# Production of sperm and oocytes in vitro

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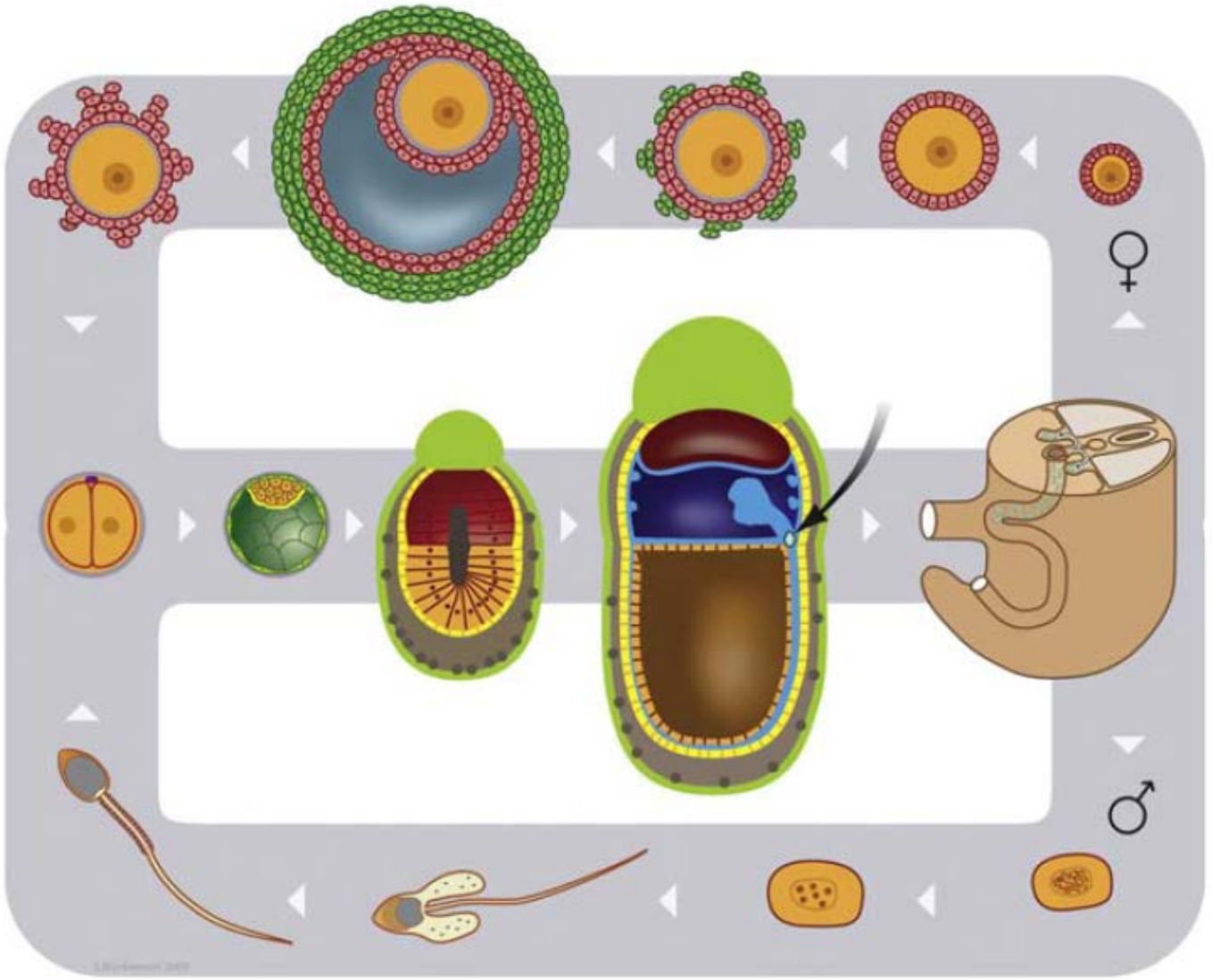
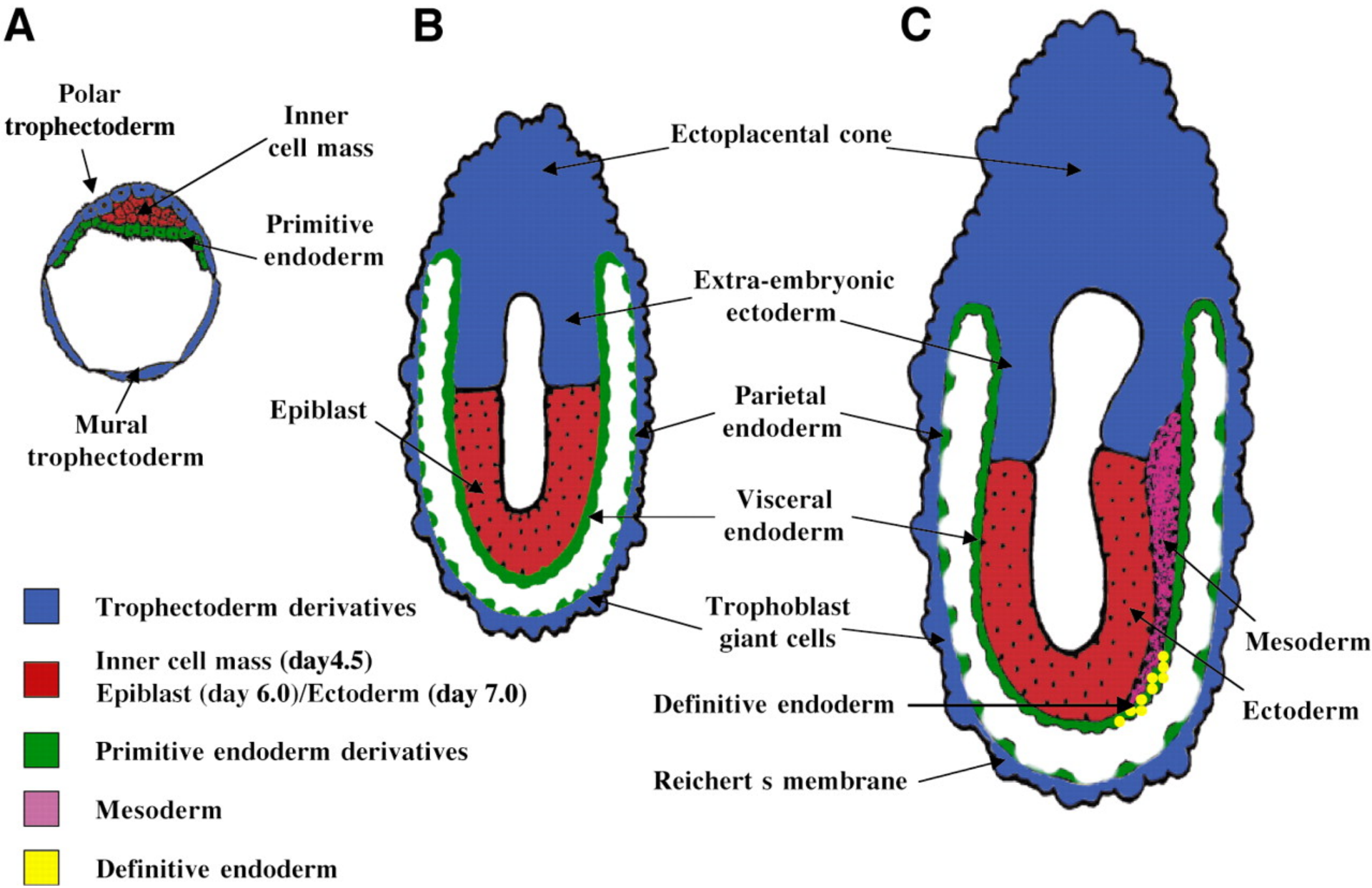
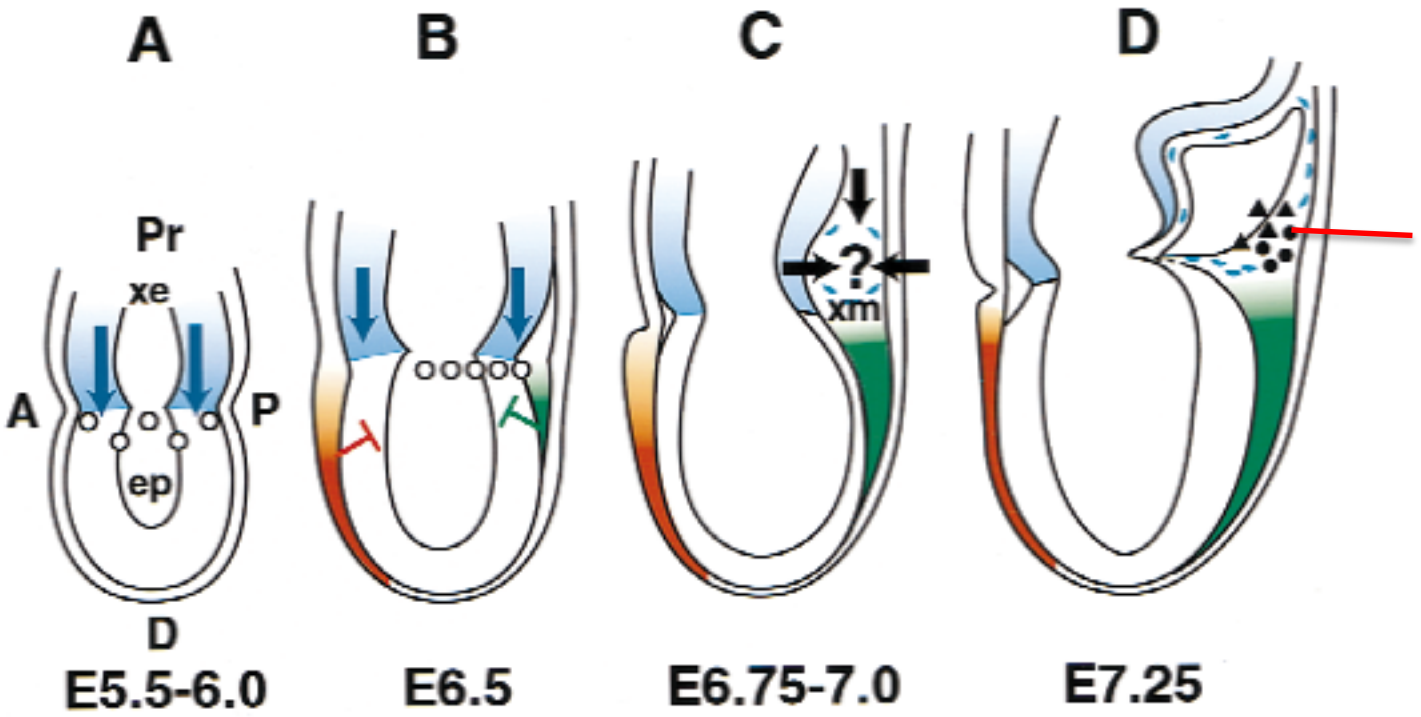
# The germ cell cycle



Chuva de Sousa Lopes & Roelen 2010 Differentiation 79, 131-140


A
B
C
Polar trophectoderm
Inner cell mass
Primitive endoderm
Mural trophectoderm
Ectoplacental cone
Extra-embryonic ectoderm
Epiblast
Parietal endoderm
Visceral endoderm
Trophoblast giant cells
Mesoderm
Definitive endoderm
Ectoderm
Reichert s membrane
Trophectoderm derivatives
Inner cell mass (day4.5)
Epiblast (day 6.0)/Ectoderm (day 7.0)
Primitive endoderm derivatives
Mesoderm
Definitive endoderm

# Extra-embryonic BMP4 induces the formation of primordial germ cells (PGCs) in the proximal epiblast



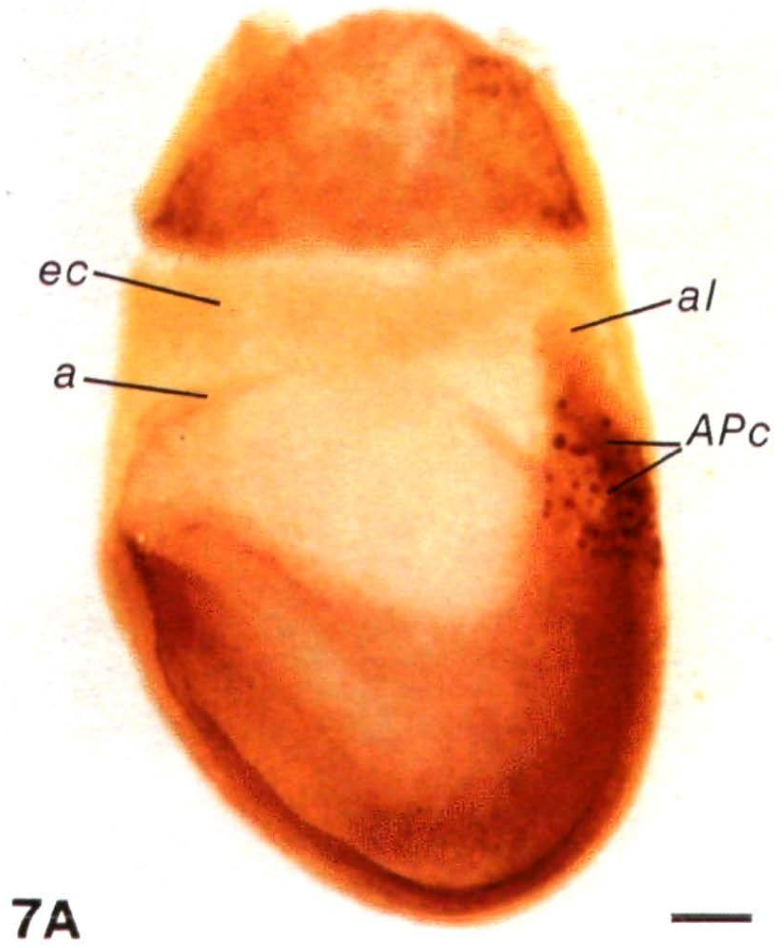

All cells of the epiblast have the capacity to adopt a PGC fate

Generation of germ cells from pluripotent cells would need to follow a similar program

Lawson *et al*., 1999 Genes Dev 13, 424-436

Chuva de Sousa Lopes *et al*., 2004 Genes Dev 18, 1838-1849

# PGCs are first recognized as a small cluster of ALP-positive cells



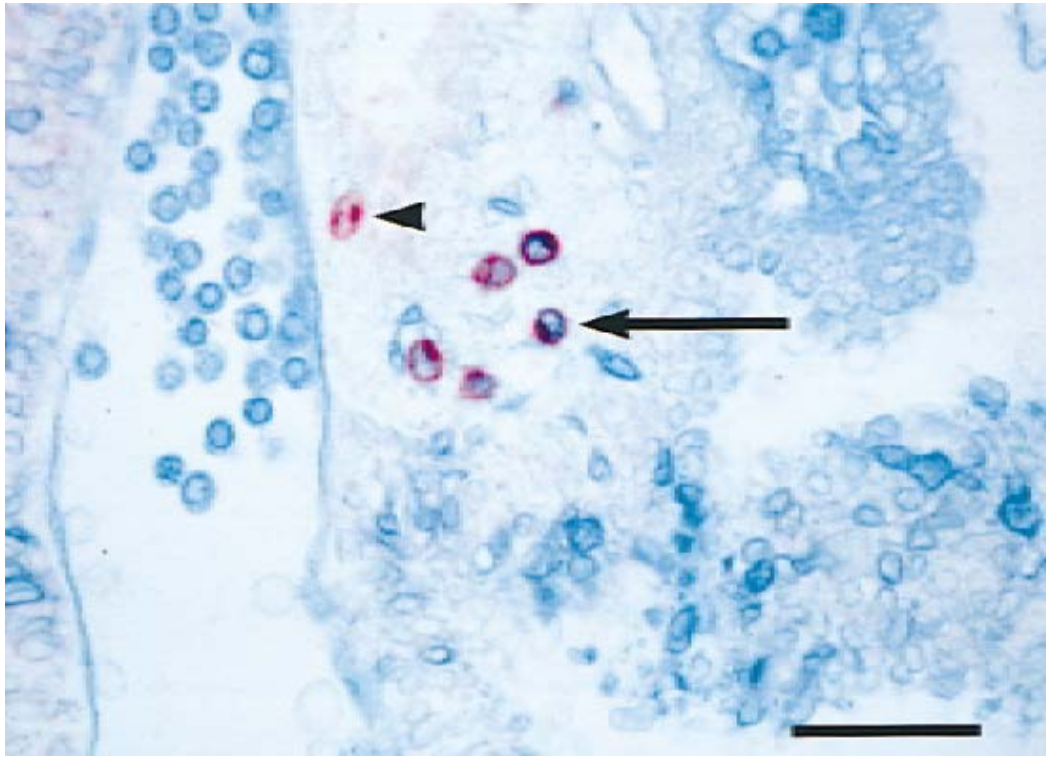
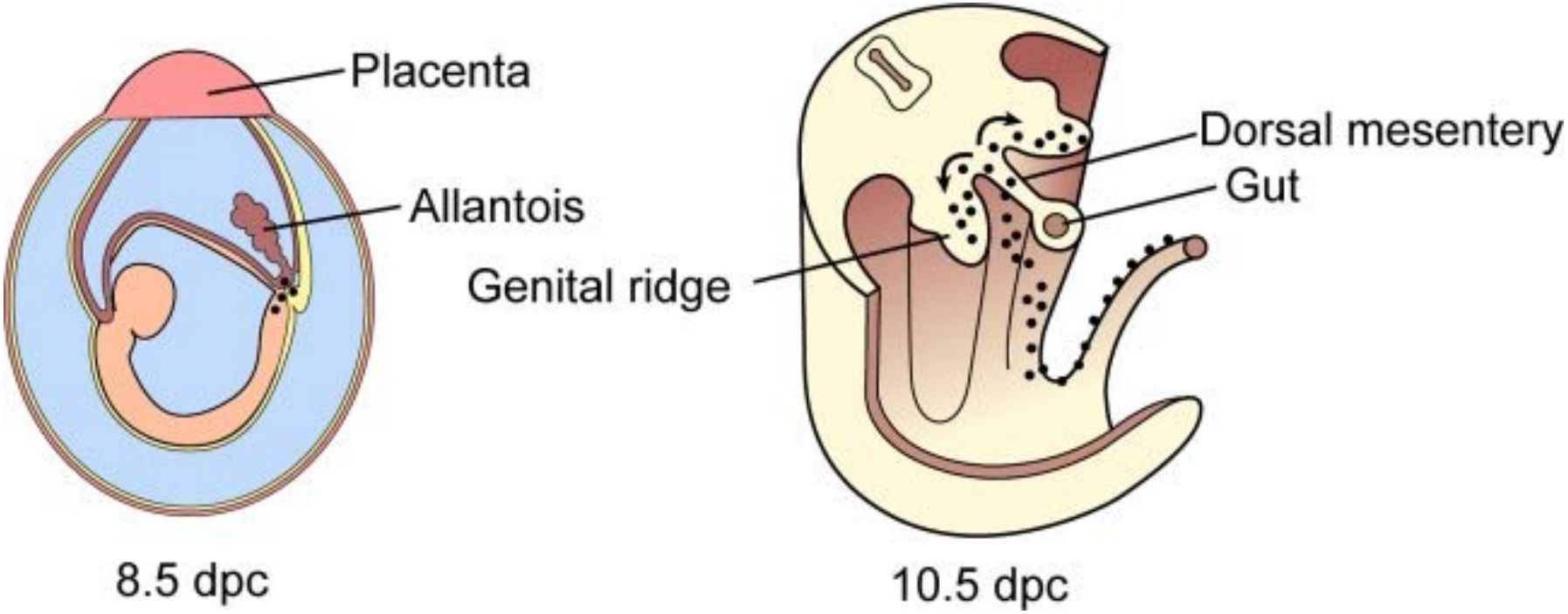



Fig. 7. (A) Stage 7-IV embryo stained as whole-mount for ALP activity.

Ginsburg *et al.*, 1990, Development 110: 521-528

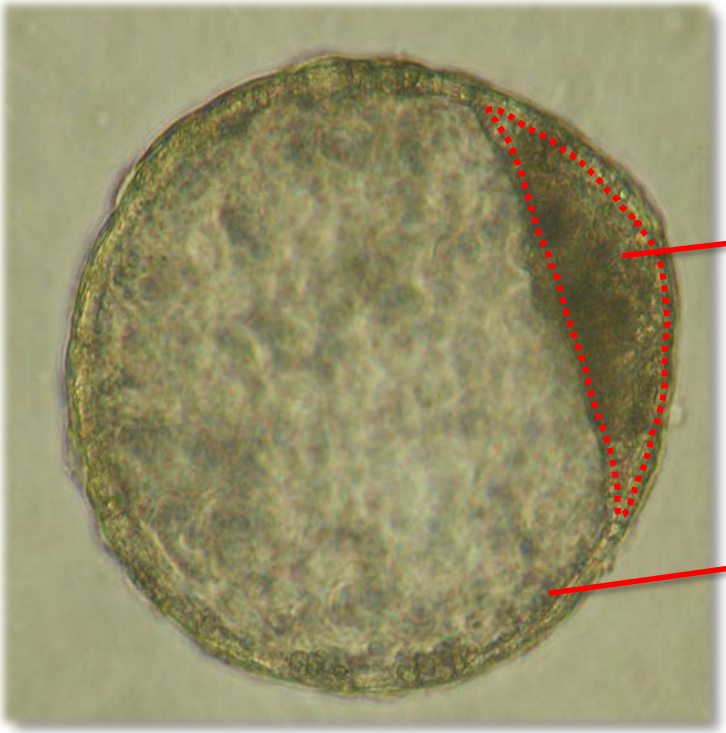
Lawson *et al.*, 1999 Genes Dev 13, 424-436

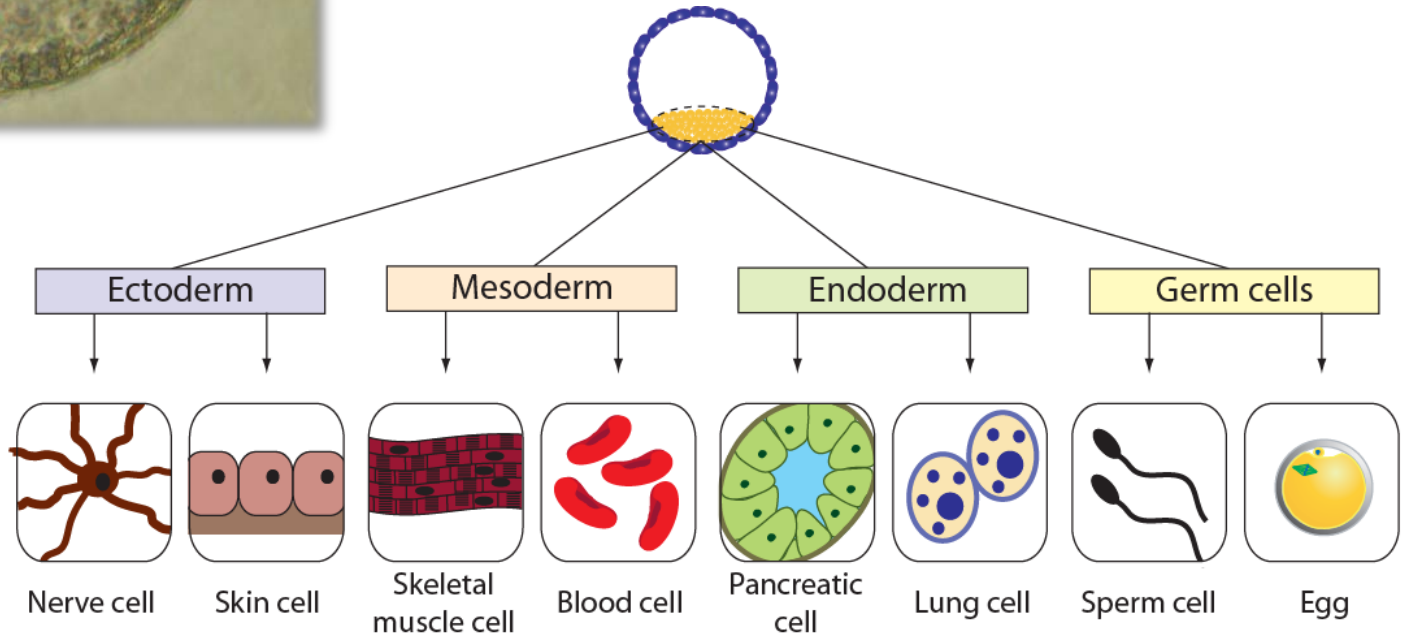
# PGCs migrate through the hindgut to colonize the developing gonads



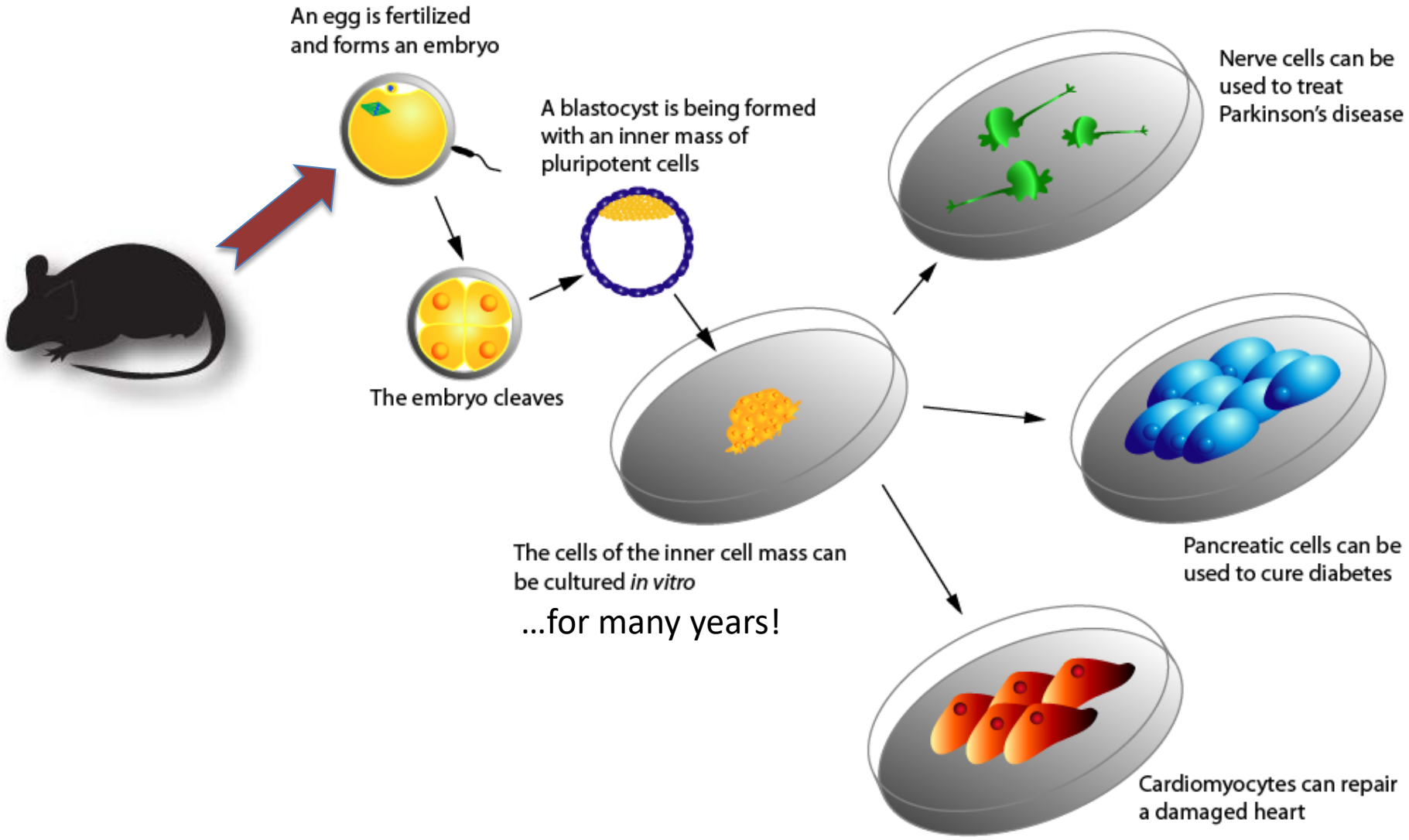

Wilhelm *et al*., 2007, Phys Rev 87: 1-28

# The cells that form the inner cell mass are *pluripotent*

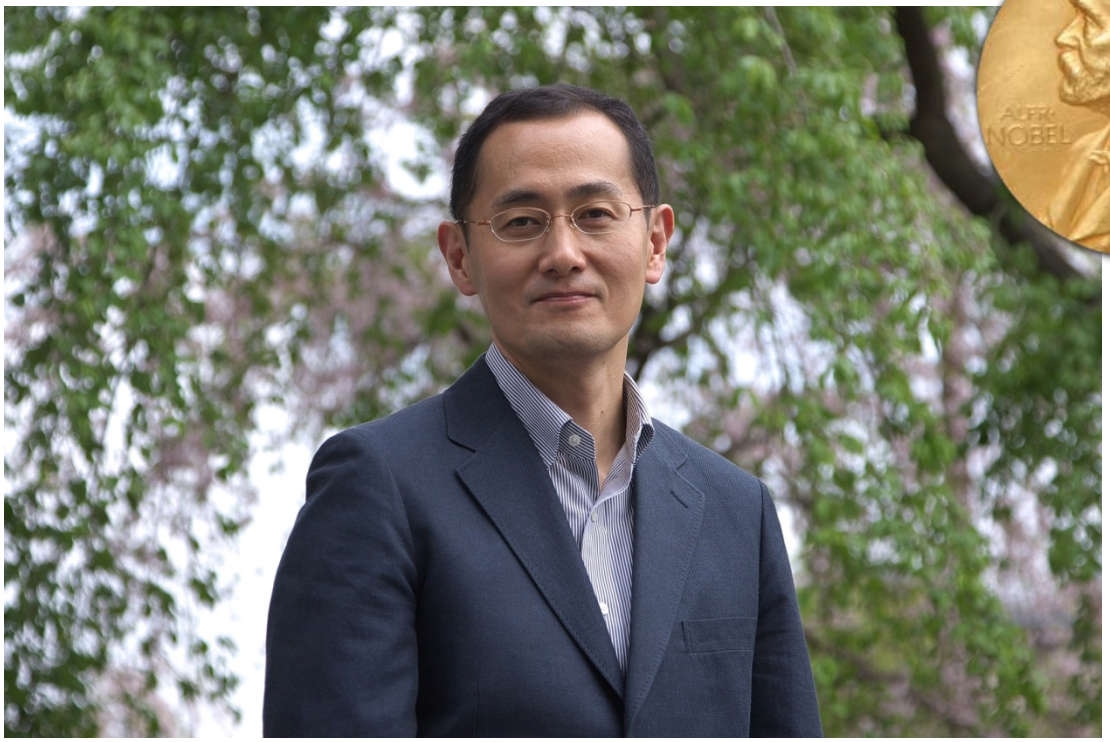




# Embryonic stem (ES) cells are derived from blastocysts




Mummery, vd Stolpe, Roelen & Clevers 2014, Stem Cells




# Induction of Pluripotent Stem Cells from Adult Human Fibroblasts by Defined Factors

Kazutoshi Takahashi,[1] Koji Tanabe,[1] Mari Ohnuki,[1] Megumi Narita,[1,2] Tomoko Ichisaka,[1,2] Kiichiro Tomoda,[3] and Shinya Yamanaka[1,2,3,4,*]

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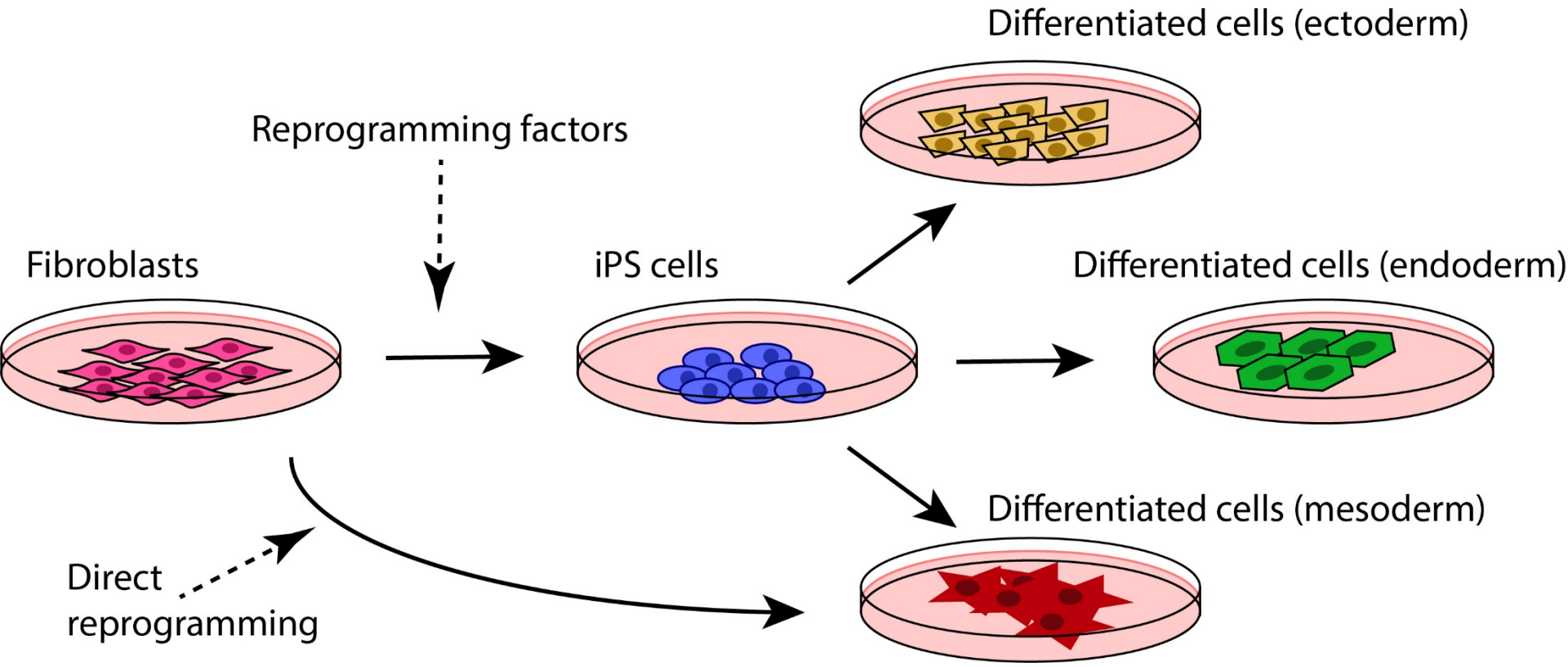
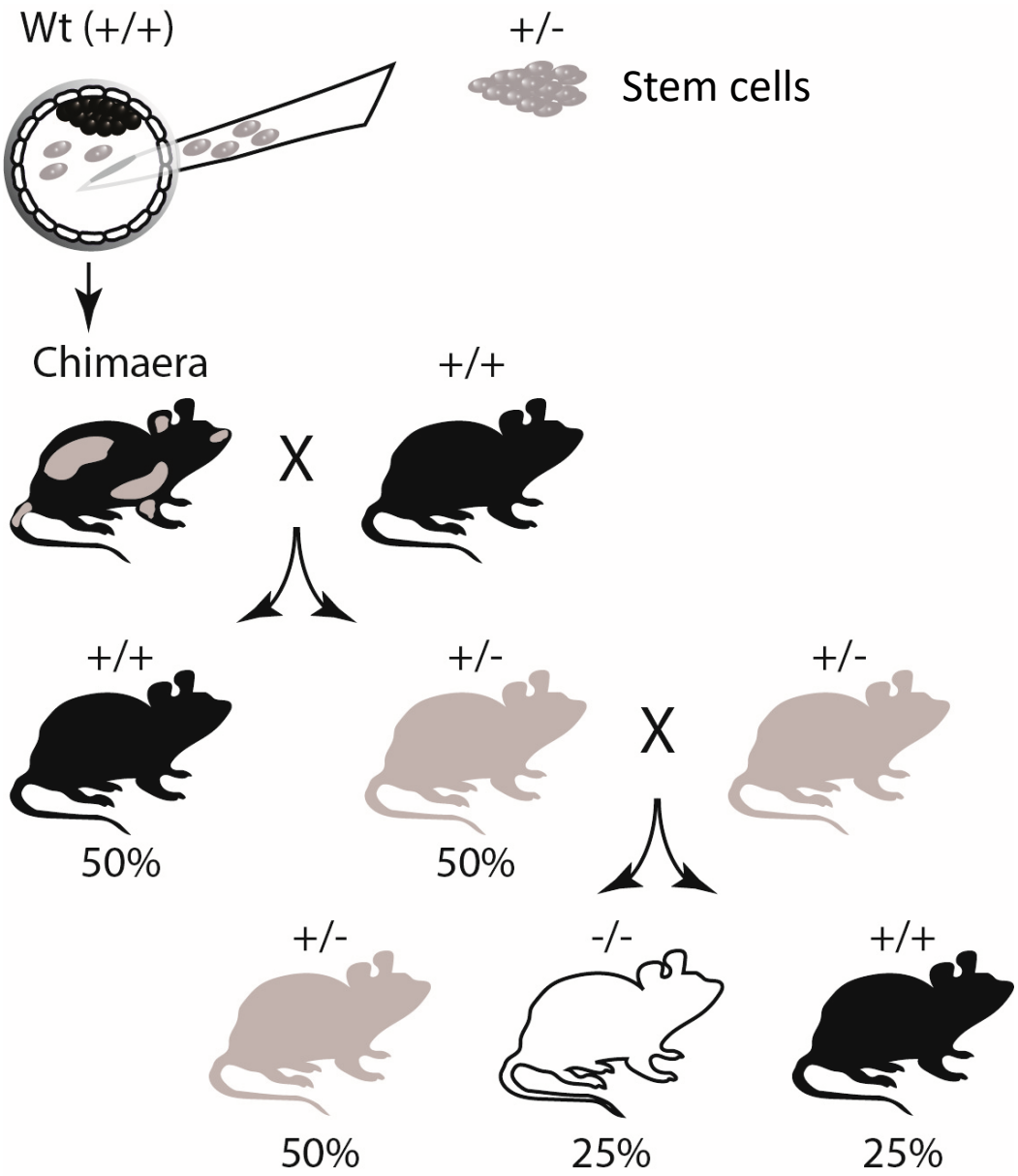
DOI 10.1016/j.cell.2007.11.019

Cell

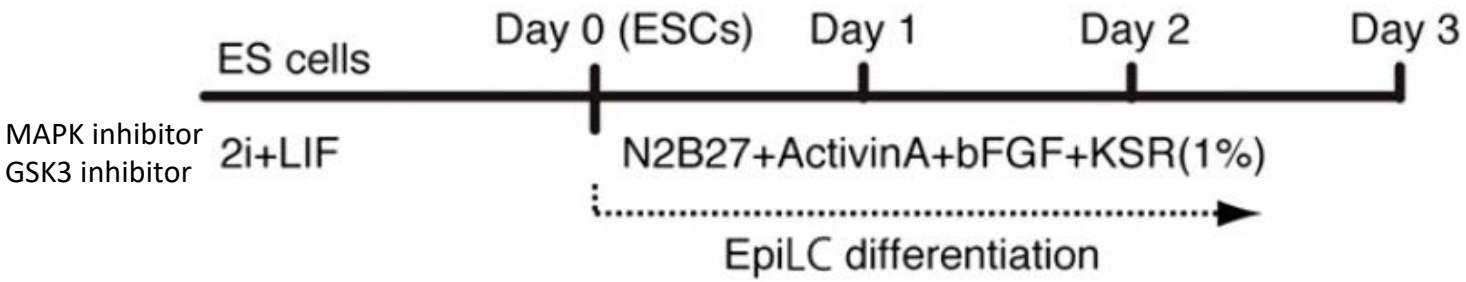
# iPS cells are pluripotent



# ES and iPS cells can form functional germ cells in vivo: chimaera



# Differentiation to pre-gastrulating epiblast-like cells (EpiLC)



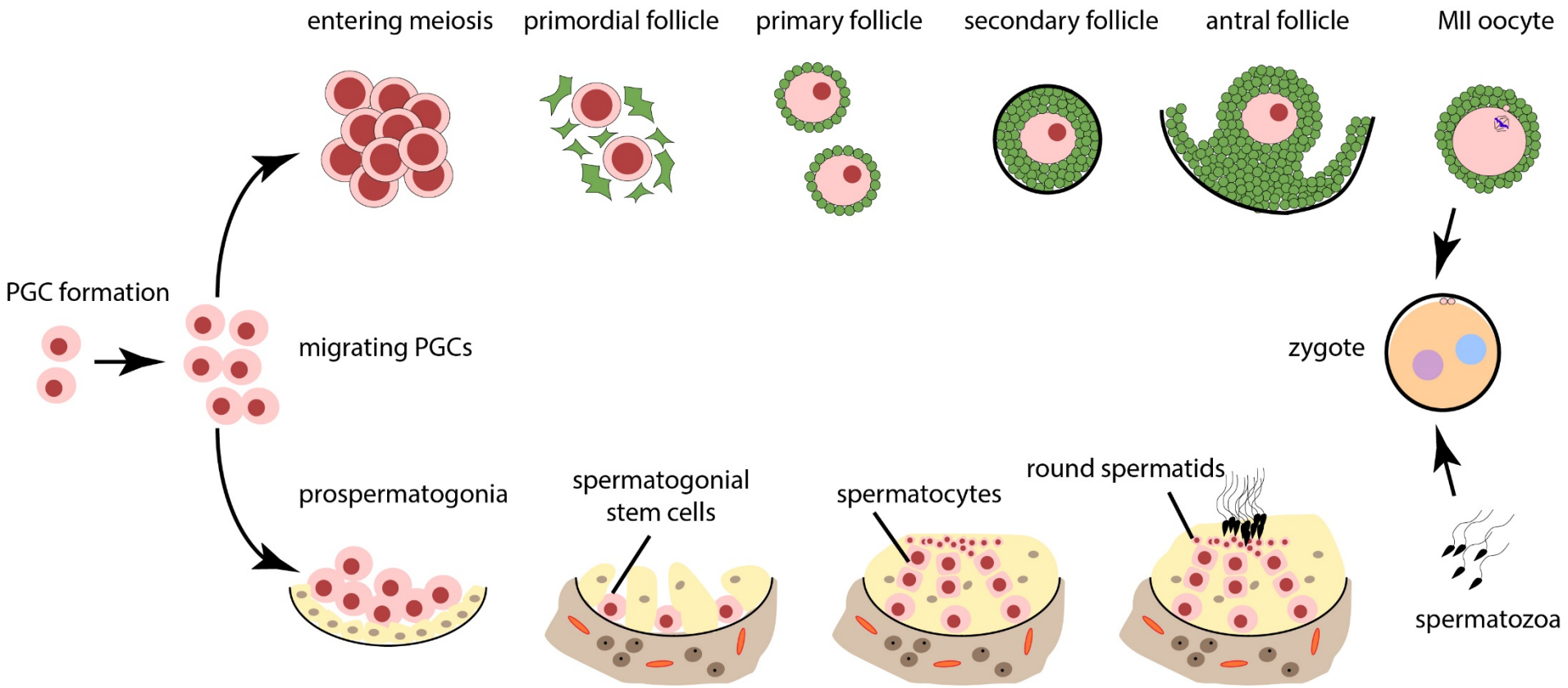

Hayashi *et al*., 2011, Cell 146: 519-532

# Germ cell formation and differentiation

Kojima *et al*., 2017, Cell Stem Cell 21: 517-532

Hayashi *et al*., 2011, Cell 146: 519-532

# Somatic gonadal cells direct sex determination



# Somatic tissue is needed for the final differentiation

Cells sorted from aggregates for Blimp1-Venus
Transplantation into the seminiferous tubules of $W/W^v$ mice lacking endogenous spermatogenesis

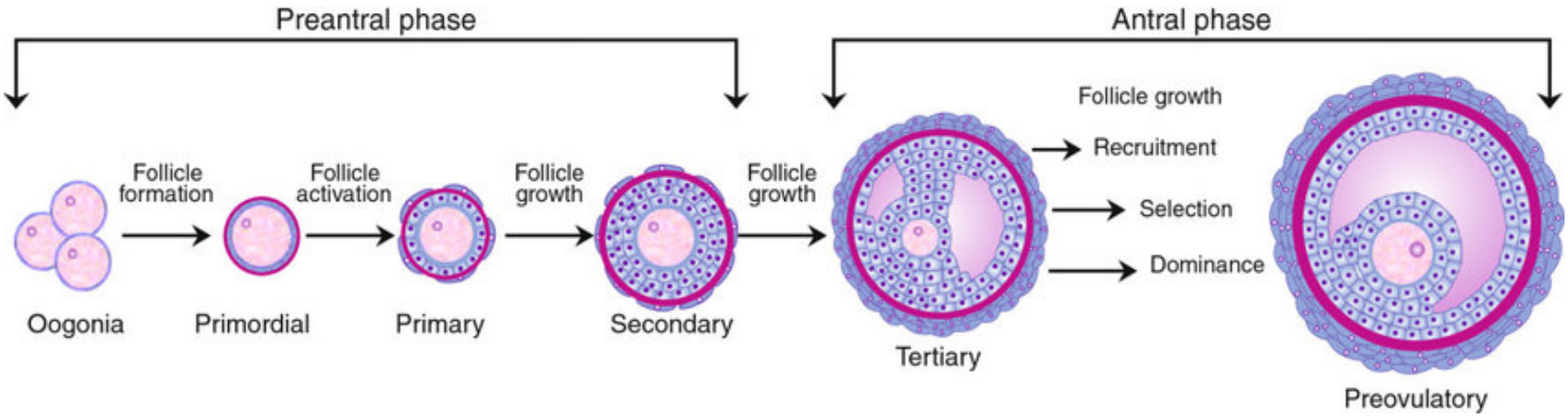
Hayashi *et al*., 2011, Cell 146: 519-532

Hayashi *et al.,* 2012, Science 338: 971-975

# Reconstitution *in vitro* of the entire cycle of the mouse female germ line

Hikabe *et al.,* 2016, Nature 539: 299-303

# Timing of oocyte development differs between species




Human ~175 days
Mouse ~45 days
Cattle ~100 days

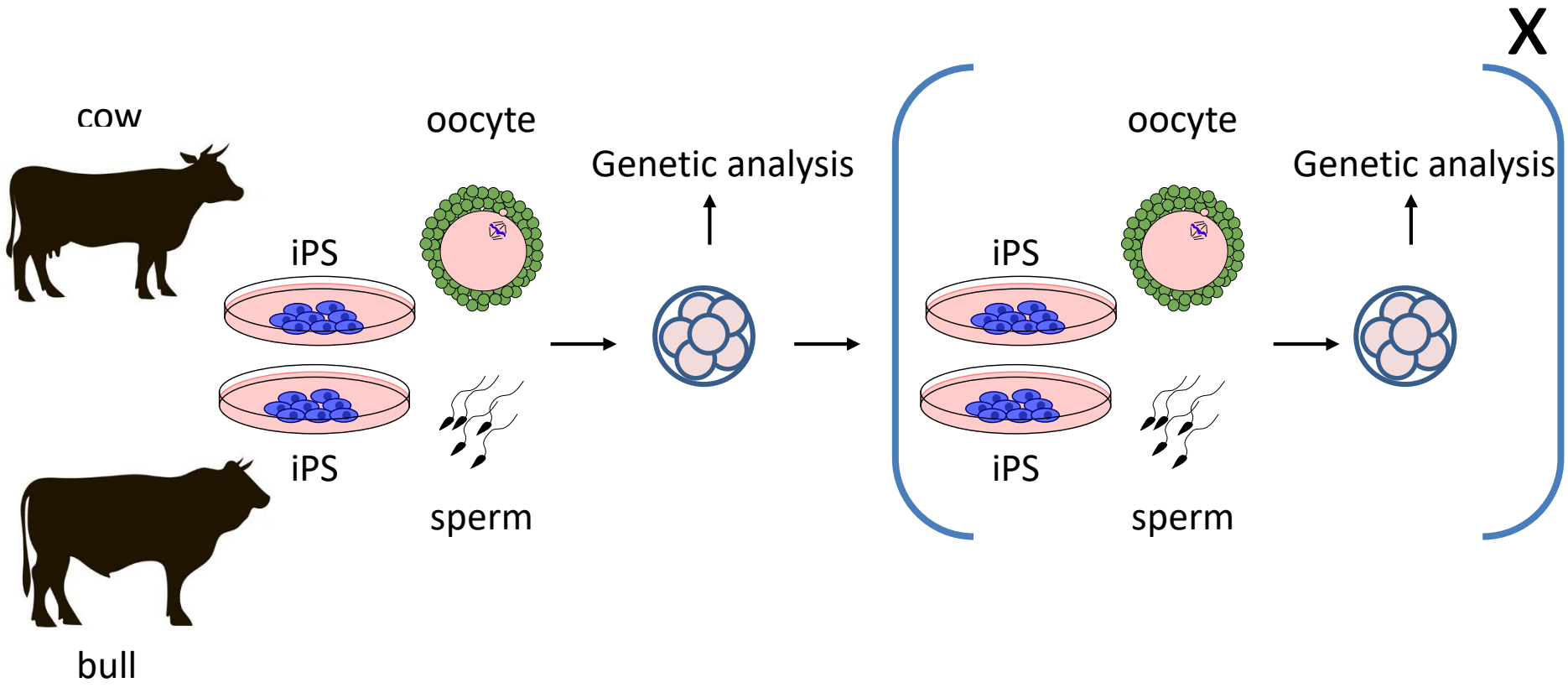
# Differences in germ cell specification

Kojima *et al*., 2017, Cell Stem Cell 21: 517-532

# Generation of human oogonia from hiPS cells in vitro

Yamashiro *et al*., 2018 Science 362, 356-360

# Genetic improvement can go much faster



# Reproduction of critically endangered species

Saragastu *et al*., 2016 Zoo Biology 35, 280-292

# Numbers of healthy eggs decrease with age

# Thank you

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