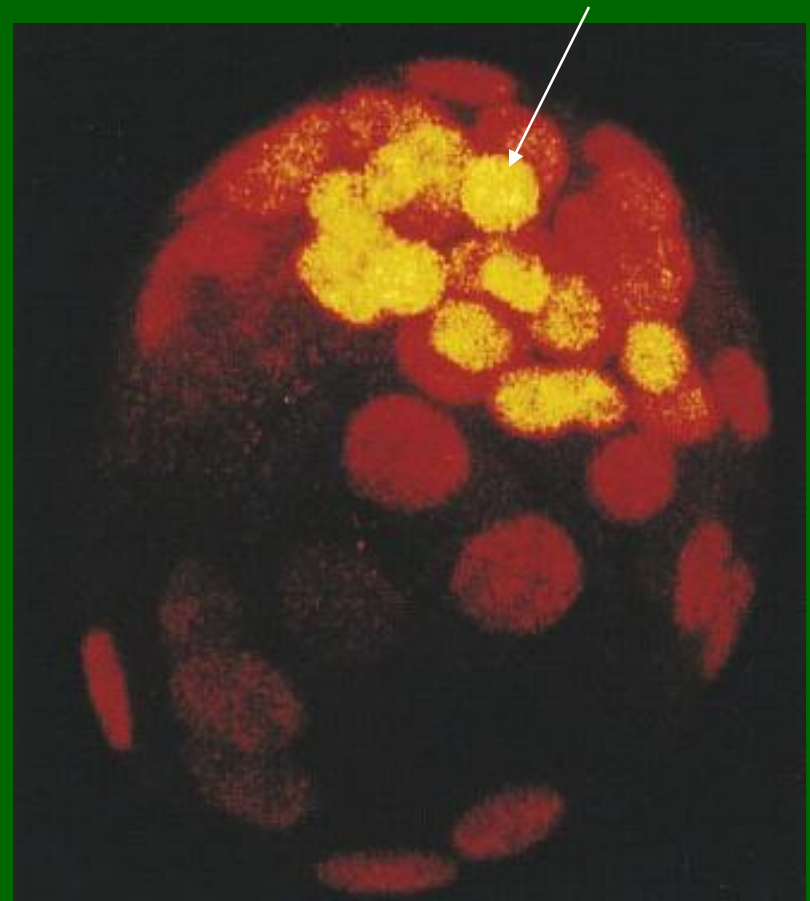


# Is There a Germ Plasm in Mammals?

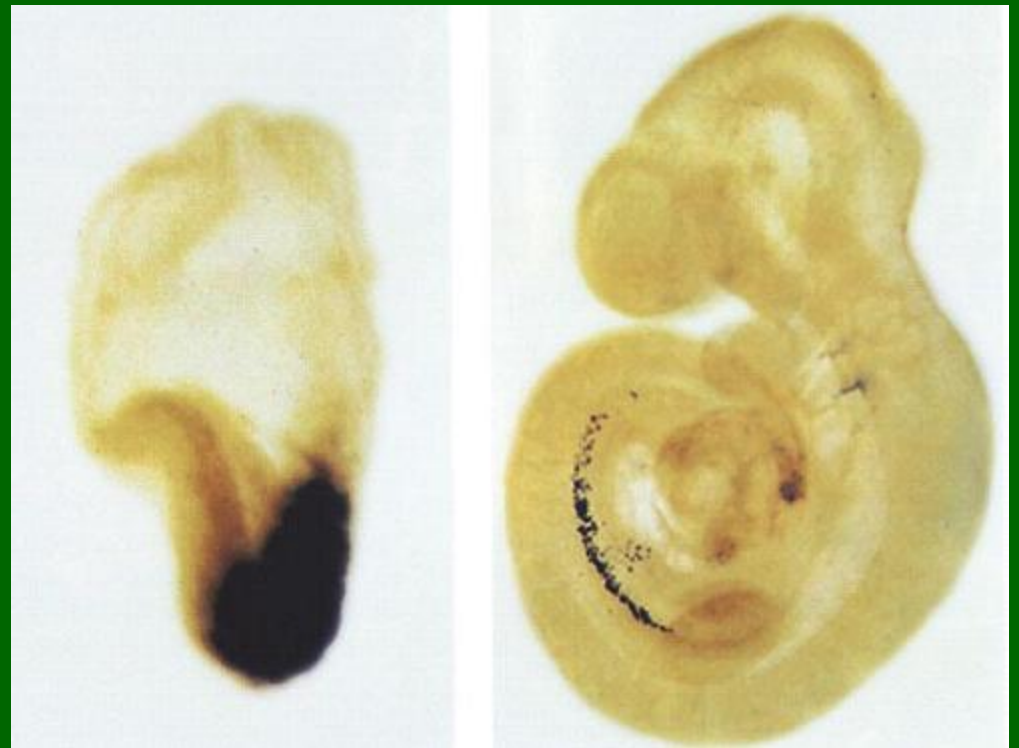
- No germ plasm yet identified in mammals
  - Induction by BMPs
  - Oct4 transcription factor: expressed in all early blastula cells, but then gradually restricted to just PGCs
  - Later only in oocytes (and spermatogonia)

Oct4 in ICM



# Oct4 Expression Pattern

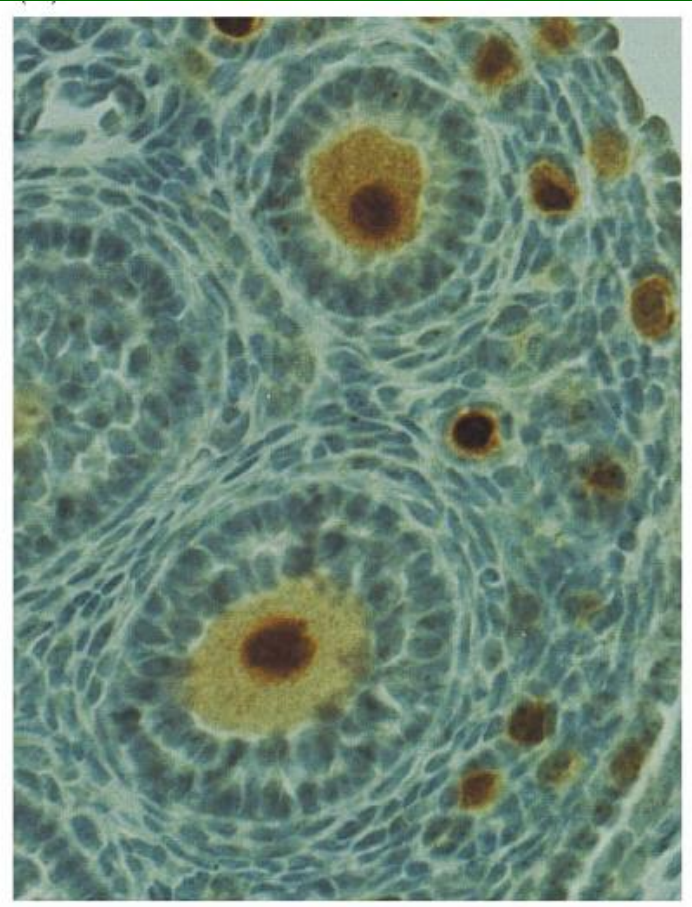
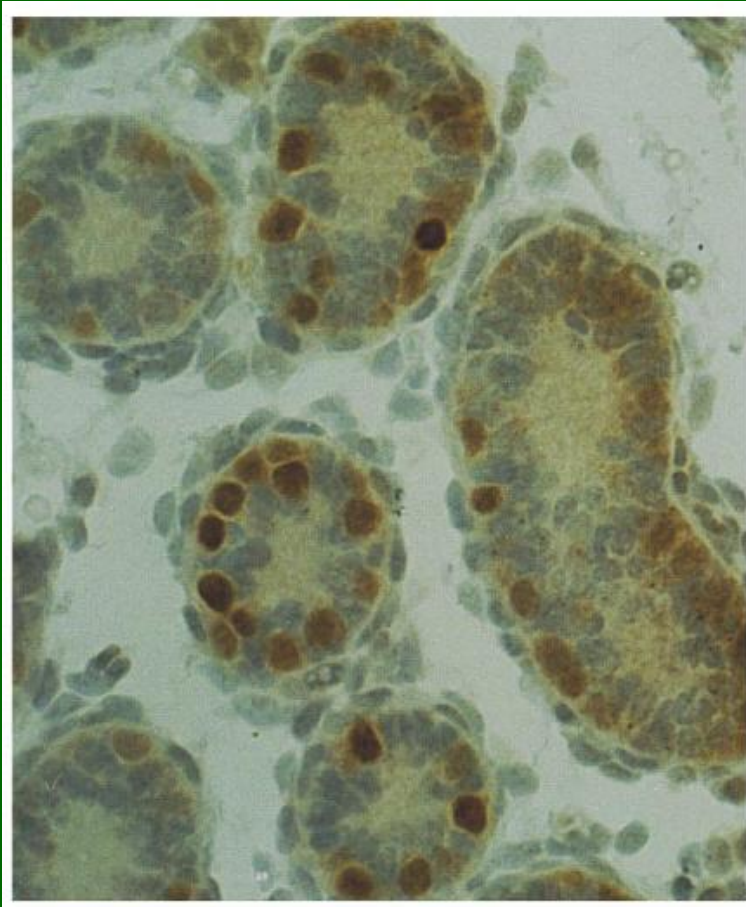
- Expression driven by Oct4 promoter in epiblast and migrating to gonad



# Oct4 Expression Pattern

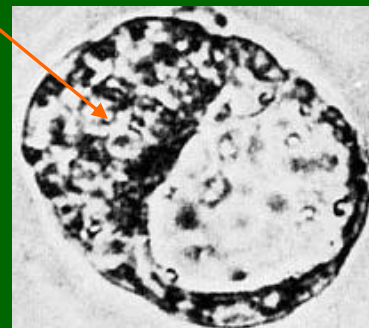
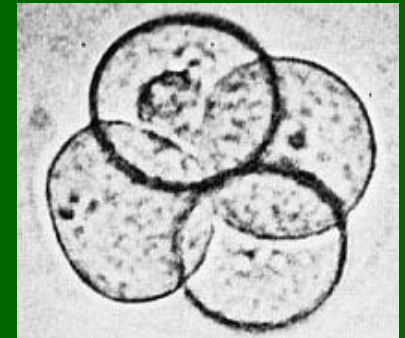
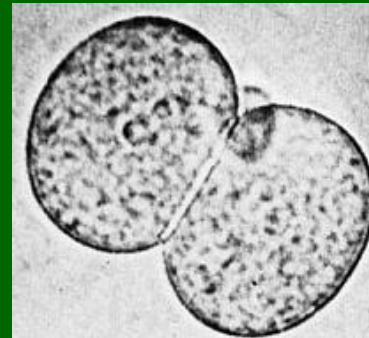
Spermatogonia

Nuclei of Oogonia/Oocytes

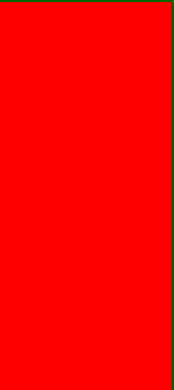


# Therapeutic Cloning for Stem Cells

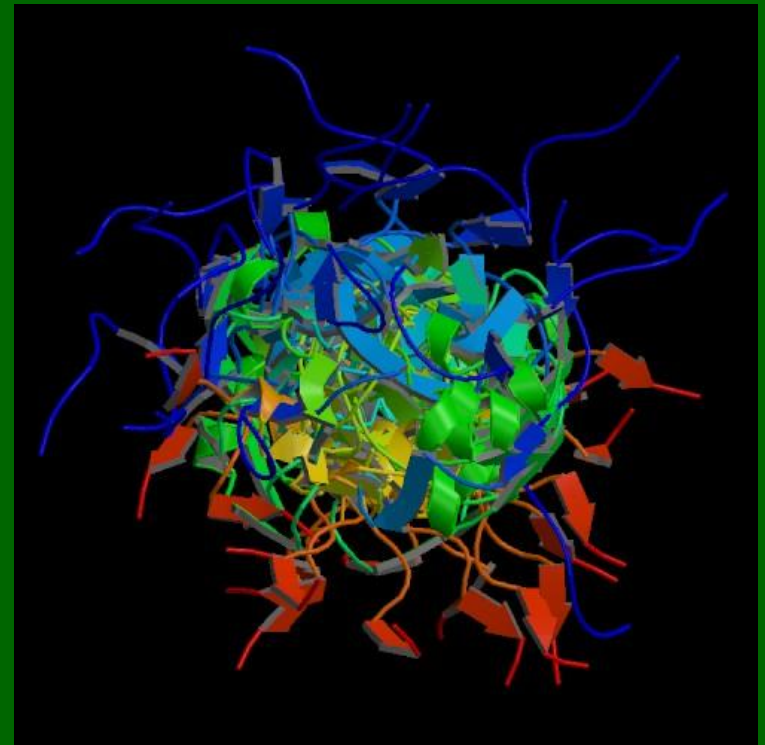
- Construction of a cloned embryo from somatic cell of an adult patient
- Culture to *blastocyst* stage to obtain ICM
- Destruction of embryo to harvest stem cells
- Growth in dish under appropriate conditions to control differentiation or in host



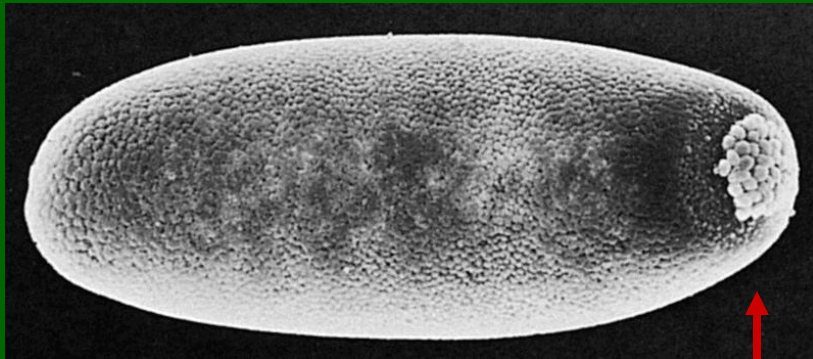
# Oct 4 and Adult Stem Cells

- keeps cells pluripotent
- pluripotent stem cells made directly from adult fibroblasts by the addition of four factors—Oct3/4, , c-Myc, and Klf4

DNA binding domain

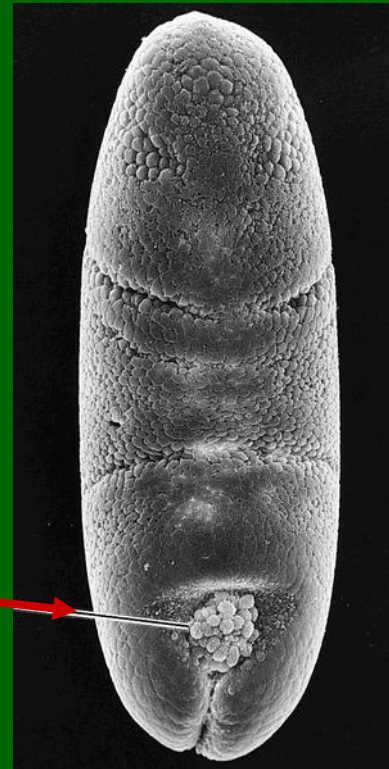


# Migration of Primordial Germ Cells to the Gonads: *Drosophila*



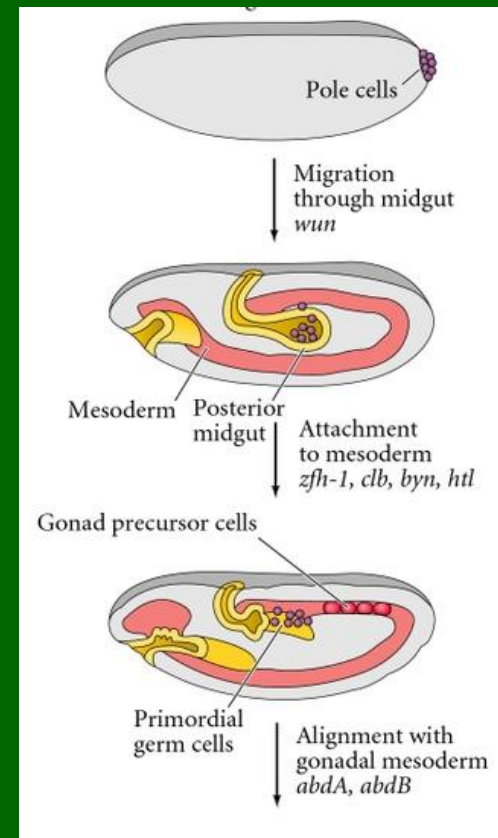
Pole cells in cellular blastoderm

Pole cells in the posterior  
midgut invagination  
during gastrulation



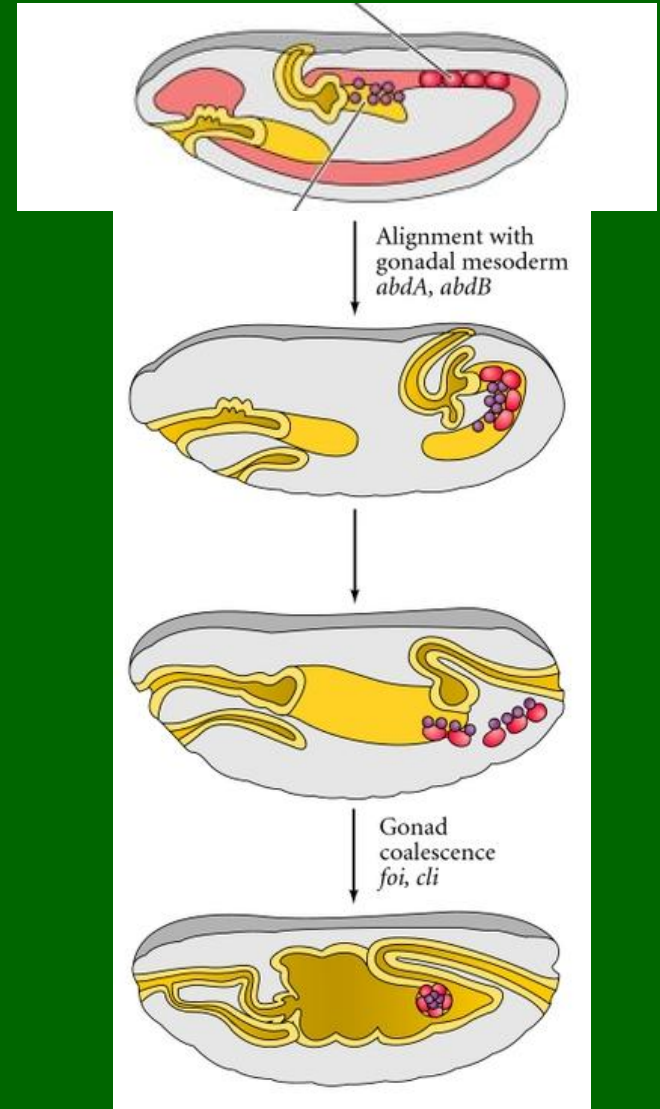
# Germ Cell Repulsion

- 1) passively carried by gastrulation
- 2) gut endoderm triggers PGCs to move out
  - *wunen* protein expressed in endoderm
  - repels PGCs from endoderm so enter mesoderm



# Germ Cell Attraction

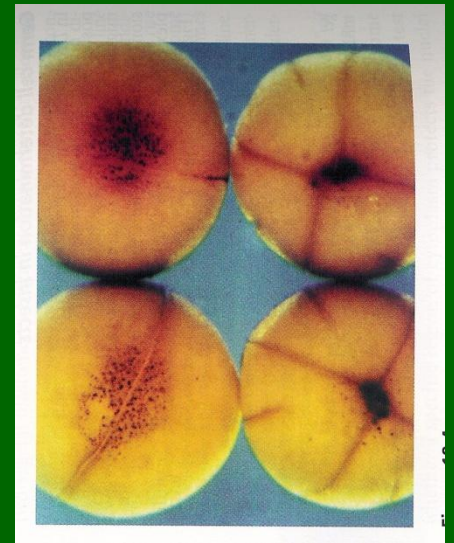
- 3) PGCs migrate to gonads
  - (gonads are derived from lateral mesoderm)
  - *columbus* and *hedgehog* protein expressed by mesodermal gonad cells to help guide PGCs
  - mutants that lack *clb*
    - PGC not attracted to gonad
  - mutants that miss-express *clb*
    - PCG attracted to wrong place
- 4) gonad coalesces around germ cells





# PGC Migration in Frogs

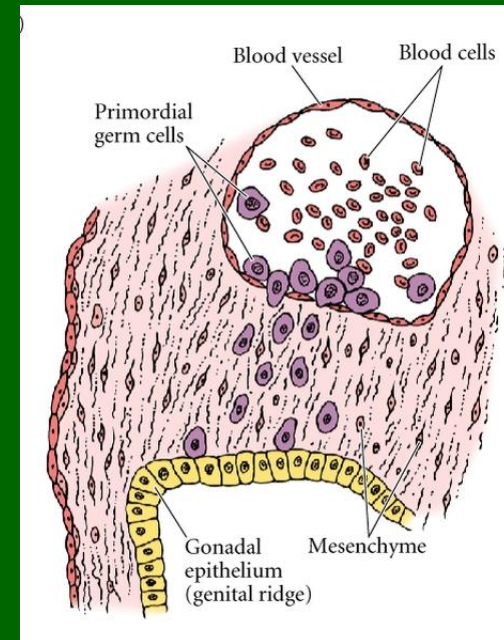
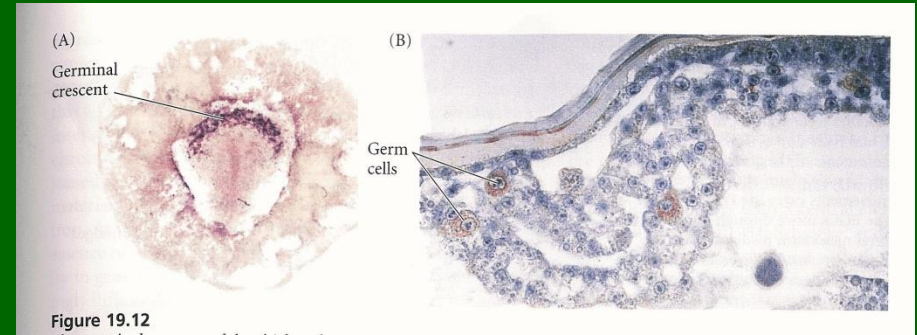
- Ventral region of egg has determinants
- In endodermal cells at posterior larval gut
- Migrate along gut and into genital ridges
- Crawl with filopodia over oriented fibronectin coated ECM
- Modest proliferation until reach gonad (30 cells)
- In newts, pgc's are induced



Nanos

# PGC Migration in Birds

- PCGs accumulate in extraembryonic germinal crescent region and proliferate
- Enter bloodstream
- Carried to hindgut and deposited at region of genital ridge
- Chemotaxis specifically to gonad rudiments *in vitro*



# Germ Cells Mammals

- Germ cells are induced by BMPs, not set aside
- Groups of responding cells express *fragilis*
  - transmembrane protein (proliferation?)
- In center of cluster express *stella* (nuclei acid binding?) -> germ cells
- Migrate into the endoderm, then gut, finally exiting into genital ridge

# Germ Cell Migration in Mammals

- Migration between day 7 and day 12
- Divide as they migrate
  - (10-100 → 2500-5000)
  - Stem cell factor stimulates proliferation
- Move by extending filipodia
  - integrin - ECM (fibronectin) interactions?
  - Soluble chemo-attractants (TGF $\beta$ 1)?

