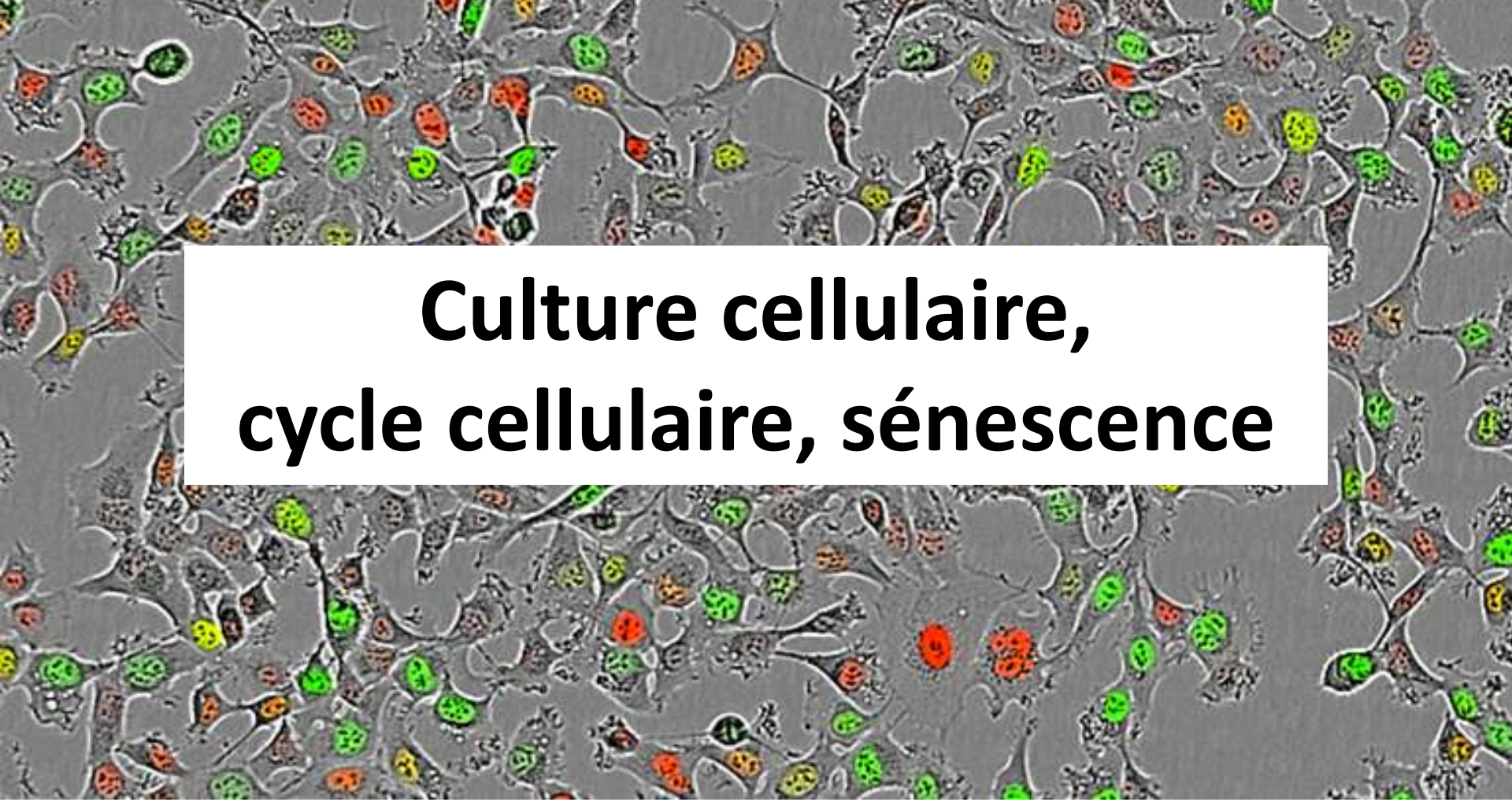


Culture cellulaire, cycle cellulaire, sénescence

M1 Sciences des médicaments et des produits de Santé

université PARIS-SACLAY

FACULTÉ DE PHARMACIE

Cells in culture

Primary cells : represent the tissue of origin

Difficult to culture and maintain, variability from donors

1917, aseptic and nutrients

Keratinocyte, enterocyte, endothelial cell, myocyte, fibroblast, hematopoietic stem cells ...

Transformation of primary cells in immortalized secondary cell line

Spontaneous / chemically or virally induced, easy to culture, no variability

HeLa, 1951, human cell line, derived from cervix cancer from Henrietta Lacks

Stem cells

Embryonic stem cells (ESCs) : (totipotent) pluripotent

1981 (mouse), 1998 (human)

Induced pluripotent stem cells (iPSCs)

2006 (from mouse, human fibroblasts)

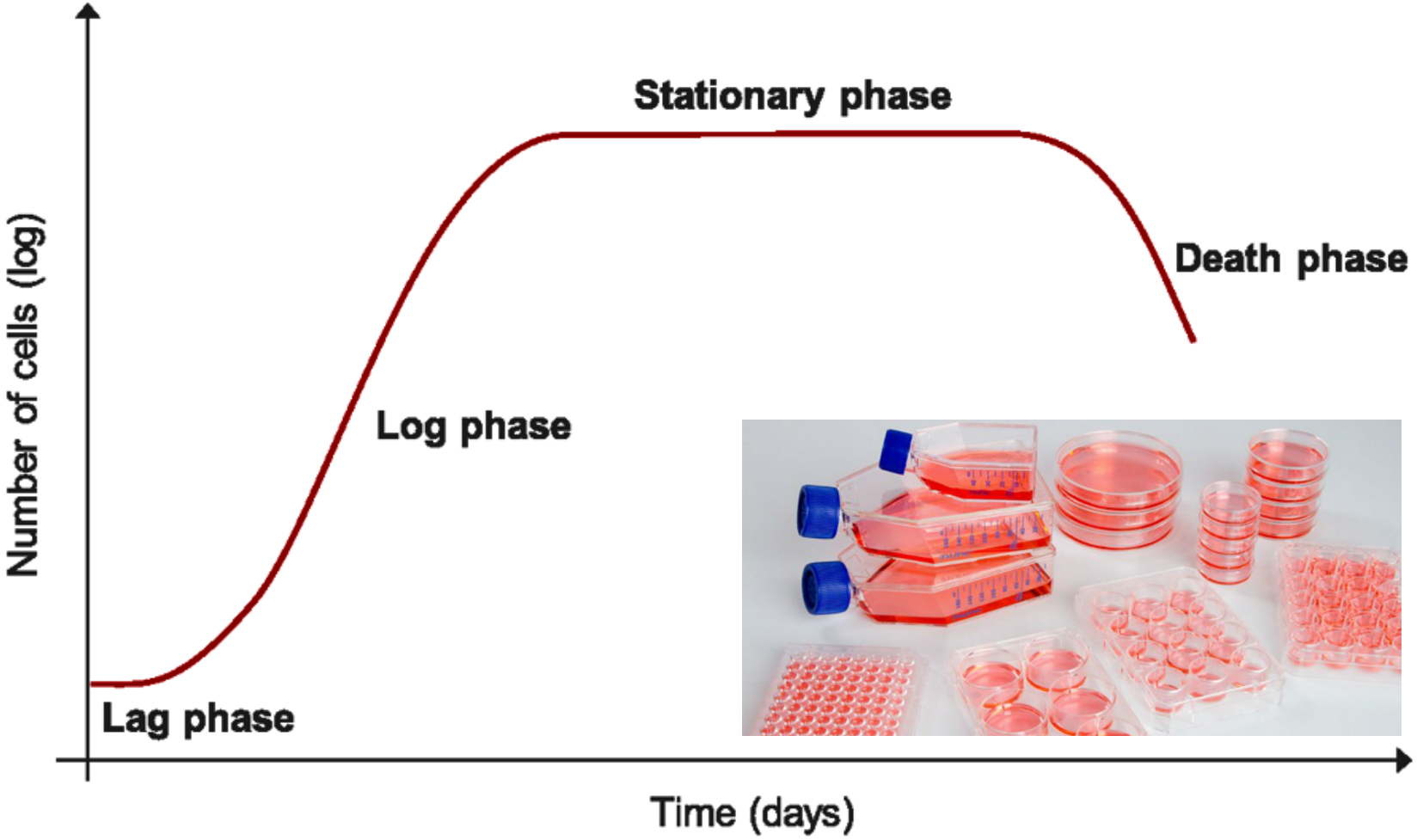
Nobel Prize in Physiology or Medicine 2012 John B. Gurdon & Shinya Yamanaka

Induced multipotent stem cells (ex : induced neural stem cell iNSCs)

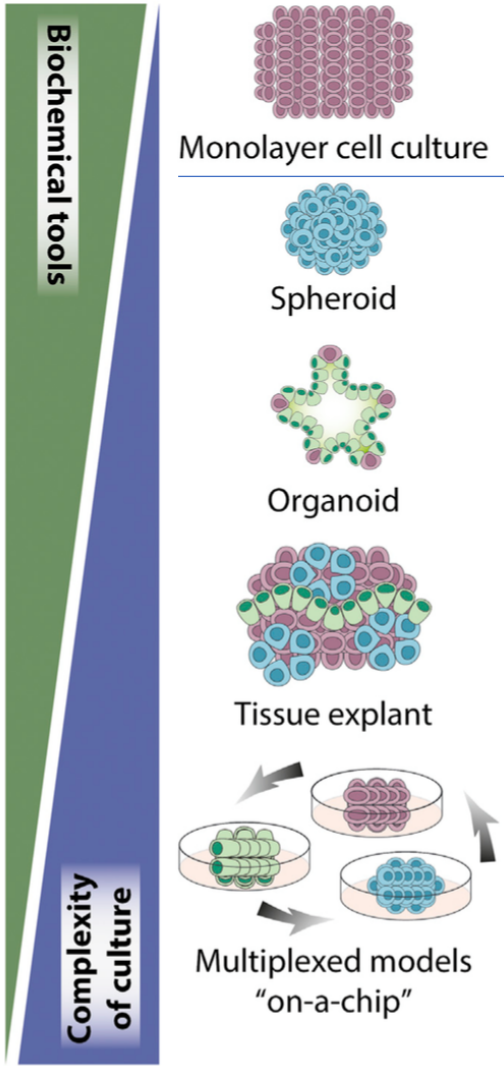
2012 (from fibroblasts). Reduced carcinogenic potential compared to iPSCs

Sakalem et al, Biotech. J., 2020

Cell line in 2D culture



2D versus 3D cell culture



Primary cells
Immortal cell lines
Stem cells

2D

3D

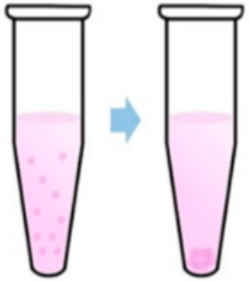
At least one cell type

At least one epithelial and one mesenchymal cell type

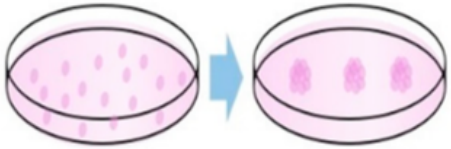
Yinet al, Cell Stem Cell, 2016

Spheroid/organoid scaffold-free culture methods

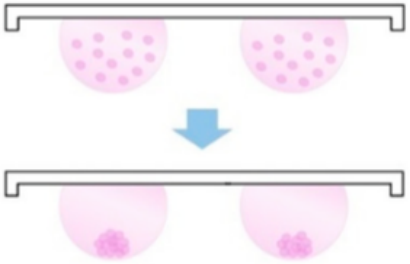
pellet



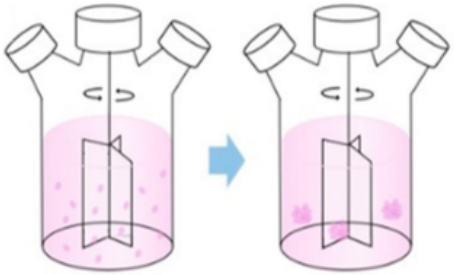
non adhesive flask

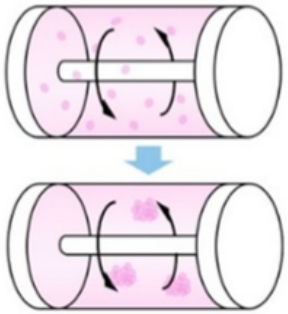


hanging drop

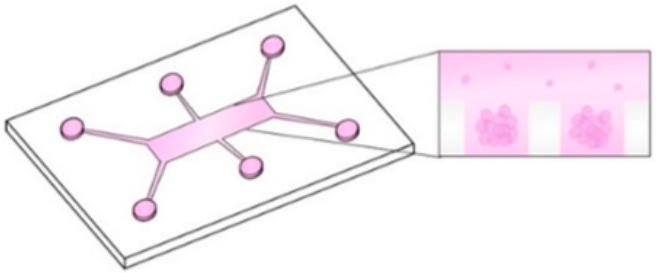


strirring vessel

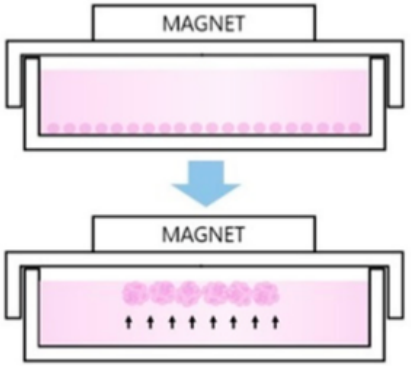




rotating vessel



Microfluidic
(organ on a chip)

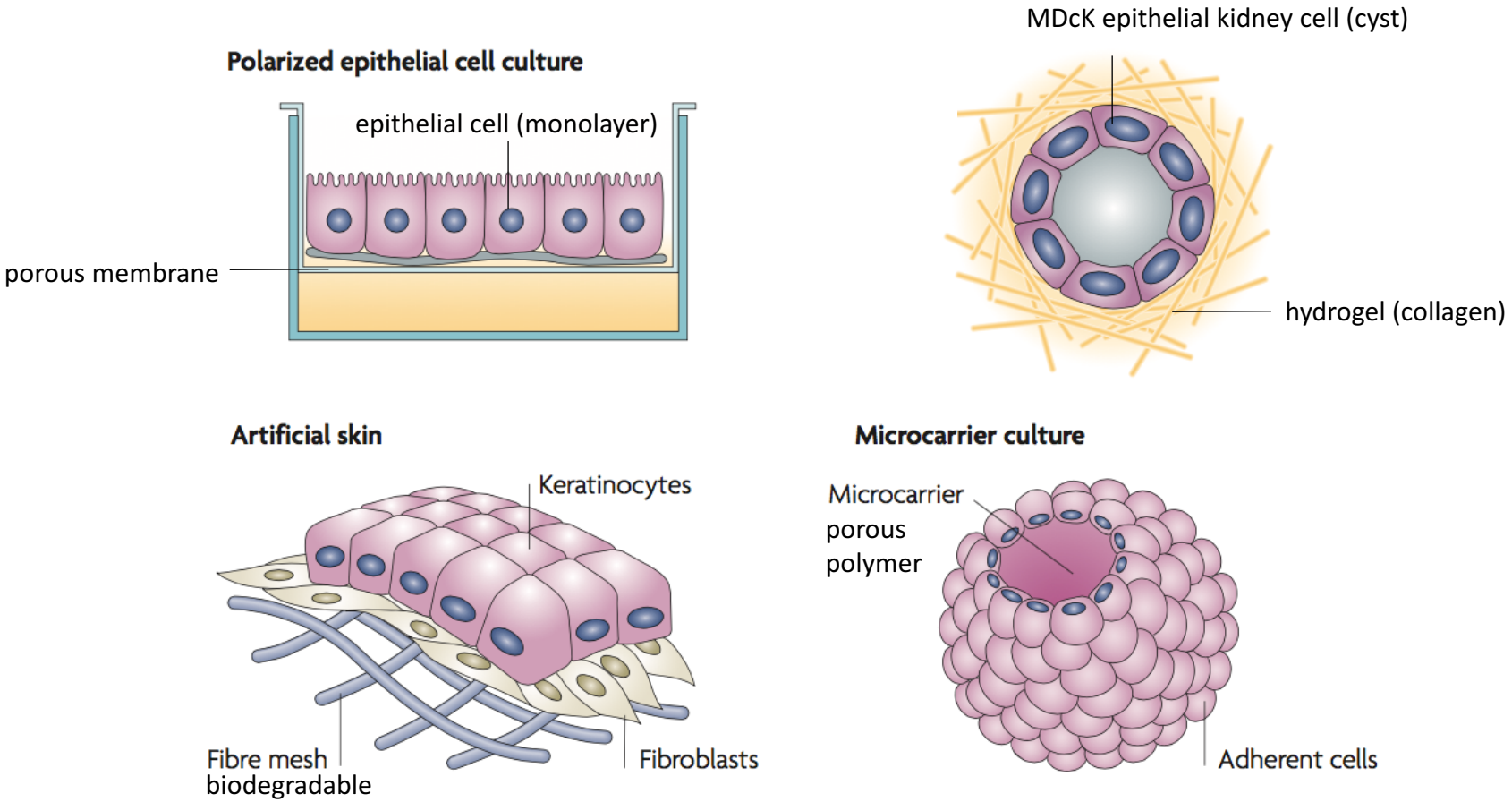


Magnetic levitation

Rely on cell self-assembly and prevention of cell adhesion to the flask

Ryu et al, Cells, 2019

Scaffolds for 3D culture : natural or synthetic hydrogel or porous



Adapted from Pampaloni et al, Nat. Rev. Mol. Cell. Biol., 2007

Before becoming a drug blockbuster…

Complex, long, expensive and risked

AFM-Téléthon, Code de santé publique

Cell fate

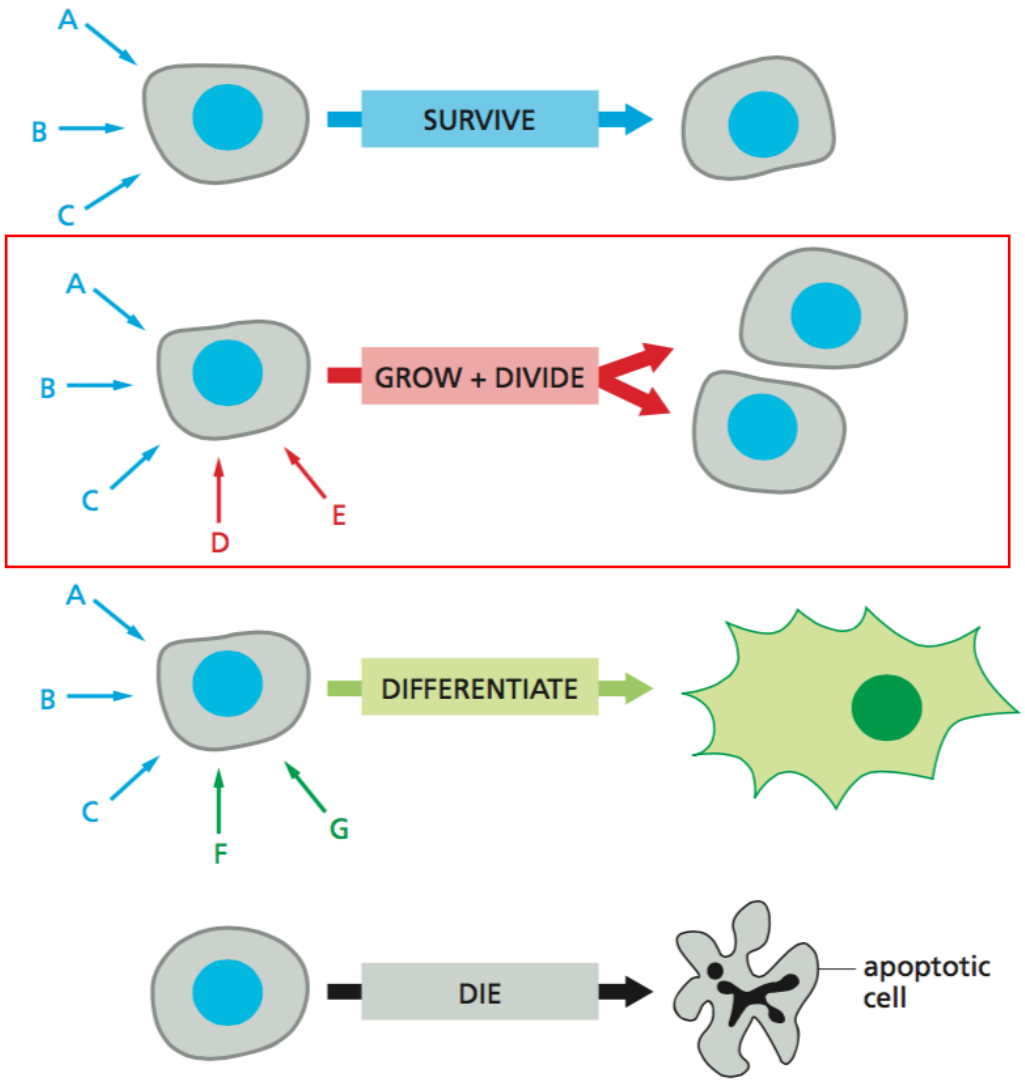
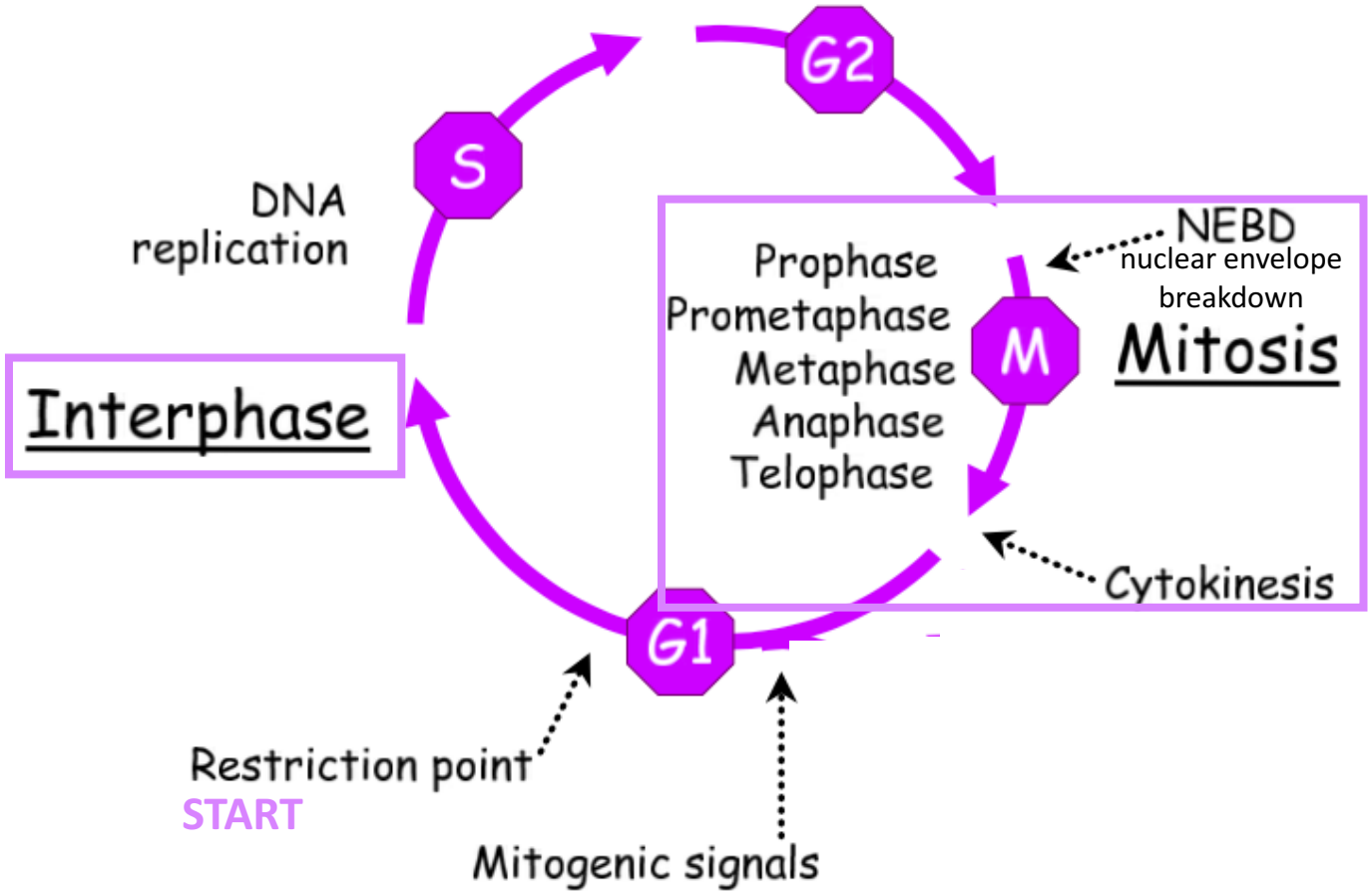


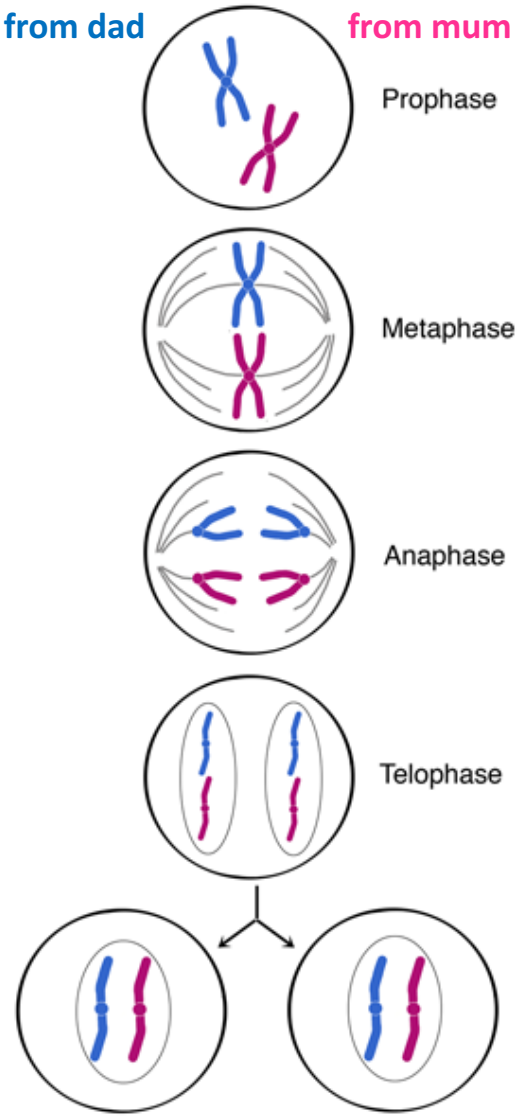
Figure 15-4 Molecular Biology of the Cell 6th

Usually 4 phases in eukaryotic cell cycle



Meijer, Oncology, 2003

Mitosis : 2 daughter cells with identical DNA content



diploid 2N, 2n
46 chromosomes

sister chromatids separation

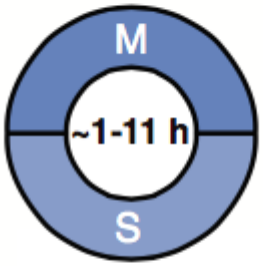
diploid 2N, 1n
46 chromosomes

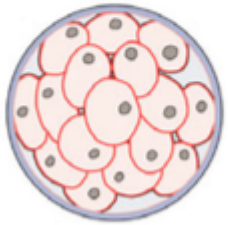
Adapted from http://cyberbridge.mcb.harvard.edu/

Cell cycle variation in different cell types

Early embryonic cells

morula





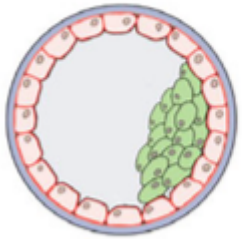
no transcription

totipotent

Embryonic stem cells

ES cells

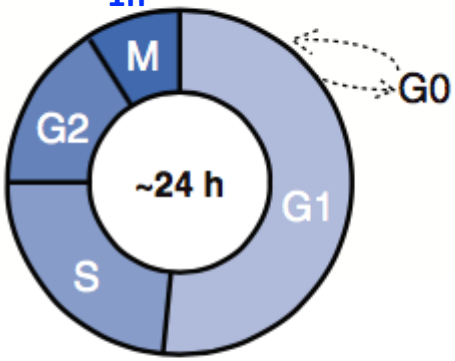
ESCs

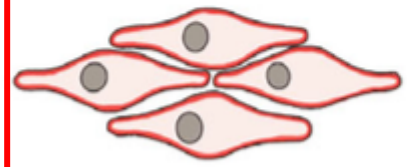


pluripotent

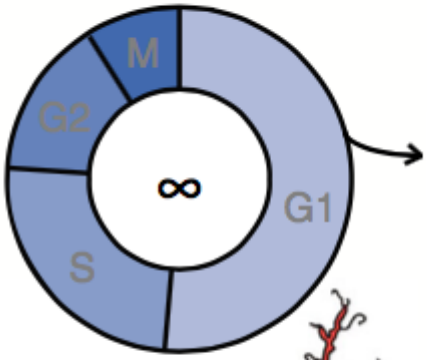
Somatic cells

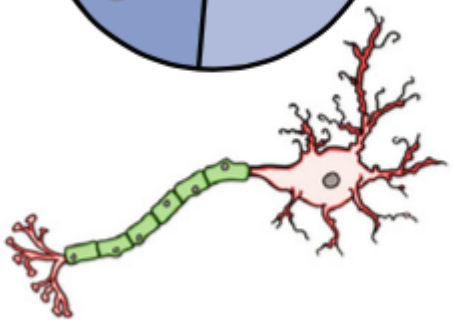
1h





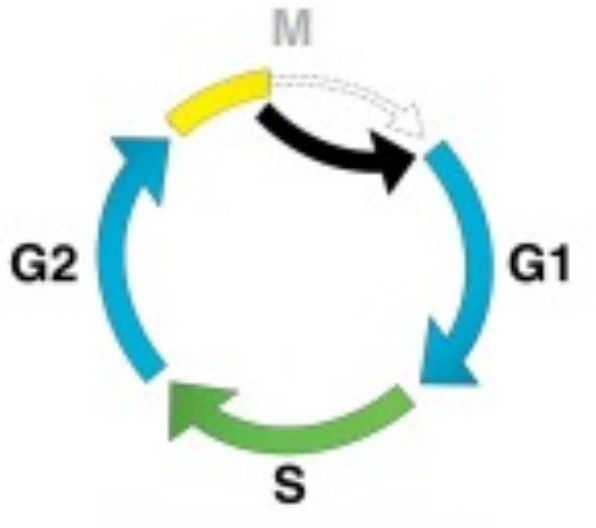
Post-mitotic cells





Padgett & Santos, FEBS letters, 2020

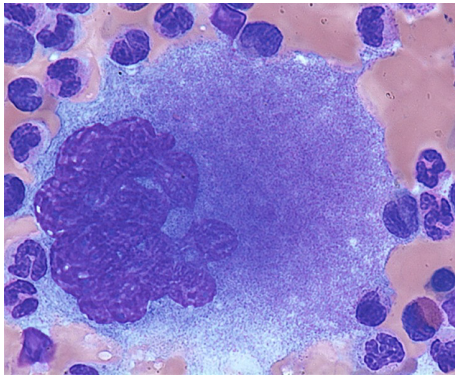
Cell cycle variation : endoreplication



Curr Opi Plant Biol

Megacaryocyte (platelet)

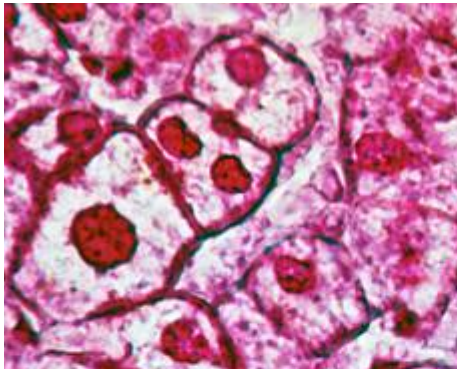
endomitosis



Peter Maslak

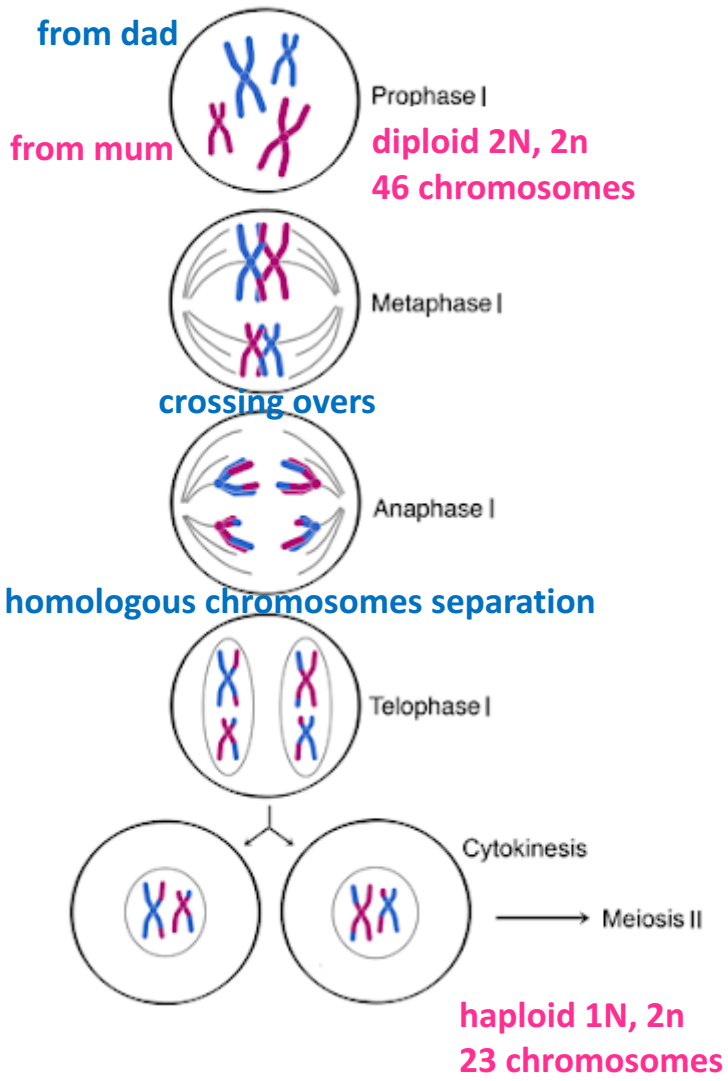
Hepatocyte **Cardiomyocyte**

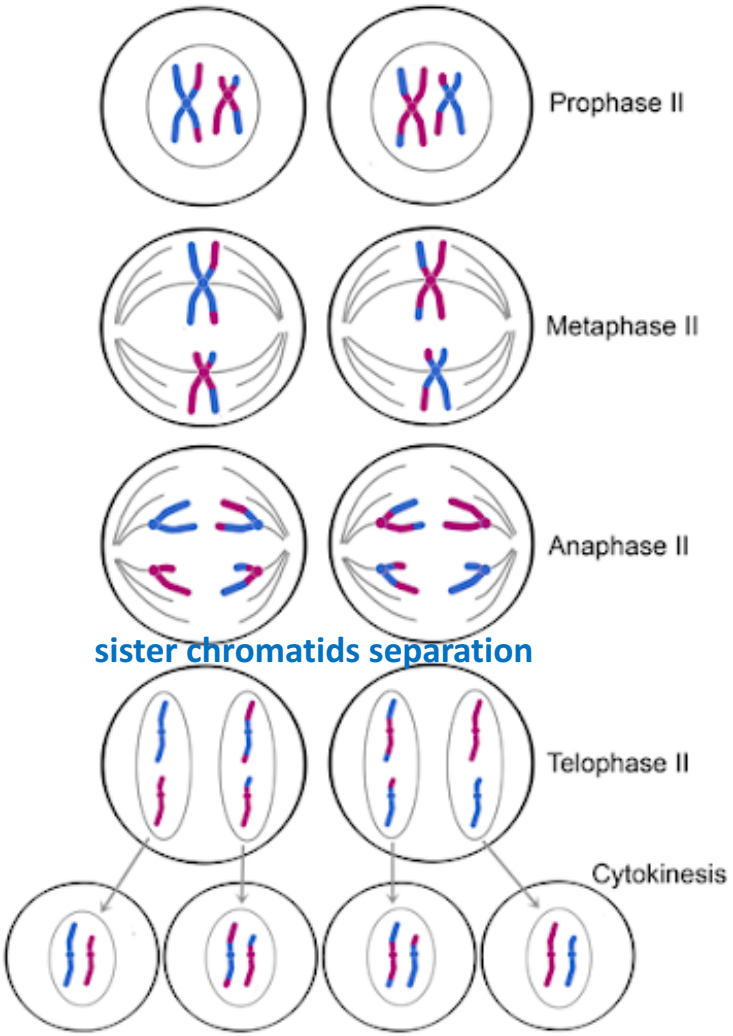
acytokinetic mitosis



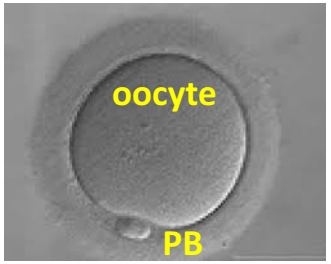
DeAgostini/Getty Images *Miko et al., Biologia, 2017*

Cell cycle variation : meiosis (gametes formation)

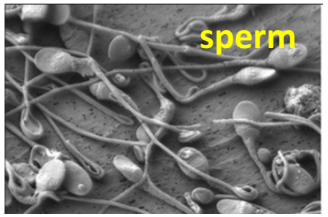




haploid 1N, 2n

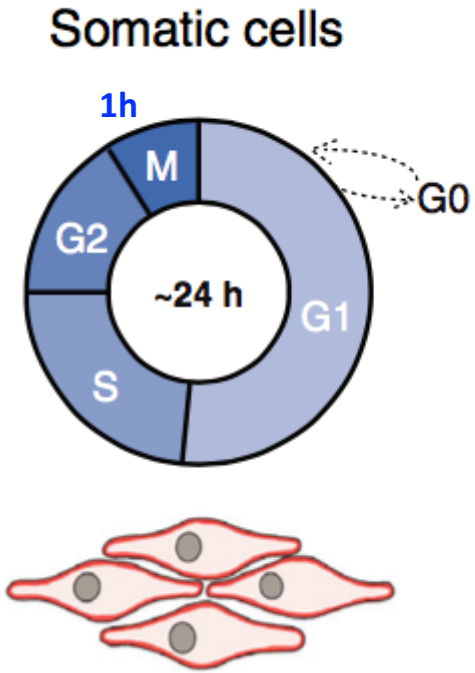


haploid 1N, 1n



Adapted from http://cyberbridge.mcb.harvard.edu/
Atlas of human enbryology, fig 37
Nussdorfer et al., Bosnian J Basic Med Sci, 2019

Cell cycle control system



- Orderly sequence of events (4 phases)
- Binary (switches on/off) : complete and irreversible
- Remarkably robust and reliable
- Adaptable

- Reversible exit : possible in G0-quiescence
- Permanent exit : terminal differentiation, senescence, death

Padgett & Santos, FEBS letters, 2020