Carnegie Stages of Human Development

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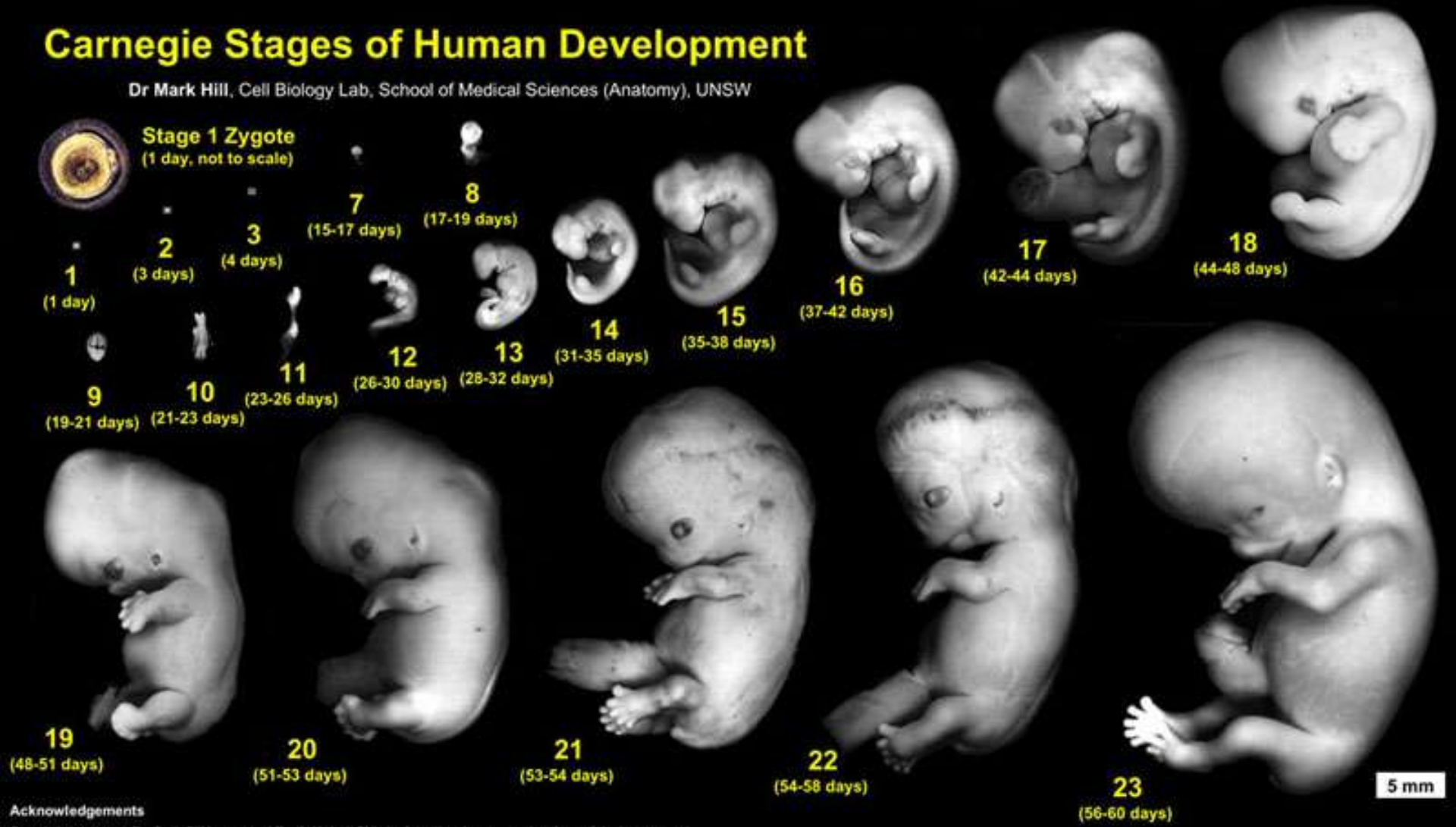

Acknowledgements

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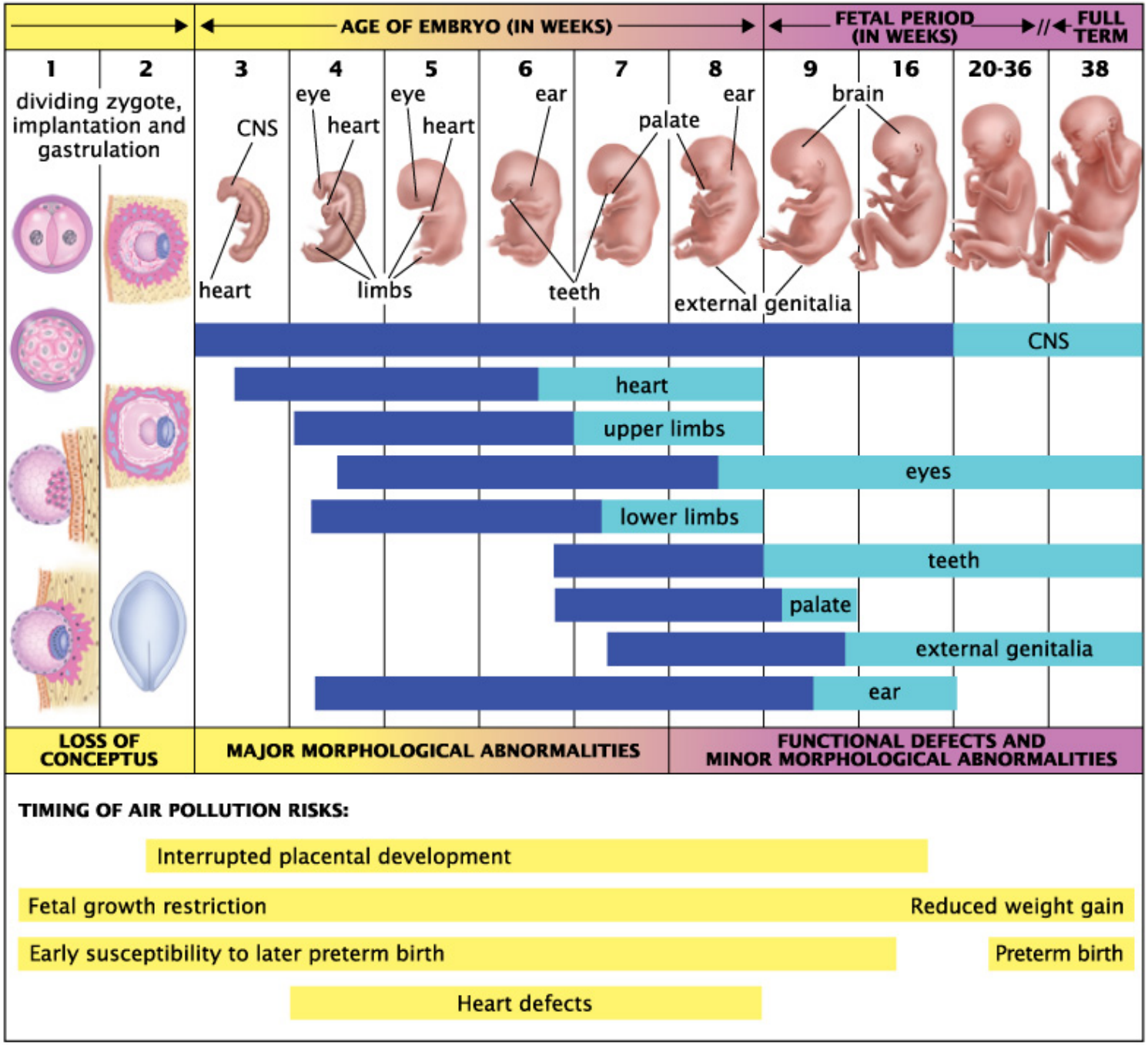
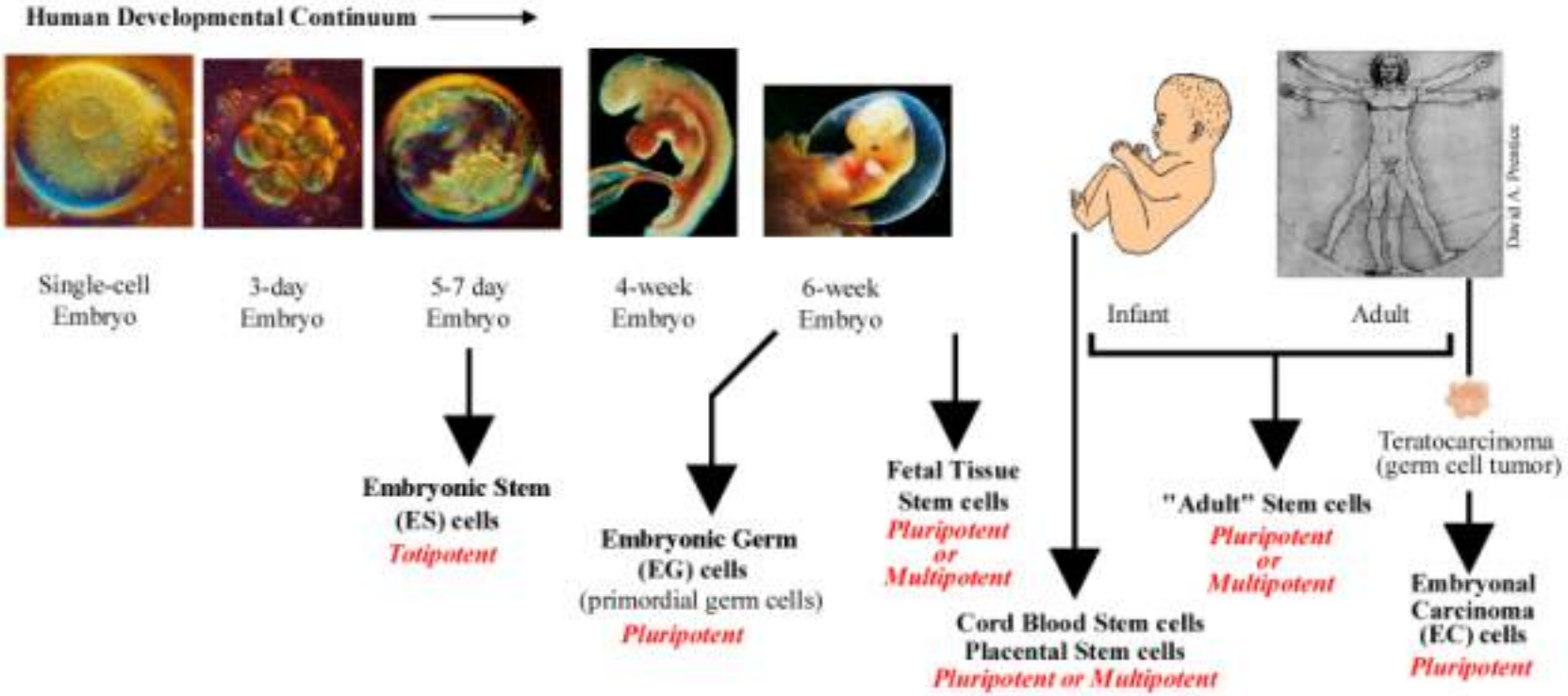


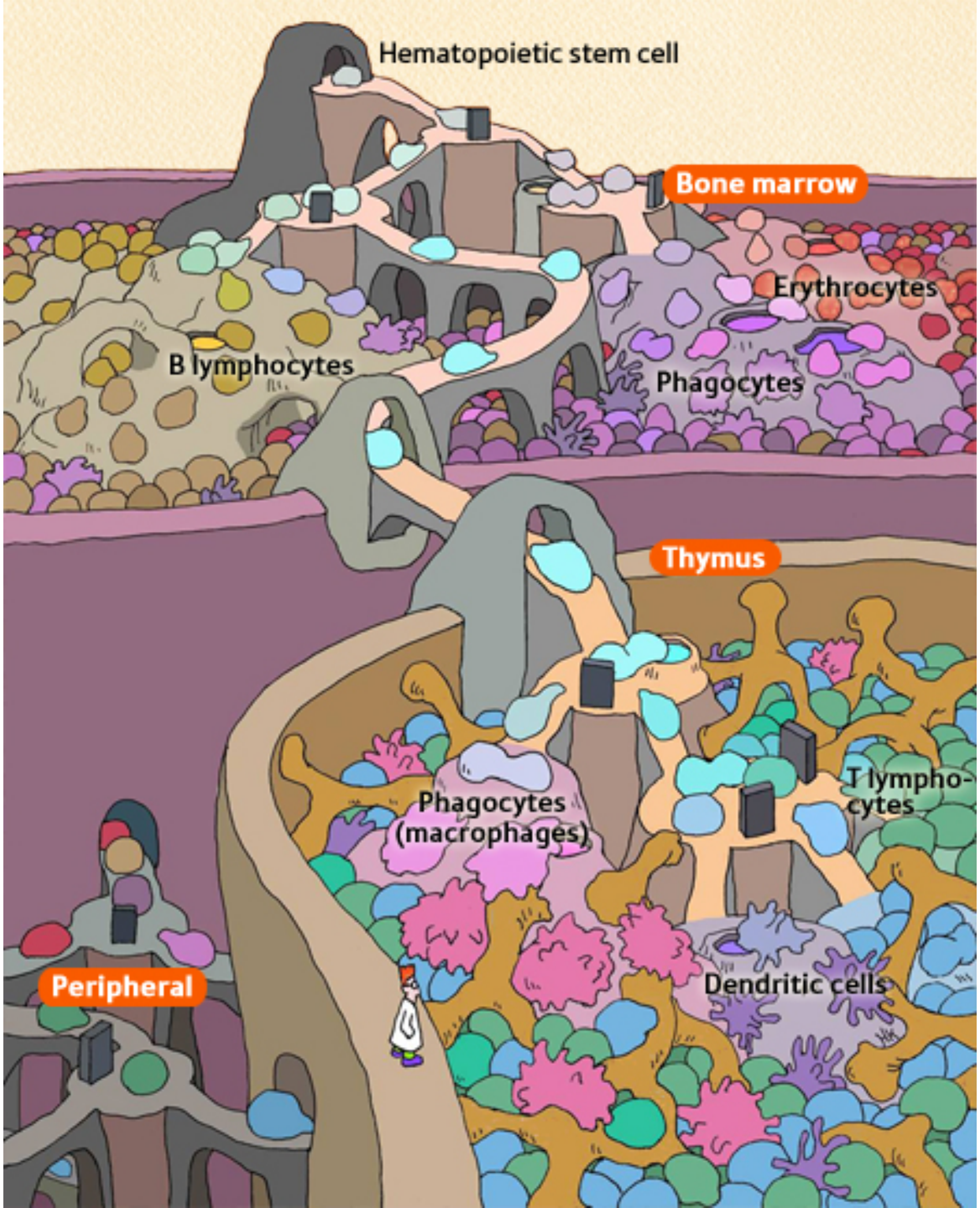
TIMING OF AIR POLLUTION RISKS:

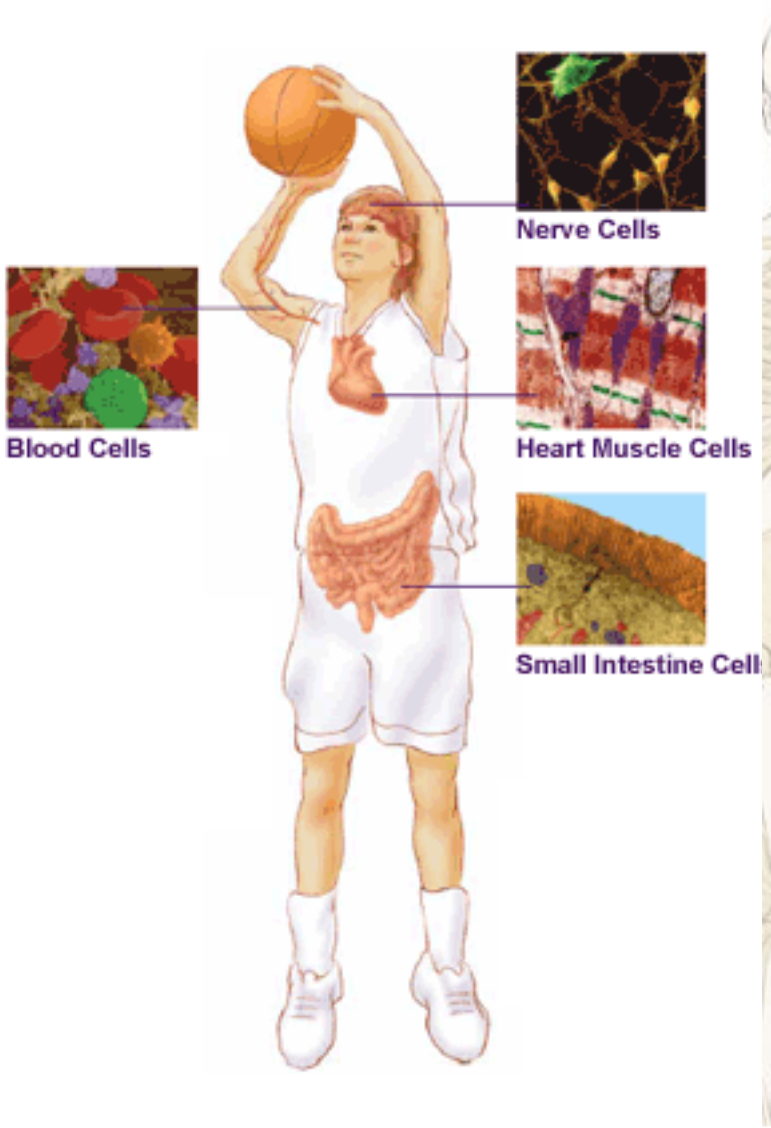
- Interrupted placental development
- Fetal growth restriction — Reduced weight gain
- Early susceptibility to later preterm birth — Preterm birth
- Heart defects

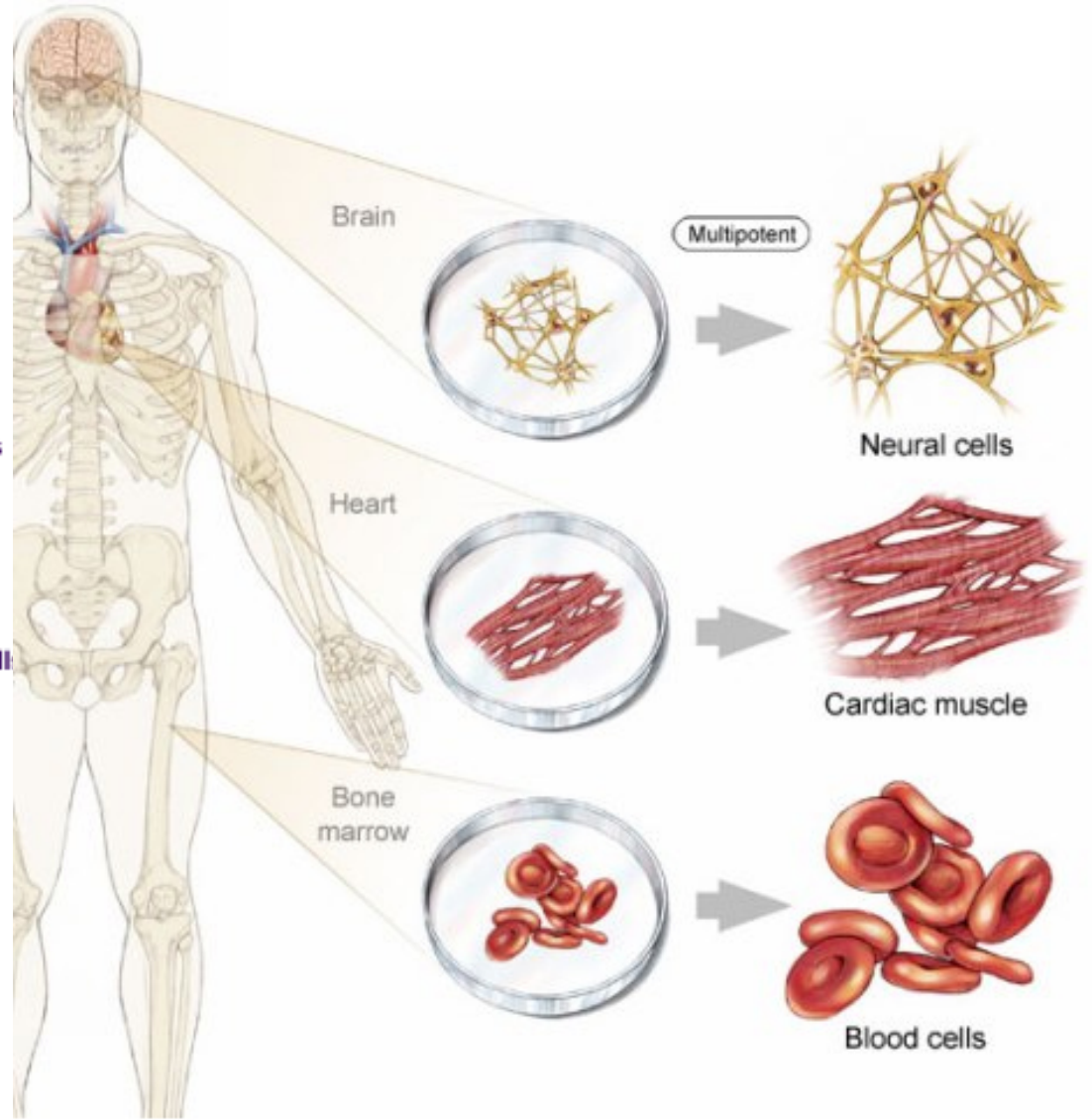
Note: Blue bars indicate time periods when major morphological abnormalities can occur, while light blue bars correspond to periods at risk for minor abnormalities and functional defects.

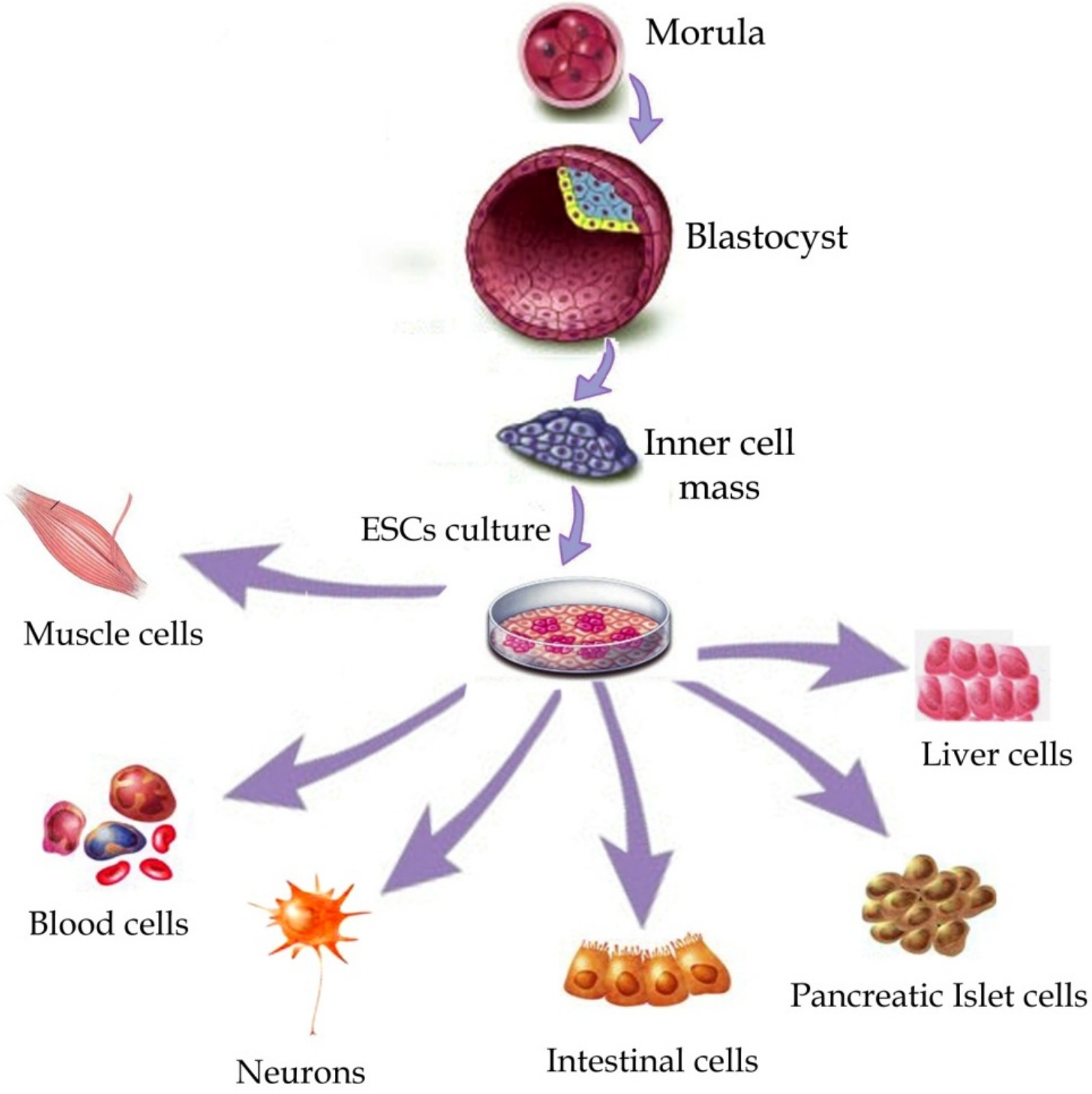
Stem Cells

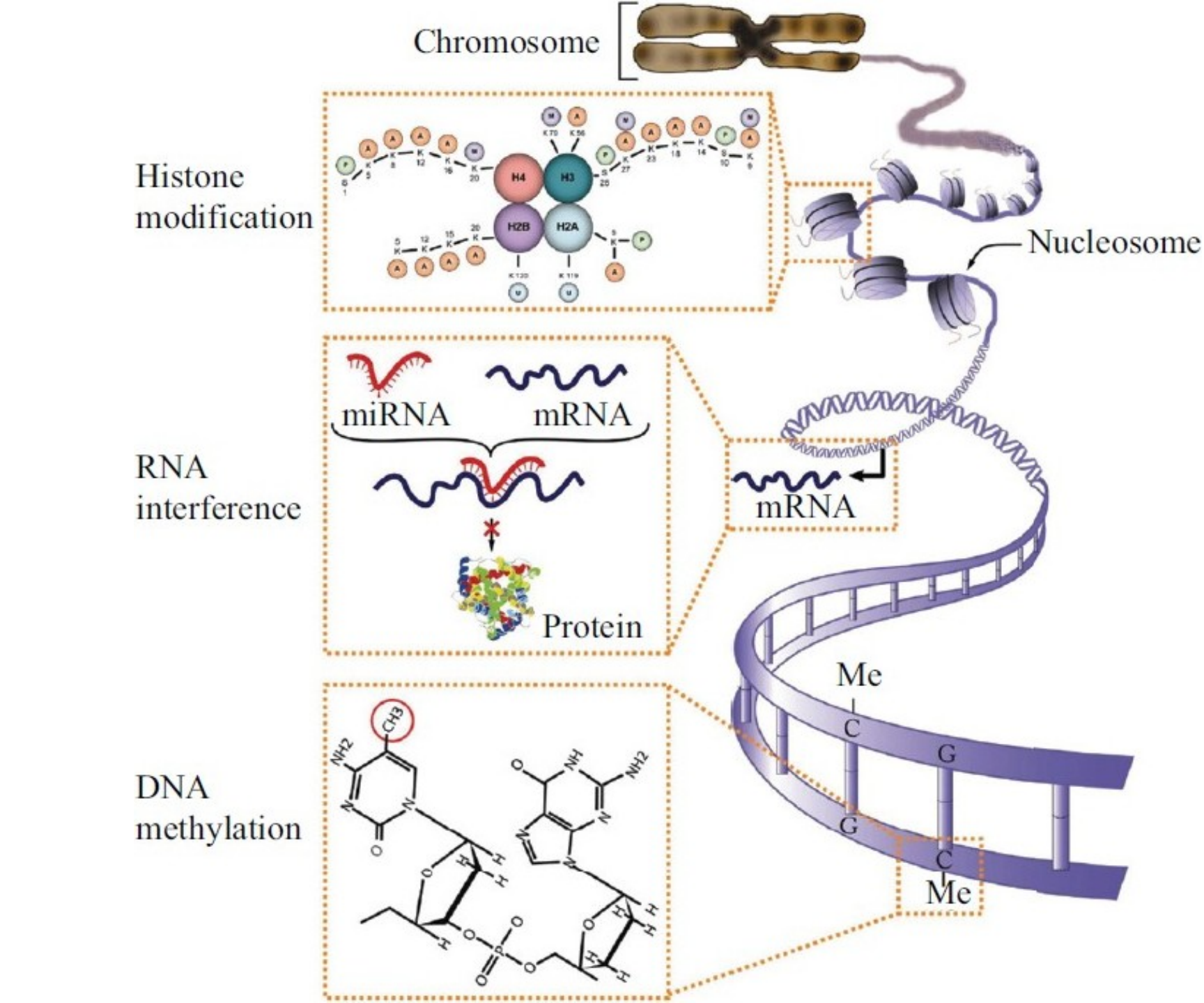

Human Developmental Continuum
Single-cell Embryo
3-day Embryo
5-7 day Embryo
4-week Embryo
6-week Embryo
Infant
Adult
Embryonic Stem (ES) cells
Totipotent
Embryonic Germ (EG) cells
(primordial germ cells)
Pluripotent
Fetal Tissue Stem cells
Pluripotent or Multipotent
Cord Blood Stem cells
Placental Stem cells
Pluripotent or Multipotent
"Adult" Stem cells
Pluripotent or Multipotent
Teratocarcinoma (germ cell tumor)
Embryonal Carcinoma (EC) cells
Pluripotent

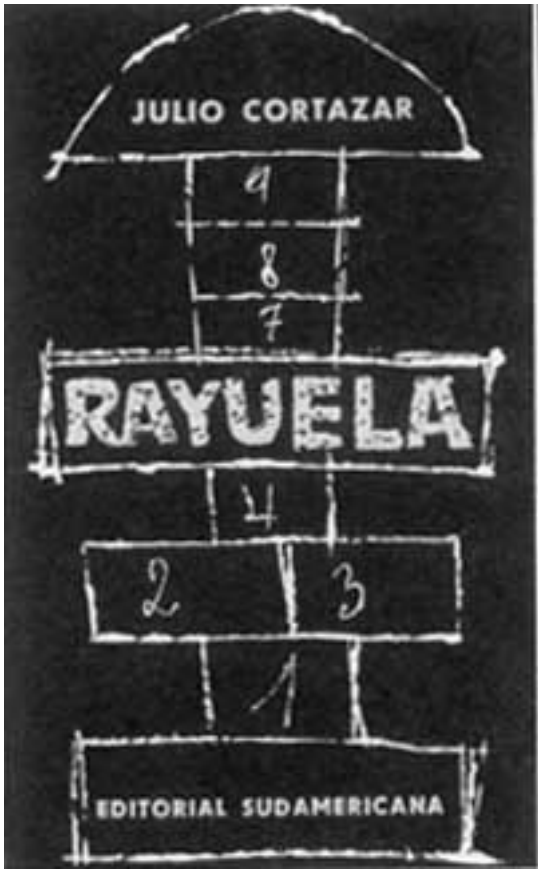

Hematopoietic stem cell
Bone marrow
Erythrocytes
B lymphocytes
Phagocytes
Thymus
Phagocytes (macrophages)
T lympho-cytes
Peripheral
Dendritic cells

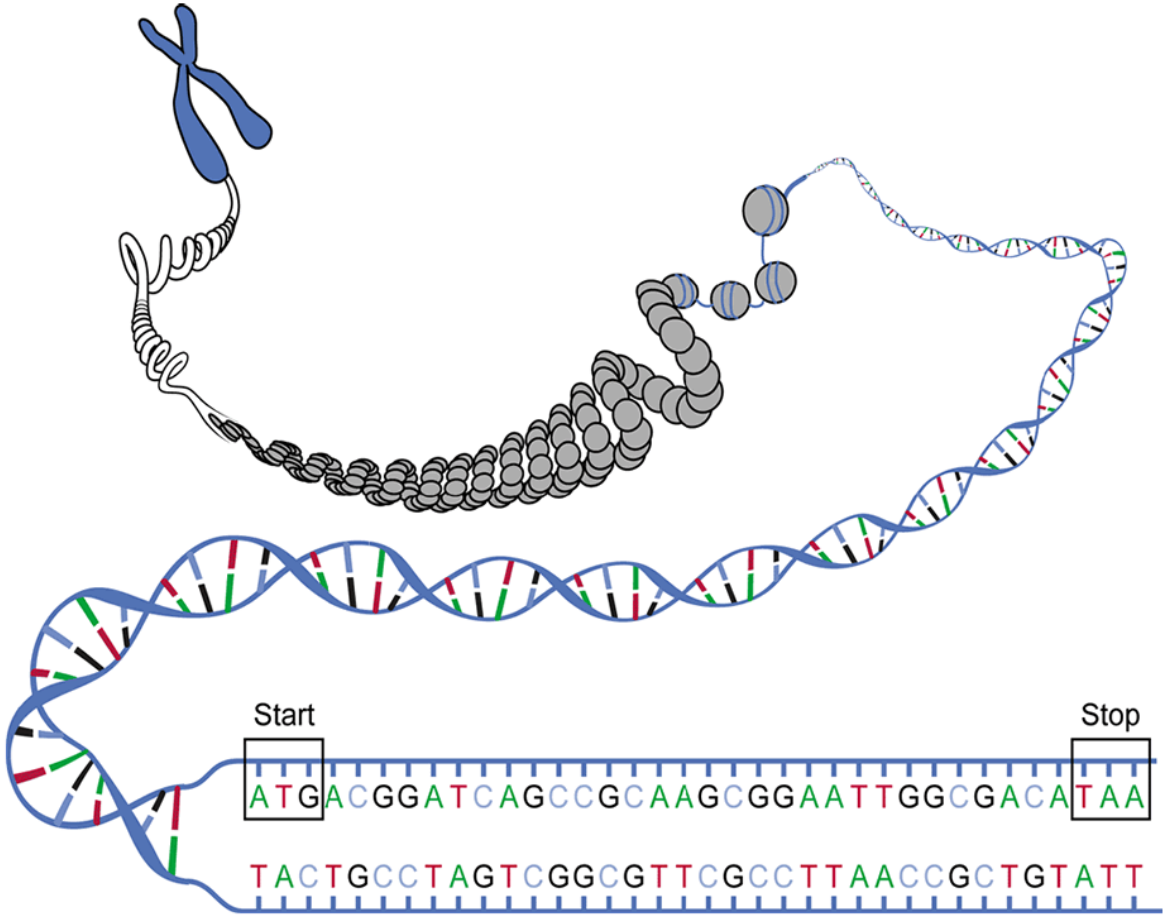

Nerve Cells
Blood Cells
Heart Muscle Cells
Small Intestine Cell


Brain
Multipotent
Neural cells
Heart
Cardiac muscle
Bone marrow
Blood cells

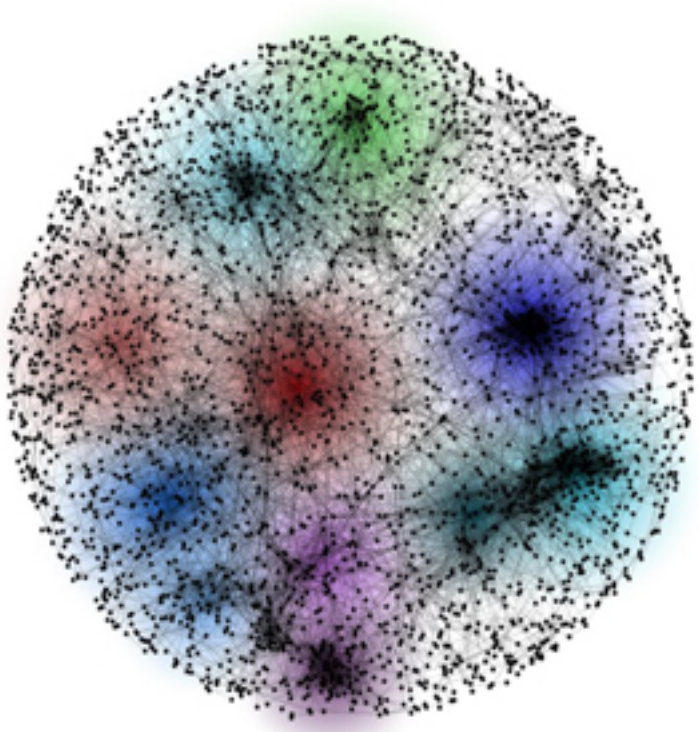

Morula
Blastocyst
Inner cell mass
ESCs culture
Muscle cells
Liver cells
Blood cells
Neurons
Intestinal cells
Pancreatic Islet cells

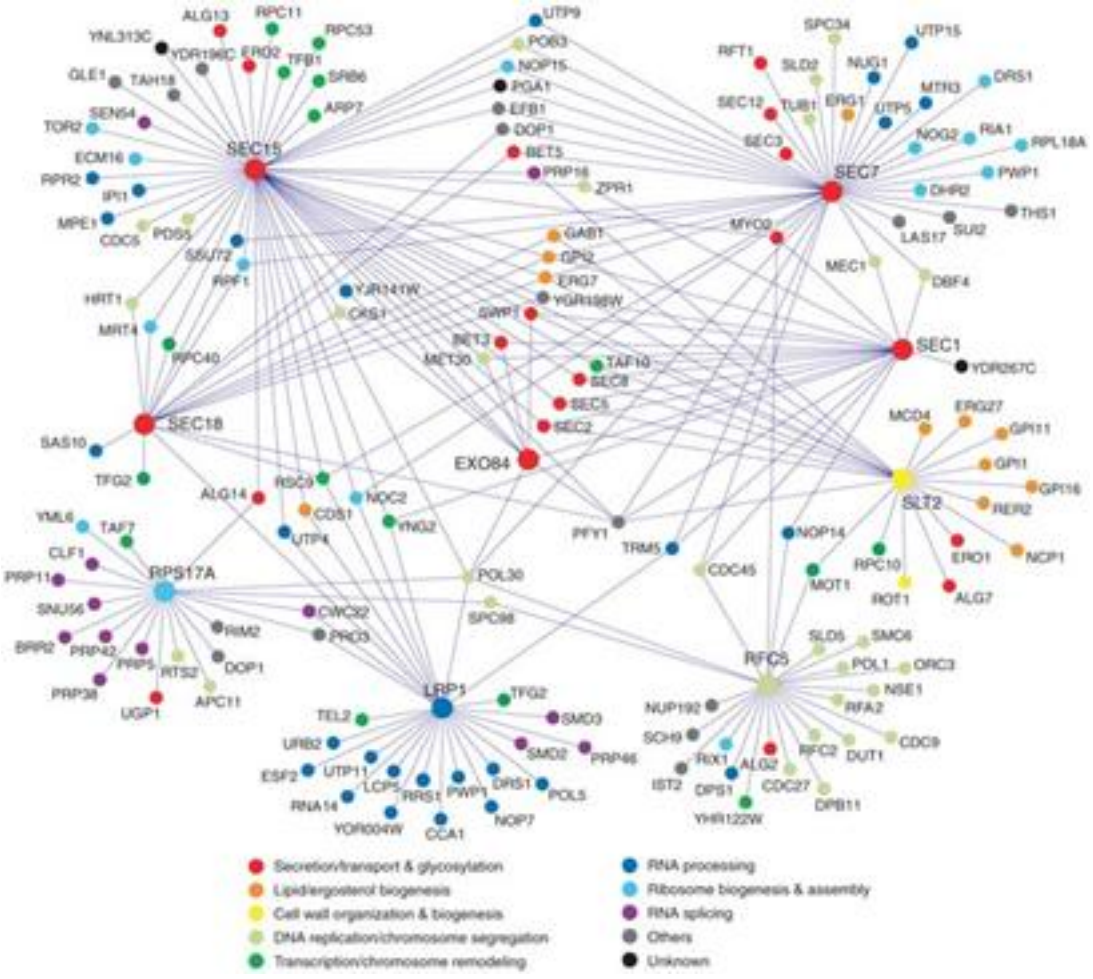

Chromosome
Histone modification
H4
H3
H2B
H2A
Nucleosome
RNA interference
miRNA
mRNA
Protein
mRNA
DNA methylation
CH3
NH2
Me
C
G
G
C
Me

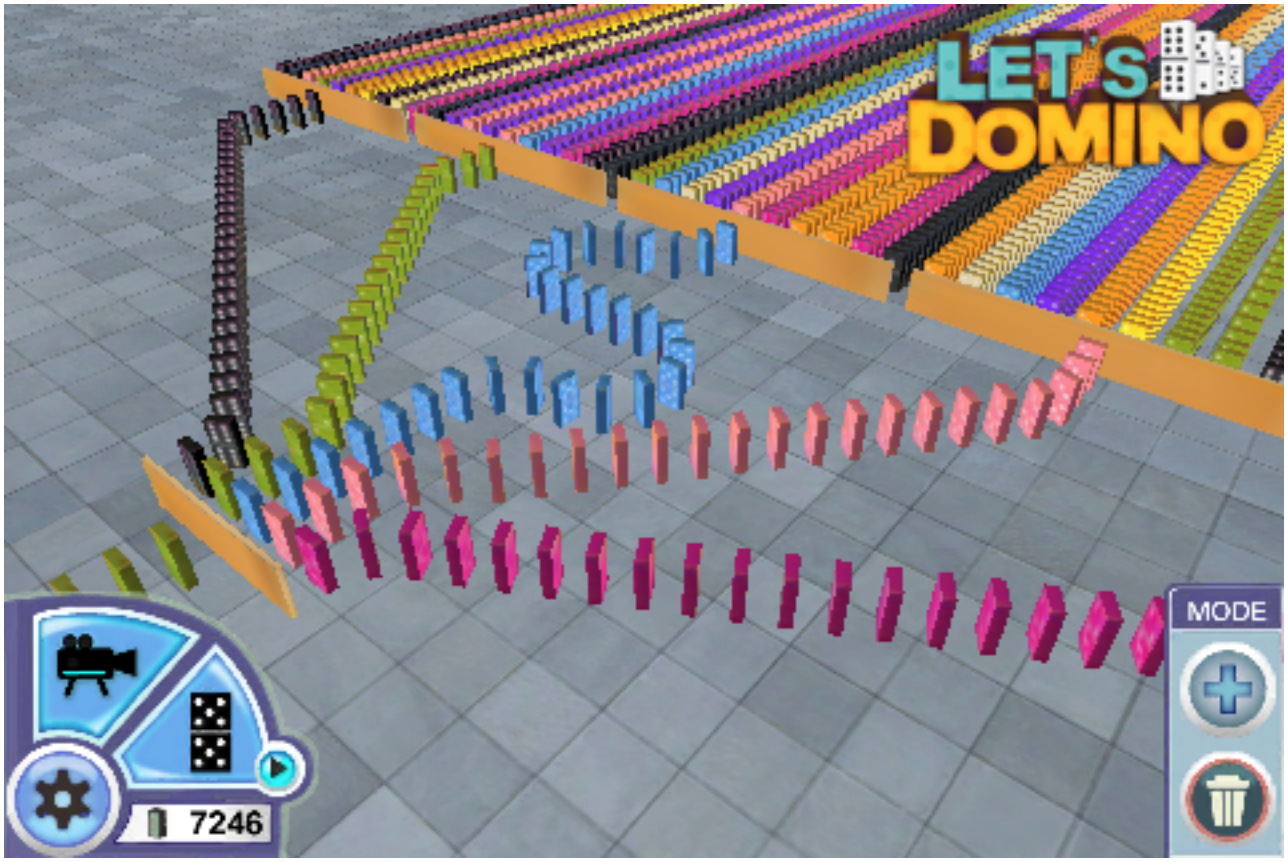

JULIO CORTAZAR
9
8
7
RAYUELA
4
2
3
1
EDITORIAL SUDAMERICANA

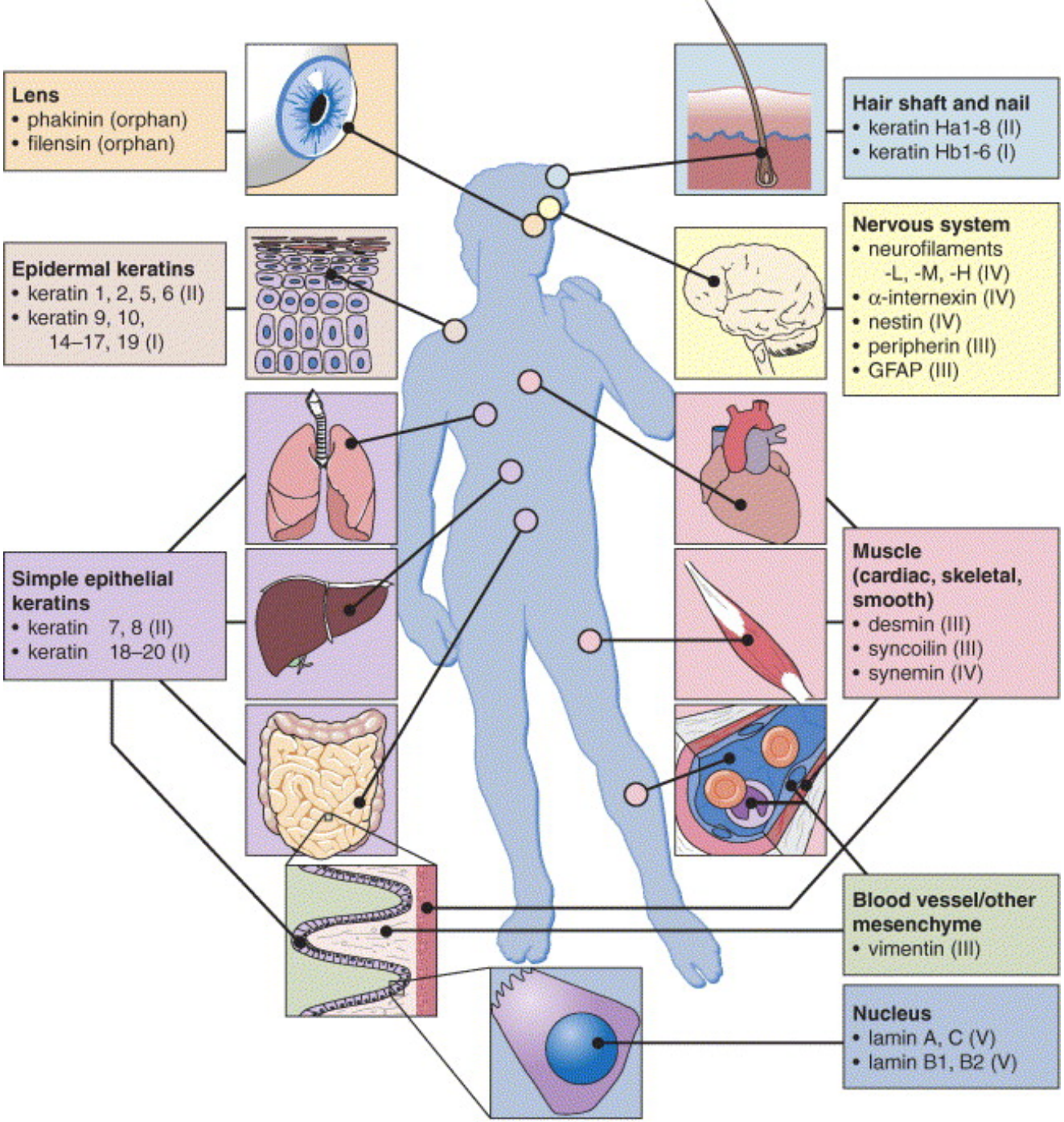

Start
Stop
ATGACGGATCAGCCGCAAGCGGAATTGGCGACATAA
TACTGCCTAGTCGGCGTTCGCCTTAACCGCTGTATT


TWINS

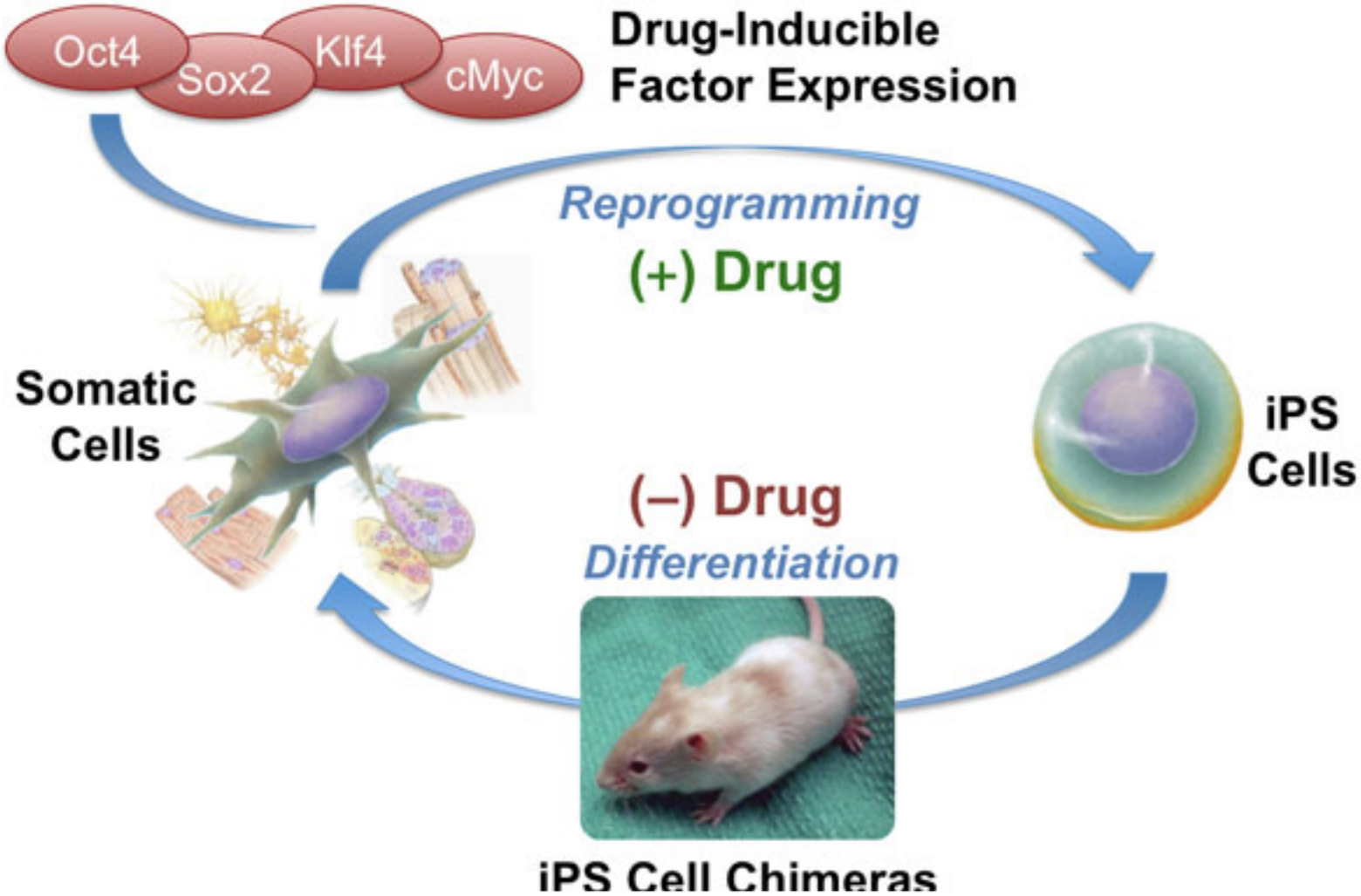


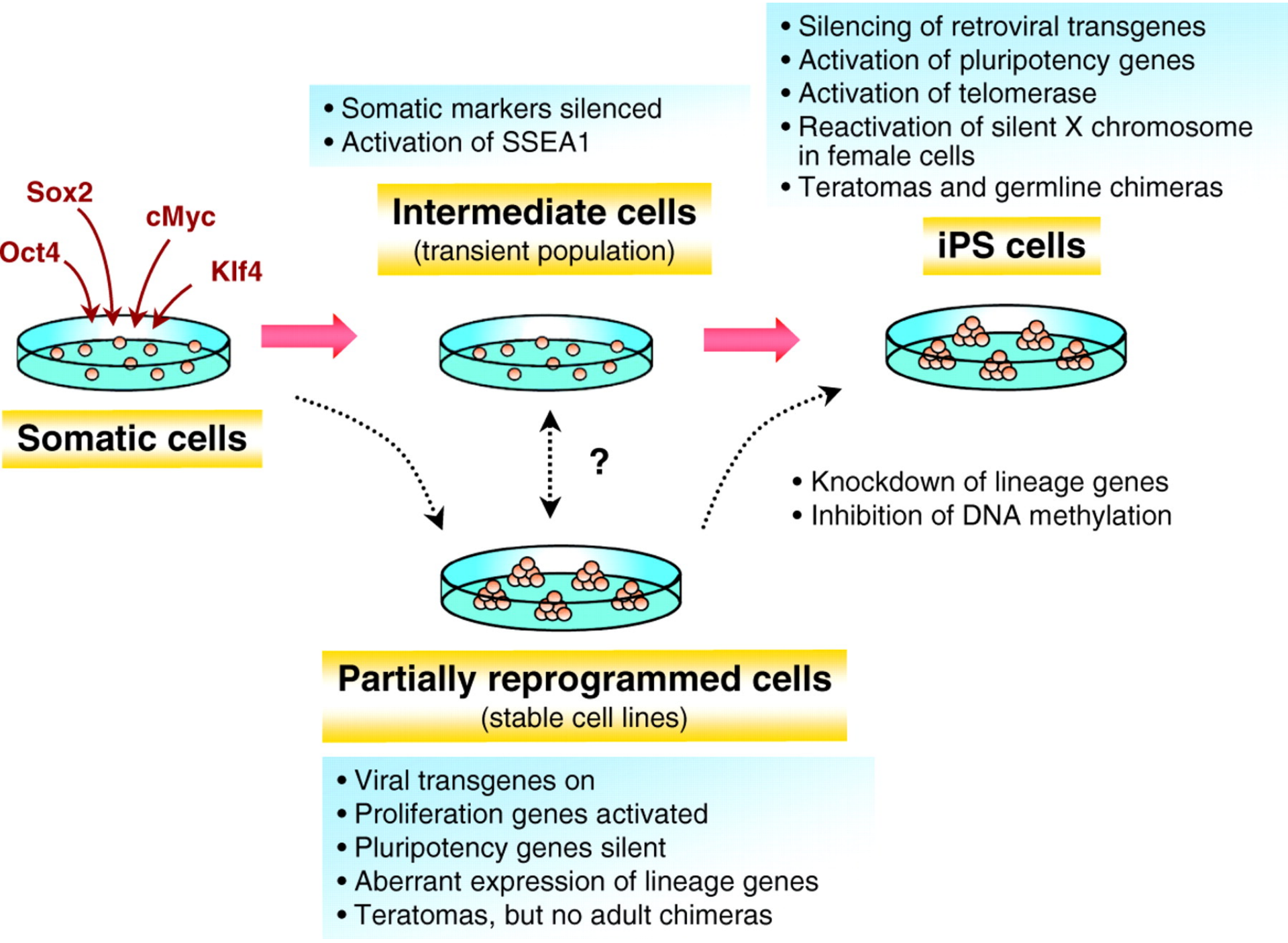

SEC15
SEC7
SEC1
SEC18
EXO84
SLT2
RPS17A
LRP1
RFC5
Secretion/transport & glycosylation
Lipid/ergosterol biogenesis
Cell wall organization & biogenesis
DNA replication/chromosome segregation
Transcription/chromosome remodeling
RNA processing
Ribosome biogenesis & assembly
RNA splicing
Others
Unknown

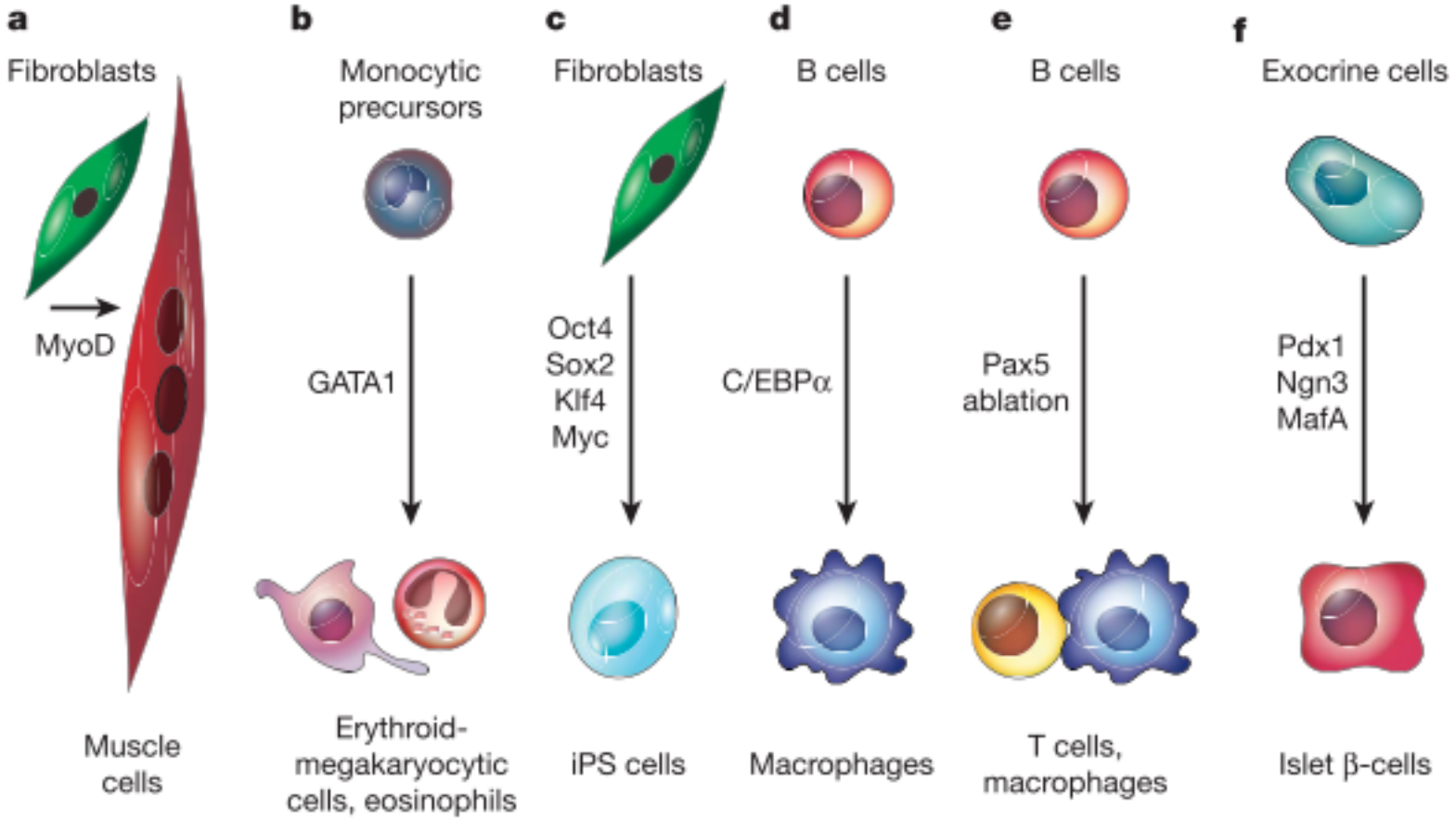

LET'S
DOMINO
MODE
7246



TRENDS in Cell Biology


Oct4
Sox2
Klf4
cMyc
Drug-Inducible
Factor Expression
Reprogramming
(+) Drug
Somatic
Cells
iPS
Cells
(–) Drug
Differentiation
iPS Cell Chimeras


• Silencing of retroviral transgenes
• Activation of pluripotency genes
• Activation of telomerase
• Reactivation of silent X chromosome in female cells
• Teratomas and germline chimeras
• Somatic markers silenced
• Activation of SSEA1
Intermediate cells
(transient population)
iPS cells
Sox2
cMyc
Oct4
Klf4
Somatic cells
?
• Knockdown of lineage genes
• Inhibition of DNA methylation
Partially reprogrammed cells
(stable cell lines)
• Viral transgenes on
• Proliferation genes activated
• Pluripotency genes silent
• Aberrant expression of lineage genes
• Teratomas, but no adult chimeras


a
Fibroblasts
MyoD
Muscle cells
b
Monocytic precursors
GATA1
Erythroid-megakaryocytic cells, eosinophils
c
Fibroblasts
Oct4
Sox2
Klf4
Myc
iPS cells
d
B cells
C/EBPα
Macrophages
e
B cells
Pax5 ablation
T cells, macrophages
f
Exocrine cells
Pdx1
Ngn3
MafA
Islet β-cells

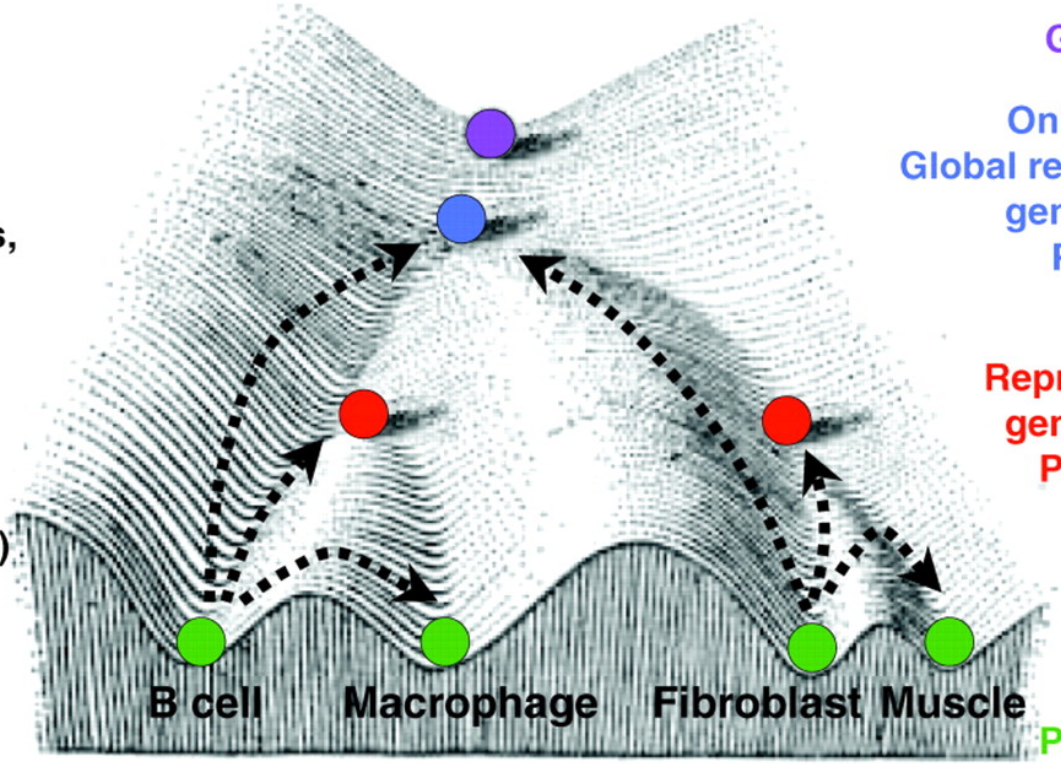
Developmental potential

Totipotent
Zygote

Pluripotent
ICM/ES cells, EG cells, EC cells, mGS cells iPS cells

Multipotent
Adult stem cells (partially reprogrammed cells?)

Unipotent
Differentiated cell types



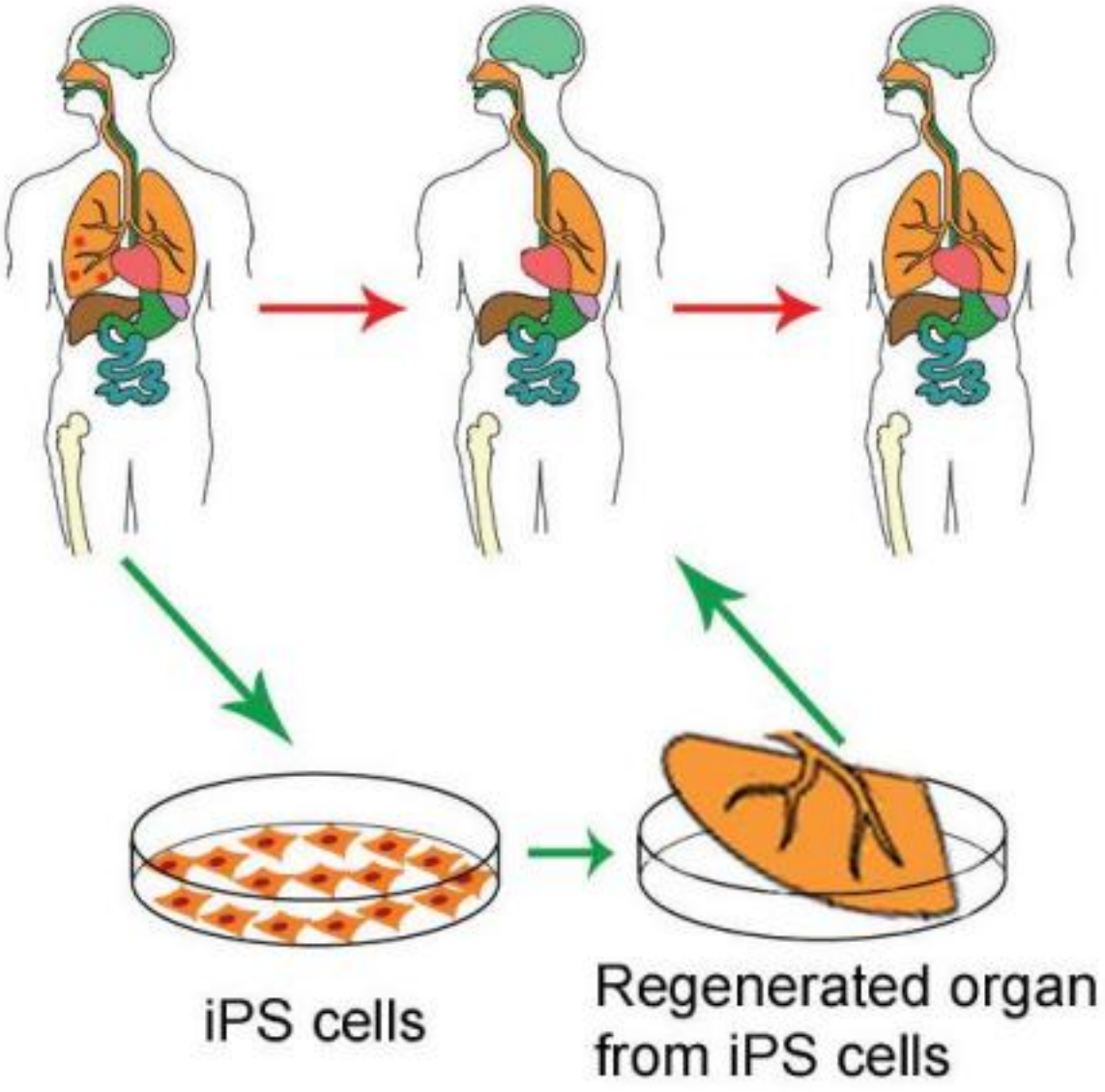
Epigenetic status

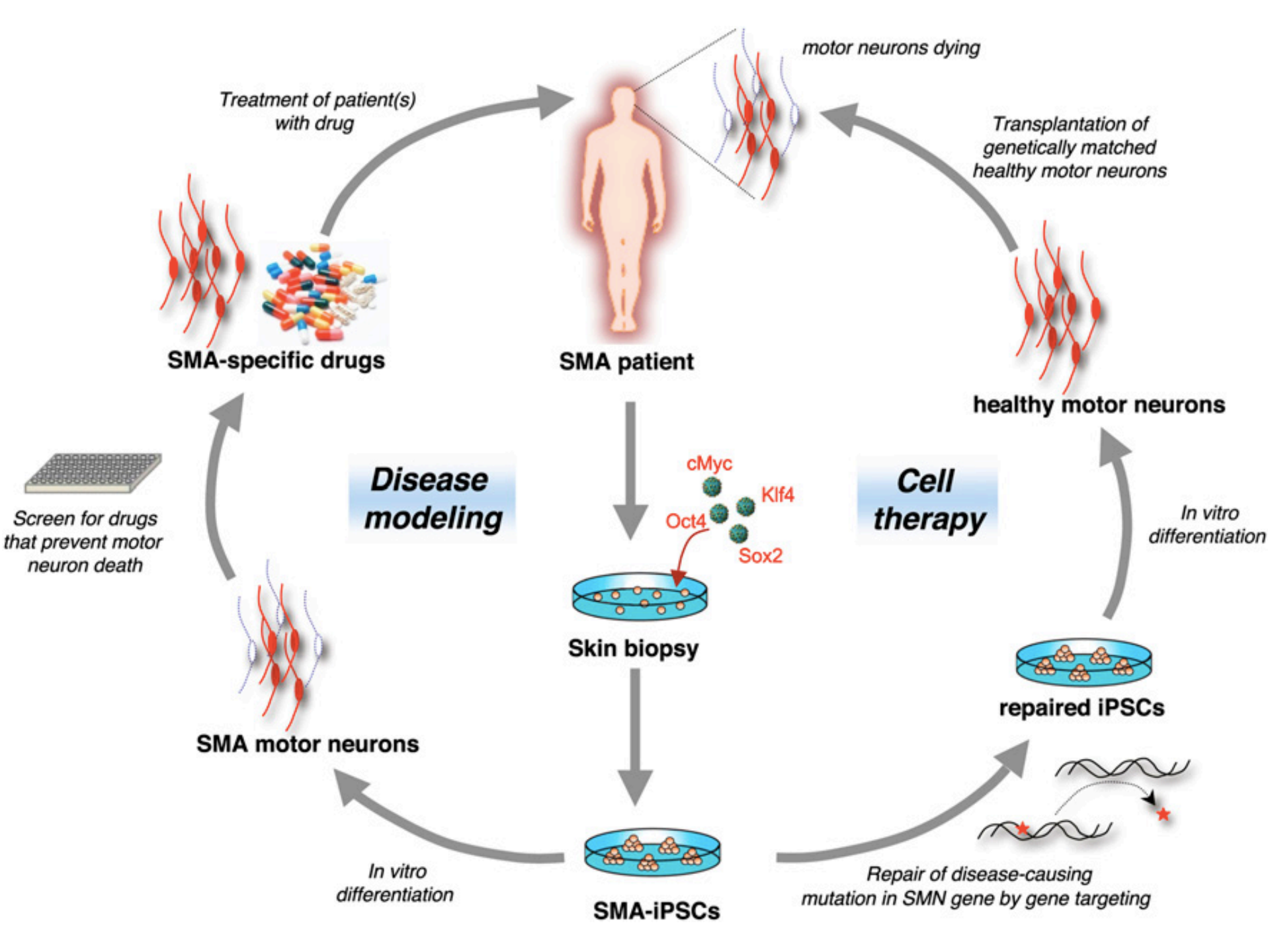
Global DNA demethylation

Only active X chromosomes; Global repression of differentiation genes by Polycomb proteins; Promoter hypomethylation

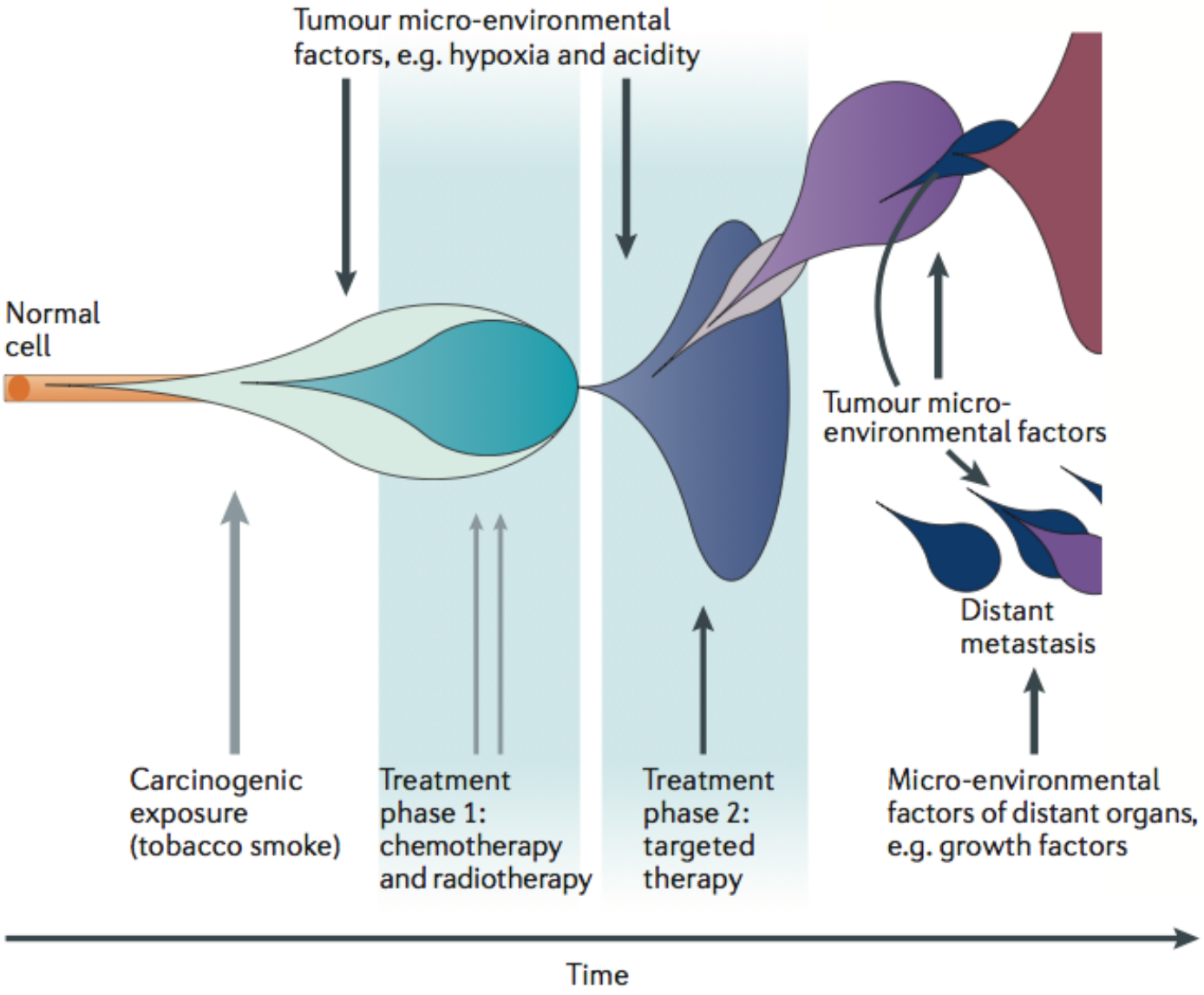
X inactivation; Repression of lineage-specific genes by Polycomb proteins; Promoter hypermethylation

X inactivation; Derepression of Polycomb silenced lineage genes; Promoter hypermethylation


iPS cells
Regenerated organ
from iPS cells


motor neurons dying
Treatment of patient(s) with drug
Transplantation of genetically matched healthy motor neurons
SMA-specific drugs
SMA patient
healthy motor neurons
Screen for drugs that prevent motor neuron death
Disease modeling
cMyc
Klf4
Oct4
Sox2
Cell therapy
In vitro differentiation
Skin biopsy
repaired iPSCs
SMA motor neurons
In vitro differentiation
SMA-iPSCs
Repair of disease-causing mutation in SMN gene by gene targeting

РАК?


Tumour micro-environmental factors, e.g. hypoxia and acidity
Normal cell
Tumour micro-environmental factors
Distant metastasis
Carcinogenic exposure (tobacco smoke)
Treatment phase 1: chemotherapy and radiotherapy
Treatment phase 2: targeted therapy
Micro-environmental factors of distant organs, e.g. growth factors
Time

the evolution of bending unit 22.

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