Phil 173: Genetic Engineering

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Introduction

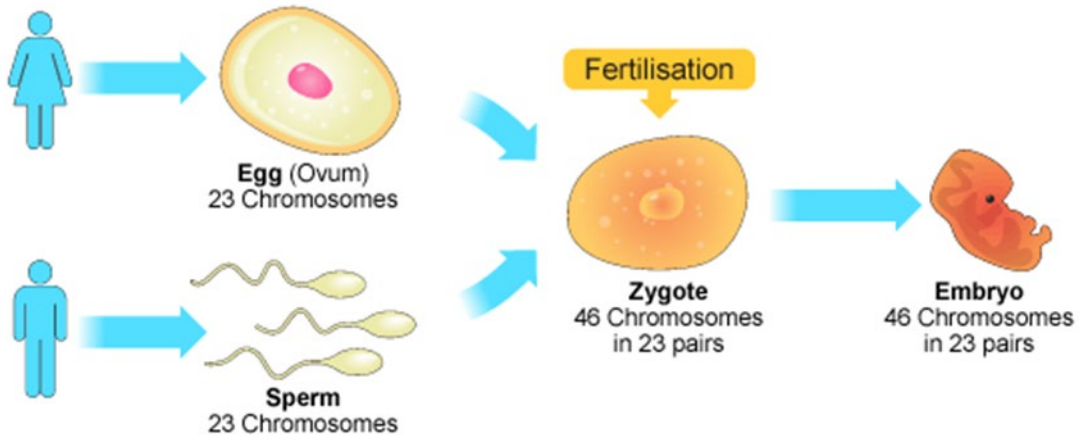
- Genetic Engineering:
  - Modifying the genome
  - It is already here!
    - https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products
  - Lots of ethical questions
    - somatic vs germline
    - treatment vs enhancement
    - disability – medicalizing difference?

Somatic vs Germline

- Somatic cell engineering
  - Not heritable
    - Lower risk?
- Germline
  - Heritable!
    - Higher risk!
- But what about cost-effectiveness, fairness etc?
- Currently germline genetic engineering is prohibited
- But the devil is in the details!

Sexual Reproduction: A more detailed look

Standard (simplified) picture:



- Brushes over some important biological detail

Sexual Reproduction: A more detailed look

Two cellular divisions take place in order to create a female gamete capable of forming a zygote through fusion with sperm:

- At ovulation, a follicle completes meiosis I by dividing, and produces a cell called a secondary oocyte
  - This is the cell that is sometimes called the human egg cell
  - This cell does contains 23 chromosomes, but each chromosome is made up of two identical chromatids
  - The secondary oocytes starts meiosis II, but pauses
- After fertilization meiosis II resumes
  - The secondary oocyte complete meiosis II by dividing again, reducing its chromosomes size to one copy of each chromatid
  - The secondary oocyte is now considered an ovum
  - The nucleus of the sperm and the nucleus of the ovum fuse to create a zygote

Sexual Reproduction: A more detailed look

In sum, the process an ovarian follicle's maturation to form an ovum involves two radical alterations to the DNA of the cell:

- Division to form the secondary oocyte that is released during menstruation
  - Half the DNA is excised (first polar body)
- Division following fertilization
  - Half the DNA is excised (second polar body)

Law/Regulation governing genetic modification

Why is the biological detail relevant?

- Law and policy often appeal to alterations to DNA when delineating procedures that are gene-effecting from those that are not
- As will be shown, this ends up prohibiting a host of interventions generally thought to be uncontroversial

Regulations - UK

UK - Human Fertilization and Embryology Act:

(2)A permitted egg is one—

(a)which has been produced by or extracted from the ovaries of a woman, and

(b)whose nuclear or mitochondrial DNA has not been altered.

(4)An embryo is a permitted embryo if—

(a) it has been created by the fertilisation of a permitted egg by permitted sperm,

(b)no nuclear or mitochondrial DNA of any cell of the embryo has been altered, and

(c)no cell has been added to it other than by division of the embryo's own cells.

Regulations - UK

Many reproductive treatments involve stimulating ovulation:

- IVF / IVM

Using chemical agents to induce the completion of meiosis causes the cell to lose half its DNA – this is clearly an alteration of its DNA!

Response: But really we have just helped along a 'natural process' and the DNA in the resultant secondary oocyte is no different from what would have arisen naturally

Appeals to nature are problematic – where do we place the natural/unnatural distinction?

- Is assisted reproduction really just helping nature?

What about 'restorative' DNA modifications?

- Possibly opening Pandora's box…

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Policy

It is not just governmental agencies that define genetic engineering in terms of modifications to DNA:

"At the Napa meeting, "genome modification" and "germline engineering" referred to changes in the DNA of the nucleus of a germ cell…

In the near term, we recommend that steps be taken to:

1) Strongly discourage, even in those countries with lax jurisdictions where it might be permitted, any attempts at germline genome modification for clinical application in humans…"

"A prudent path forward for genomic engineering and germline gene modification" Science 03 Apr 2015:Vol. 348, Issue 6230

Appeal to genes

- But there is much debate over the definition of 'gene', and it has changed considerably since first introduced
- Loci on chromosomes, protein blue prints, open reading frames,
- Why not consider epigenetics 'genetics' ? (Keller)
  - Why should the particular molecular basis for a hereditary effect be ethically important?

Morgan's discussion of the gene (1933):

"There is not consensus of opinion amongst geneticists as to what genes are—- whether they are real or purely fictitious—because at the level at which genetic experiments lie, it does not make the slightest difference whether the gene is a hypothetical unit, or whether the gene is a material particle."

How should we limit genetic engineering?

- Treatment vs Enhancement
  - Why might enhancement be problematic?
    - Safety
    - Fairness
    - Hubris
    - Changes to our nature?
  - What about treatment?

How should we limit genetic engineering?

- Treatment vs Enhancement
  - How do we draw the line?
- Normal species functioning?
  - What about those with great natural ability?
    - Denied treatment?
  - What about normal age-related decline?
  - What about prevention?
  - What compensatory benefits?

How should we limit genetic engineering?

- Maybe we can distinguish enhancement from treatment by appeal to disease
- But how do we define disease?
  - Harmful variation from normal species functioning?
  - Whatever medical professionals defines as disease?
    - Short stature vs skeletal dysplasia
    - Should the cause matter? Or just the effect on wellbeing?

Are harmful differences diseases?

- Medicalization of difference
- Disability implies that a trait is harmful
- Whether a certain trait is harmful and the extent to which it is so depends largely on social norms, social structures, etc.
  - Height
  - Literacy
  - Mobility
- But how far does this go?

Are harmful differences diseases?

- Claims of harmfulness often overstated
- Based on individuals imagining what having / not have a trait would be like, rather than self-reports from individuals
- Difference between created with a difference/disability and having a trait changed later in life
  - “transition costs”