Epigenetic Inheritance

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Beyond Genetics: Hope or Burden?

“It’s in your genes!”

- presumption: genetics determines attributes
- sex determination in humans – yes
- obesity, intelligence, bad habits – no
  → genes fix predisposition

“It’s in your hands!”

- environmental factors and lifestyle exert an influence on genes
- negative: smoking increases disease risk
- positive: proper nutrition reduces disease risk

**hope:** living responsible will benefit your health

**burden:** living irresponsible may have serious effects on your children, grandchildren and others
Inheritance (Vererbung)

- heredity – Vererbung (das Konzept)
- hereditary – “durch Vererbung”
- heritable – erblich
- heritability – Erblichkeit
- inheritance – Vererbung (der Prozess)
- to pass/transmit/transfer sth. to – etw. vererben an
- to inherit sth. from so. – etw. von jmdm. erben

**Genetic inheritance** – the passing of traits from parents to their offspring that are “encoded” in the genetic material

**Epigenetic inheritance** – the passing of traits from parents to their offspring that are not “encoded” in the genetic material
Passing traits from parents to offspring

- **“minitatures”**
  a whole miniature organism (human → homunculus) within a germ cells

- **“gemmule”**
  all body parts shed gemmule into the blood which accumulate in the germ cells

- **“genes”**
  blueprints/instructions for building the organism are present in cells; those of germ cells are passed on (germ/soma separation)

→ backboard, funny Barbapapa cartoons

**Epigenesis**
starting from a zygote, resulting from fusion of undifferentiated germ cells, development gives rise to adult tissues and organs
The genotype-phenotype Map

- development maps a genotype onto a phenotype
- changes in genotype can give rise to changes in phenotype
- only heritable changes to genotype can give rise to heritable changes in phenotype
- changes to the phenotype are only heritable iff the changes in phenotype are a result of changes in genotype
  → not consistent with observations

→ blackboard
Development

**genetically determined**

- number of cell divisions and lineage commitment is deterministic

  example: *Caenorhabditis elegans* hermaphrodite: 959 somatic cells, about 1000-2000 germ cells
  male: 1031 somatic cells, about 2000 germ cells

**environmentally determined**

- cell identity is determined by cell-cell interaction, communication and environmental factors

  example: most other complex multicellular organisms

**genetics – environment**

- high predisposition – low adaptiveness
- low predisposition – high adaptiveness
Inheritance at Cellular an Organismal Level

**mitotic inheritance**
- cell division: from cell to daughter cells
- integrated in the cell cycle
- default mainly **maintainance** of epigenetic information

**meiotic inheritance**
- sexual reproduction: from parent(s) to offspring
- integrated in the life cycle
- only in germ line cells
- mainly **removal** of epigenetic information
  - genomic information $\rightarrow$ long lived (many generations)
    beneficial in slow changing environment (relative to lifespan)
  - epigenetic information $\rightarrow$ short lived (lifetime of the individual)
    beneficial in fast changing environment (relative to lifespan)
Mitotic Inheritance: Replicating Epigenetic Information

DNA methylation

- semi-conservative replication of 5mC marks
- hemi-methylated DNA replicated by DNMT1
- modified 5mC, e.g. hydroxy-5mC, is NOT replicated

Mitotic Inheritance: Replicating Epigenetic Information

**Histone modification**

- no direct copying machinery
  - delution of marked histones during replication
  - recomputation of modification pattern
- newly synthetized histones are marked with replication-dependent H3.1 and H3.2 variant and H4K5ac and H4K12ac
- multiple replication models
- maybe preferential attachment of “old” histones with one particular strand

![Diagram of histone modification and inheritance](image)
Meiotic Inheritance: Removal of Epigenetic Information

Germline reprogramming in mice

- post-fertilization reprogramming:
  - mother brings more epigenetic marks and a lot more proteins and RNAs to the zygote than the father
  - early: passive demethylation (maternal and paternal epigenome) and active demethylation of paternal epigenome by maternal proteins
  - global remethylation by maternal proteins

- imprints are maintained

- germline reprogramming:
  - somatic programs are erased together with imprints
  - parent-specific imprints are laid down
Meiotic Inheritance: Removal of Epigenetic Information

IAP... type of retrotransposon; PGC... premordial germ cell

Heard et al. (2014) “Transgenerational Epigenetic Inheritance: Myths and Mechanisms”
**Intergenerational** epigenetic inheritance: information is passed across a limited amount of generations, decaying as it goes.

**Transgenerational** epigenetic inheritance: information can be passed from generation to generation infinitely many times. (Only replicating information would be able to do so.)

**Maternal effect**: phenotypic characteristics induced by “environmental” effects stemming from the mother ($F_{-1}$) (e.g. maternally store proteins, RNAs or maternal care).

**Grand-Maternal effect**: phenotypic characteristics induced by “environmental” effects stemming from the mother ($F_{-2}$) of a pregnant mother. (Characteristic appears in Grand-mother and child but not in the mother.)
Why Epigenetics is NOT the same as Lamarckism

Lamarckism: a model of evolution where characteristics acquired by an individual become manifest in the heritable material and are pass on to its progeny

Darwinism: a model of evolution driven by natural selection of small, inherited variations that increase the individual’s ability to compete, survive, and reproduce.

The genome sequence of an individual doesn’t change as as a result of adaptation to different environments. Instead, the information on where, when, and how a gene is read and expressed changes.