How to clone
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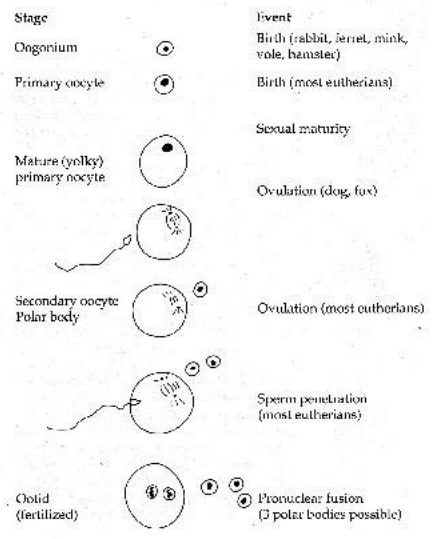
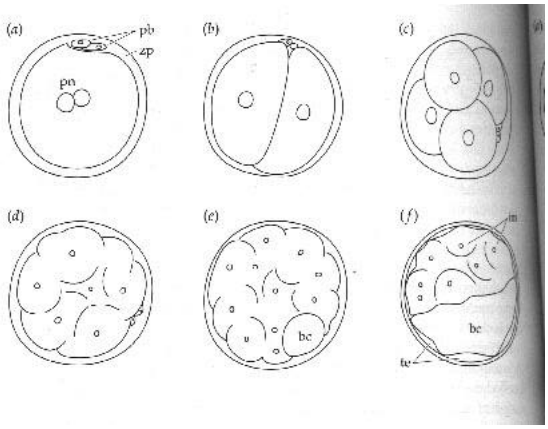
Chem 210

4/10/00

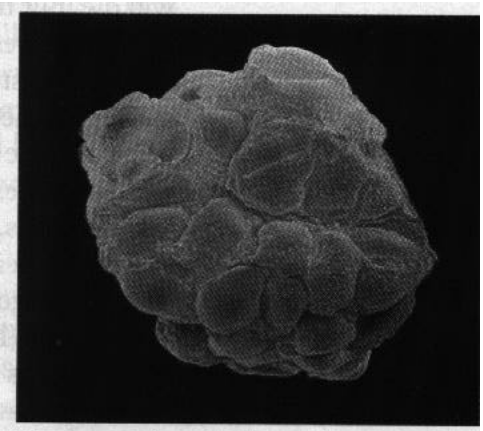
Fertilization: The traditional method of making an embryo



The fertilized egg develops into a *blastocyst*



Early embryo is a clump of cells

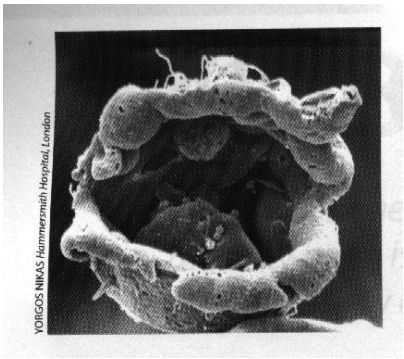


Human embryo is shown five days after fertilization.

Blastocyst cells are undifferentiated

- Yet to undergo changes into specific types of tissues
- All of the cells should still have the potential to develop into any type of tissue.
- Challenge: can these cells be manipulated/have their development controlled?
  - Use these cells to grow specific tissues
  - Make “copies” of embryos

Blastocysts can be divided to make multiple embryos



- Steen Willadsen develops the method in Cambridge in the early 1980s.
- An embryo at the 8 cell stage can be divided into 2 or more fragments.
- These cells can then develop into independent embryos (sometimes).

Embryos can be cloned by fusion with enucleated eggs

- Removed the chromosomes from an unfertilized egg
- Isolated individual cells from a young blastocyst
- "Fuse" the egg and embryonic cell together
  - Either using the Sendai virus or via an electric current
- The resulting egg can develop into an embryo with the same chromosomes as the embryonic cell and be implanted within the uterus of an adult female.
- This technique has been done on cows, sheep, monkeys, etc.

For a short time, cloning embryos had potential as a big business

- In the late 1980s, several companies were created which "cloned" cattle
  - Greneda Corporation, Alta Genetics, etc.
  - Goal: make copies of the world's most valuable cattle breeds
- Most companies soon went out of business
  - Still a really expensive technique which not necessarily much more efficient than tried and true breeding methods

Ian Wilmut and co-workers sought to clone starting from cultured embryonic cells

- Embryonic cells can be grown and sustained in culture and maintain their ability to later differentiate into specific tissues--*embryonic stem cells*.
- Ian Wilmut (Edinburgh University) and coworkers tried to clone from these cultured cells.
  - Cultured cells can be modified/made transgenic
- Idea: fuse cultured cells with an enucleated egg
- Key element: make sure the cultured cells are quiescent (not replicating chromosomes or transcribing/producing RNA)

Megan and Moran: Sheep cloned from cultured cells

Can cloning work with non-embryonic cells?

- Wilmut's hypothesis: what's important is the position in the cell cycle when the cells are fused.
  - If the cells are quiescent, maybe fusion with an egg can still result in creation of an embryo.
- Experiment: select cells from mammary tissue of a pregnant sheep.
  - This is tissue which is actively growing/differentiating
- What happens….

Dolly: the first clone of an adult mammal

The technique used with Dolly appears to be general

- Has been performed again with sheep, also with cattle and mice.
- Type of tissue selected does not seem to be as important as position within the cell cycle.

Cloning can be combined with genetic engineering technology

- Introduce foreign DNA into cultured cells.
  - Wilmut is interested in producing the human protein Factor IX in sheep's milk
- Fuse cultured cells with enucleated egg.
- Implant embryo into an adult.

Polly: the first transgenic clone

New tissues for transplants may be developed by a combination of cloning and stem cell technology

- Clone cells from a human adult by fusion technique.
- Culture embryonic stem cells from the resulting embryo.
- It may be possible to generate new organs from cultured embryonic stem cells.

This cloning technique offers new options for human reproduction

- Fuse an adult cell with an enucleated egg cell from a donor.
- The new embryo will be a clone of the adult.
- The embryo can be implanted into any surrogate
- Applications:
  - Infertility
  - Expands reproduction options for singles/same sex couples

What is biological birth?

- This technology alters the way we think about the”narrative” of biological birth.
  - Embryo without conception
  - When is the embryo an embryo?
  - Who “owns” a cloned embryo?
- How will this affect our conceptions of social birth?