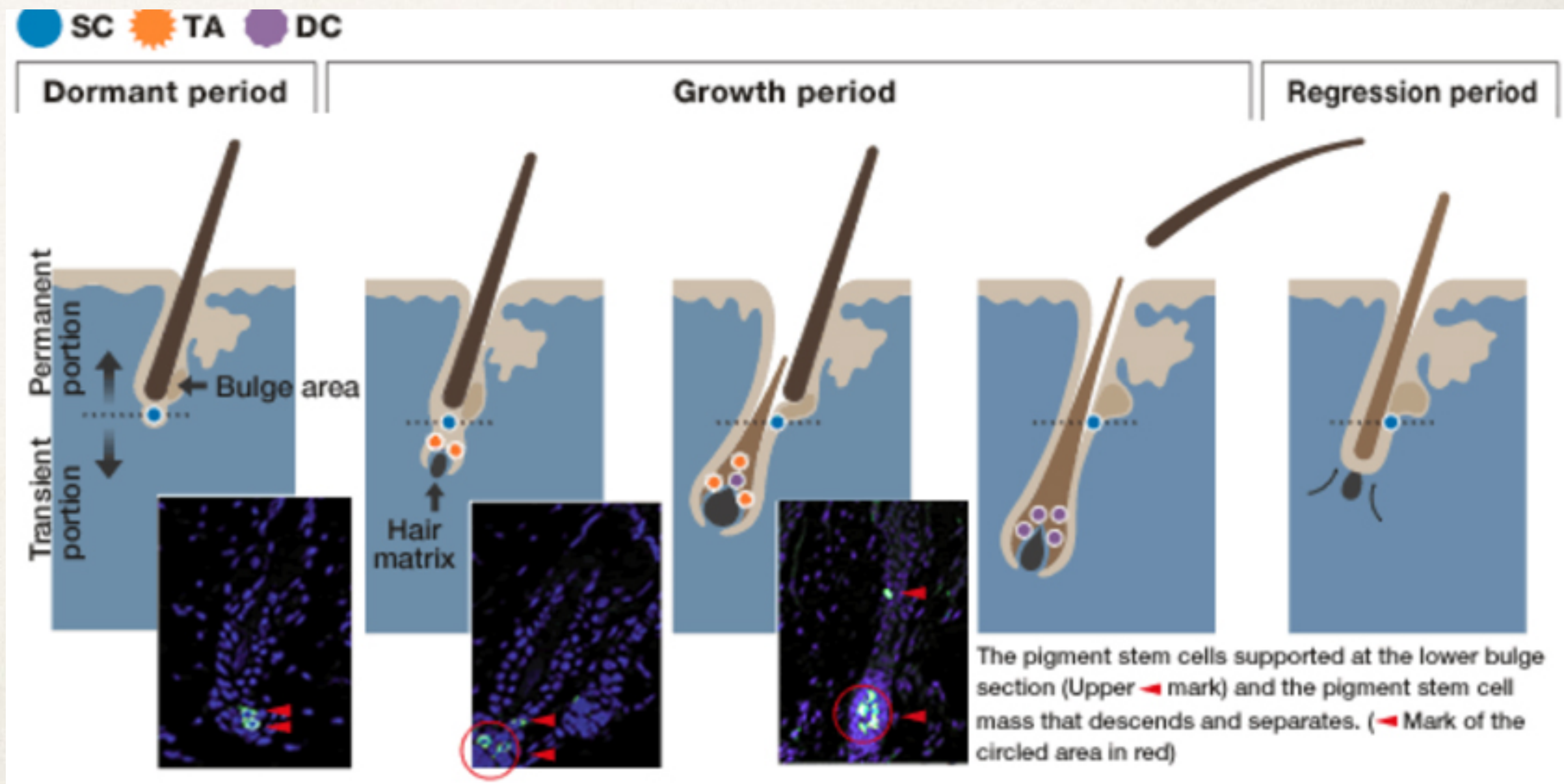
Somatiskās cilmes šūnas: (i) atrodamas dažādos orgānos; (ii) atjauno novecojušos vai aizstāj bojā gājušos audus

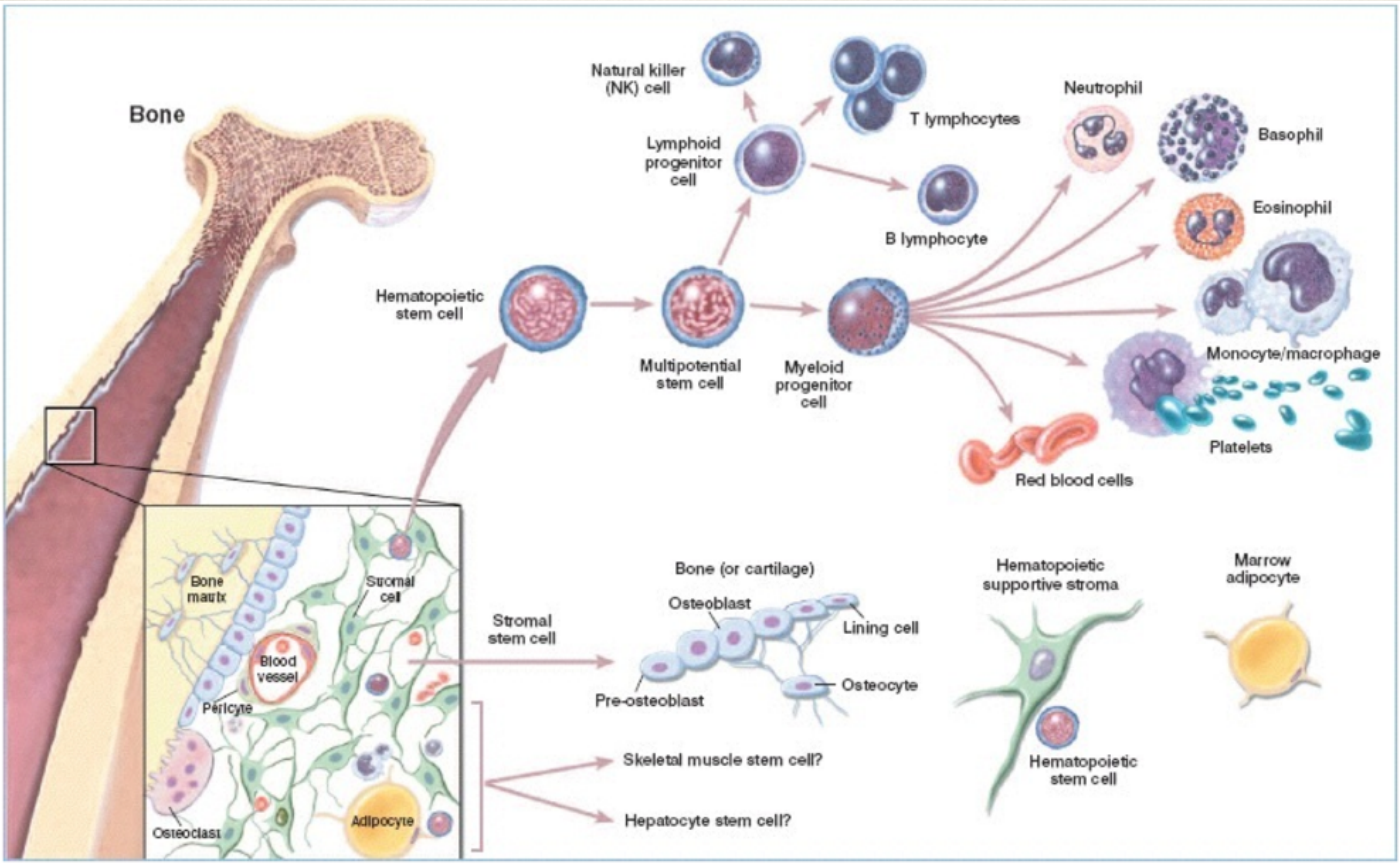


http://learn.genetics.utah.edu/content/stemcells/quickref/



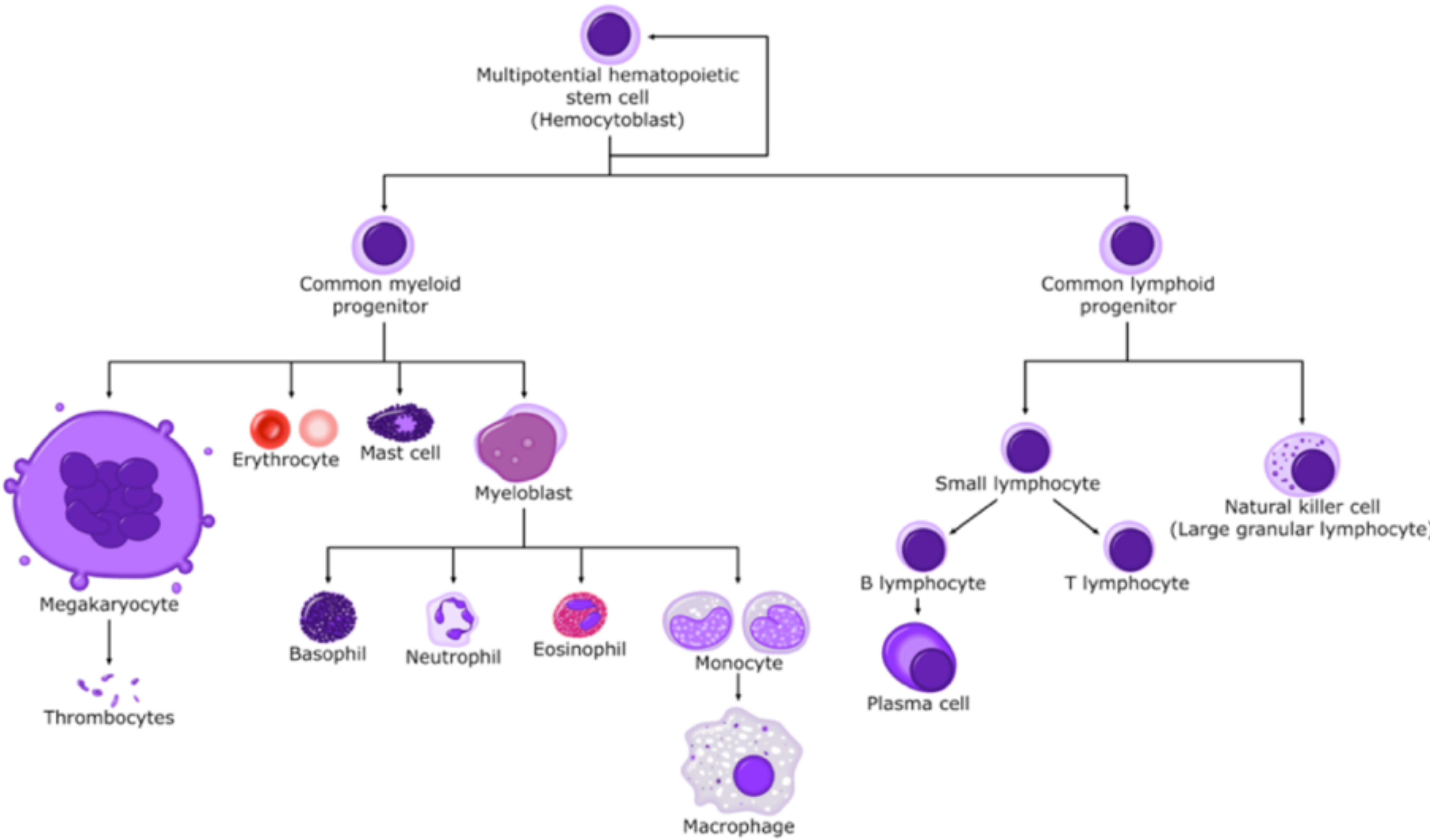
Cox and Frye, http://www.cell.com/cell_picture_show-skin





Bone
Natural killer (NK) cell
T lymphocytes
Lymphoid progenitor cell
B lymphocyte
Neutrophil
Basophil
Eosinophil
Hematopoietic stem cell
Multipotential stem cell
Myeloid progenitor cell
Monocyte/macrophage
Platelets
Red blood cells
Bone matrix
Stromal cell
Blood vessel
Pericyte
Osteoclast
Adipocyte
Stromal stem cell
Bone (or cartilage)
Osteoblast
Lining cell
Osteocyte
Pre-osteoblast
Skeletal muscle stem cell?
Hepatocyte stem cell?
Hematopoietic supportive stroma
Hematopoietic stem cell
Marrow adipocyte

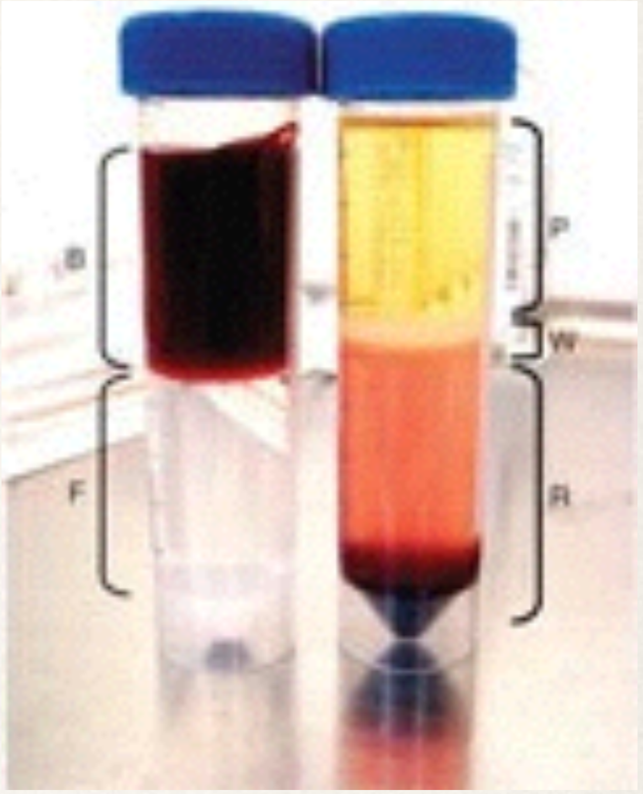
Hematopoētiskās cilmes šūnas



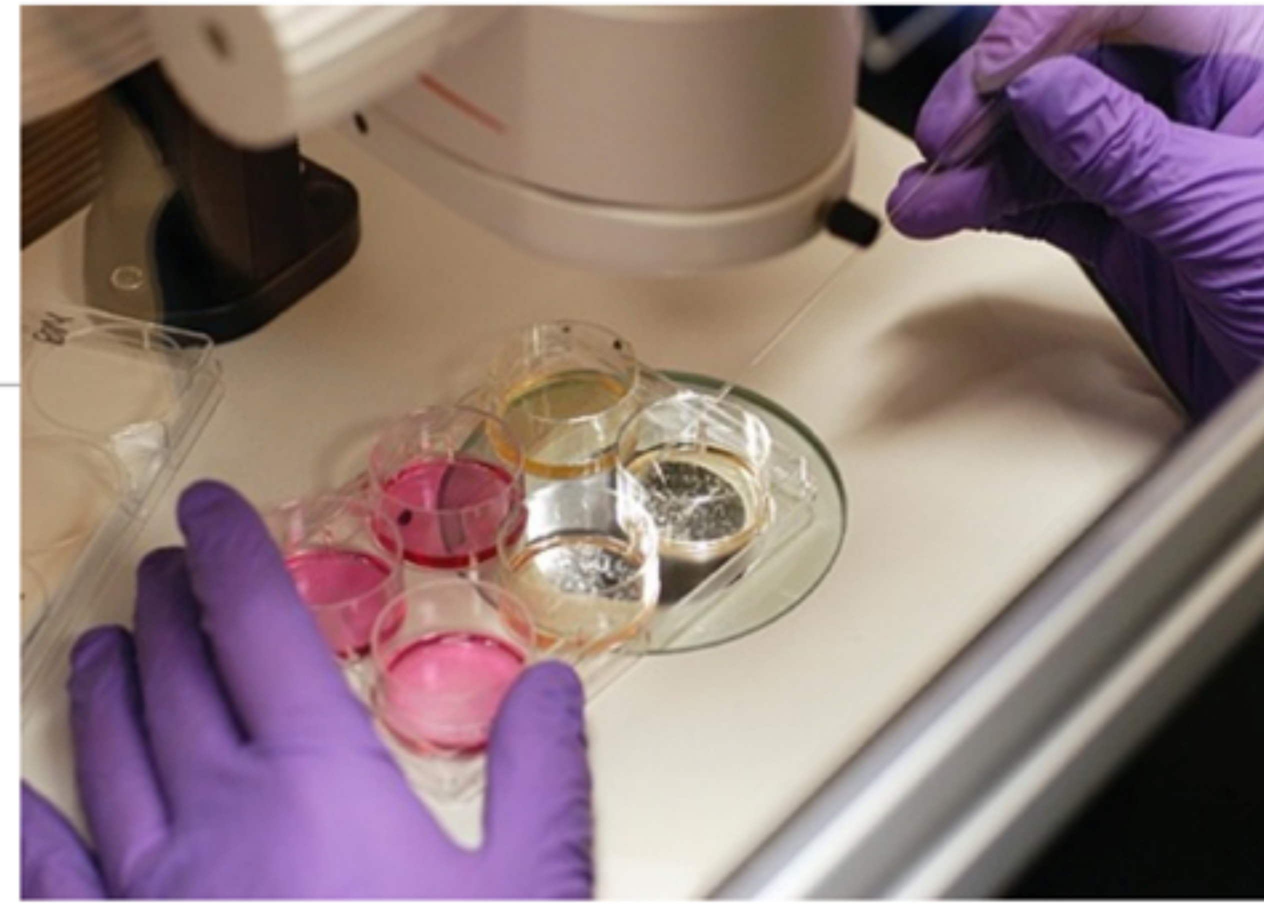
http://www.allthingsstemcell.com

Kā mēs varam iegūt SCŠ?

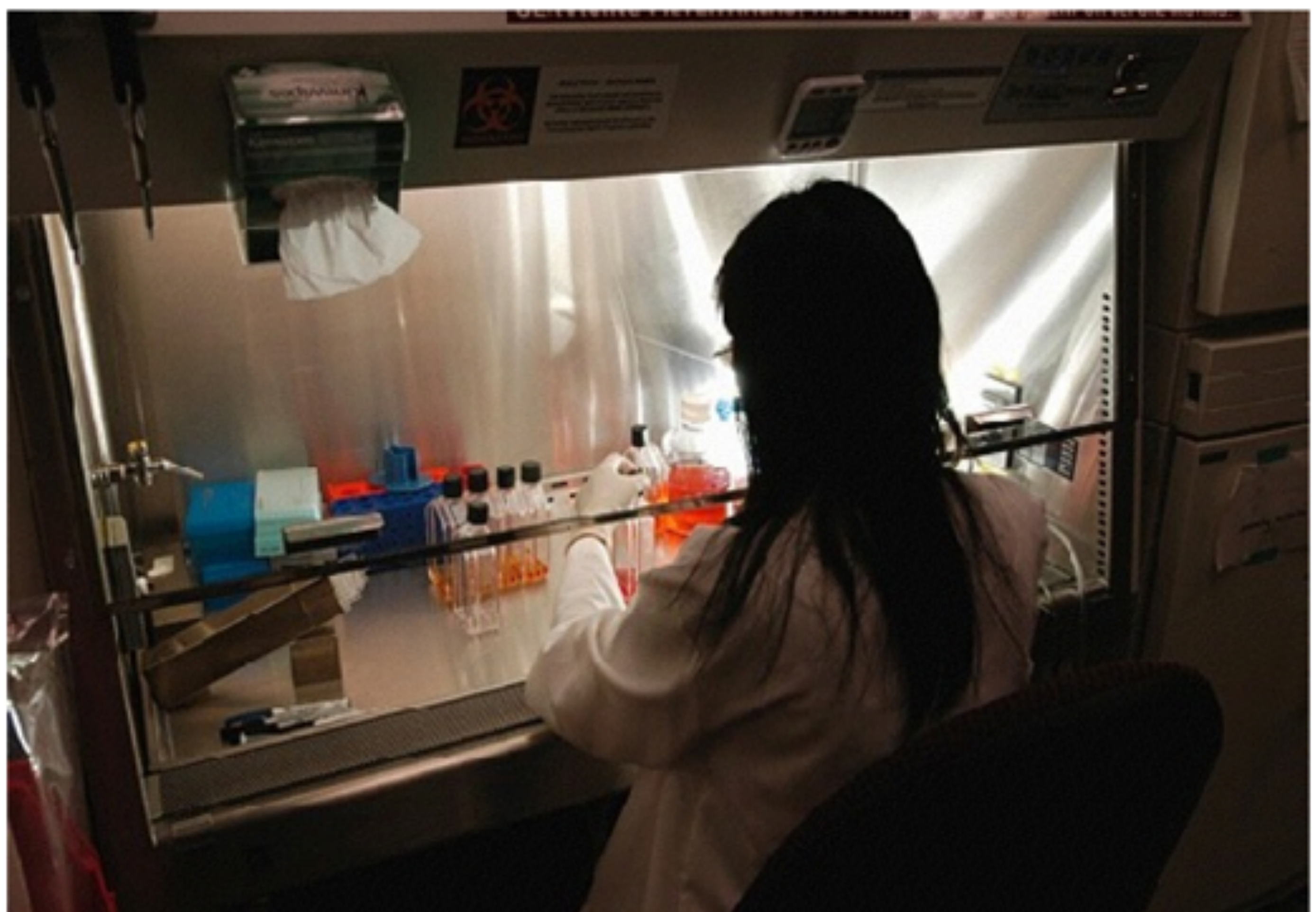
- centrifugēšana blīvuma gradientā
- atdalīšana izmantojot marķierus
- kultivējot specifiskās vidēs
- enzimātiski sadalīt audus
- kultivēšana uz cietas virsmas



http://www.nature.com/nprot/journal/v3/n6/full/nprot.2008.69.html

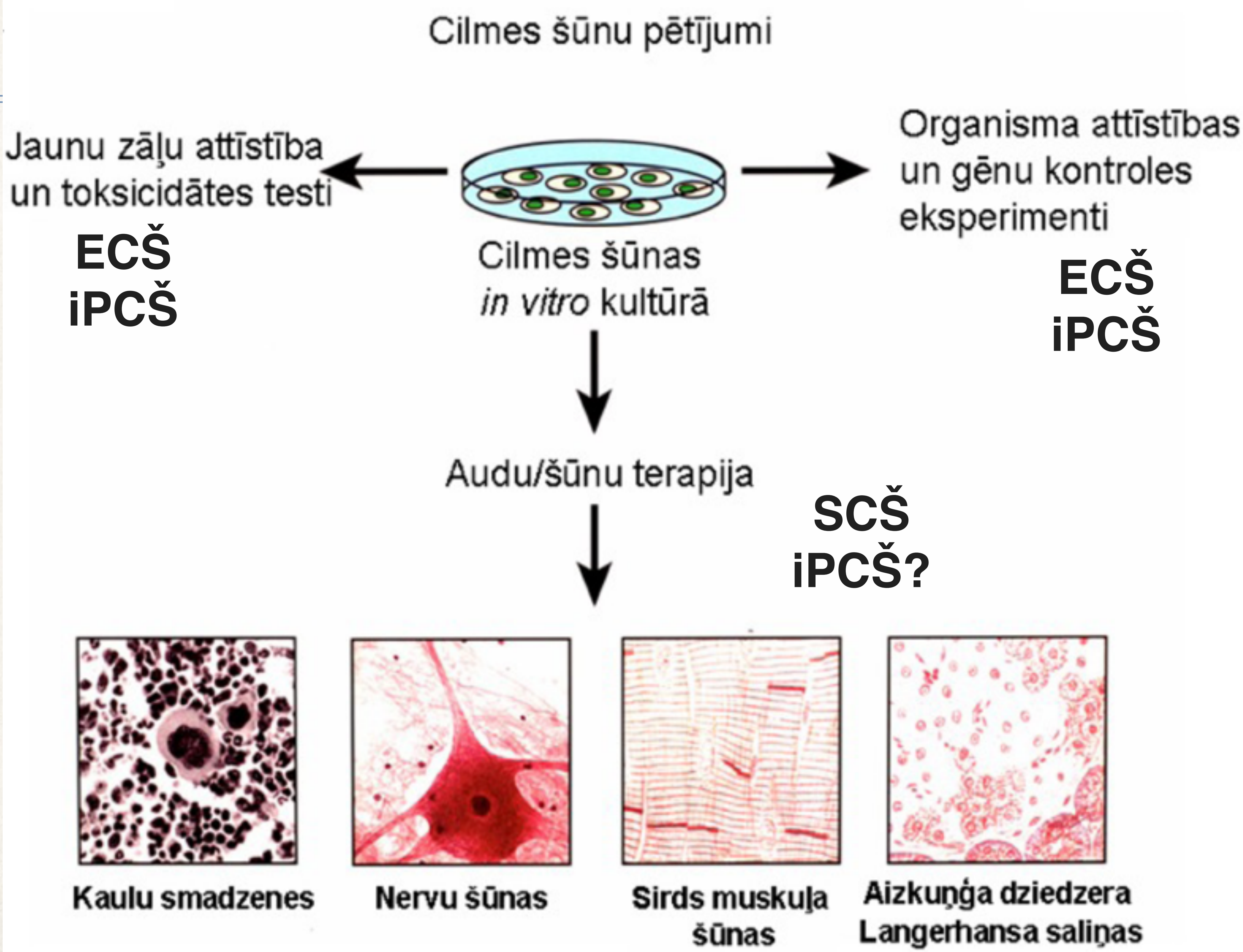


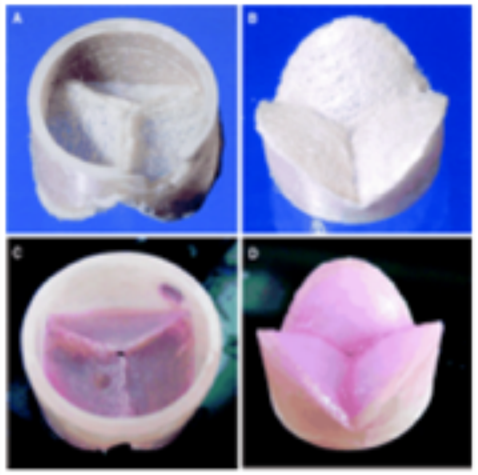
http://newsroom.stemcells.wisc.edu/gallery



Šūnu pielietojums

Šūnu praktiskais pielietojums

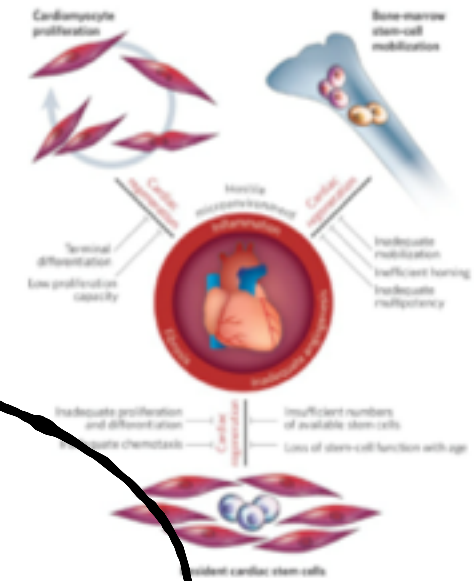




Mol et al., Circulation 2006

Audu inženierija un biomateriāli

Šūnu terapija



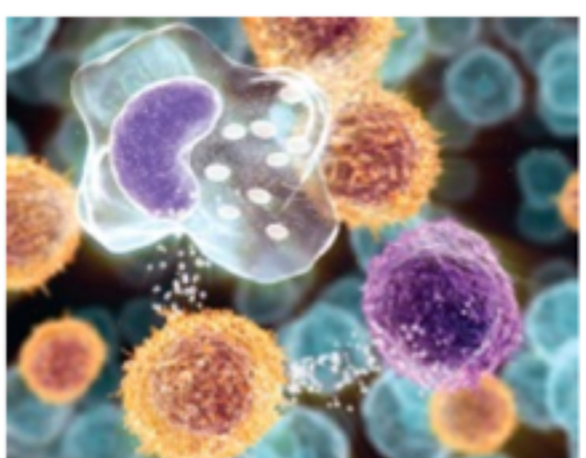
Segers and Lee, Nature, 2008

Gēnu terapija

scientificamerican.com

Reģeneratīvā medicīna

Iekšējie reģenerācijas stimulatori

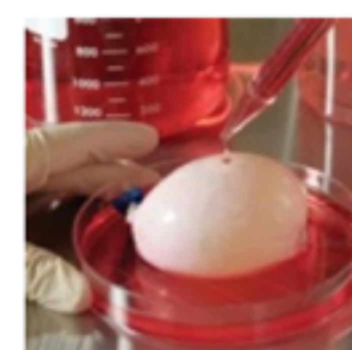


multiple-sclerosis-research.blogspot.com

Ksenotransplantācija

riaus.org.au/

Medicīnas iekārtas un mākslīgie orgāni

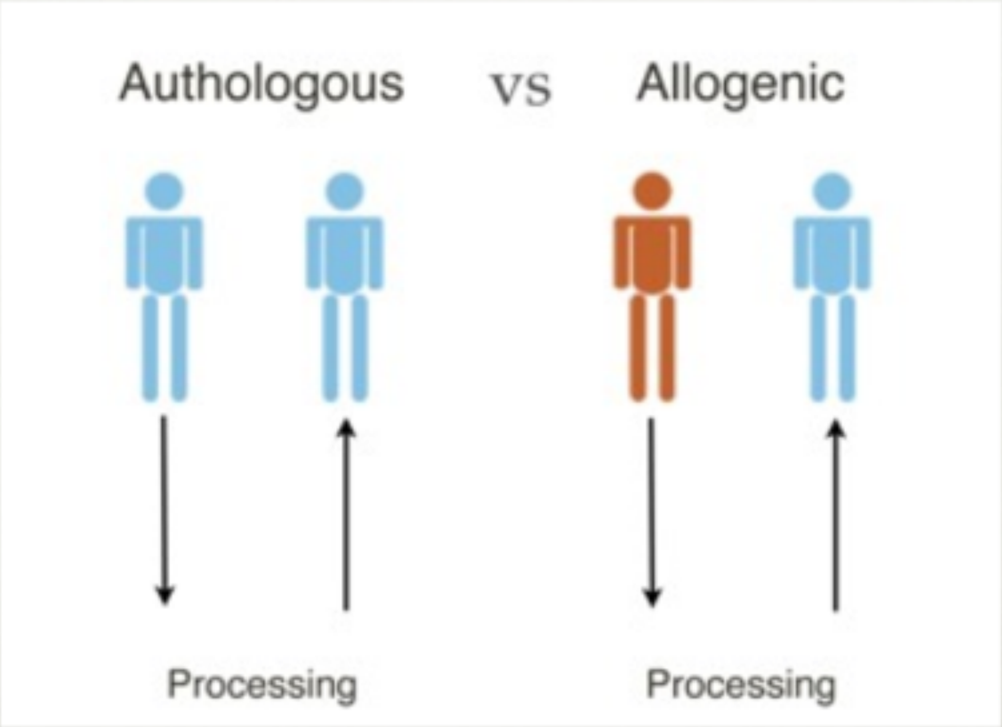


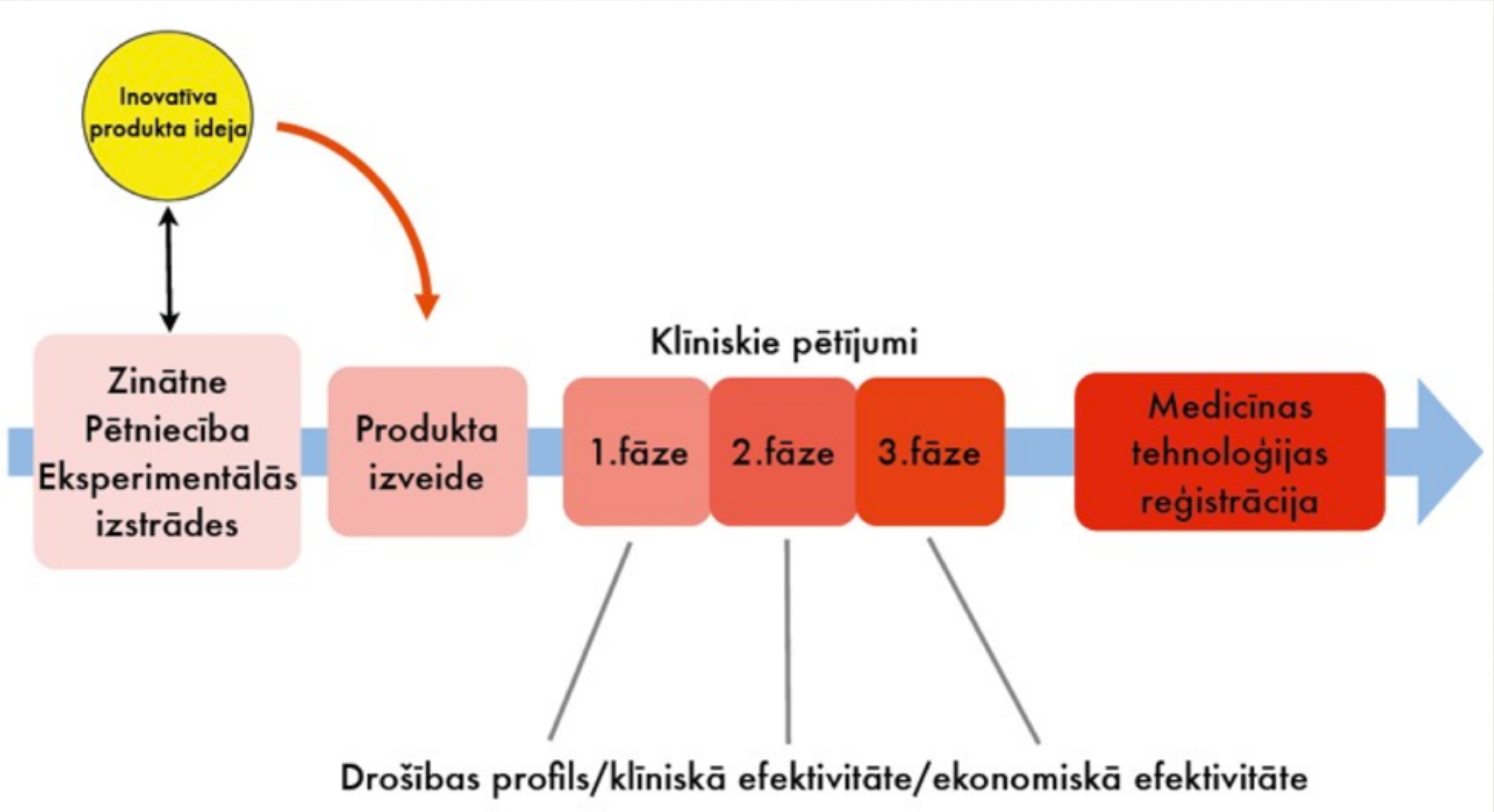
nature.com

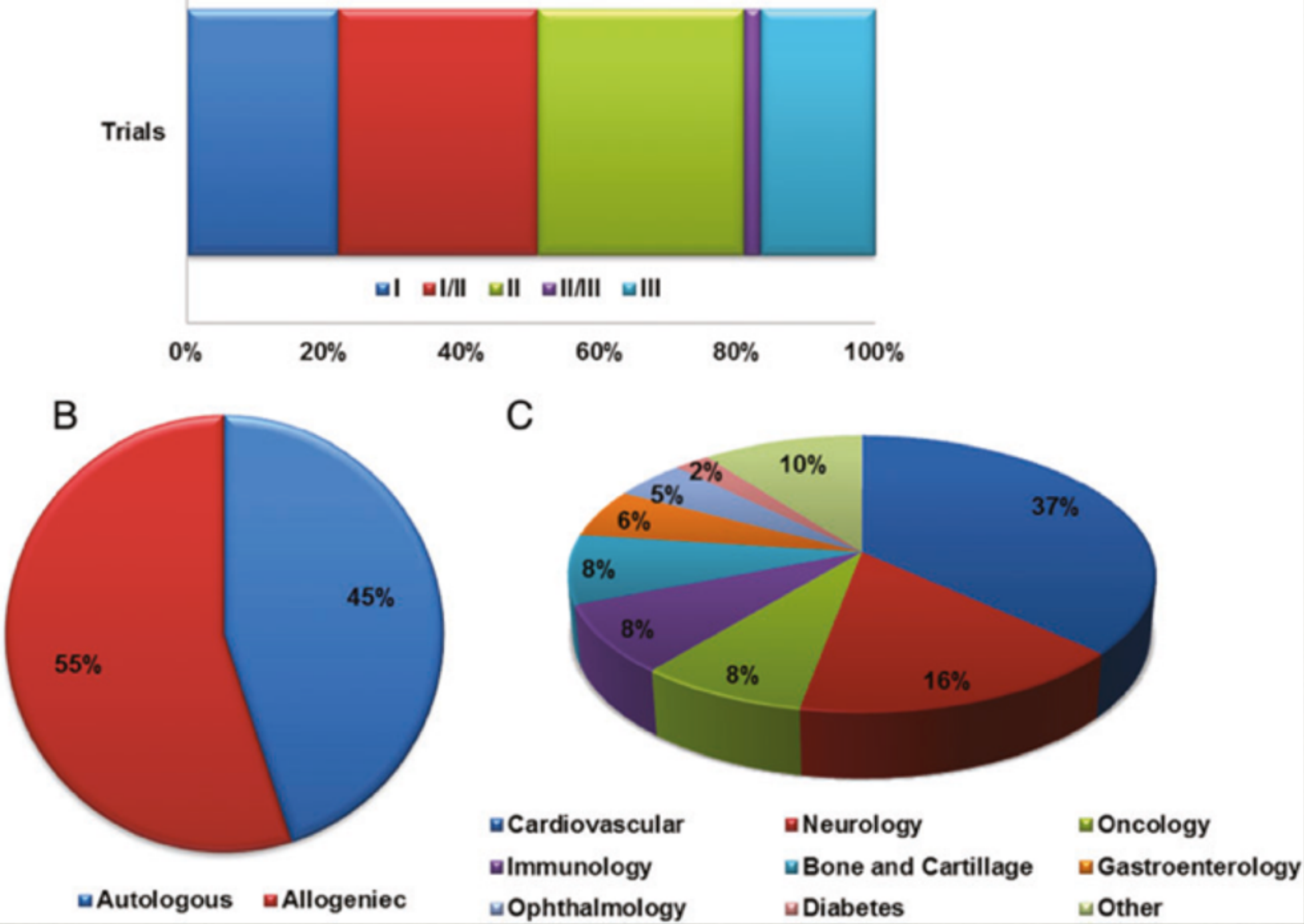
Šūnu pielietojums klīnikā

- Nekultivētas šūnas
- Kultivētas šūnas

- Autologas vai allogēnas šūnas



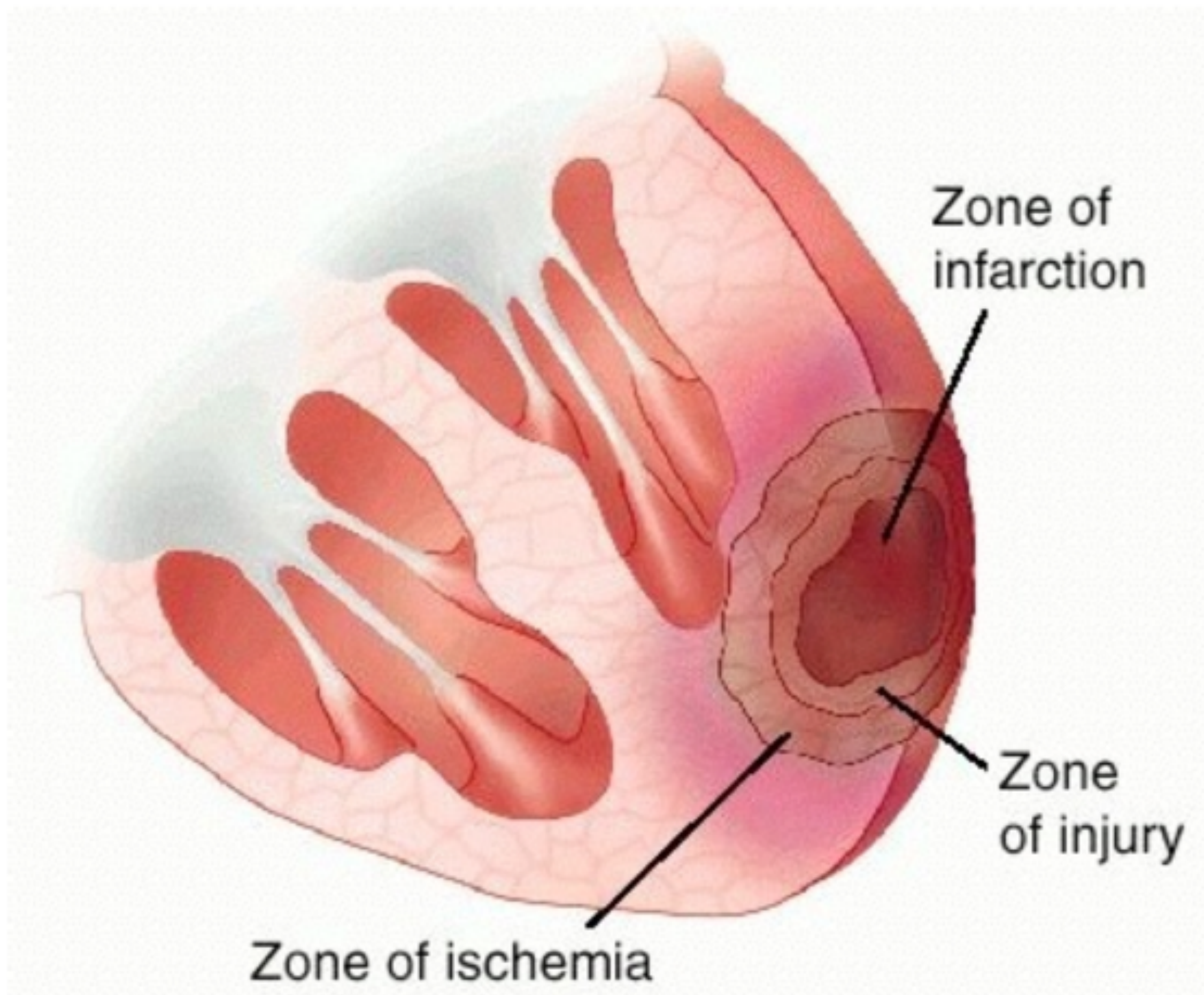

Inovatīva produkta ideja
Zinātne
Pētniecība
Eksperimentālās izstrādes
Produkta izveide
Klīniskie pētījumi
1.fāze
2.fāze
3.fāze
Medicīnas tehnoloģijas reģistrācija
Drošības profils/klīniskā efektivitāte/ekonomiskā efektivitāte



Ratcliffe et al., 2013, Brit Med Bullet

Autologo šūnu terapijas piemērs: kardioloģija

Miokarda infarkts sirds kambaru šķērsgriezumā



http://medical-dictionary.com

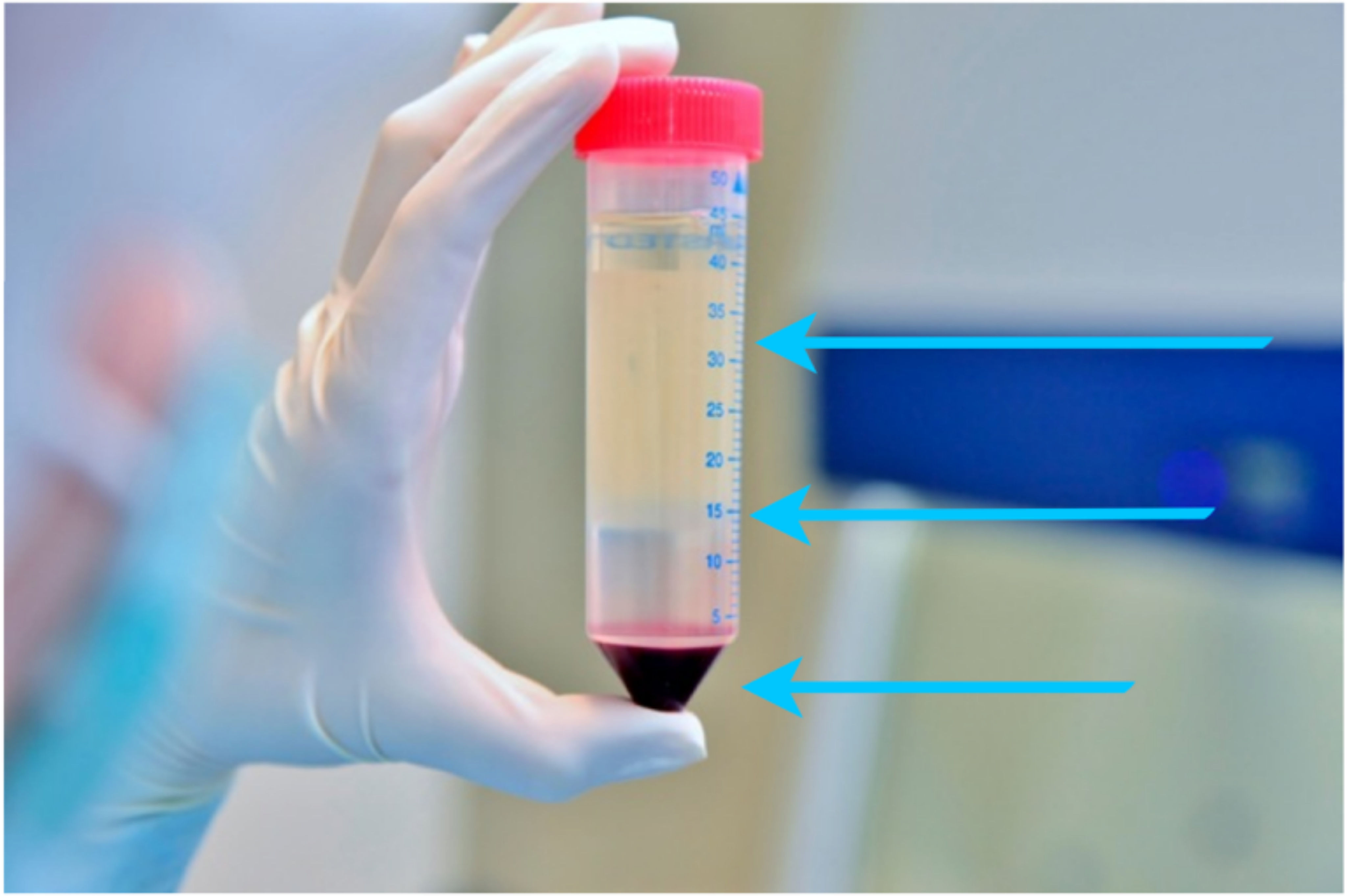


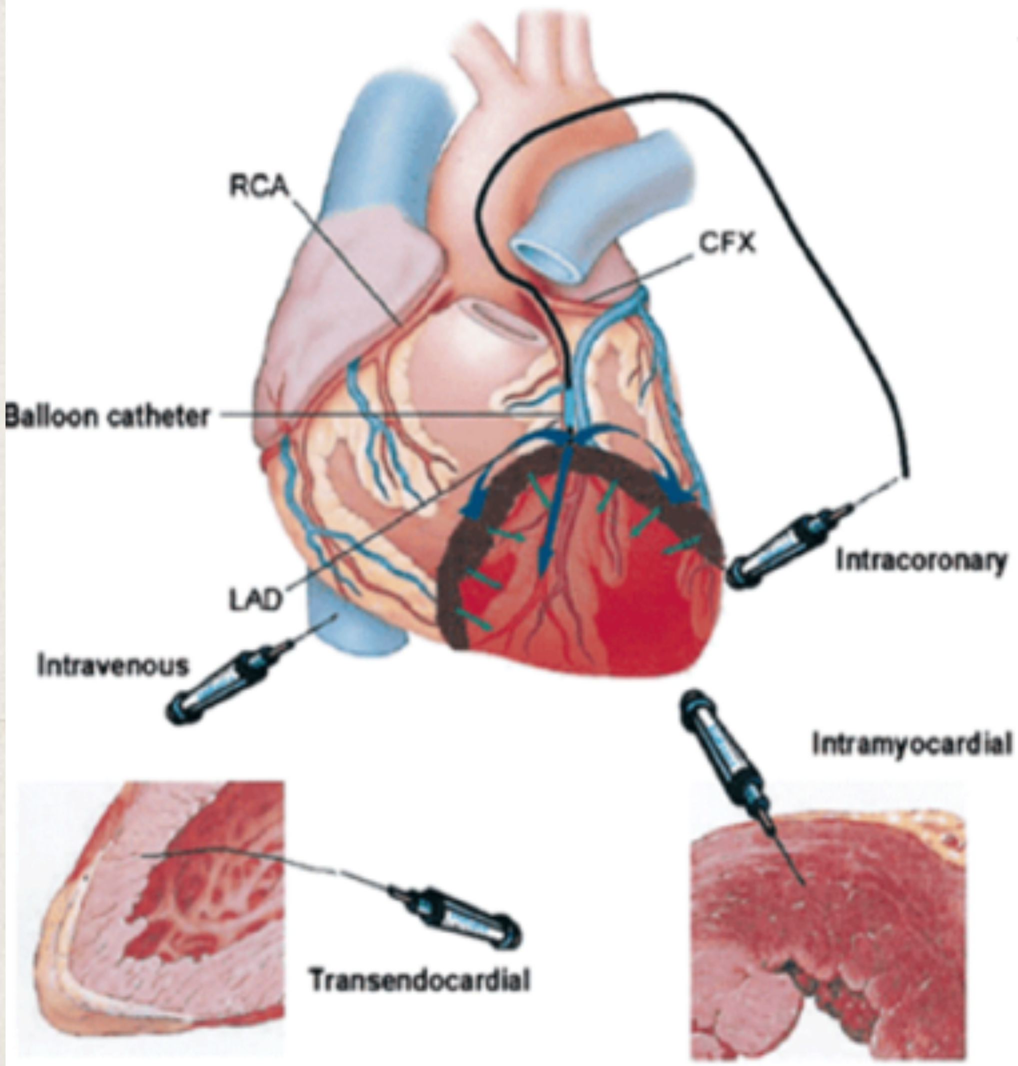
Foto: I.Prēdelis

plazma

Mono Nukleārās Šūnas

sarkanās asins šūnas

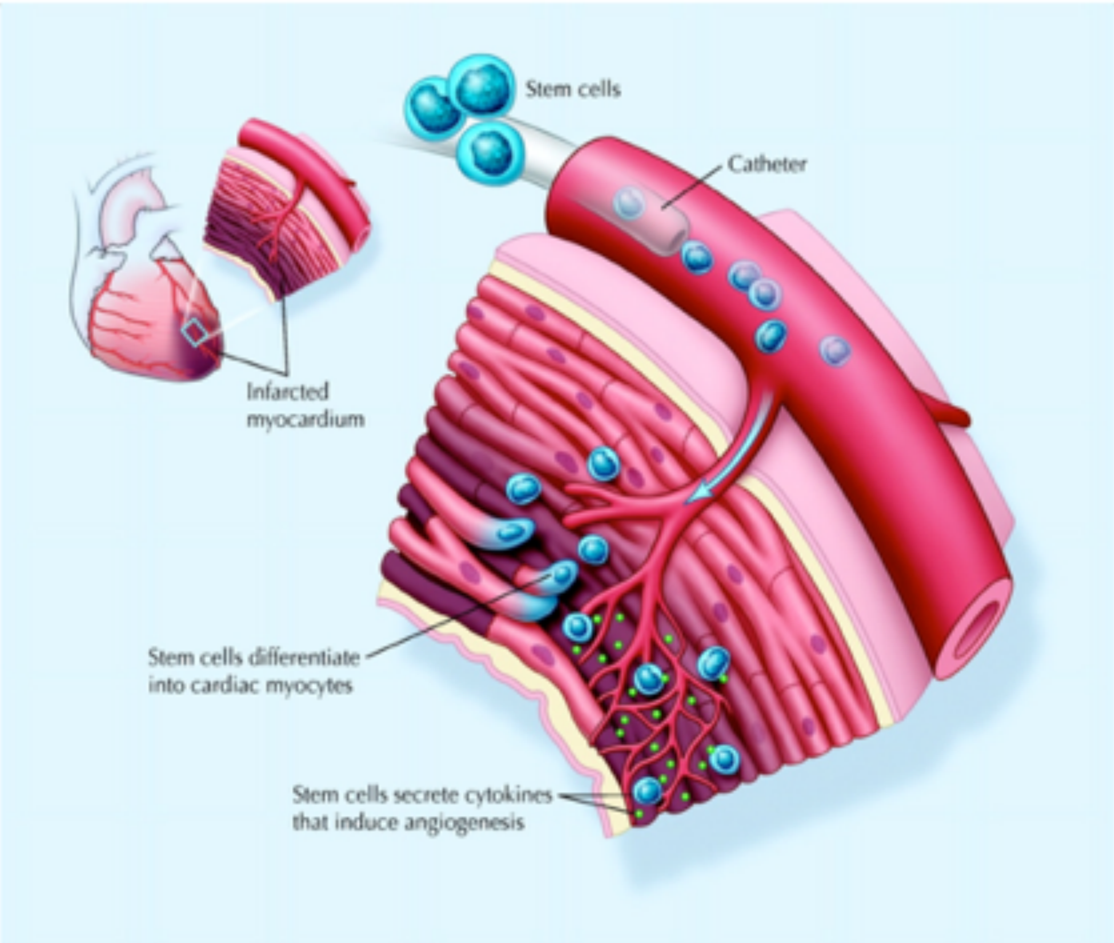
Šūnu ievadīšanas veidi



Sequeira et al., 2011, J Cell Sci Ther

šūnas ievada intrakoronāri caur katetru

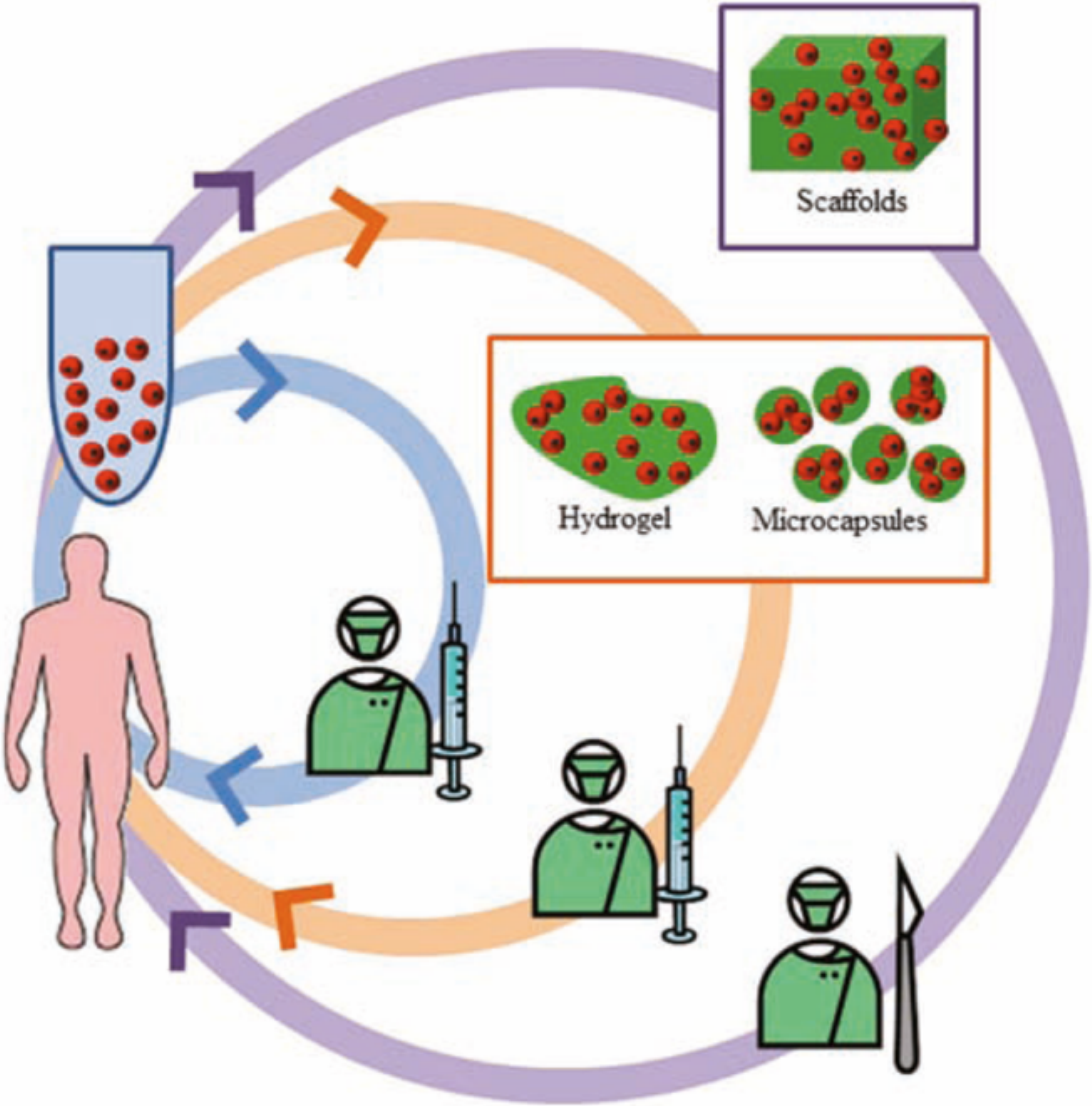
Potenciālie darbības mehānismi: diferenciācija un/vai parakrīnais efekts



CMAJ·JAMC

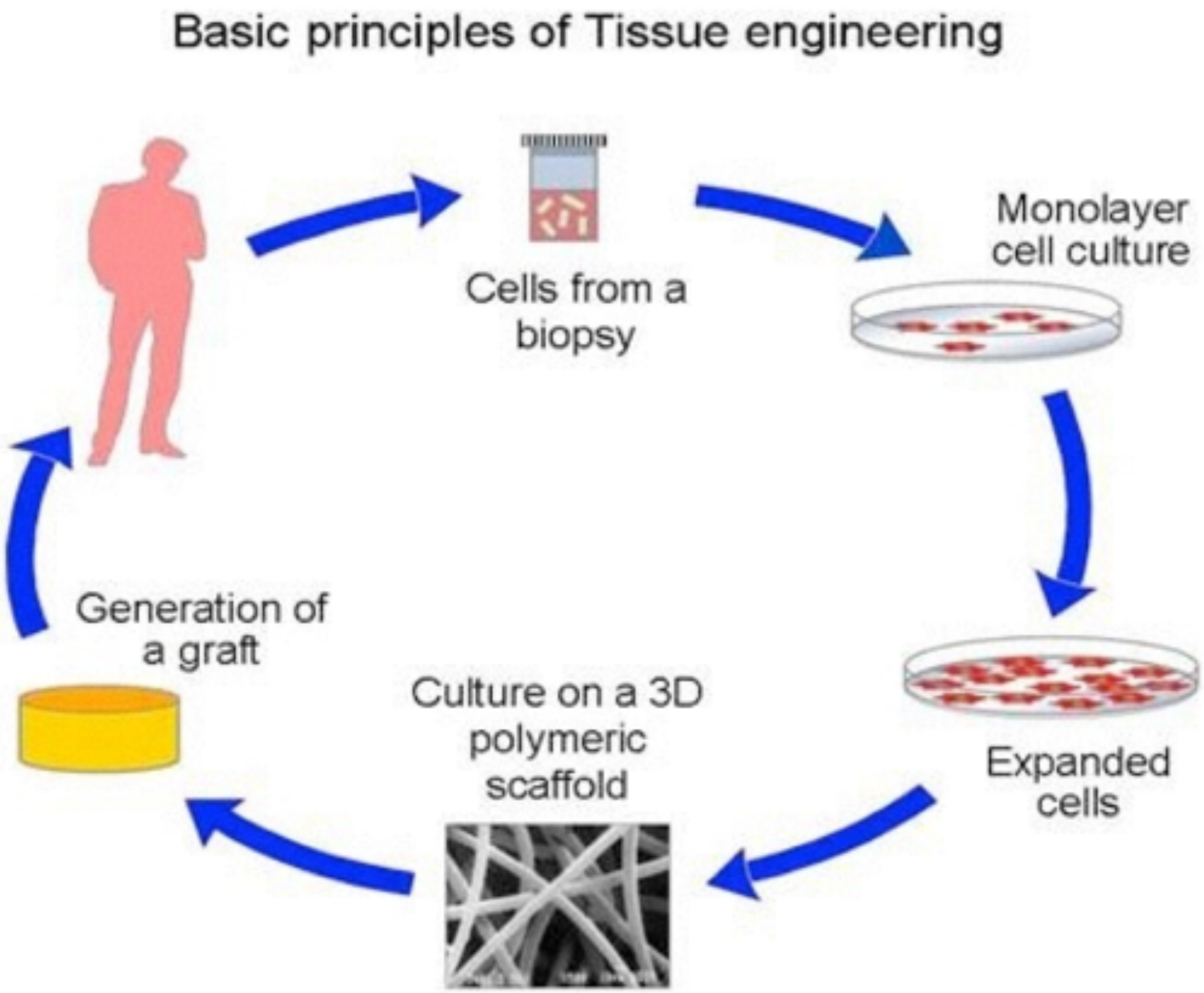
www.osiris.com

Vai pietiek tikai ar šūnām?



Girolamo et al., 2013,Current Pharmaceutical Design

Audu inženierija



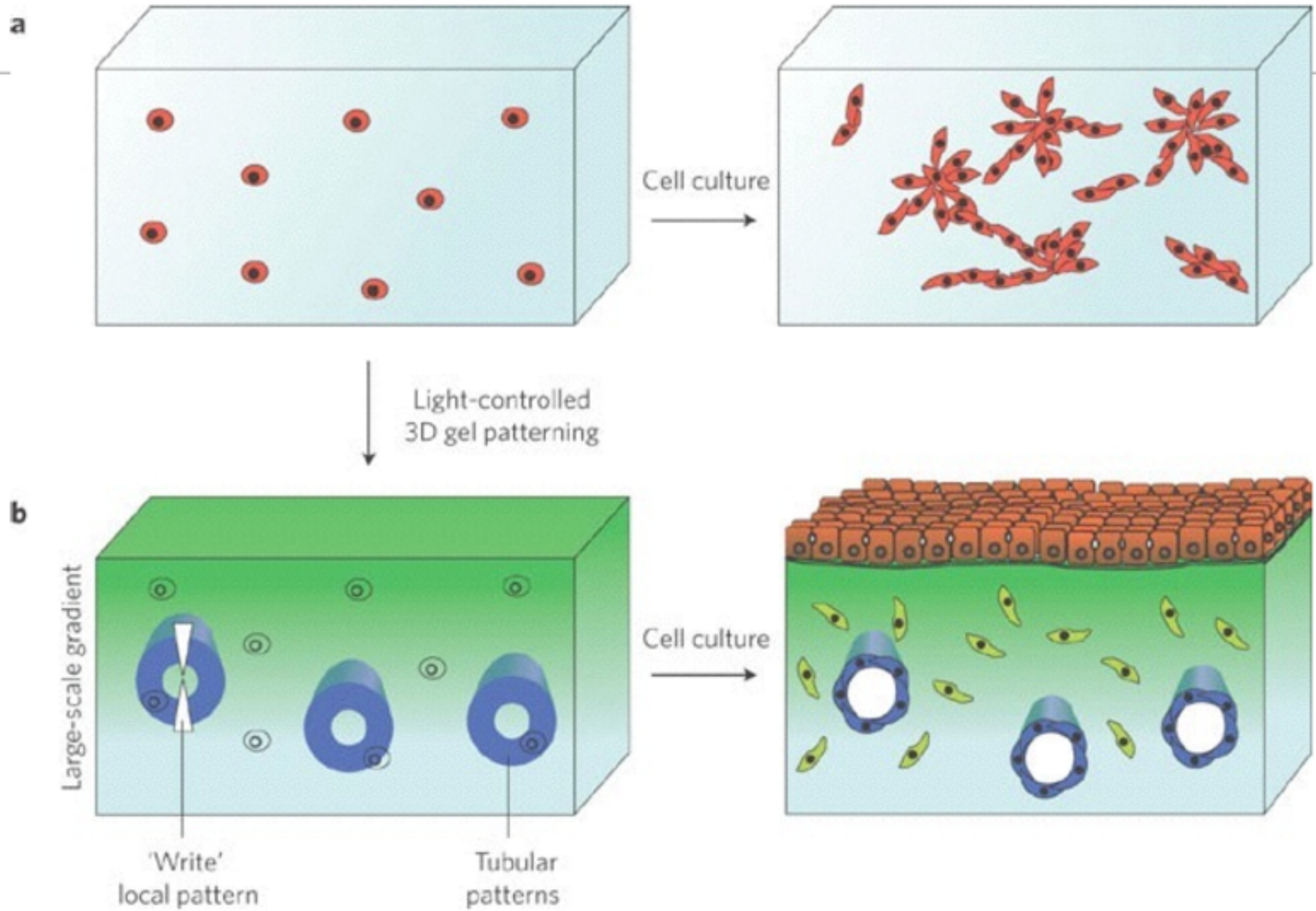
Starpdisciplināra nozare, kas izmanto dzīvības zinātņu un inženierijas principus, lai attīstītu bioloģiskus aizvietotājus, kas atjaunotu, uzturētu vai uzlabotu AUDU vai ORGĀNU funkcijas

Langer R and Vacanti J, Science, 1993

Šūnu vide pēc iespējas tuvāka *in vivo* apstākļiem

Biomateriāli

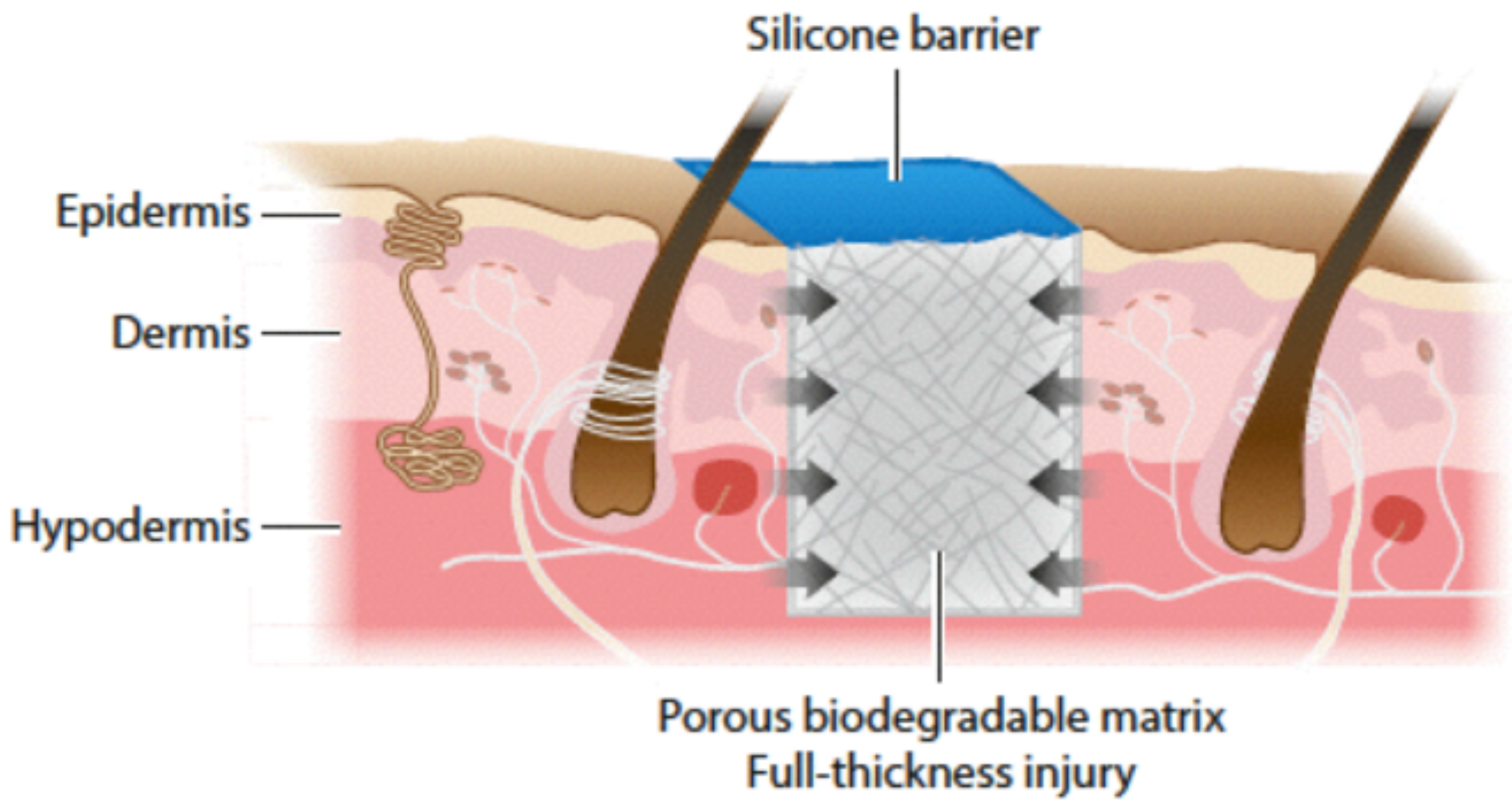
- bioloģiskā savietojamība (imūnā atbilde)
- poraina vide adekvātam barības vielu, šūnu izdalīto produktu un metabolītu transportam
- mehāniskā izturība vai elastīgums
- virsmas īpašības (stimulēt šūnu pieķeršanos, augšanu, proliferāciju un migrāciju)
- uzglabāt un padarīt pieejamu bioķīmiskos faktorus
- bionoārdīšanās (kontrolēts degradēšanās laiks)



Lutolf PM, Nature Meterials, 2009

Audu inženierijas piemērs - āda

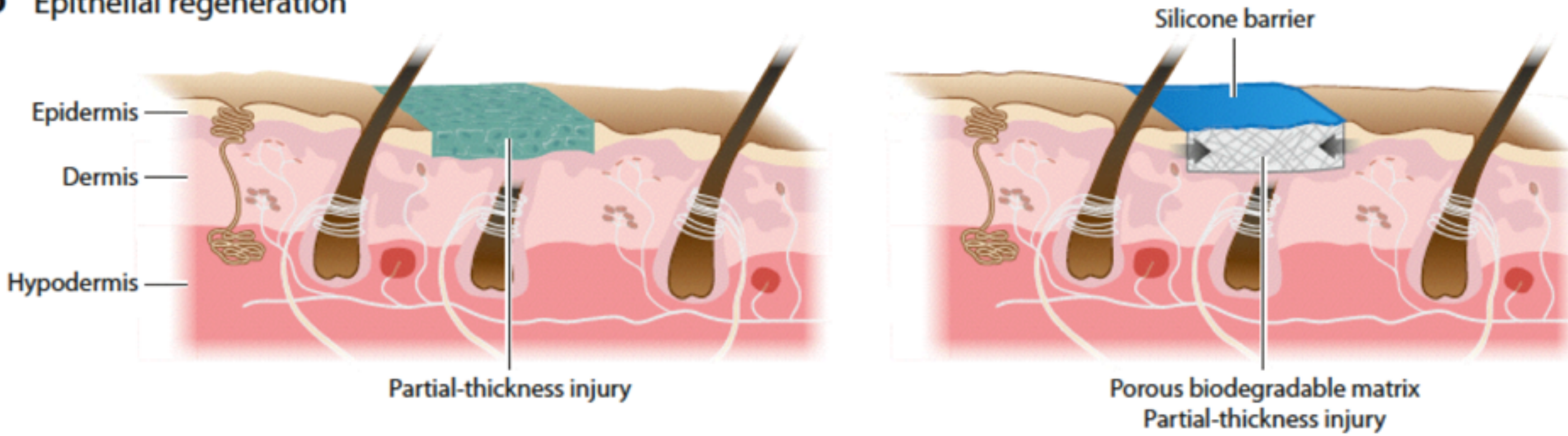
a Dermal regeneration matrix



- Porous biodegradable matrix with no cells
- Host fibroblasts and endothelial cells migrate into matrix
- Promotes regeneration of dermis
- Improves scar appearance

Berthiaume et al., 2011, Annu Rev Chem Biomol Eng

b Epithelial regeneration

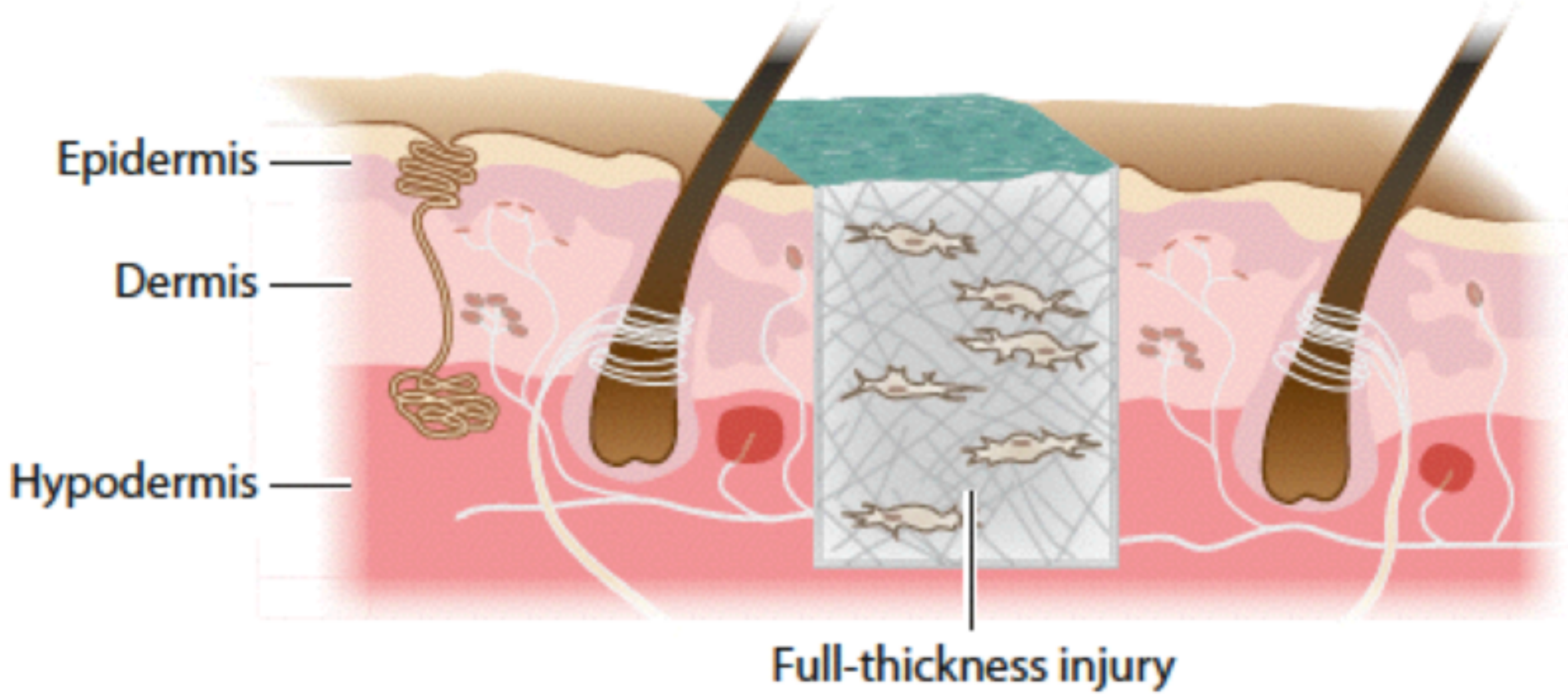


- Cultured autologous epithelial cells
- Permanent wound coverage

- Temporary matrix/growth factor cover
- Promotes host epithelial migration and proliferation

Berthiaume et al., 2011, Annu Rev Chem Biomol Eng

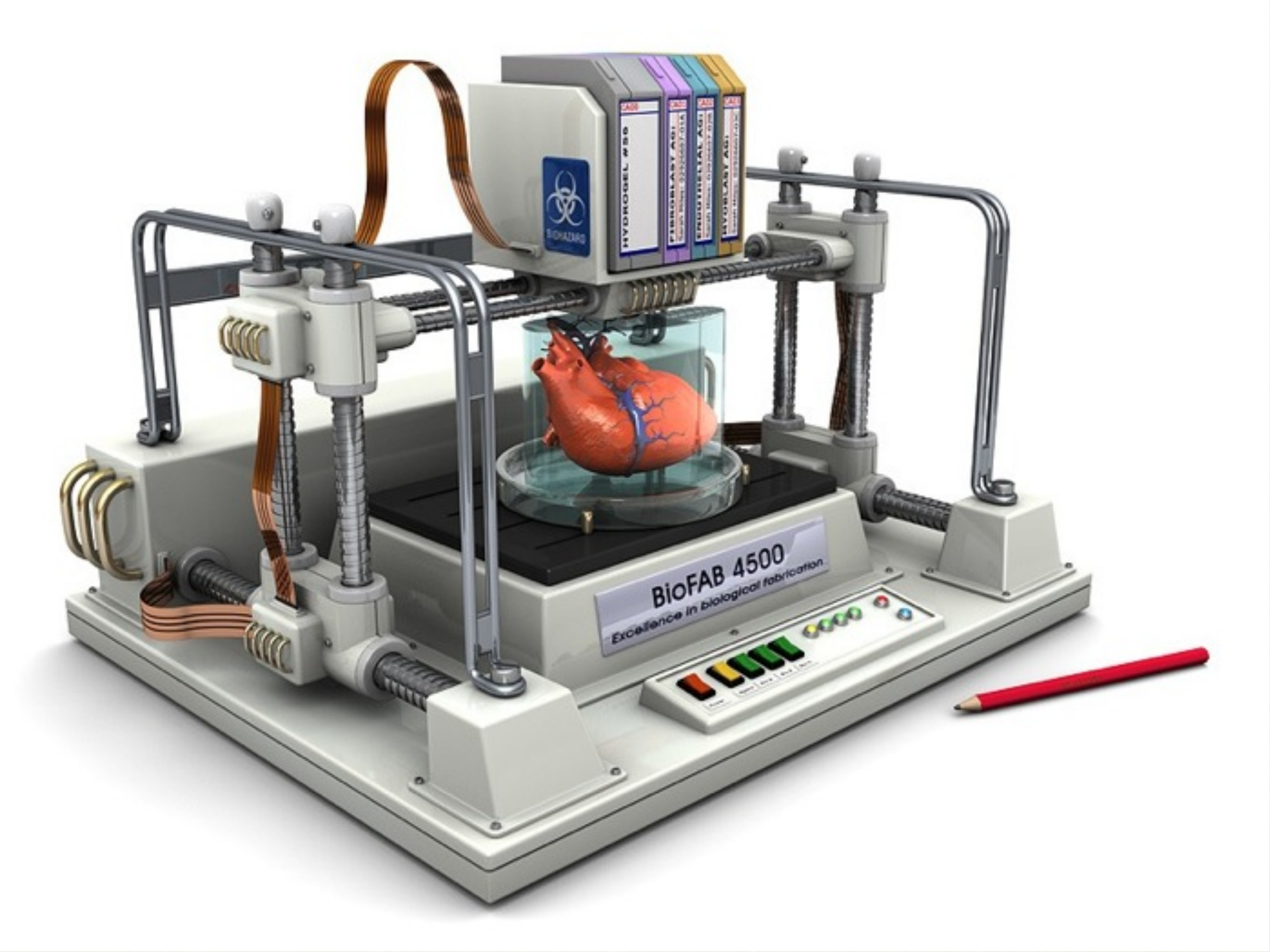
c Full-thickness composite skin



- Fibroblast-populated matrix covered with keratinocytes
- Allogeneic cells used, so coverage is temporary
- Attempts to develop technology using autologous cells are underway

Berthiaume et al., 2011, Annu Rev Chem Biomol Eng

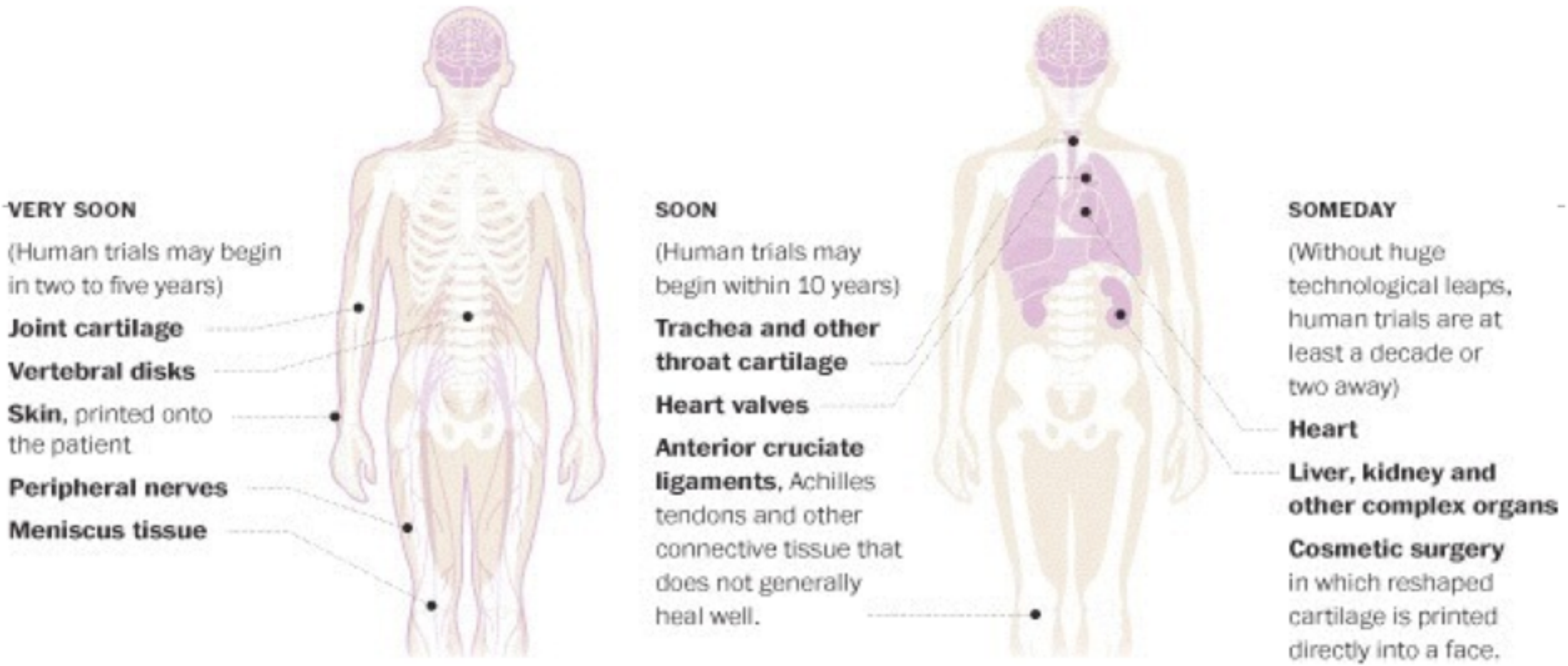
Nākotnes tehnoloģijas - bioprintēšana



http://www.explainingthefuture.com/bioprinting.html

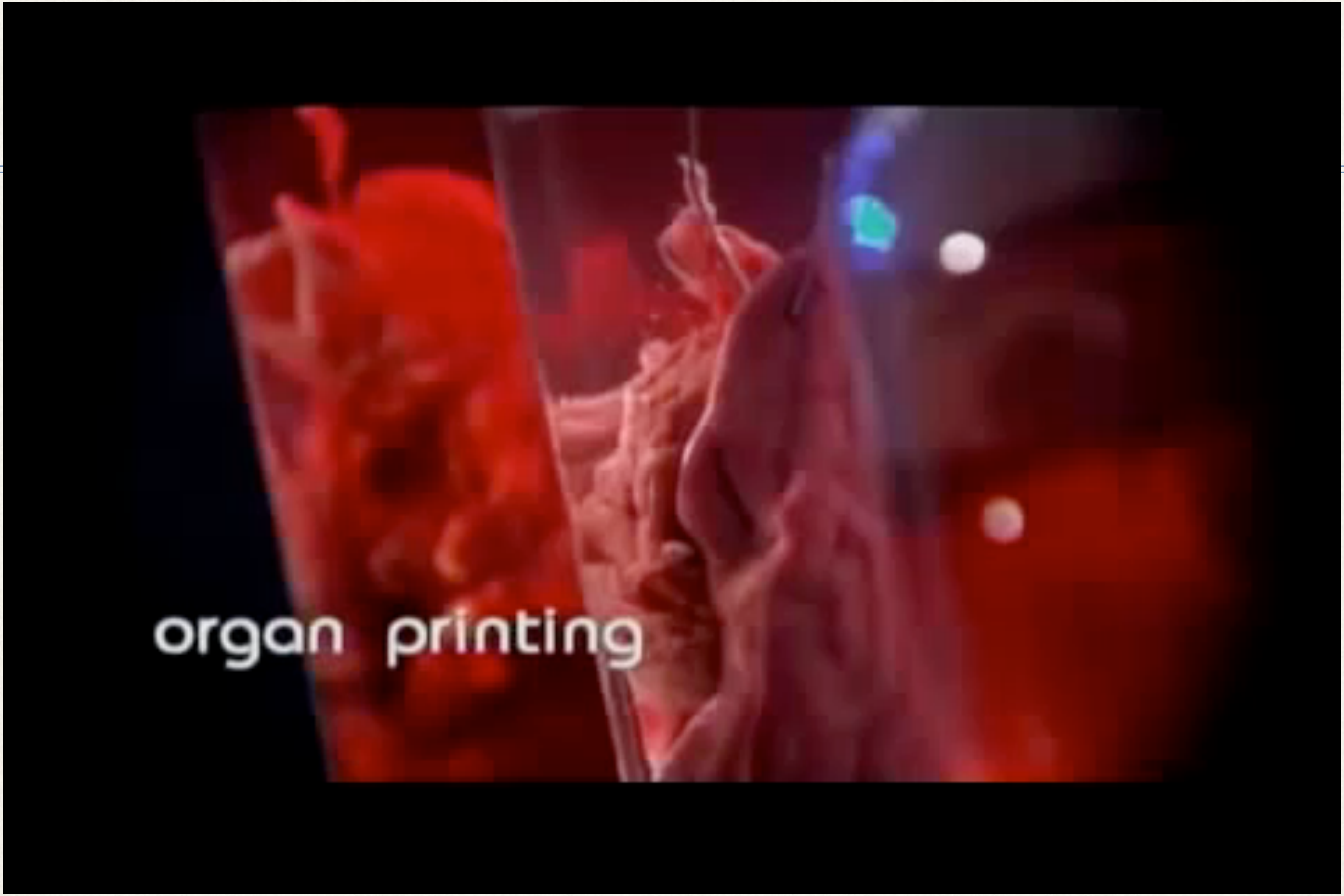
www.designboom.com/technology/3d-printed-organs-from-regenerative-living-cells/

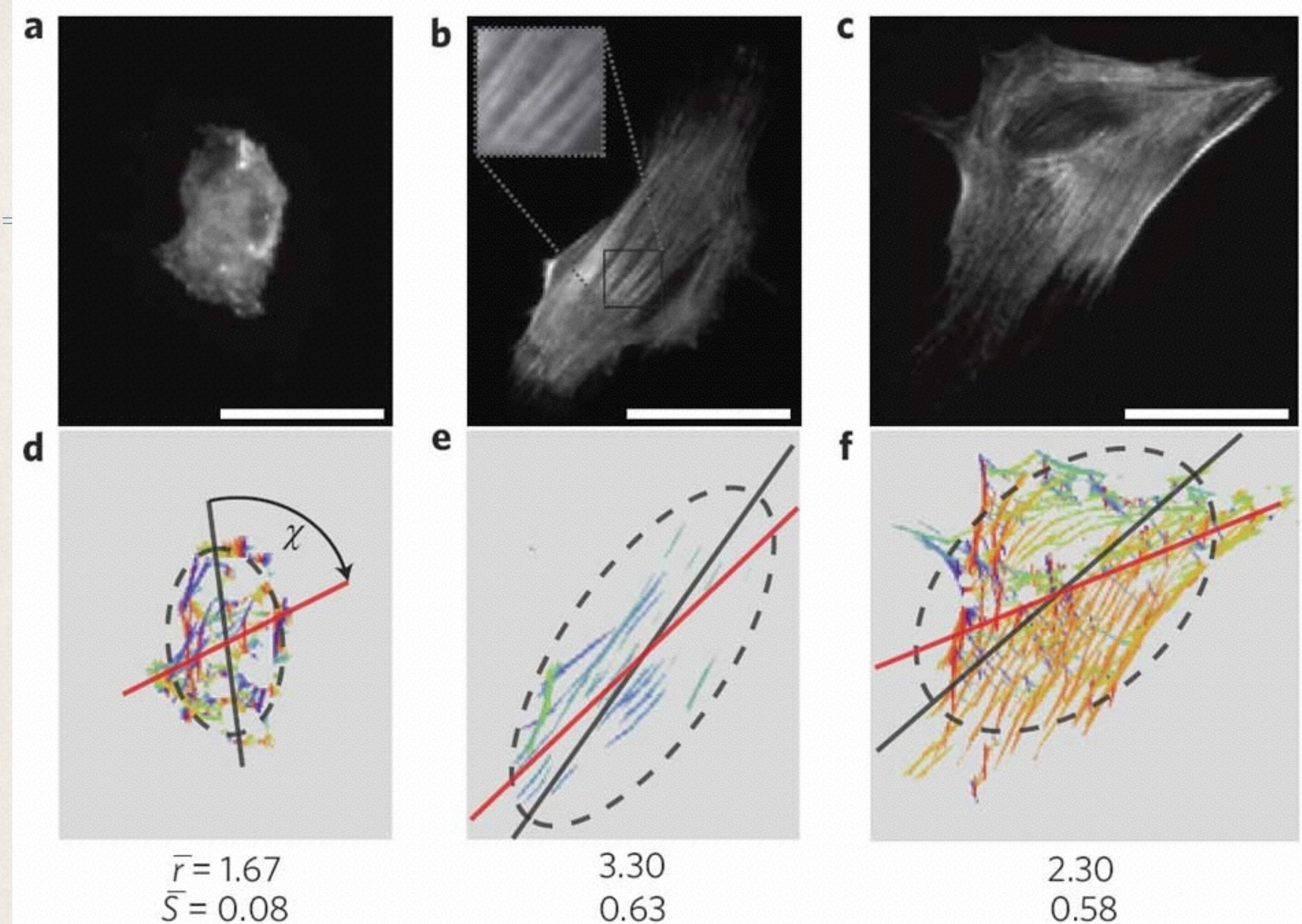
www.ted.com/talks/anthony_atala_printing_a_human_kidney.html



http://www.youtube.com/watch?v=80DhBLEhdzk

Jonathan Butcher's lab at Cornell University focuses on aortic valves, hoping to someday print replacement valves for children with heart disease

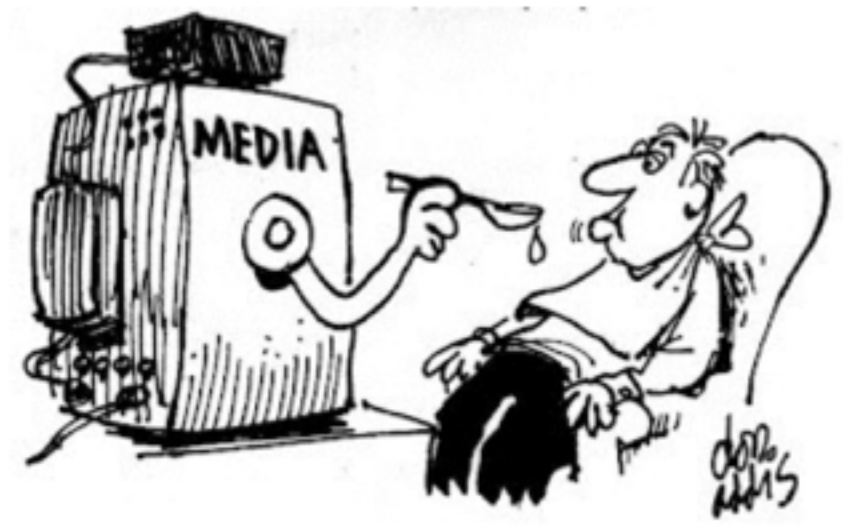

organ printing



http://www.nature.com/nphys/journal/v6/n6/fig_tab/nphys1613_F1.html

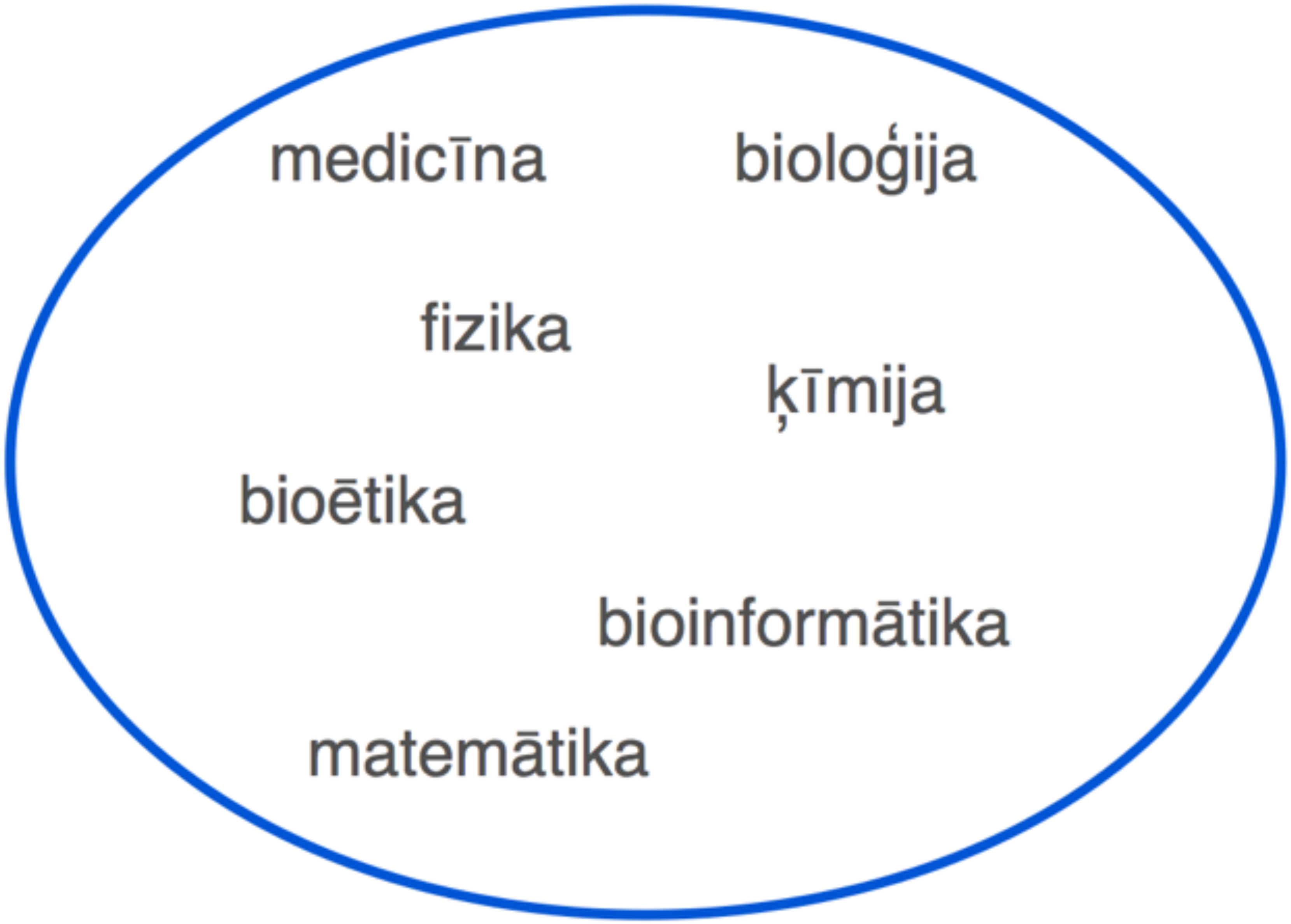
Noslēgumā…

- Vairāki klīniskie pētījumi ir parādījuši šūnu terapijas drošumu, tomēr jebkura informācija jāizvērtē kritiski



Noslēgumā…

šūnu terapija + gēnu terapija + audu inženierija



Noslēgumā…

- Joprojām nepieciešami fundamentāli pētījumi, kas sniegtu plašāku informāciju par šūnu darbības mehānismiem