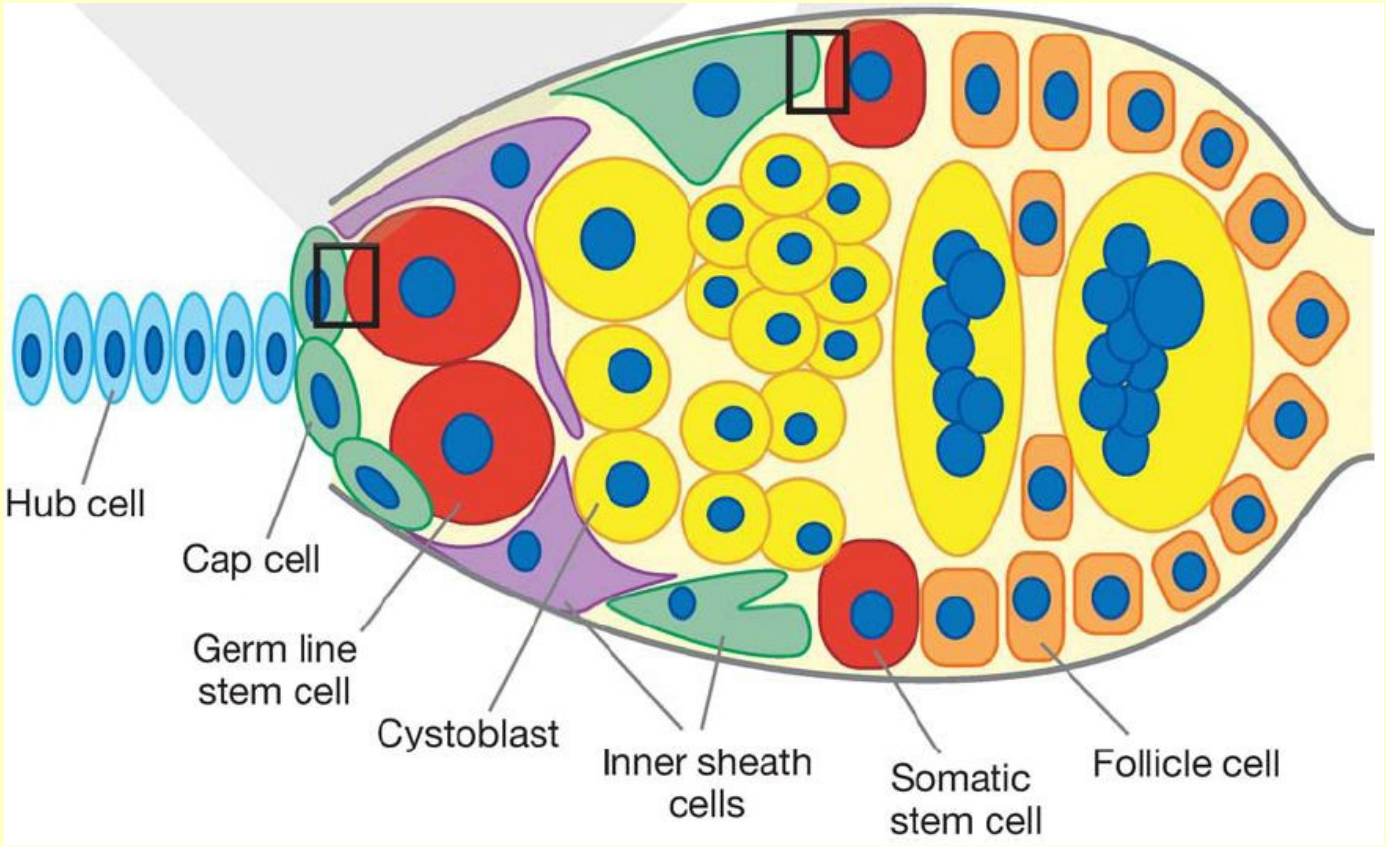
Your Genes and Your Health

http://bio84.stanford.edu/

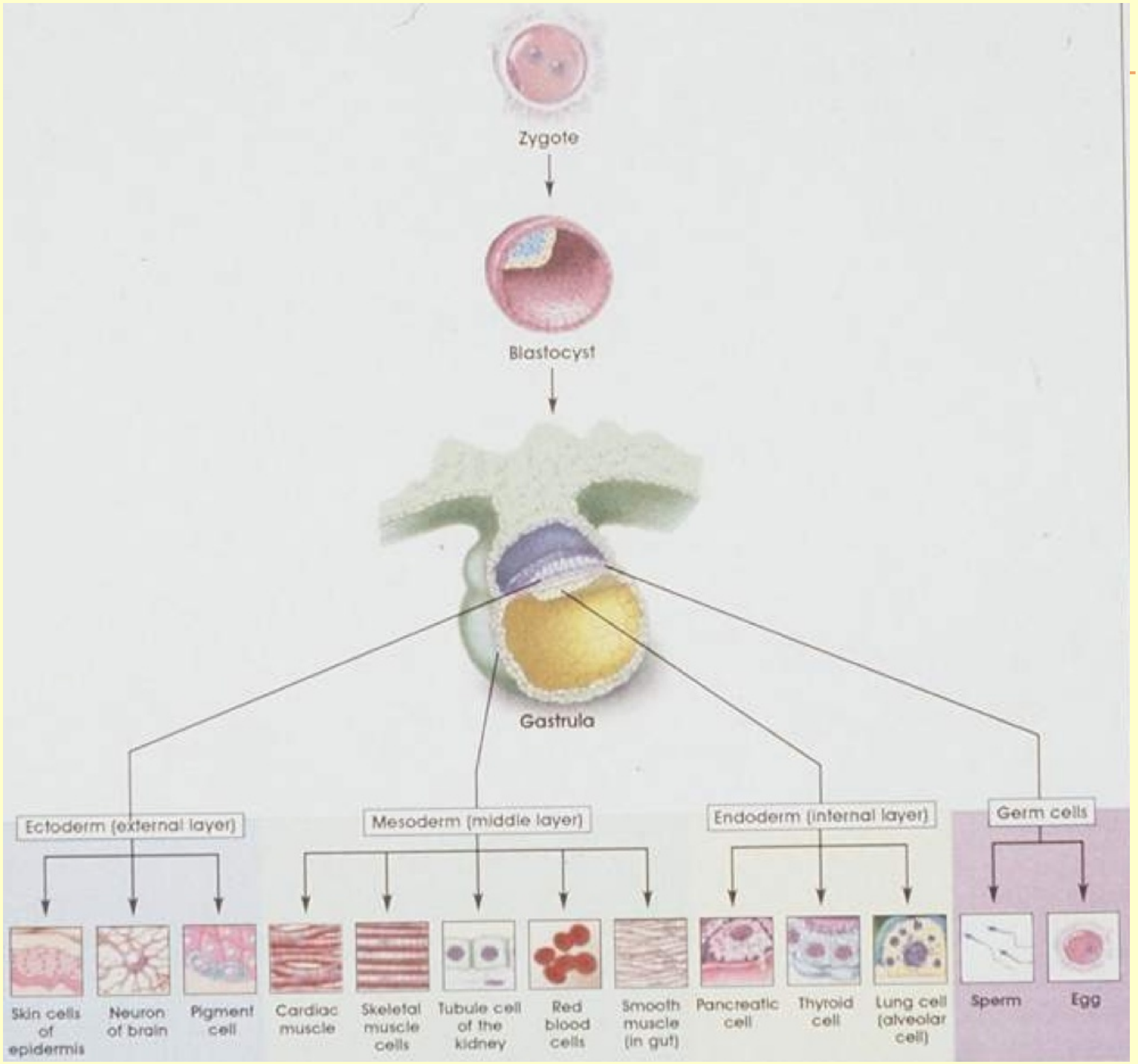
Stem Cells

http://bio84.stanford.edu/07 Stem Cell Therapy.html



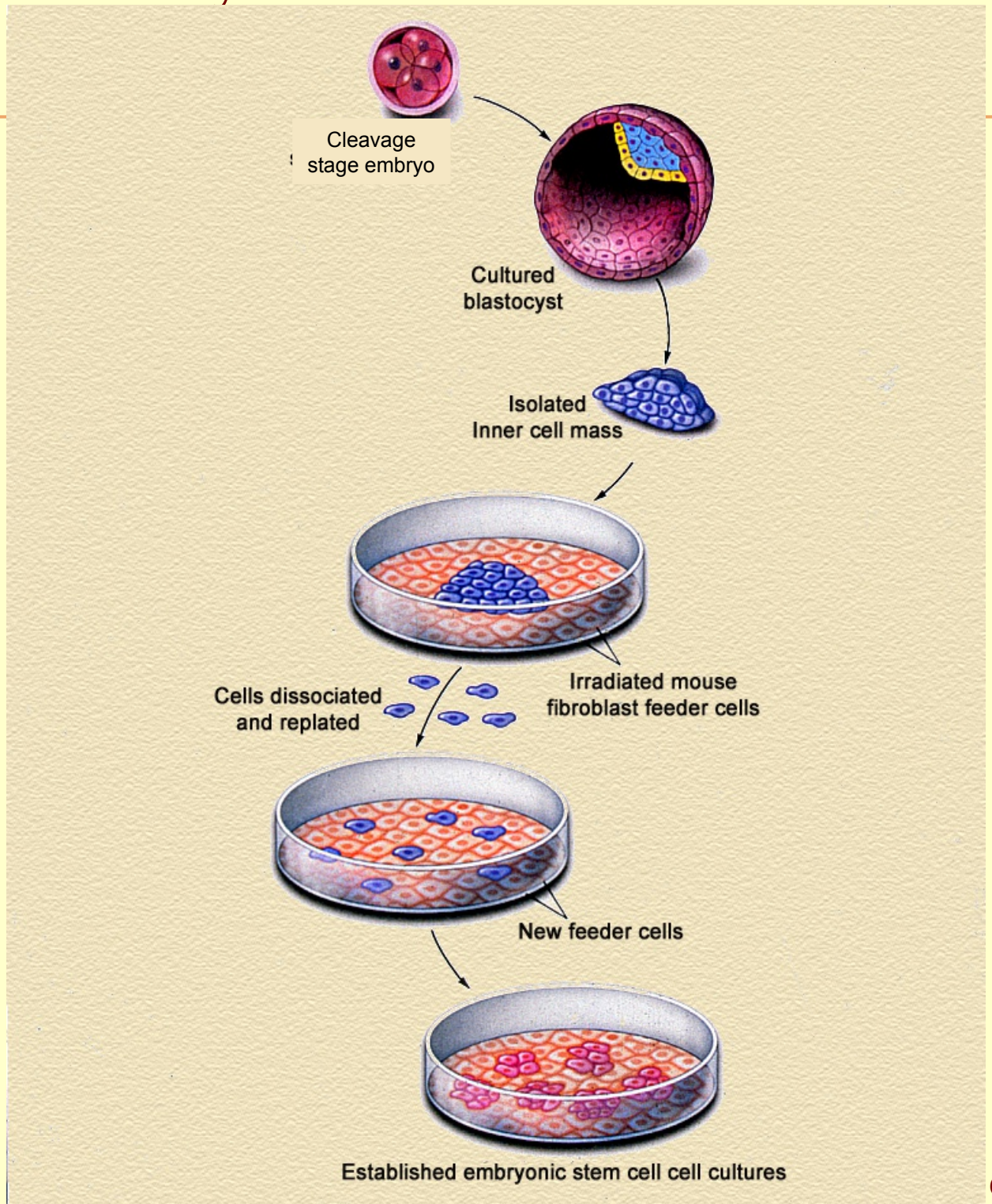
Doug Brutlag, Professor Emeritus of Biochemistry & Medicine (by courtesy)
Stanford University School of Medicine

Differentiation of Human Tissues



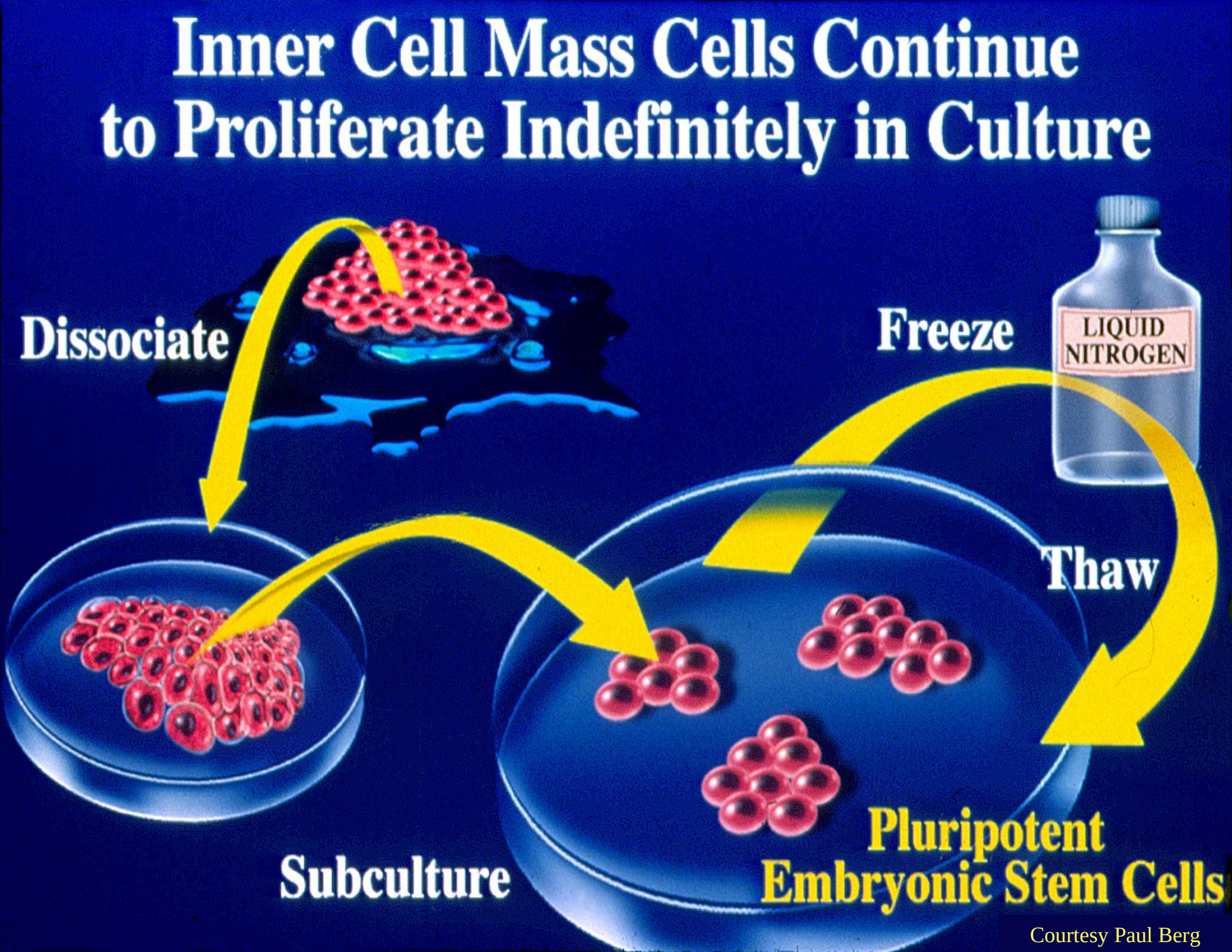
Courtesy Irv Weissman

Embryonic Stem Cell Cultures



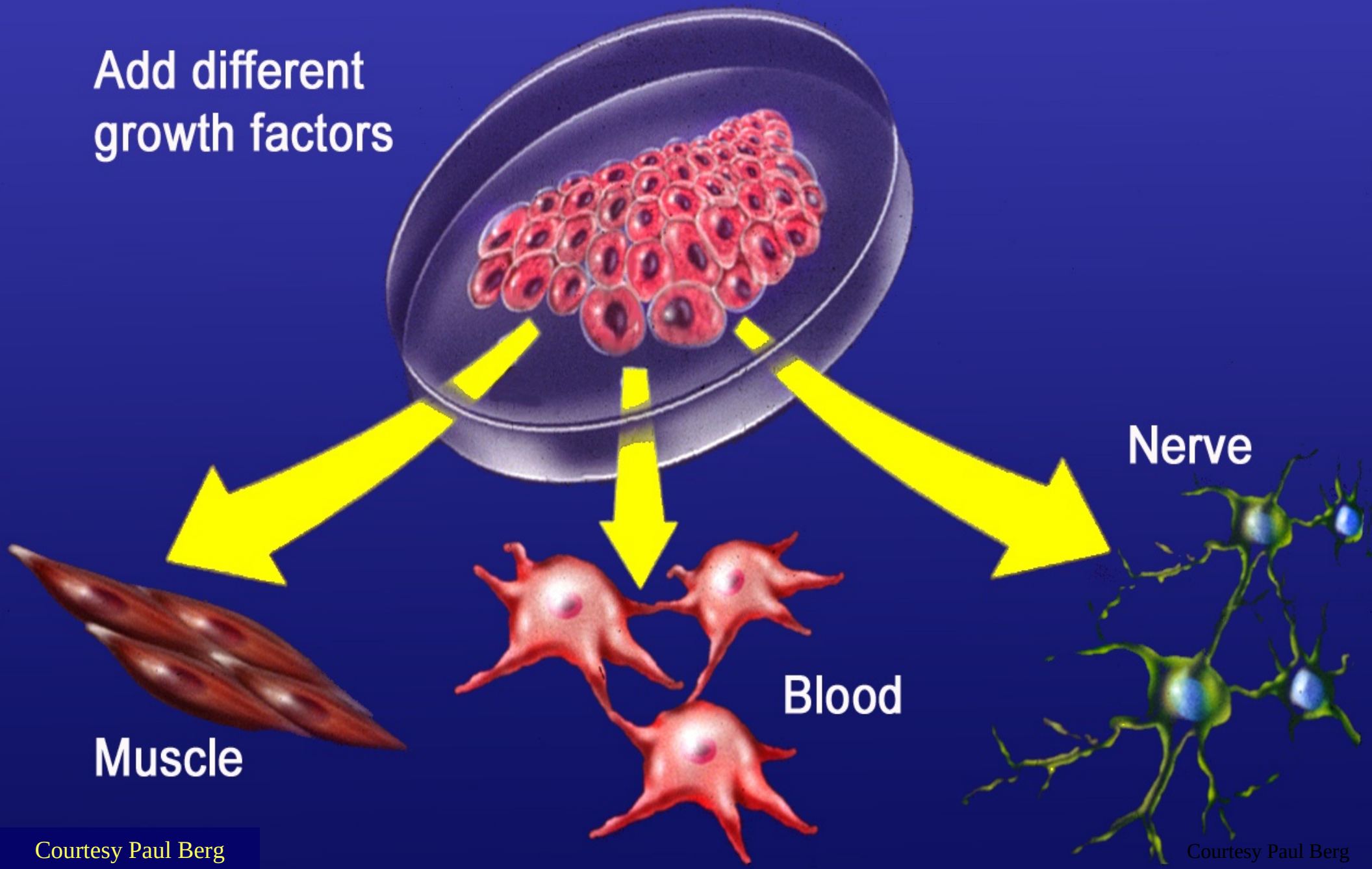
Courtesy Paul Berg

Inner Cell Mass Cells Continue to Proliferate Indefinitely in Culture

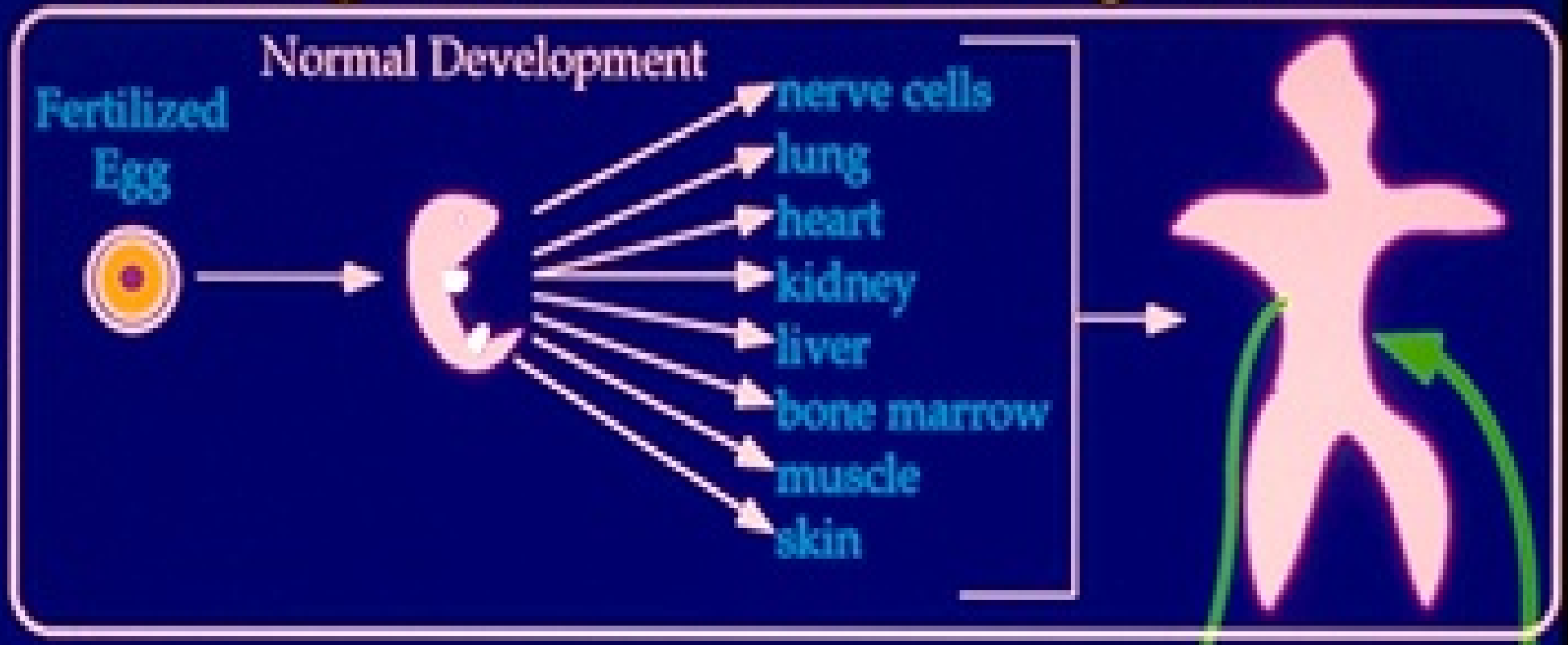


Courtesy Paul Berg

Pluripotent Stem Cells Differentiate into many Cell Types



Cloning Facilitates Tissue Regeneration



Once the embryonic state is obtained, special factors can be used to force differentiation down chosen pathways

Courtesy Paul Berg

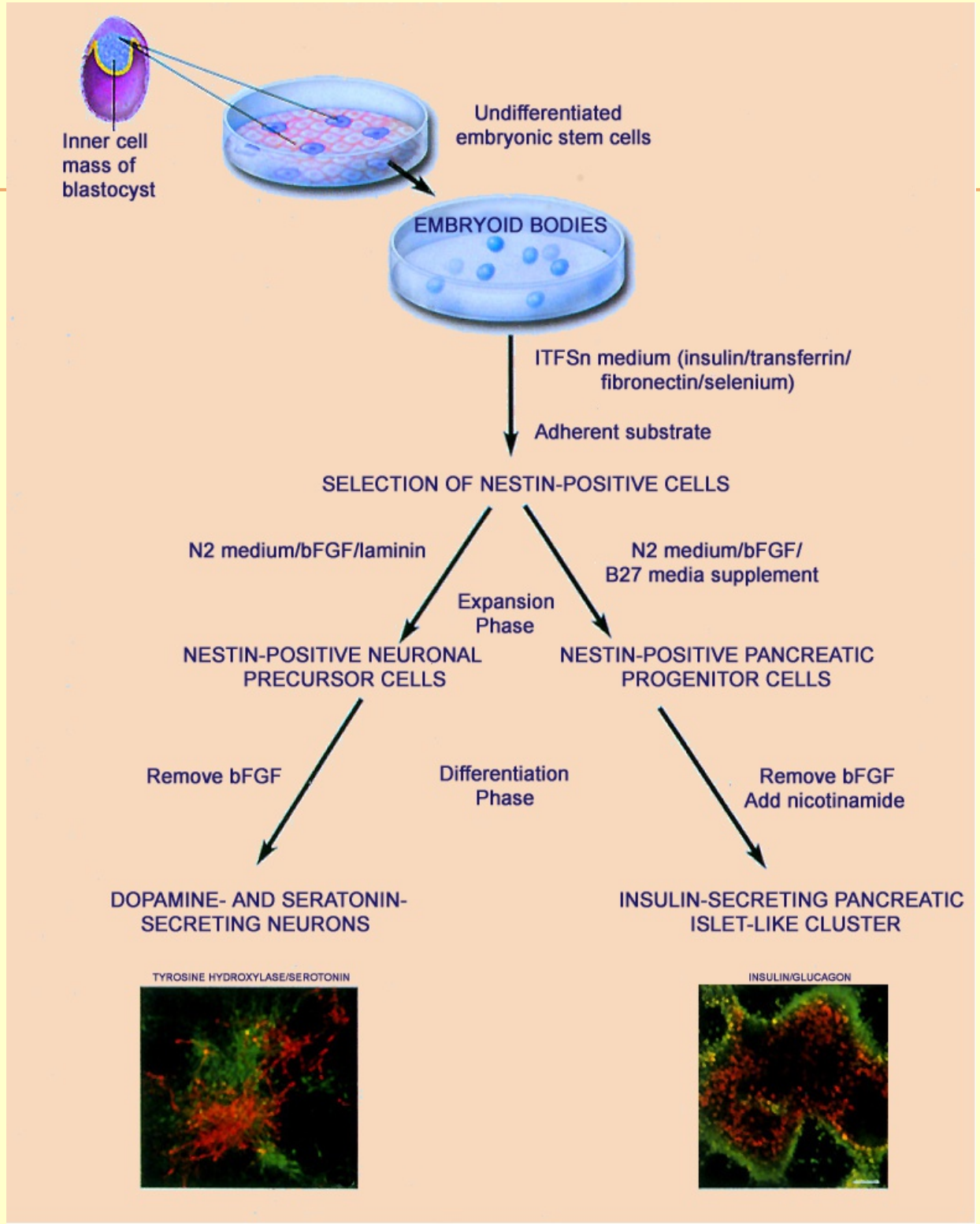
Basic Problems of Stem Cell Therapy

- HOW TO DIRECT DIFFERENTIATION OF CELLS DOWN SPECIFIC PATHWAYS?
  e.g. all into muscle or all into nerve; different "cocktails" of growth factors

- HOW TO OVERCOME IMMUNE REJECTION?
  e.g. alter histocompatibility genes; therapeutic cloning for"customized" lines

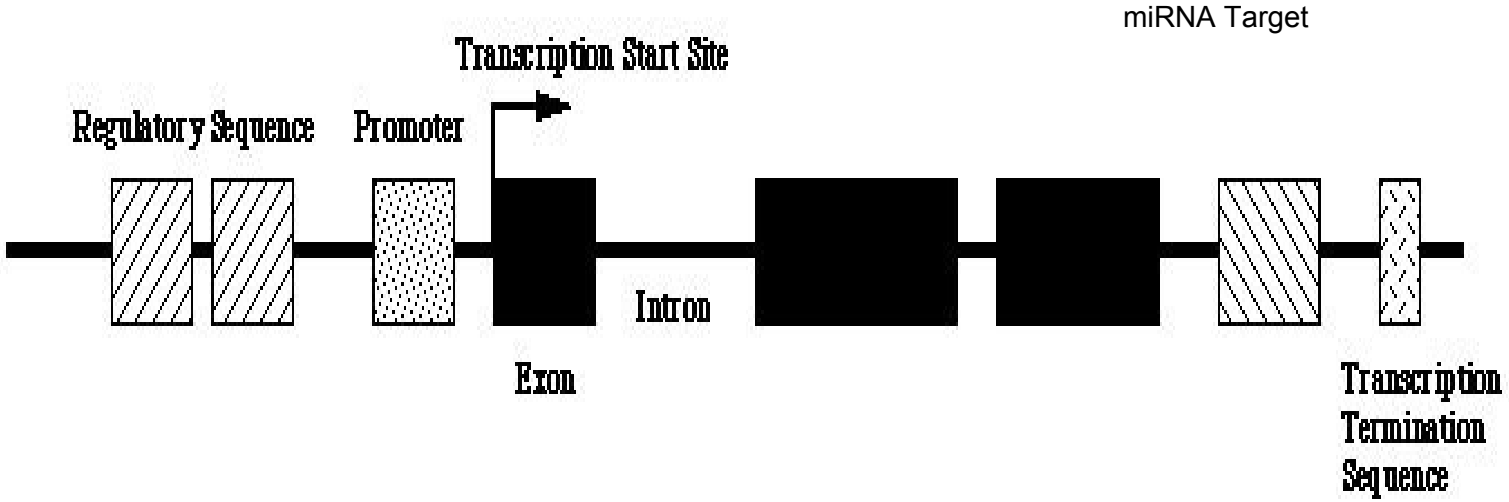
- HOW TO MAKE AN ORGAN?
  e.g. combine different cell types in three dimensional arrangements.

Courtesy Paul Berg

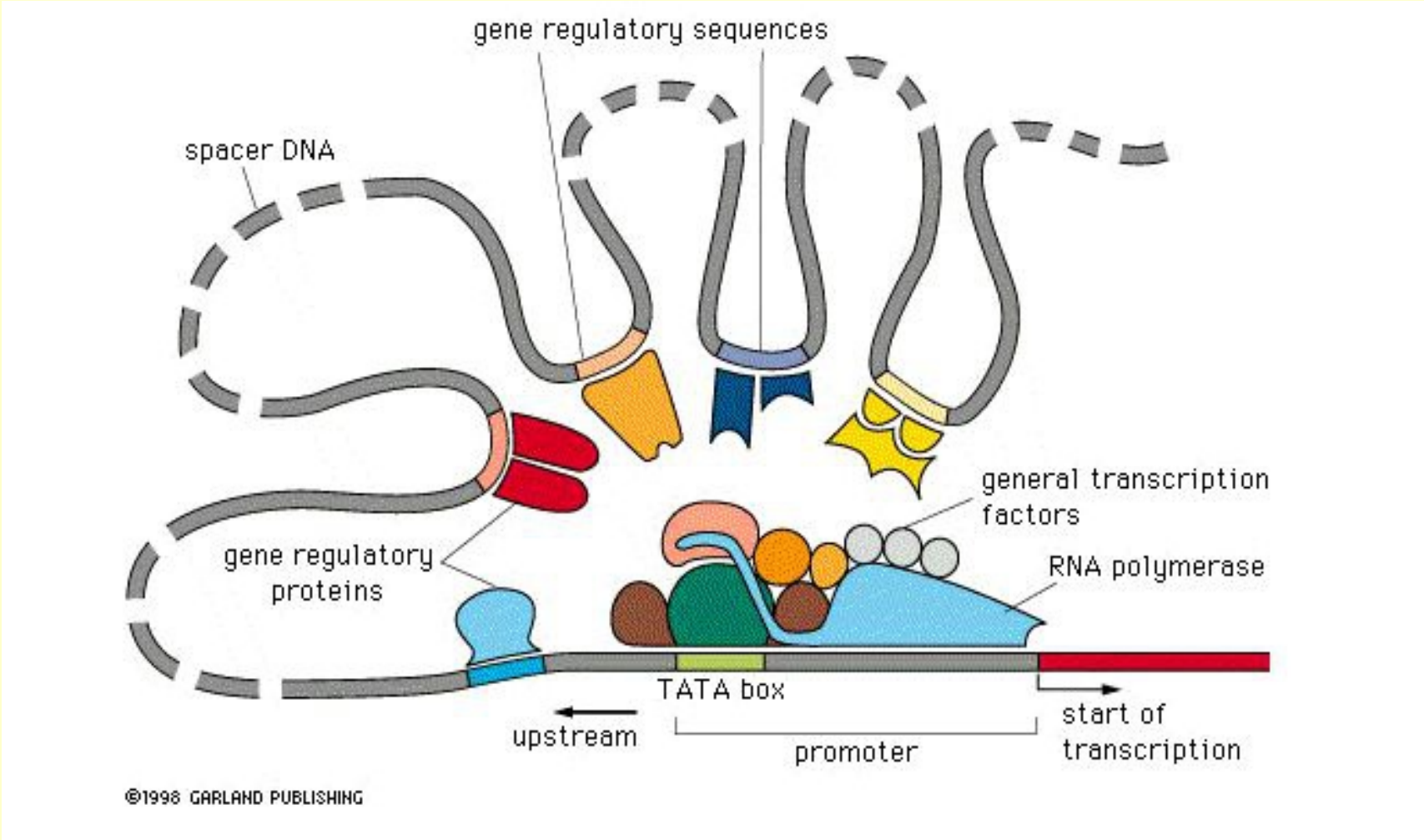


Courtesy Paul Berg

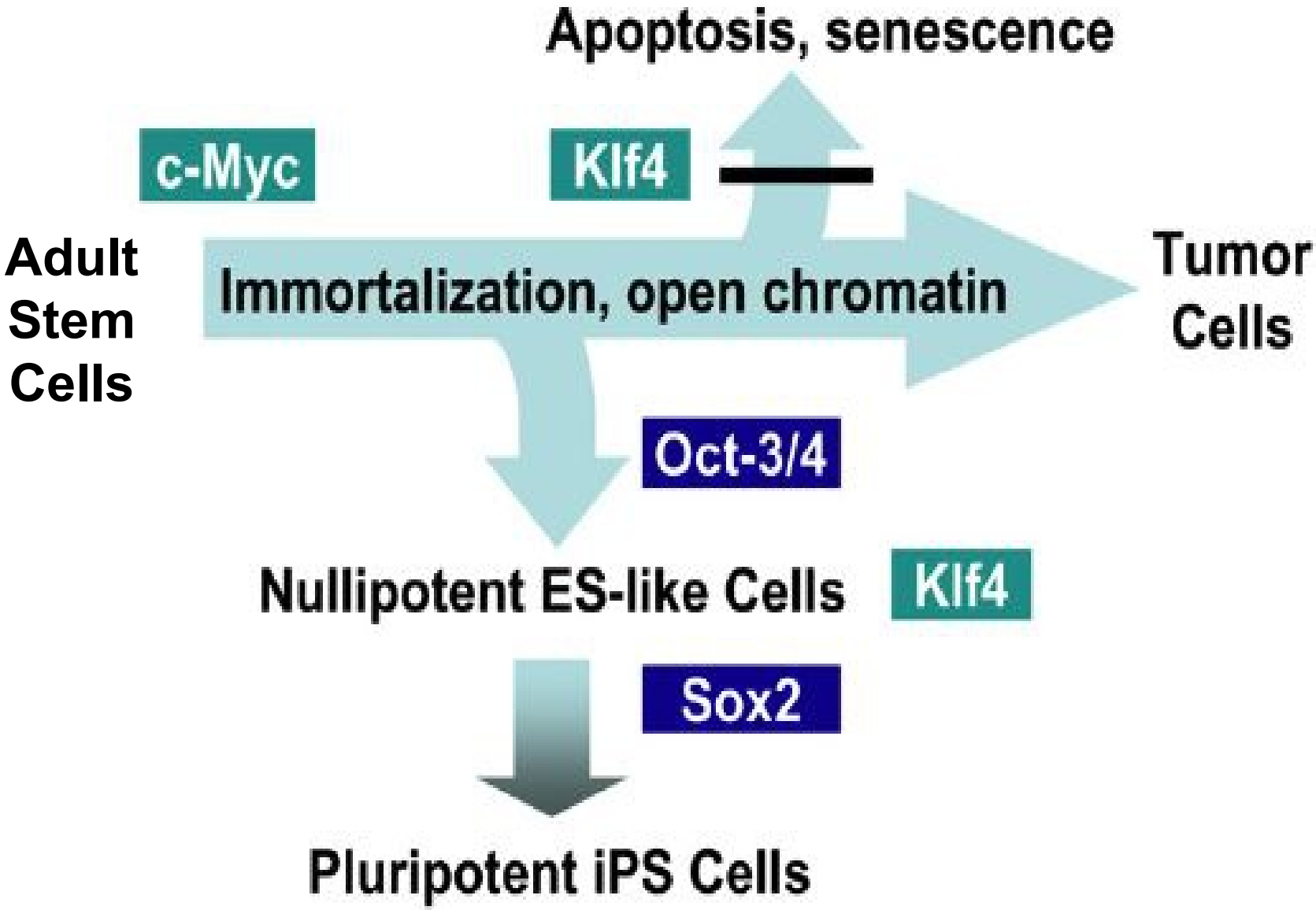
Eukaryotic Gene Structure



Multiple Enhancer Sequences



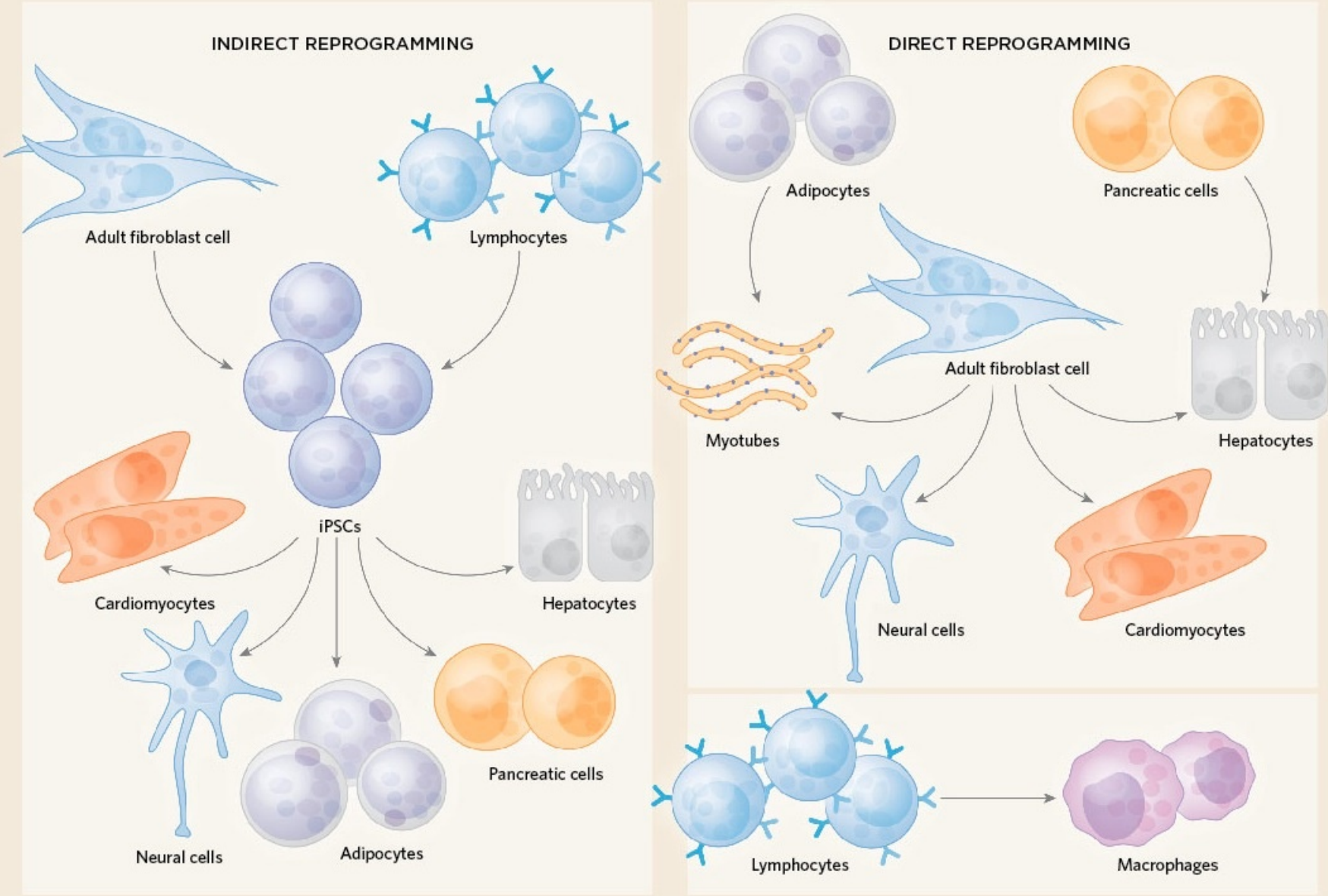
Induction of Pluripotent Stem Cells (iPS) from Somatic Stem Cells



Yamanaka. (2007) Cell Stem Cell Vol 1, pp 39-49.

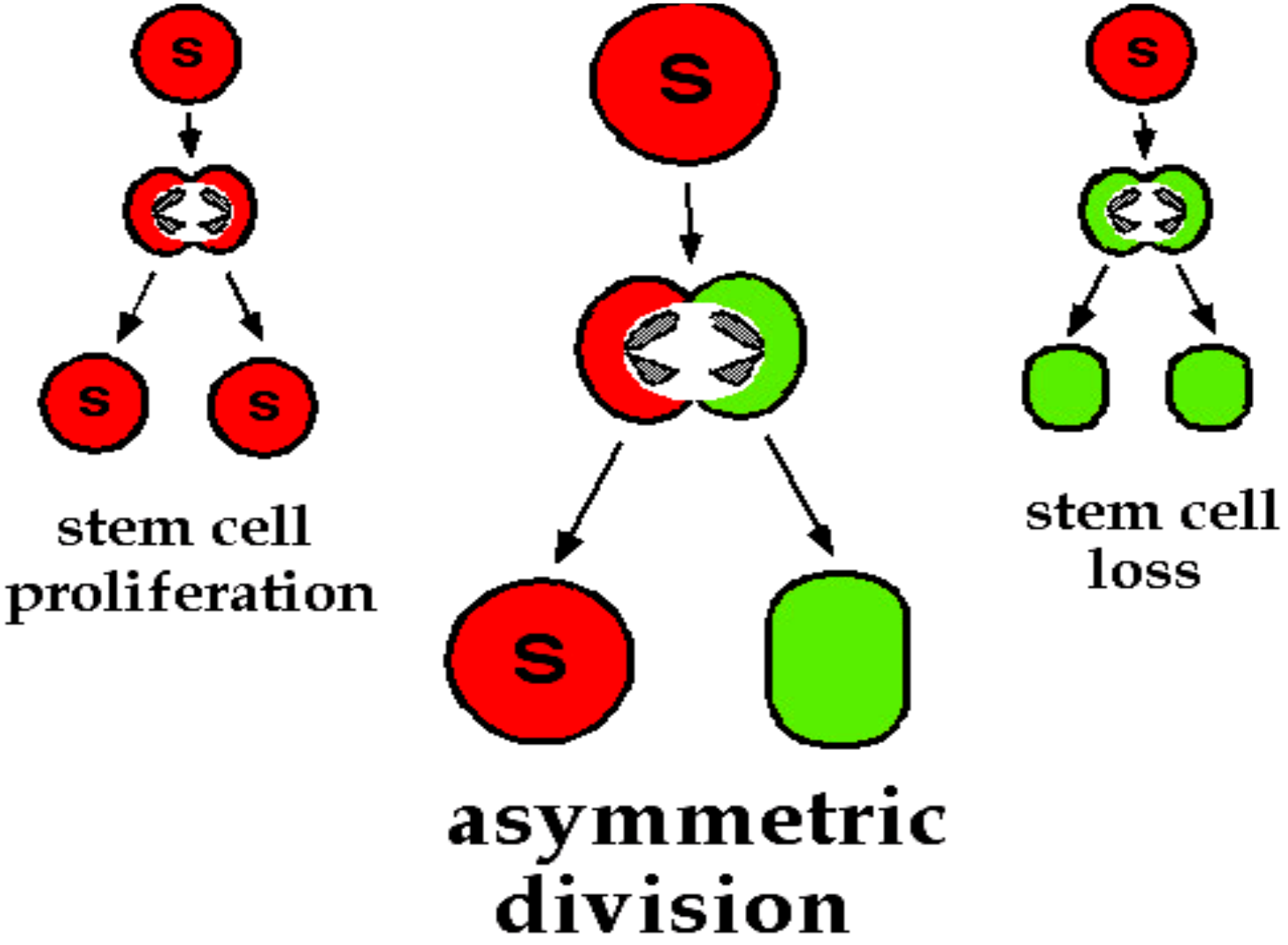
Cell Reprogramming *in vivo* & *in vitro*

http://www.the-scientist.com/?articles.view/articleNo/39241/title/A-Twist-of-Fate/

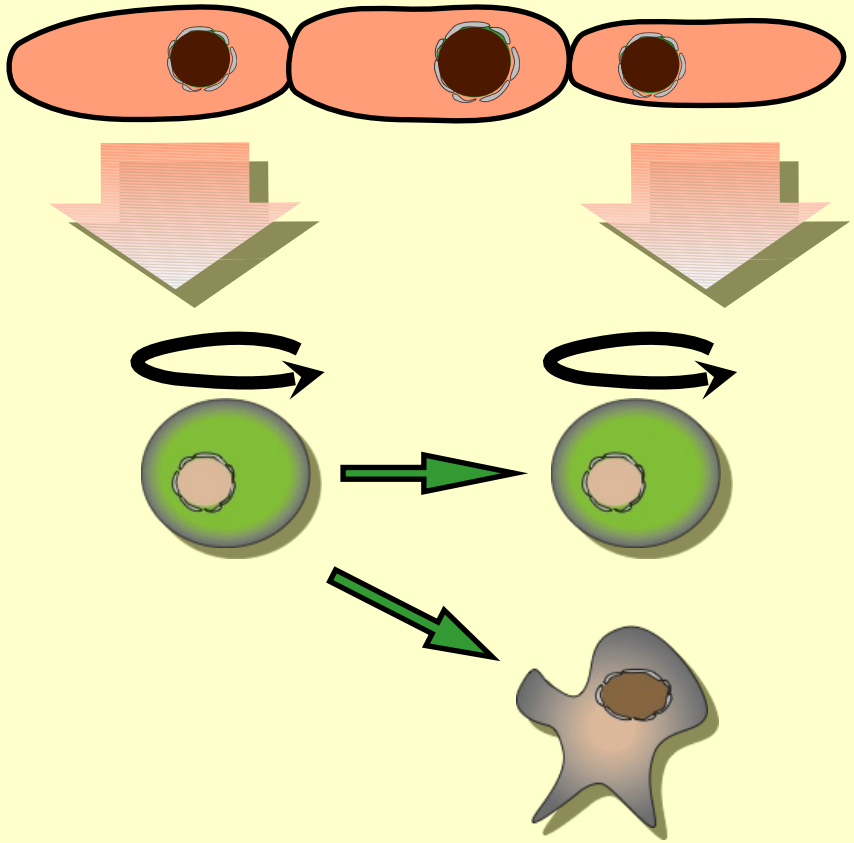


http://www.the-scientist.com/?articles.view/articleNo/39241/title/A-Twist-of-Fate/

Alternate Stem Cell Fates

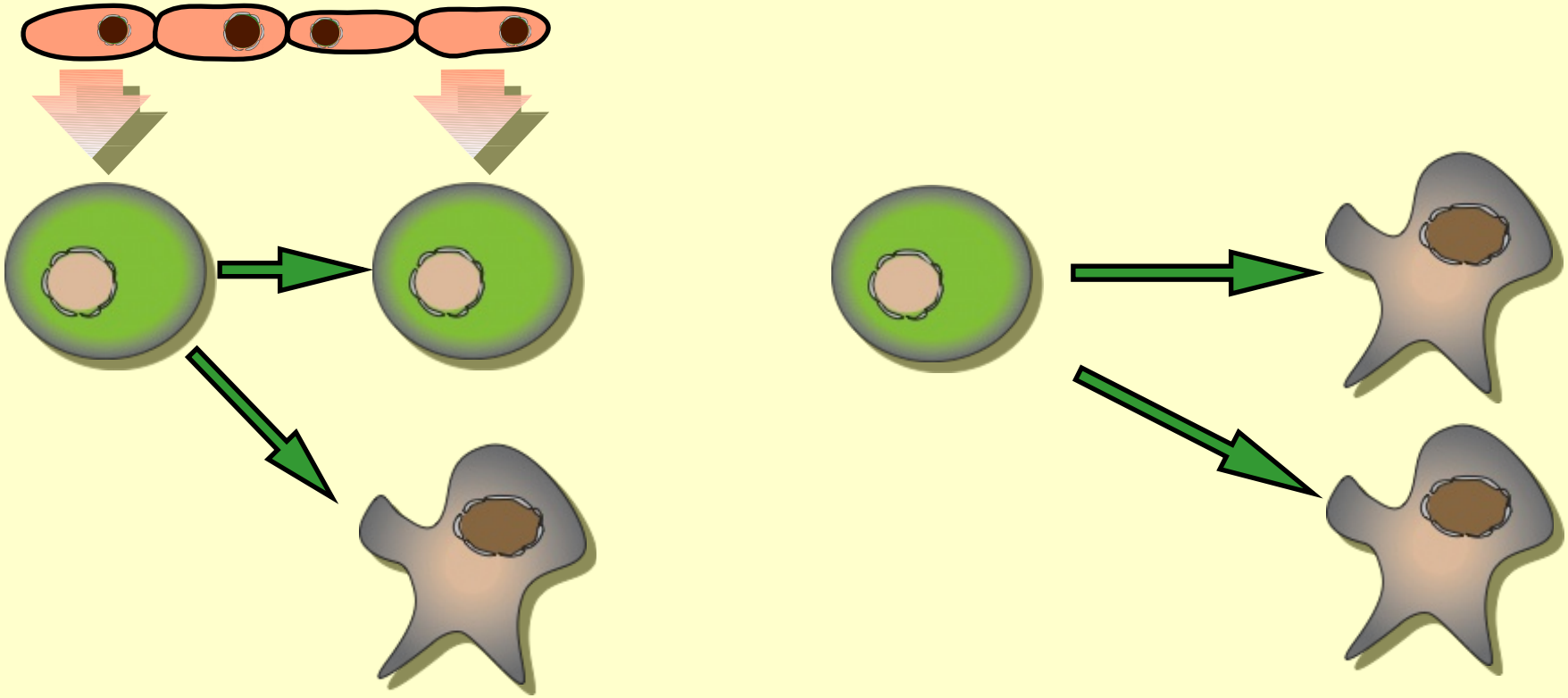


signals from niches maintain adult stem cells and tissues



Courtesy of Roel Nusse

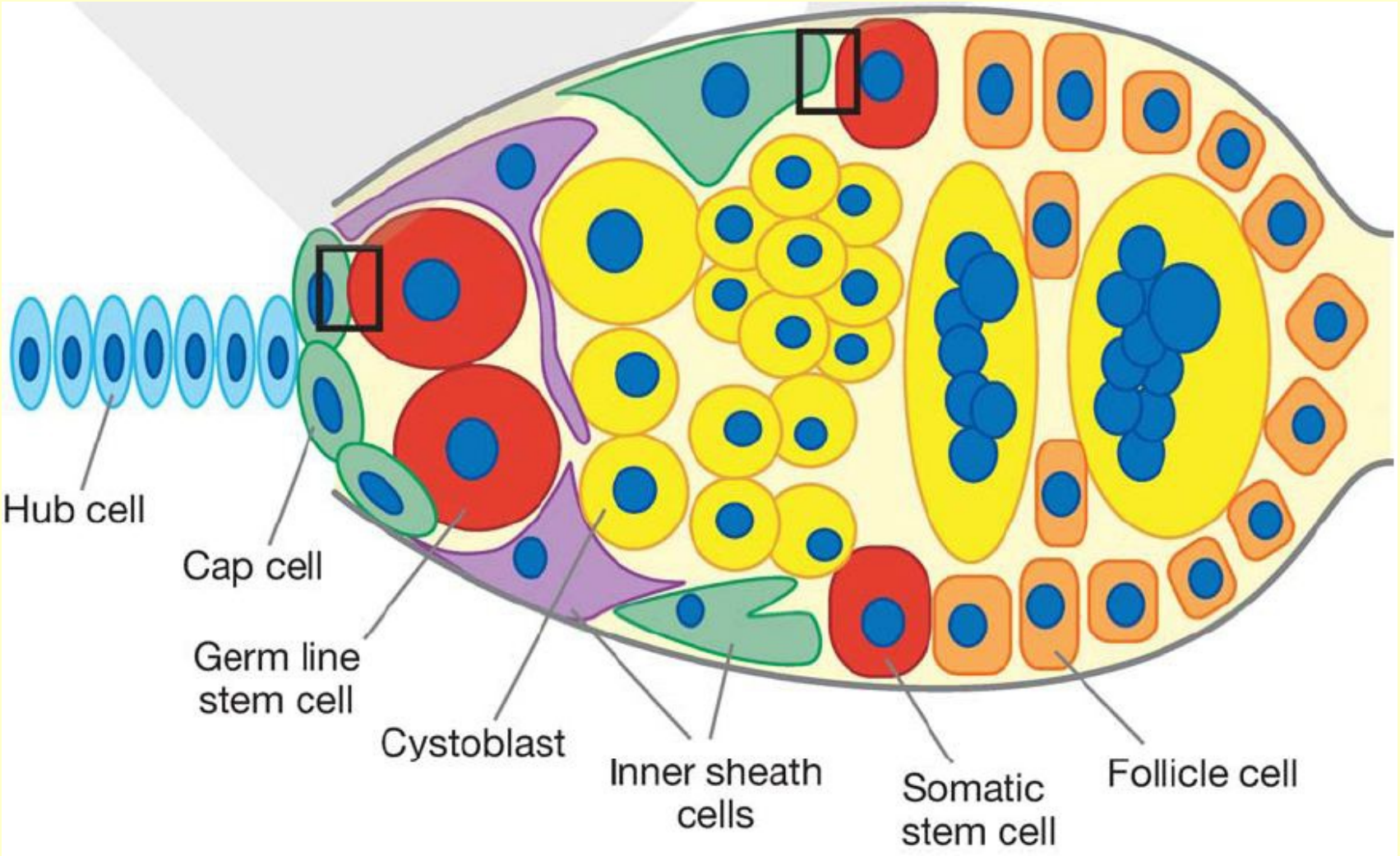
In the absence of niche signals, adult stem cells will differentiate, by default



1. Self-renewal is proliferation coupled to blocking differentiation, controlled by signals.
2. Signals are local; niches have a limited capacity and cells compete for the signals
3. The signals control tissue homeostasis, also after damage

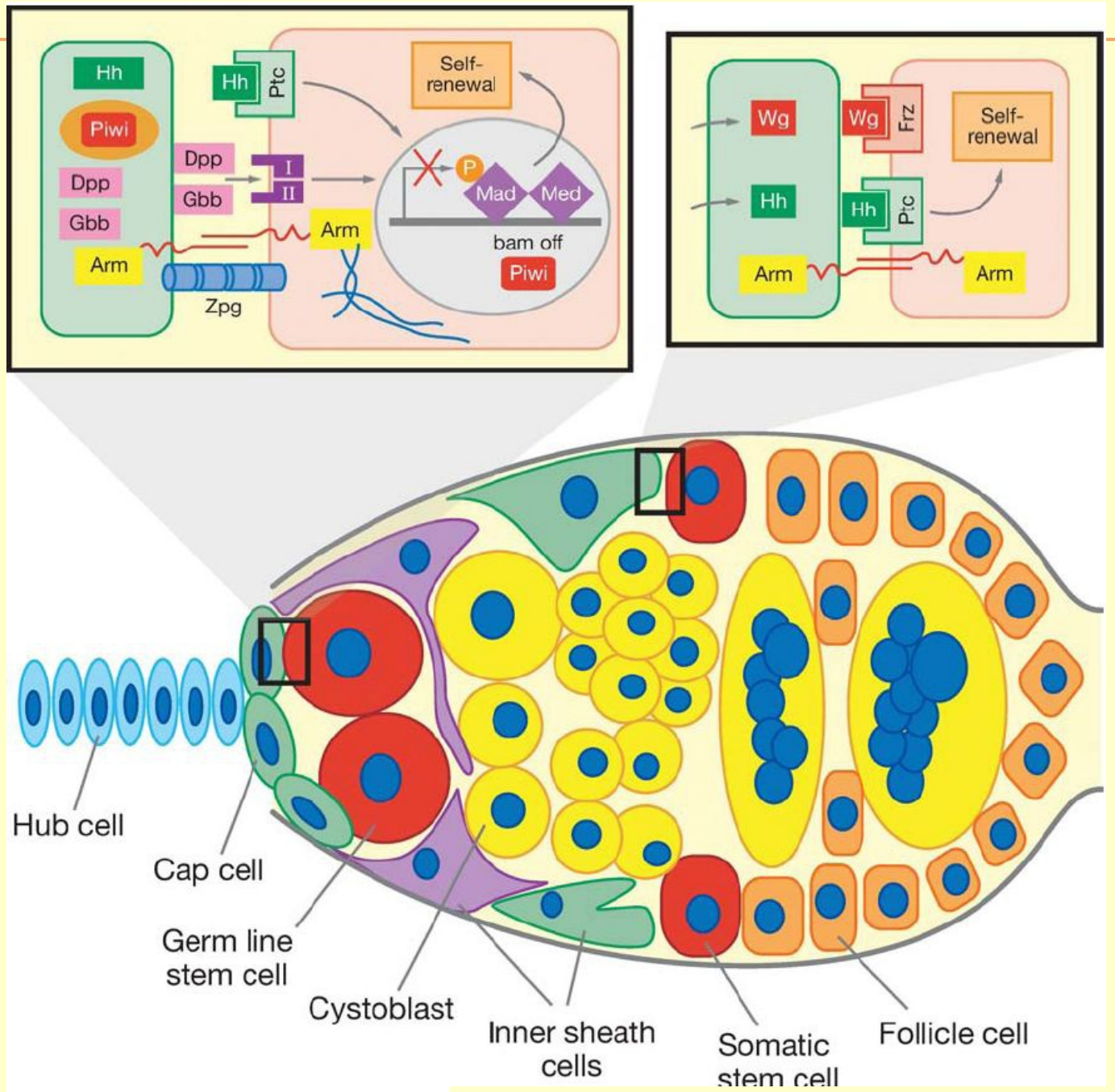
Courtesy of Roel Nusse

Oocyte Niche in the Drosophila Germarium



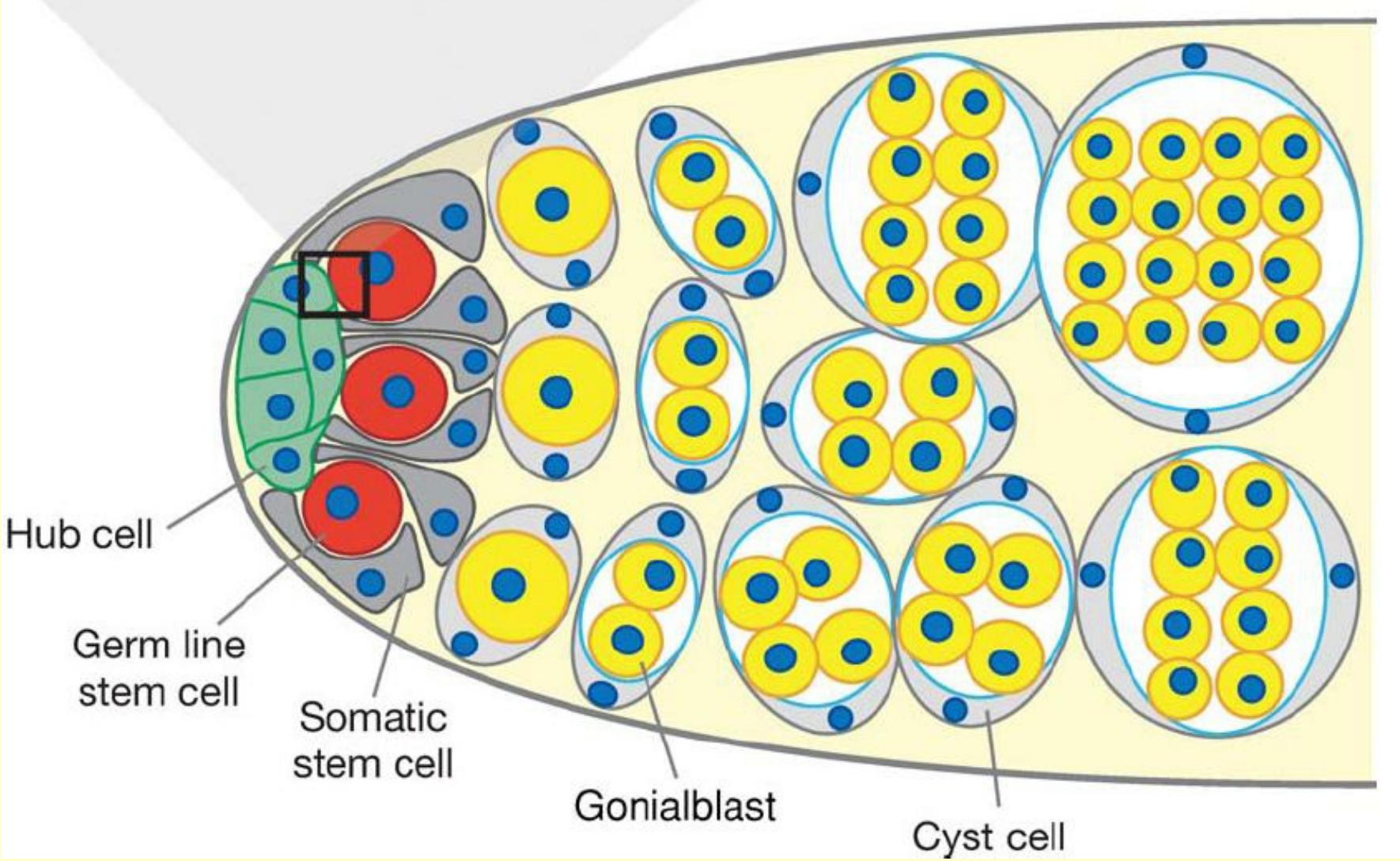
Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

Cell-Cell Interactions at Oocyte Niche



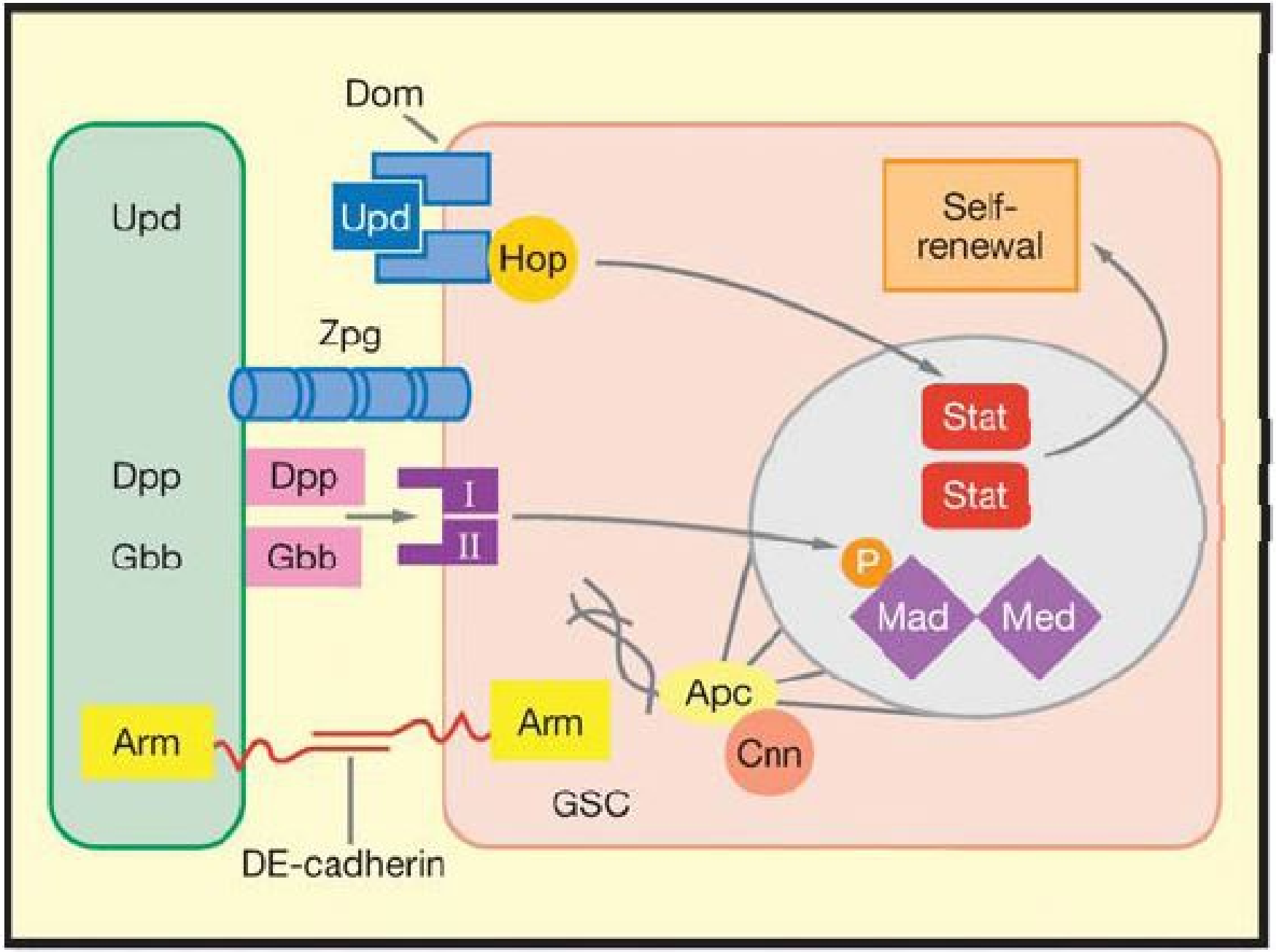
Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

Drosophila Spermatogonial Niche



Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

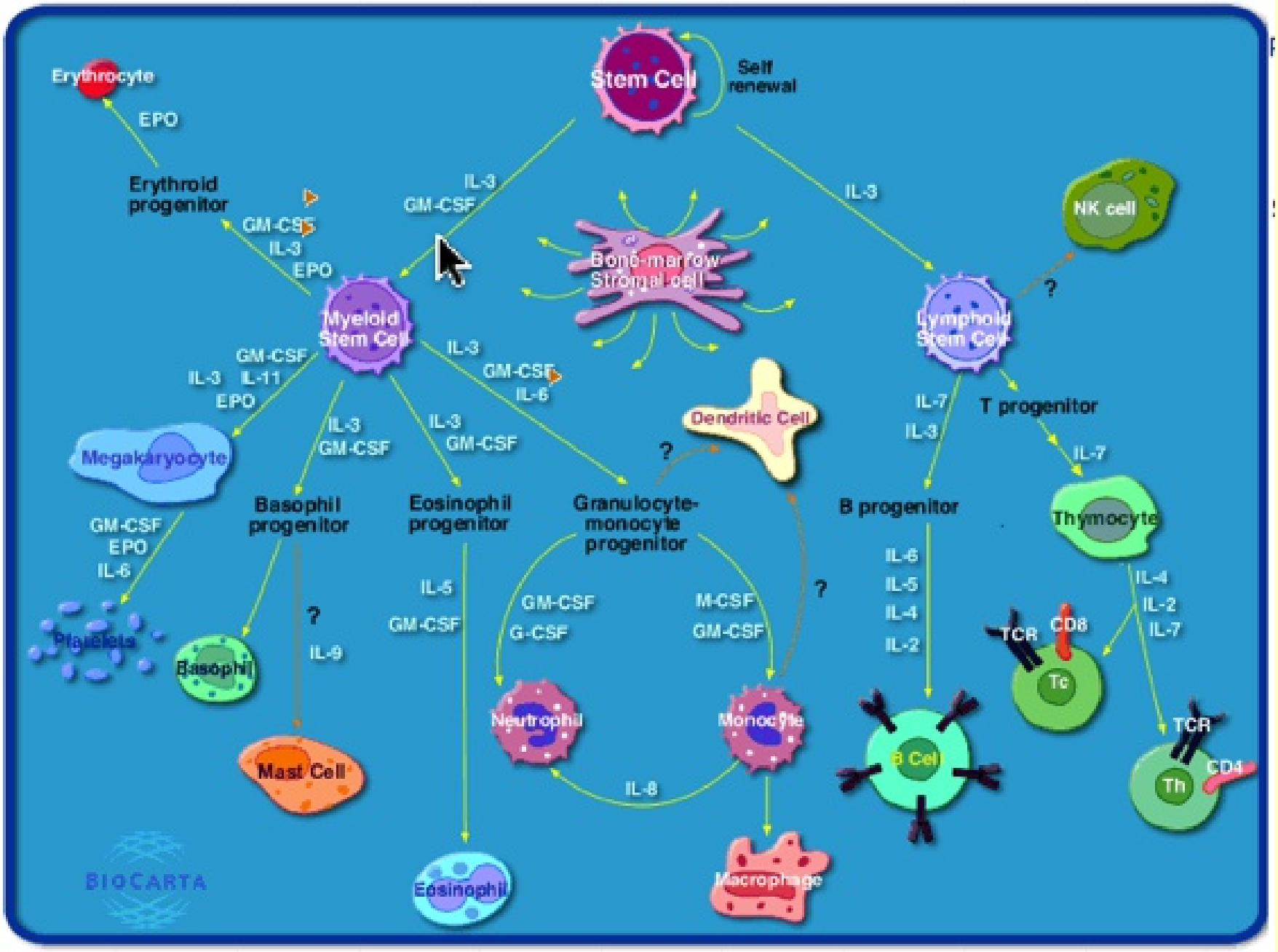
Cell-Cell Interactions at the Spermatogonial Niche



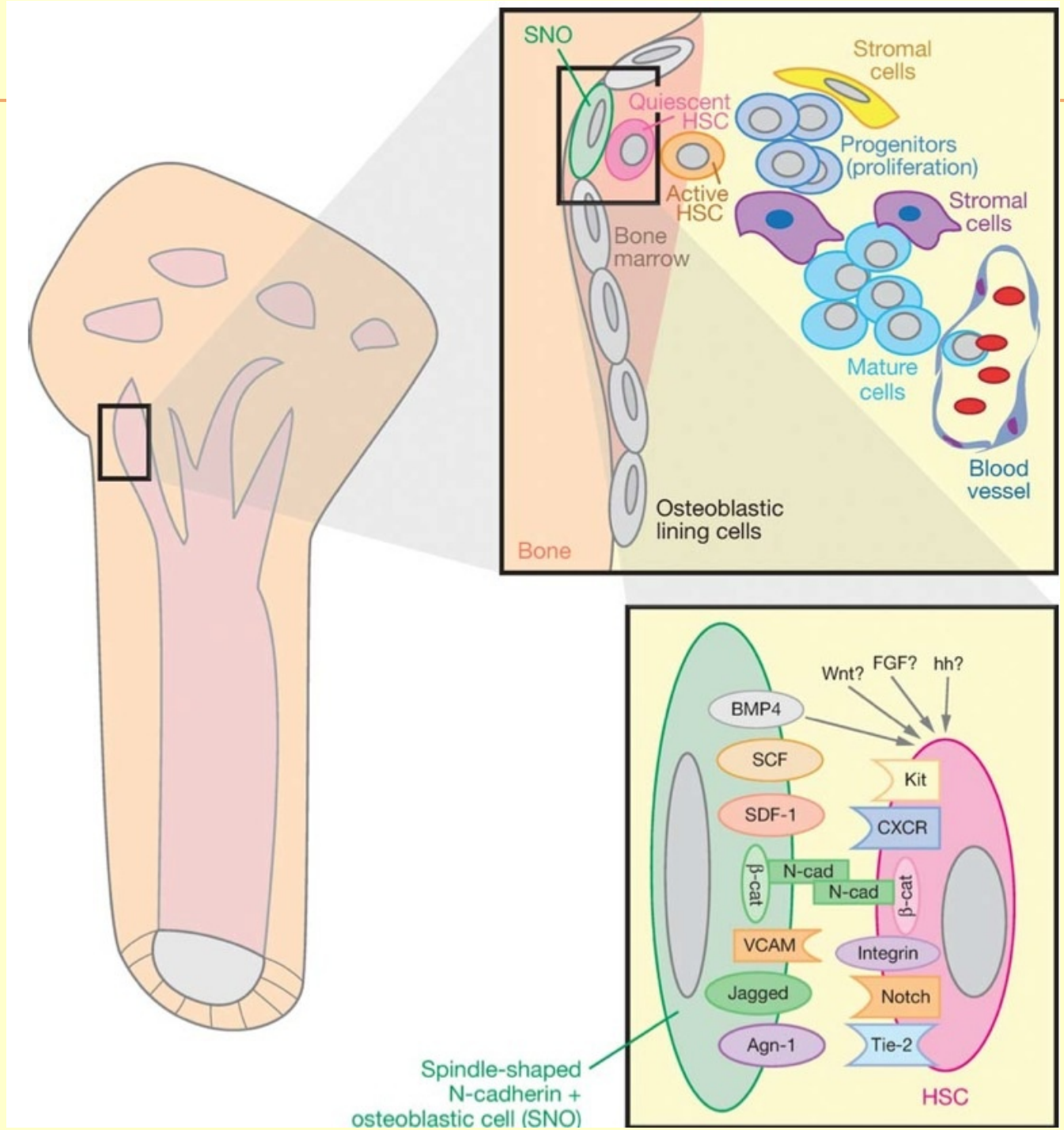
Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

Hematopoiesis

http://www.biocarta.com/pathfiles/h_stemPathway.asp



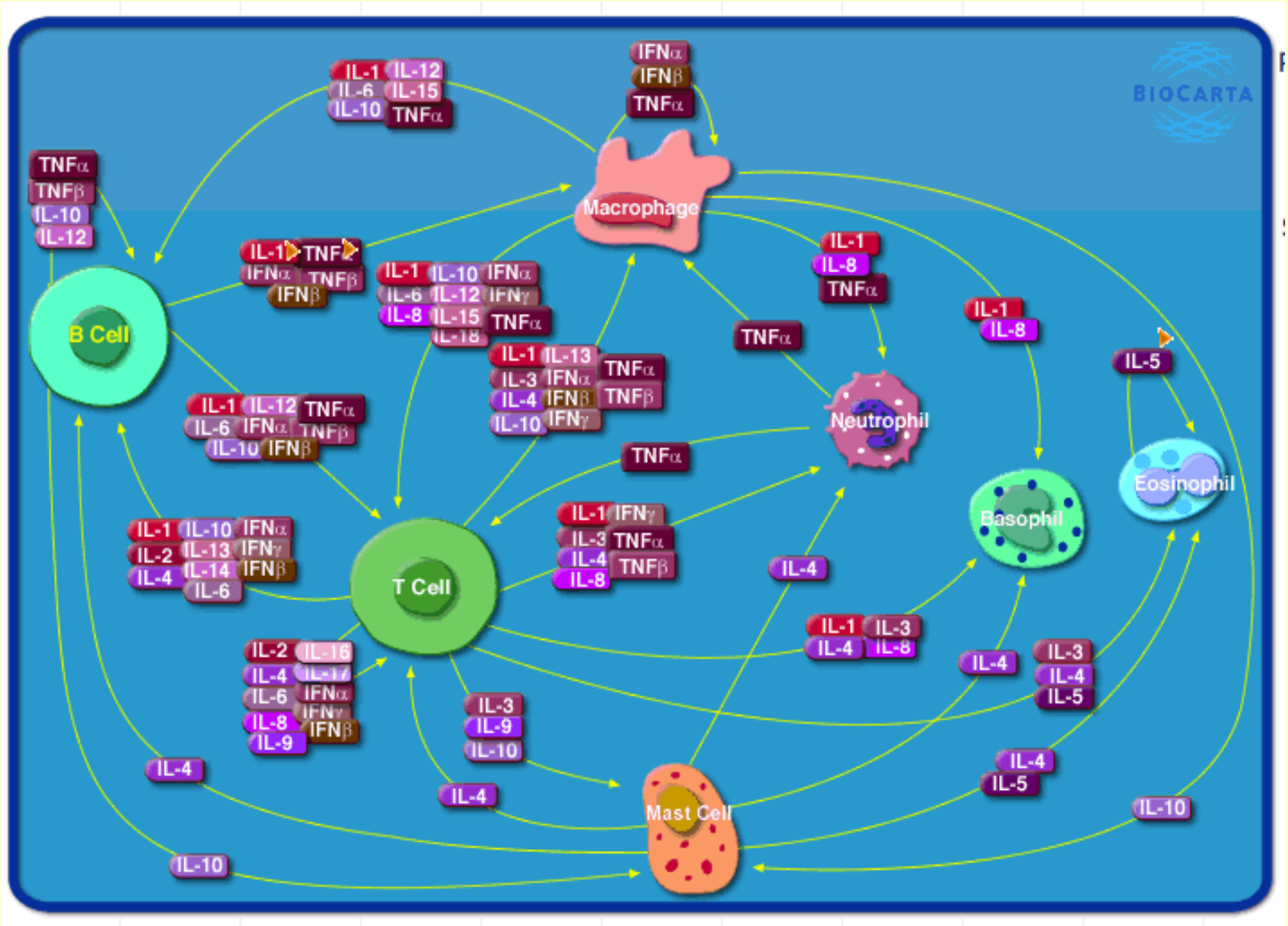
Hematopoietic Stem Cell Niche



Li and Xie, Ann. Rev. Dev. Biol. 2005, 605-663

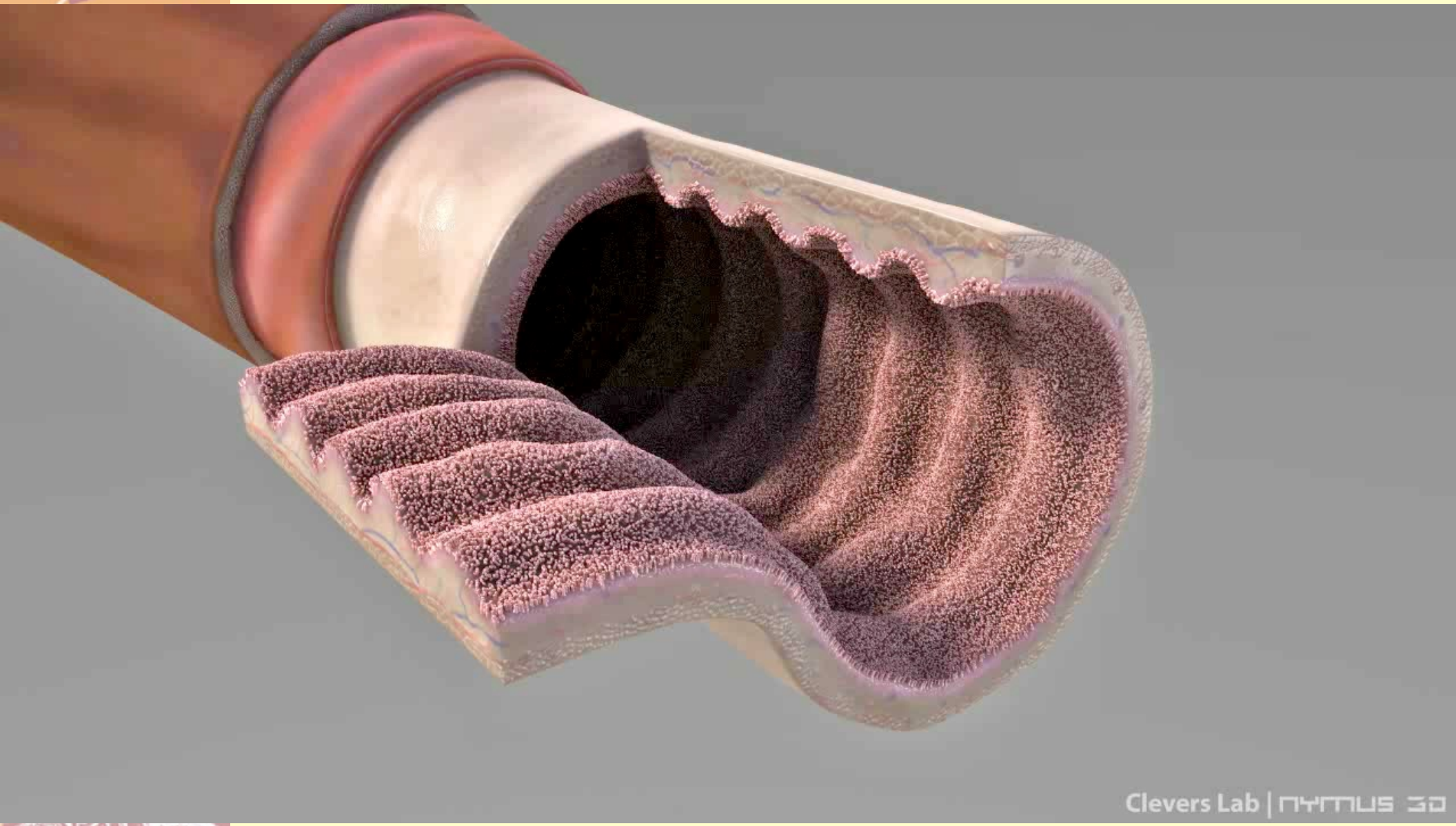
Cytokine Network

http://www.biocarta.com/pathfiles/h_cytokinePathway.asp

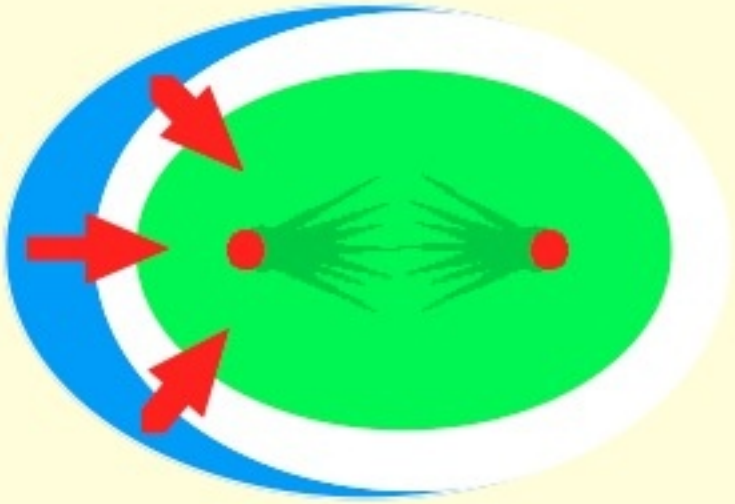


Intestinal Stem Cells in Crypts

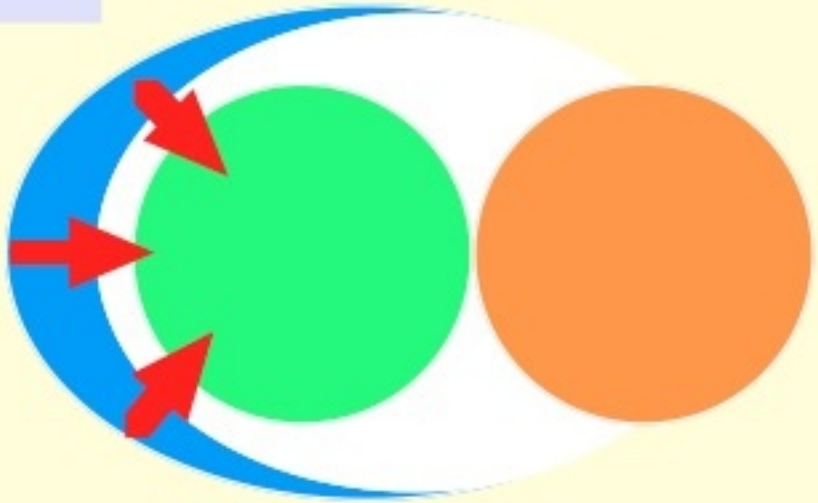
Rainbow Villi



Asymmetric stem cell divisions



Niche



John Cairns: The Immortal Parental Strands

Nature Vol. 255 May 15 1975

review article

Mutation selection and the natural history of cancer

John Cairns*

Survival of the rapidly renewing tissues of long-lived animals like man requires that they be protected against the natural selection of fitter variant cells (that is, the spontaneous appearance of cancer). This article discusses three possible protective mechanisms and shows how they could explain various features of the natural history of certain common cancers of man.

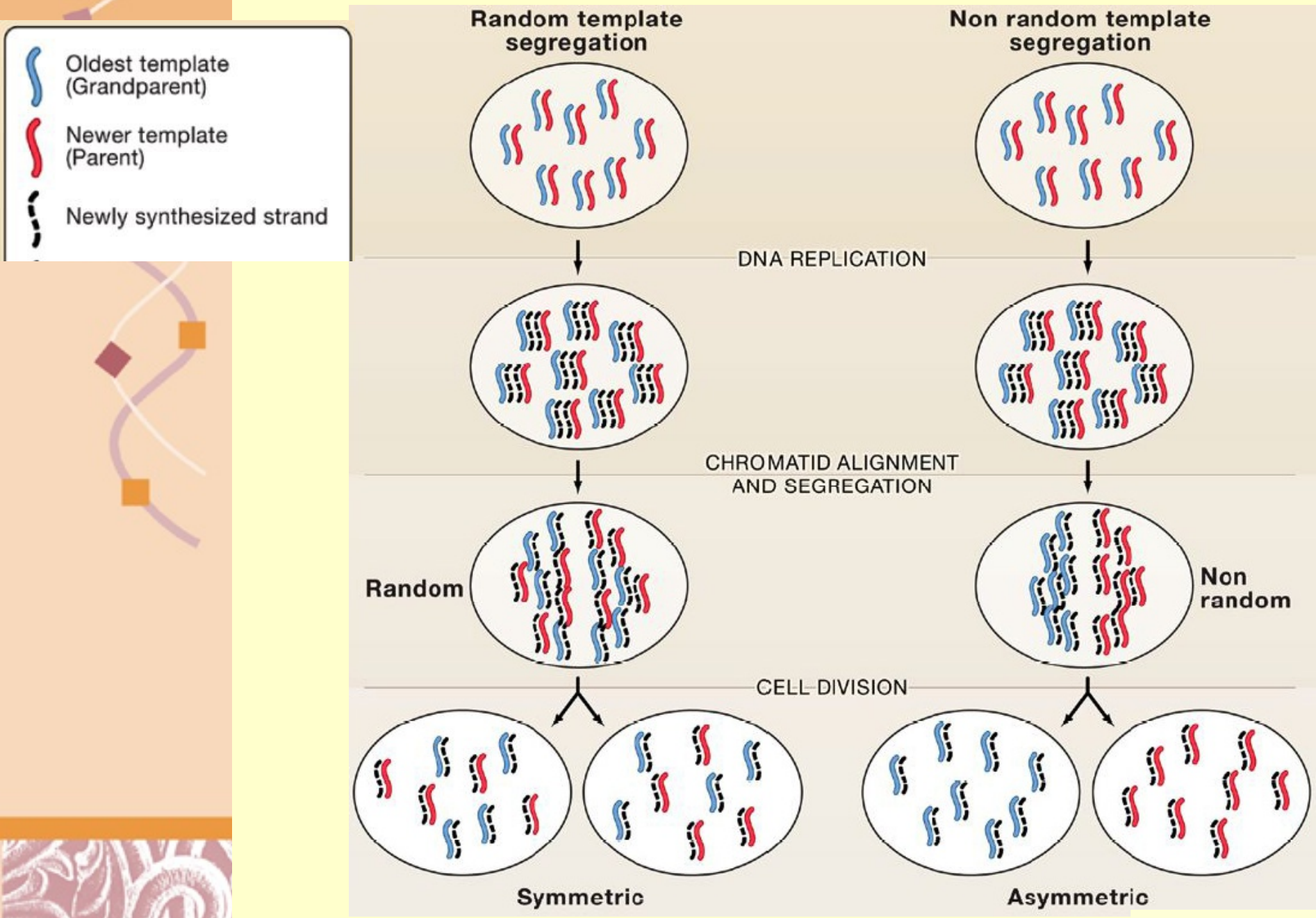
Cairns (1975) Nature **255, 197**

Motivation for the Immortal Parental Strand or Asymmetric Strand Segregation

- Adult rat contains $6x10^{10}$ cells
- In its small intestine, a rat sheds over 10^{13} epithelial cells during its lifetime.
- Requires 10^{3} symmetric cell doublings from embryo to adult followed by 10^{13} asymmetric cell doublings during its lifetime
- How do epithelial cells minimize mutations that lead to cancer?

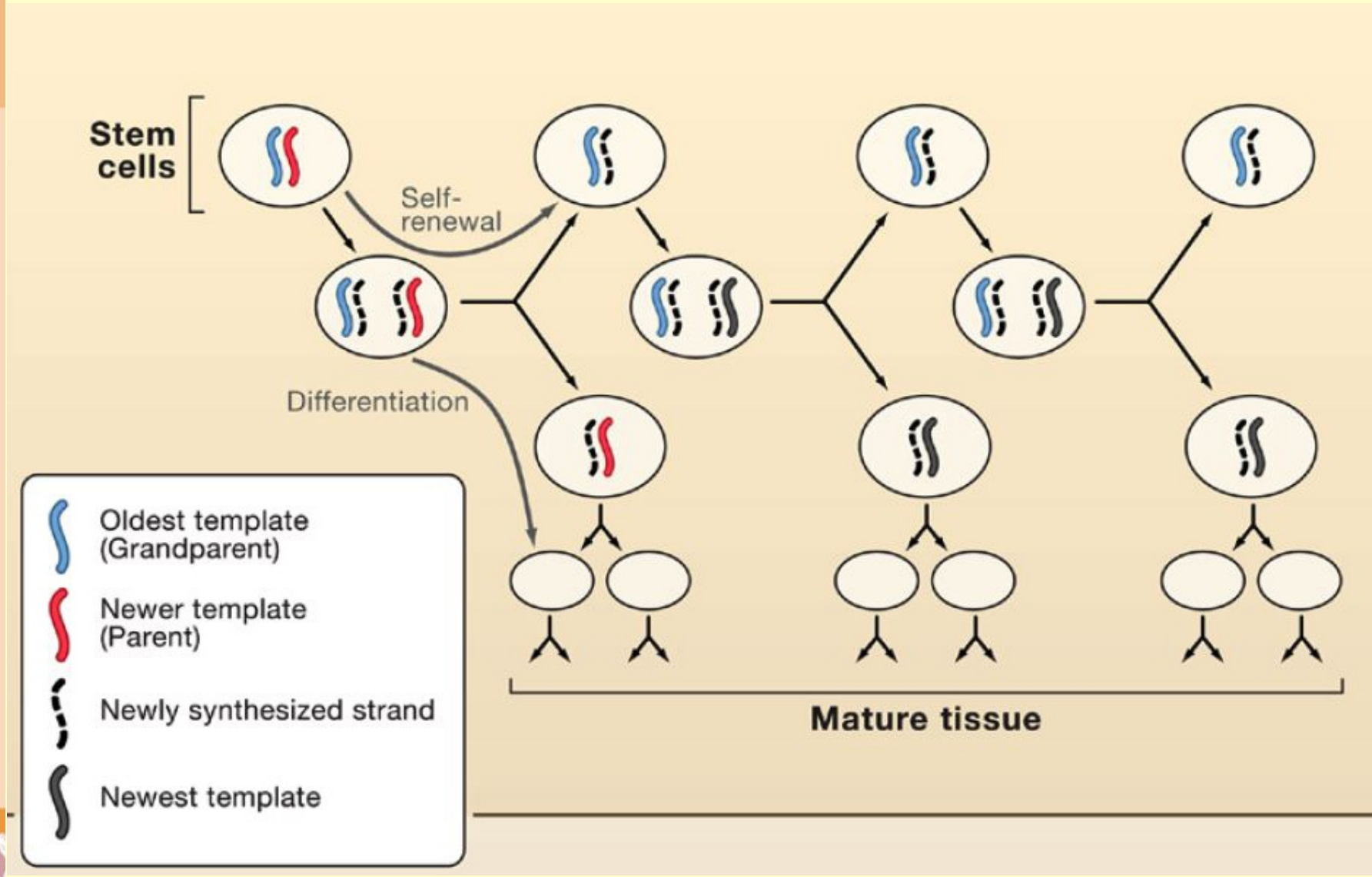
Cairns (1975) Nature **255, 197**

Asymmetric Segregation of Parental DNA Strands



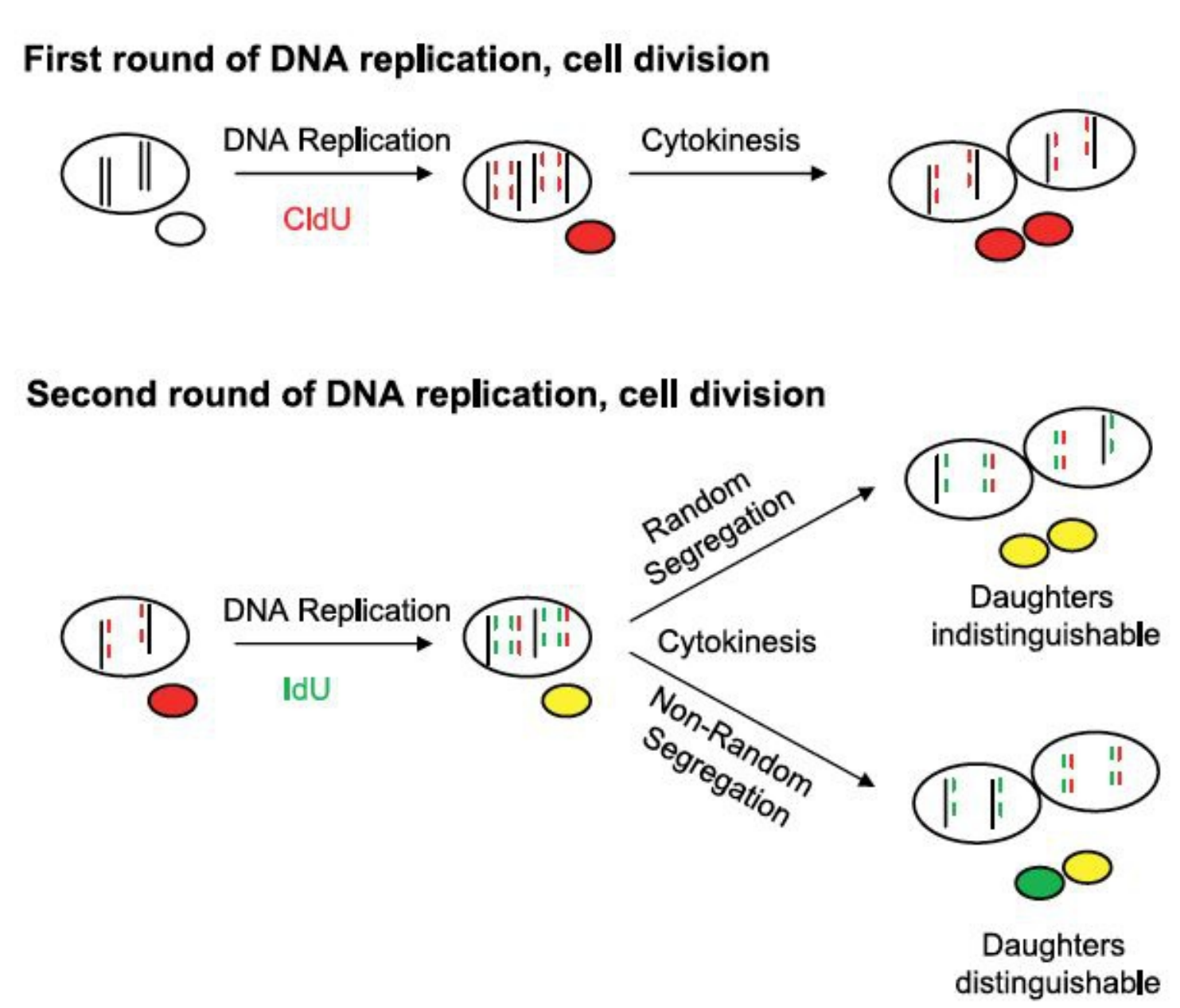
Rando (2007) Cell 129 1239

Asymmetric Stem Cell Growth with Asymmetric Parental Strand Segregation



Rando (2007) Cell 129 1239

Asymmetric DNA Labeling Patterns



Rando (2007) Cell 129 1239

Duplicating Muscle Cell Pairs Display Asymmetric DNA Labeling Patterns

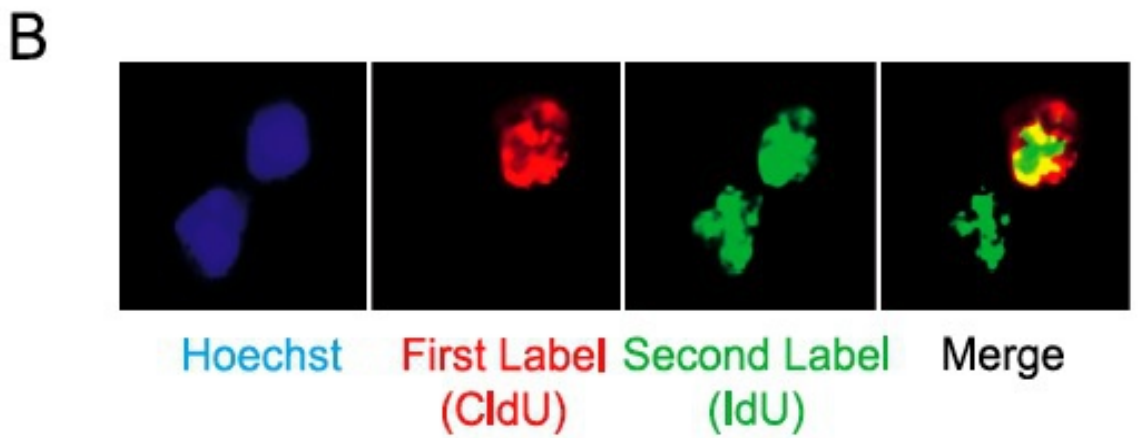
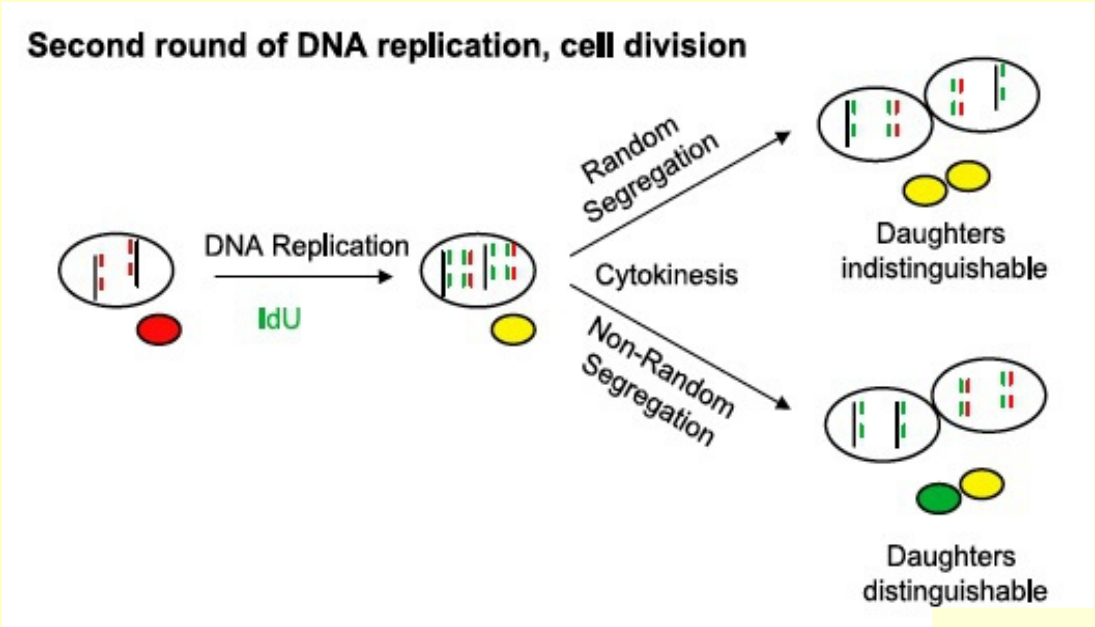
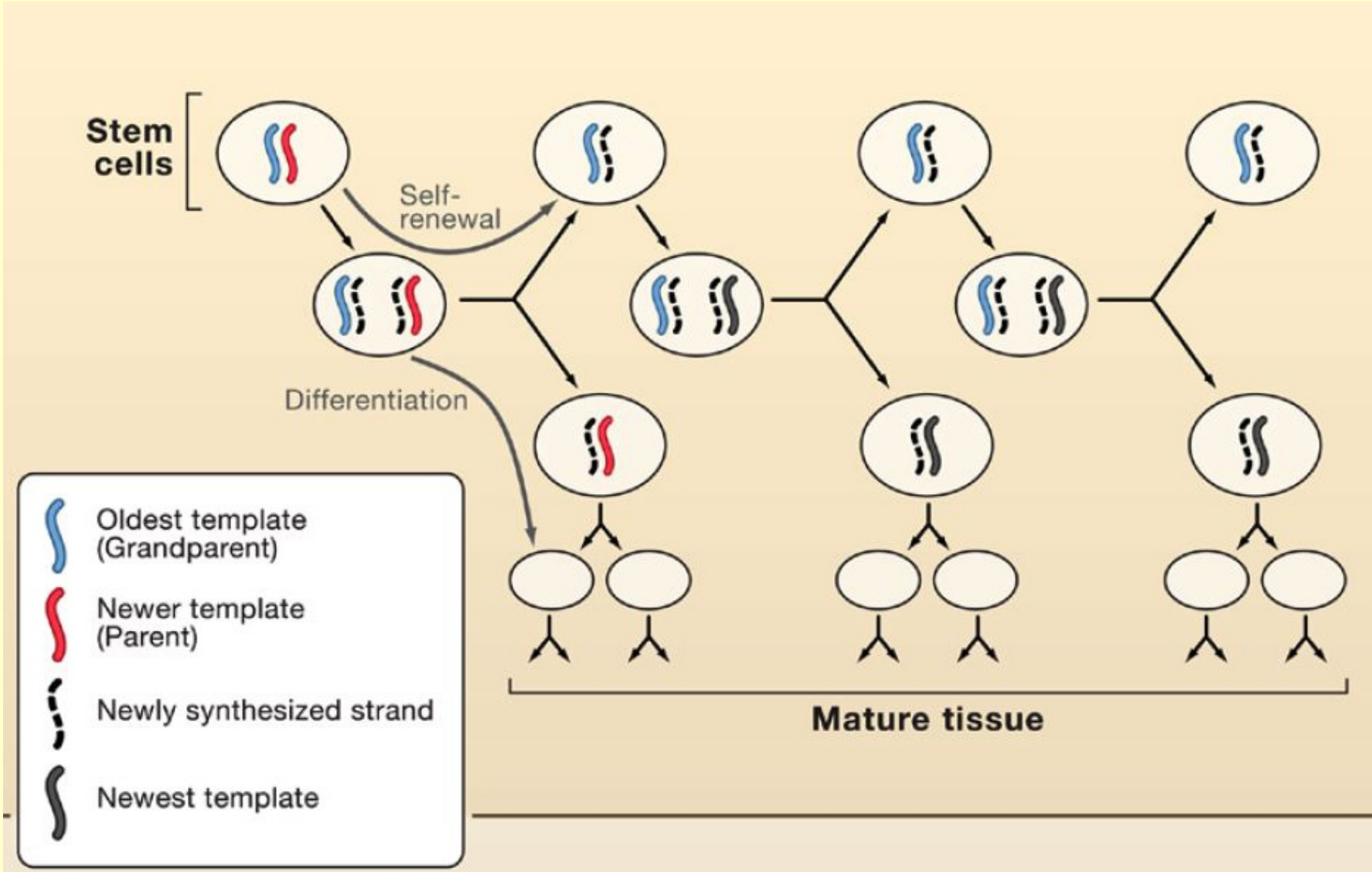


Figure 2. Evidence of Co-Segregation of DNA Template Strands during Muscle Progenitor Cell Division
(B) Cell pairs were immunostained for CldU and IdU. Shown is a representative photograph of an immunostained pair of cells, in which both daughter cells were labeled with the second label, IdU (green), but only one daughter inherited the first label, CldU (red).



Conboy et al, PLOS Biology (2007)

Asymmetric Stem Cell Growth with Asymmetric Parental Strand Segregation



Rando (2007) Cell 129 1239