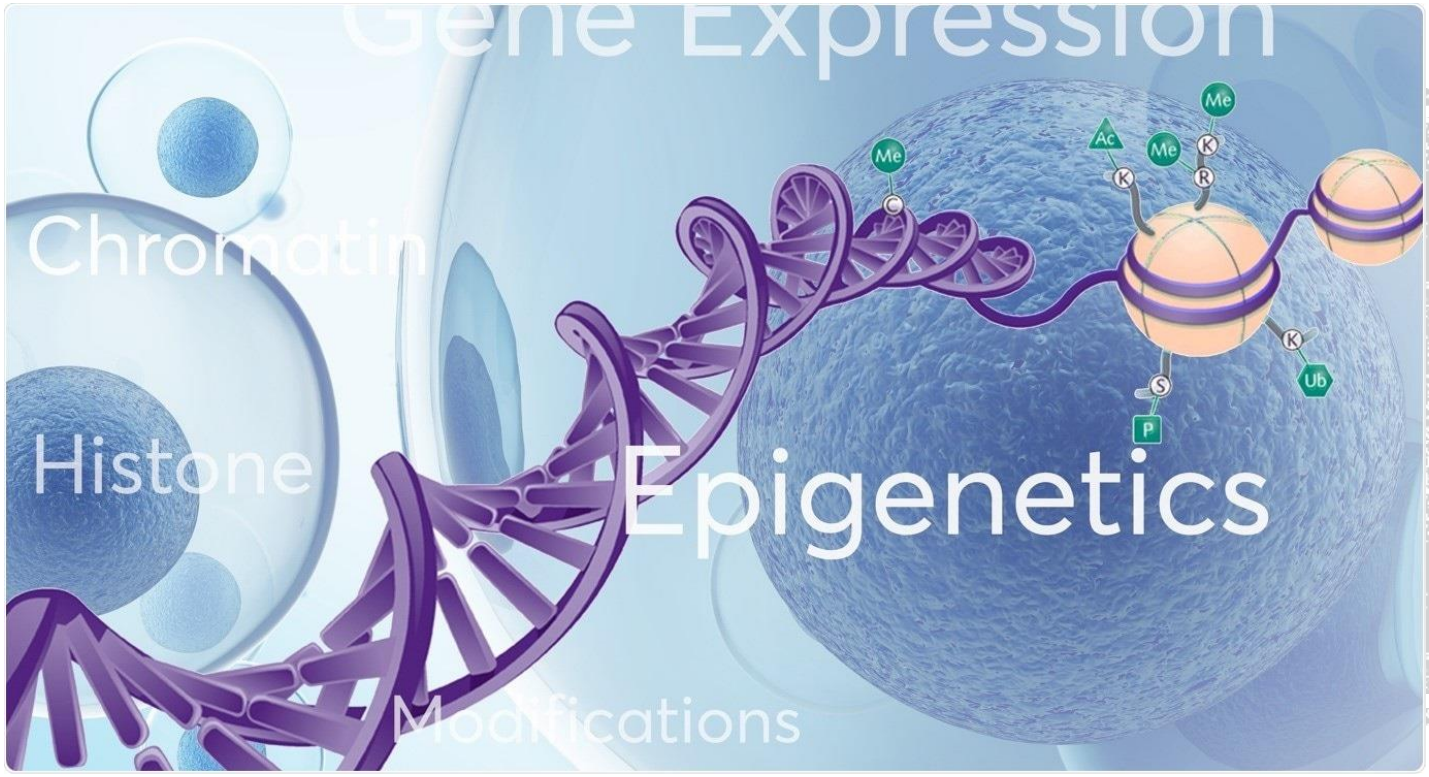

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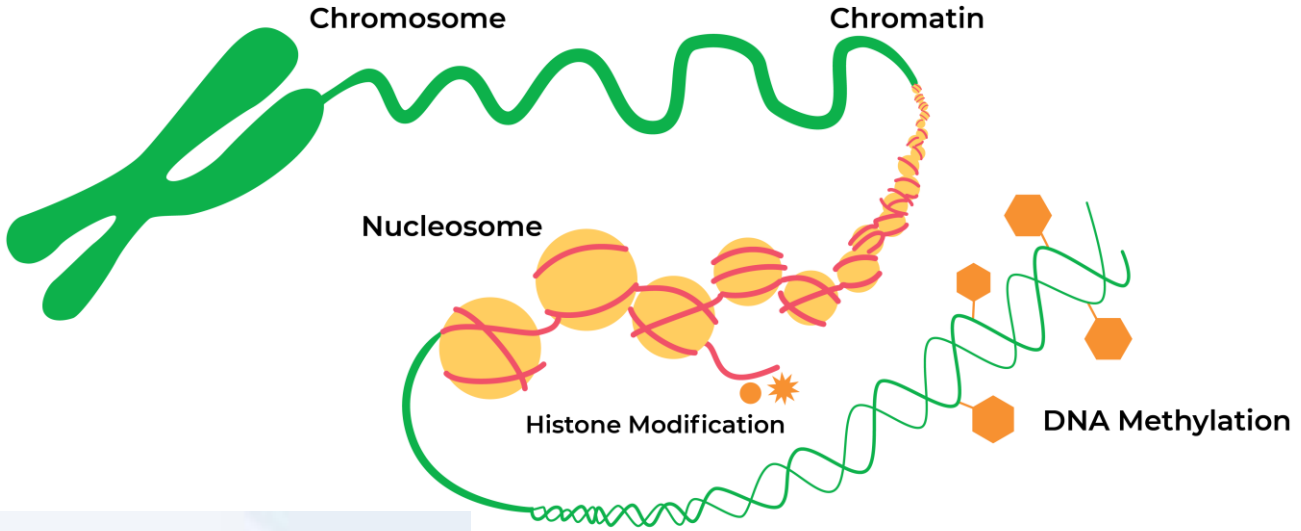
Dr. Manu Smriti Singh

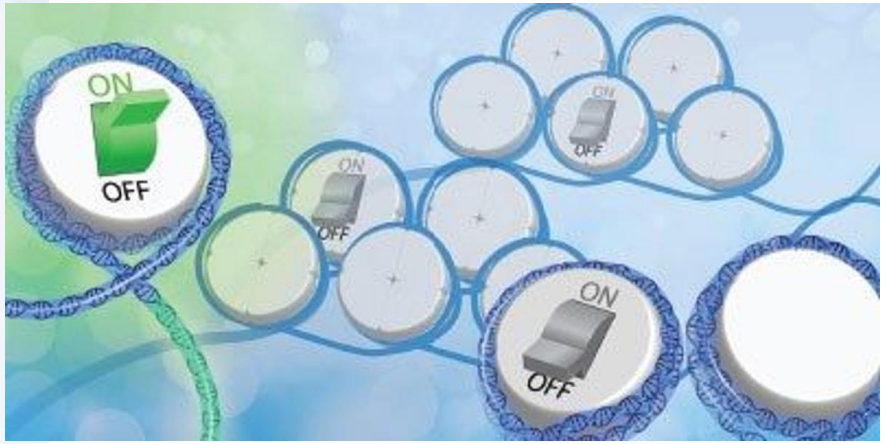
Department of Biotechnology

Bennett University

EPIGENETICS

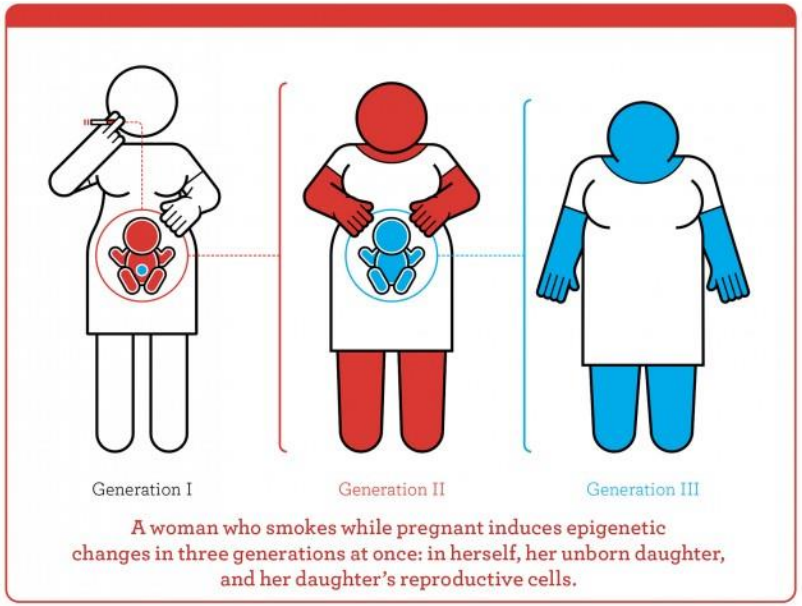


- **Epigenetics** is the study of heritable changes in gene expression or cellular phenotype, caused by mechanisms other than changes in the underlying DNA sequence
  - *epi-* (Greek: *επί-* over, above, outer) *-genetics*.
- It refers to functionally relevant modifications to the genome that do not involve a change in the nucleotide sequence.
  - DNA methylation and histone modification, both of which serve to regulate gene expression without altering the underlying DNA sequence.
  - These changes may remain through cell divisions for the remainder of the cell's life and may also last for multiple generations.

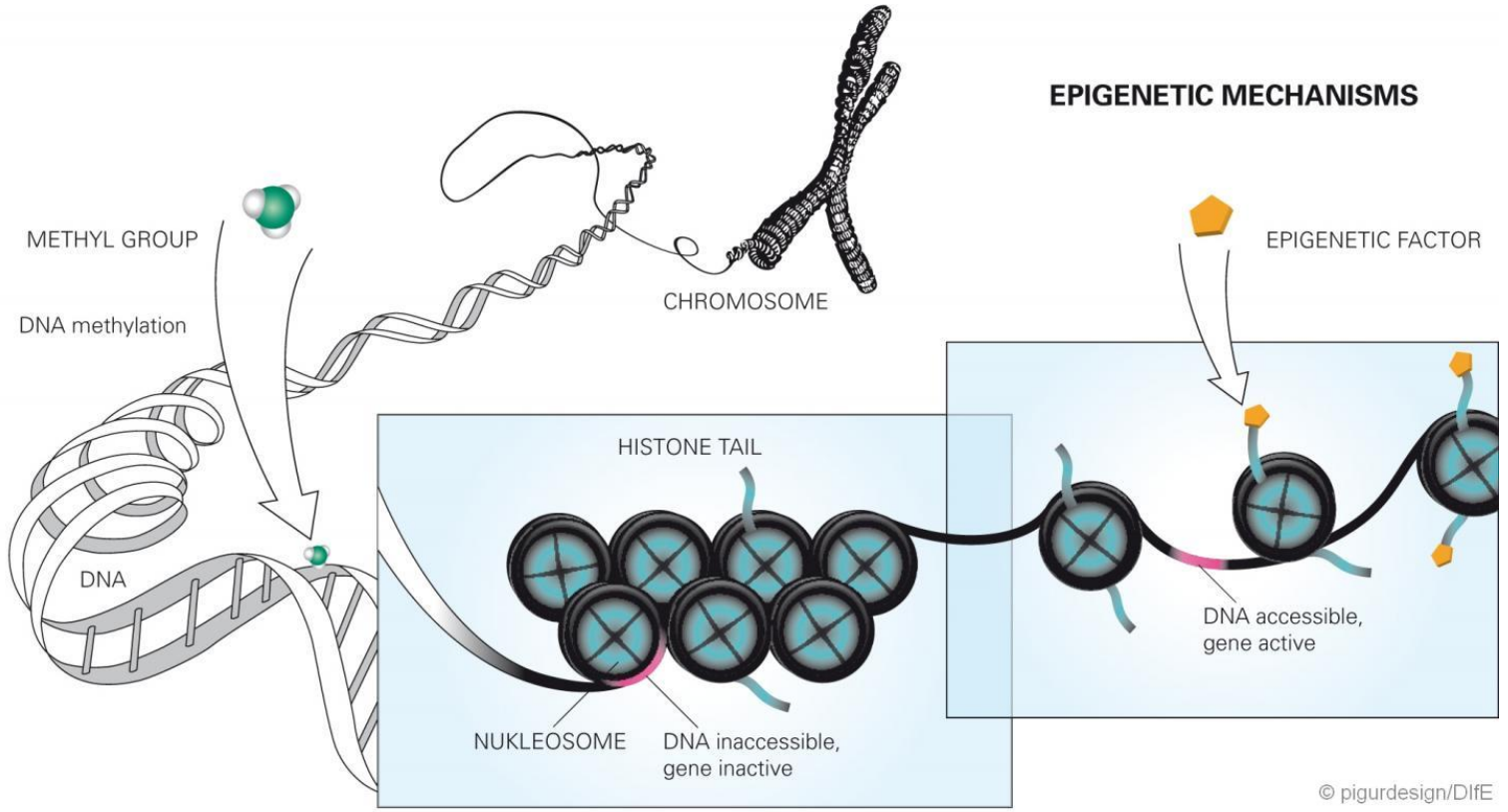


MEMES HELP!


EPIGENETICS: GENES ARE NOT YOUR DESTINY
ALSO EPIGENETICS: YOUR GRANDMOTHER'S DIET HAS DOOMED YOU
imgflip.com


Generation I
Generation II
Generation III
A woman who smokes while pregnant induces epigenetic changes in three generations at once: in herself, her unborn daughter, and her daughter's reproductive cells.

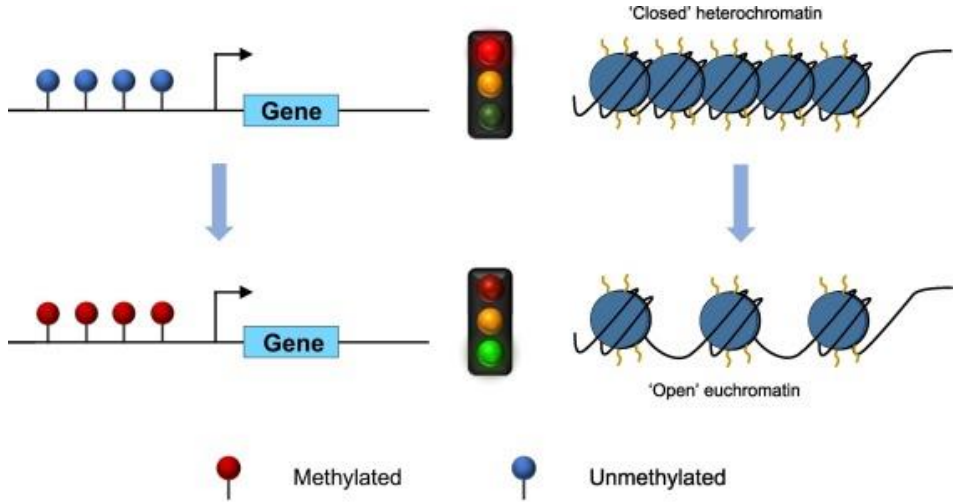
OBESITY

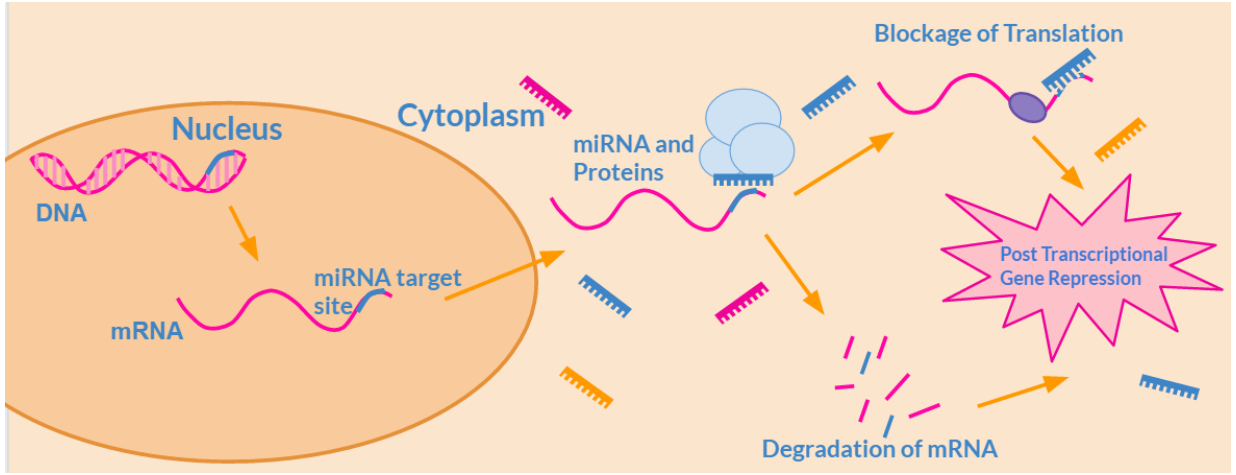


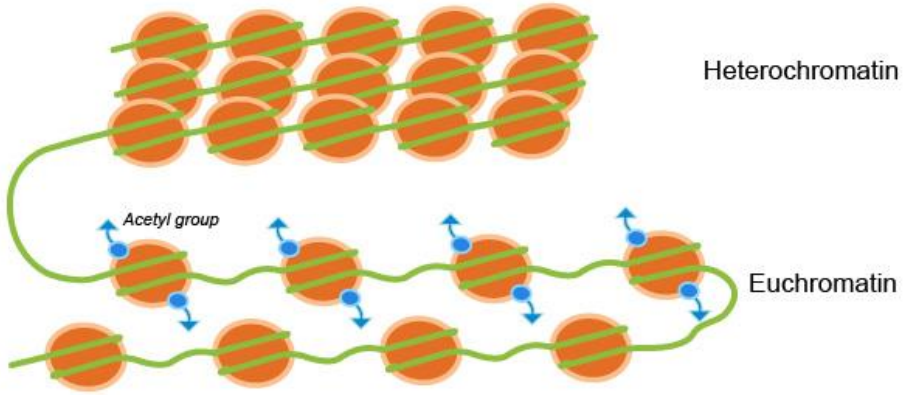
Epigenetic control of genes involved in fat metabolism

REGULATORY MECHANISMS

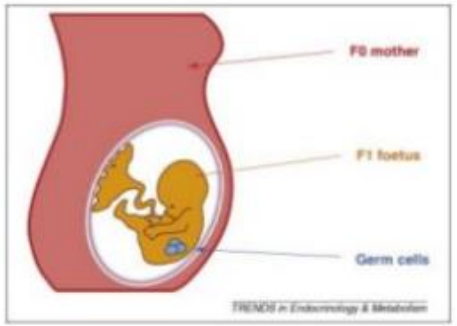
- **DNA methylation:** CH3-attached to CpG islands regulate gene activity. Renders the DNA inaccessible and suppresses gene expression
- **Histone (covalent) modifications:** methylation (Me) or acetylation (Ac) of histones determines the activity of the DNA wrapped around them
- **microRNA (miRNA):** noncoding (19-22 nucleotides) molecules that silence RNA & post-transcriptional regulation of gene expression, bind to complementary sequences in the 3′ end of mRNA and reduce the rate of protein synthesis







DUTCH FAMINE (1944-45)

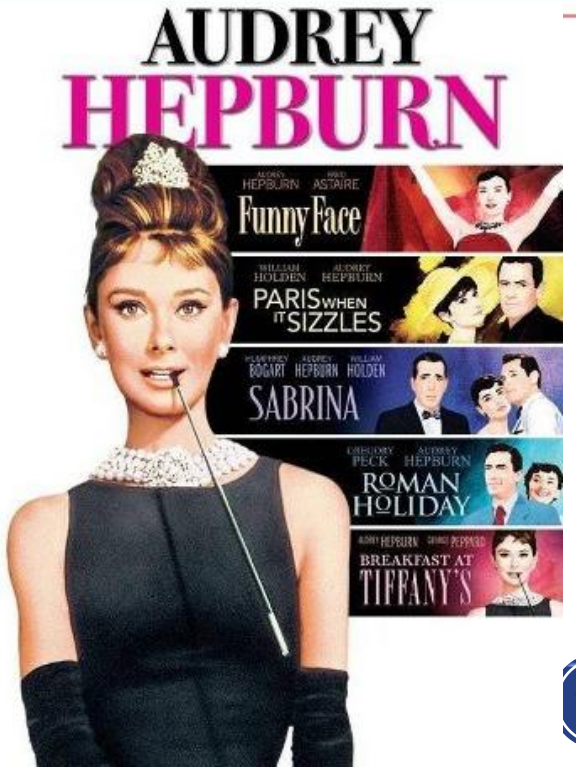


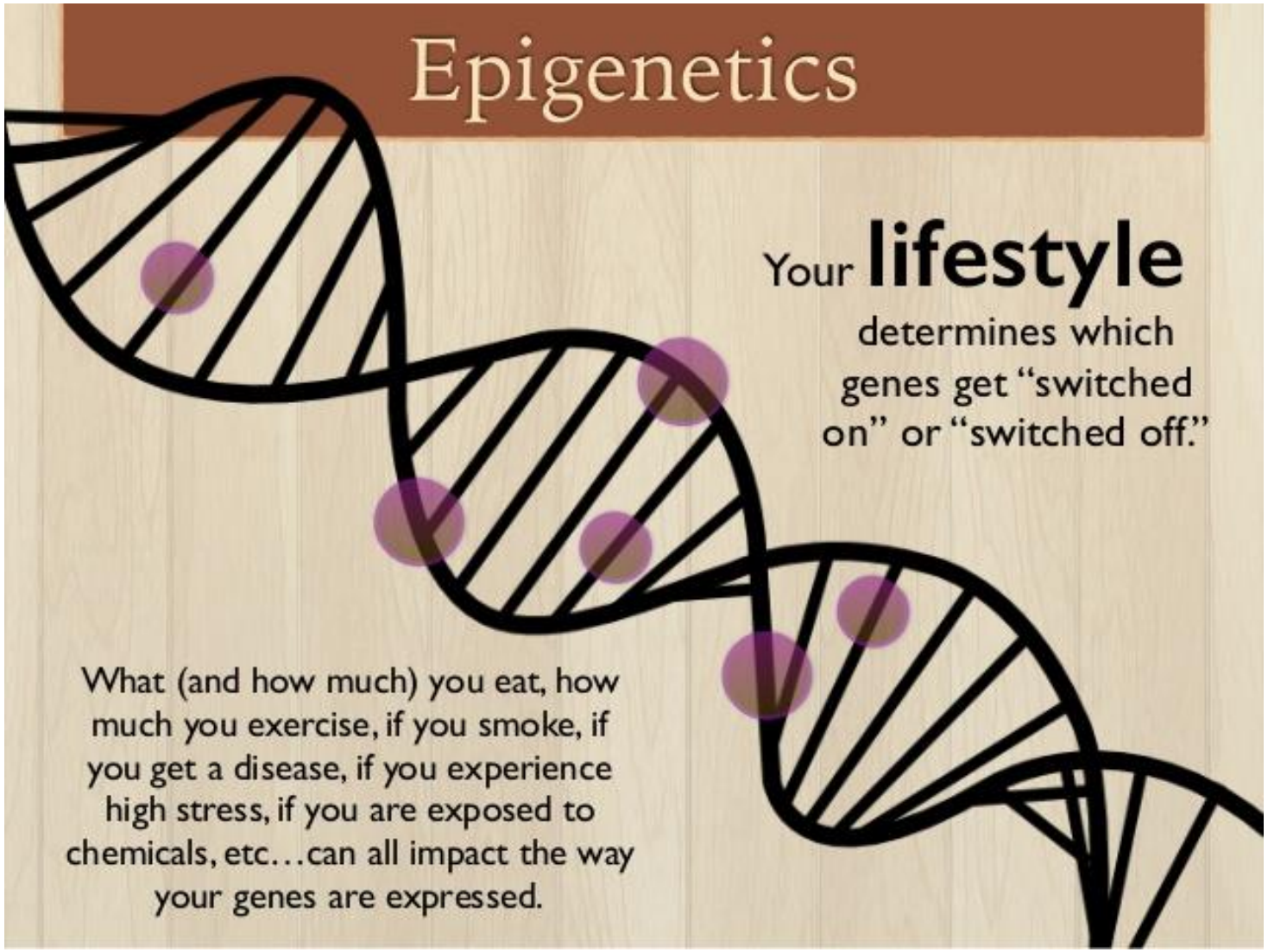
Human evidence of inheritance

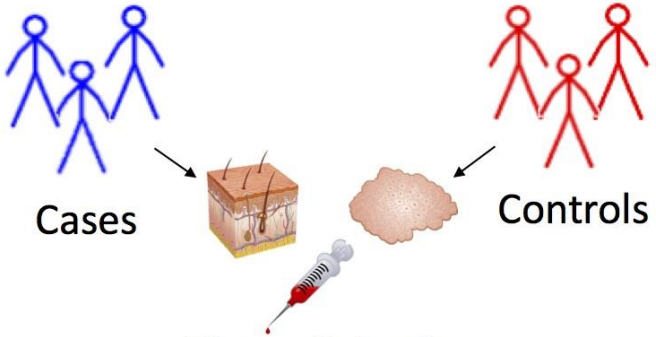
Dutch hunger winter

- Offspring born during the famine were smaller than average and risk of having smaller babies persisted 2 generations (F1 & F2)

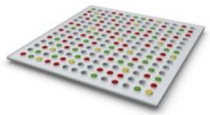
- Hongerwinter
- German-occupied Netherlands towards the end of WWII
- German blockade cut off food and fuel shipments from farm towns
- 4.5 million people affected, 22,000 deaths
- Dutch Famine Birth Cohort Study
- Children of pregnant women exposed to famine were more susceptible to diabetes, obesity, cardiovascular disease, microalbuminuria
- Audrey Hepburn → childhood in the Netherlands during the famine. Lifelong negative medical repercussions: anemia, respiratory illnesses, and œdema



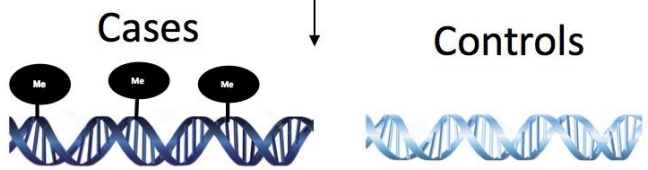




Tissue Selection



Measurement of genome-wide epigenetic marks



Epigenome Variation

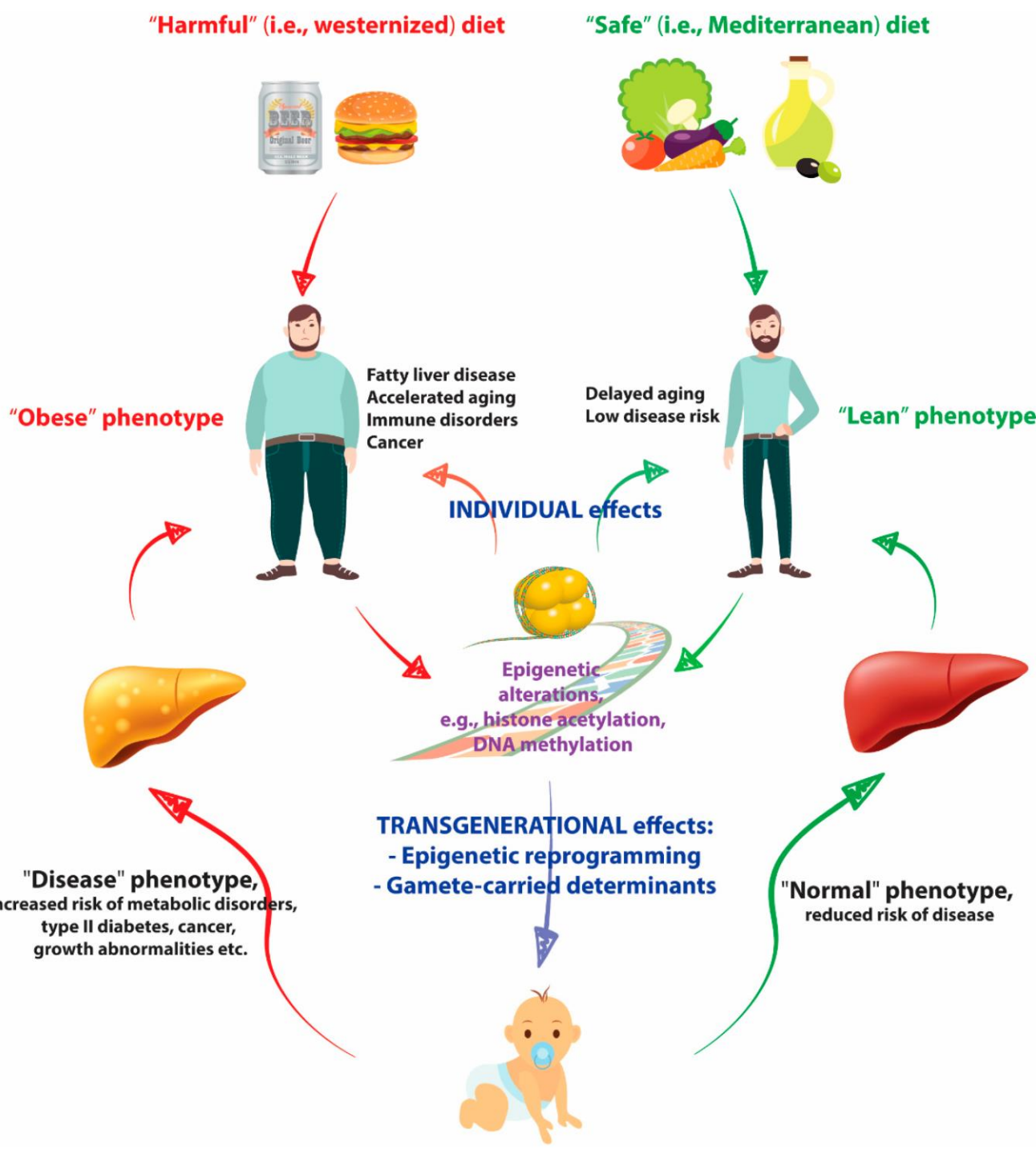
Statistically significant epigenetic variation between cases and controls

Rationale for further functional studies

TRANSGENERATIONAL MECHANISMS

Recapitulation

- The repetition of an evolutionary or other process during development
- Re-occurrence in an individual organism's development (phenotype) resembling the series of ancestral types from which it descended so offspring retraces the phylogeny of its group
- Largely environmental
  - Nutrition
  - Smoking/Alcohol/Drugs
  - Physical activity
  - Stress
  - Exposure to endocrine disruptors
  - Etc.

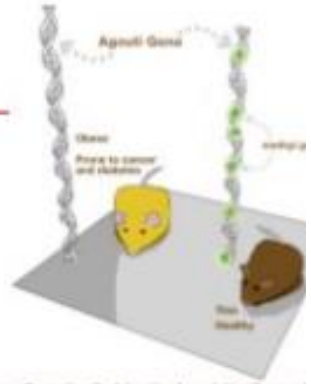


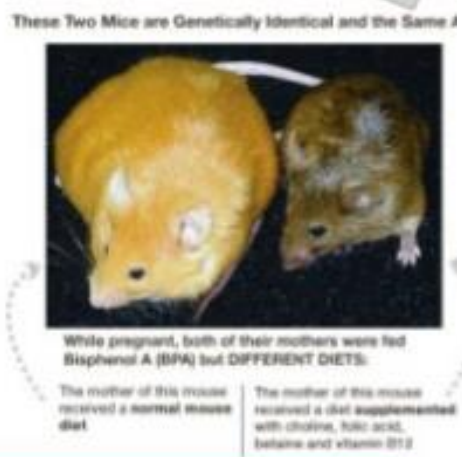
EXPERIMENT TIME!

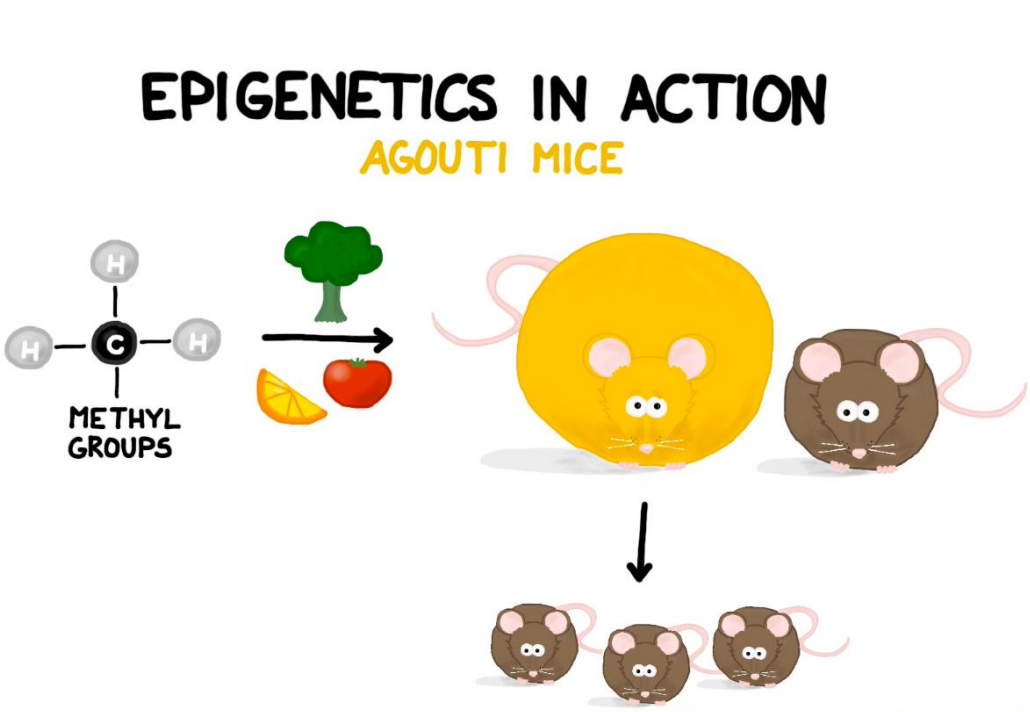
Maternal Diet in Pregnancy

Classic example of CH3-dependent Epigenetic Modification

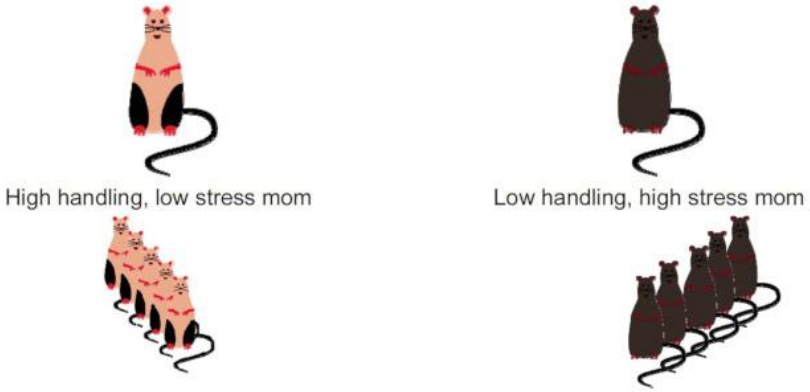
- BPA ↓ methylation of agouti gene
- When mothers fed BPA their babies were yellow & obese
- When moms fed BPA + CH3-rich foods the offspring were brown & healthy
- Supplementation counteracted exposure
- Demonstrates how environmental exposure *in utero* can alter phenotypes in isogenetic pairs



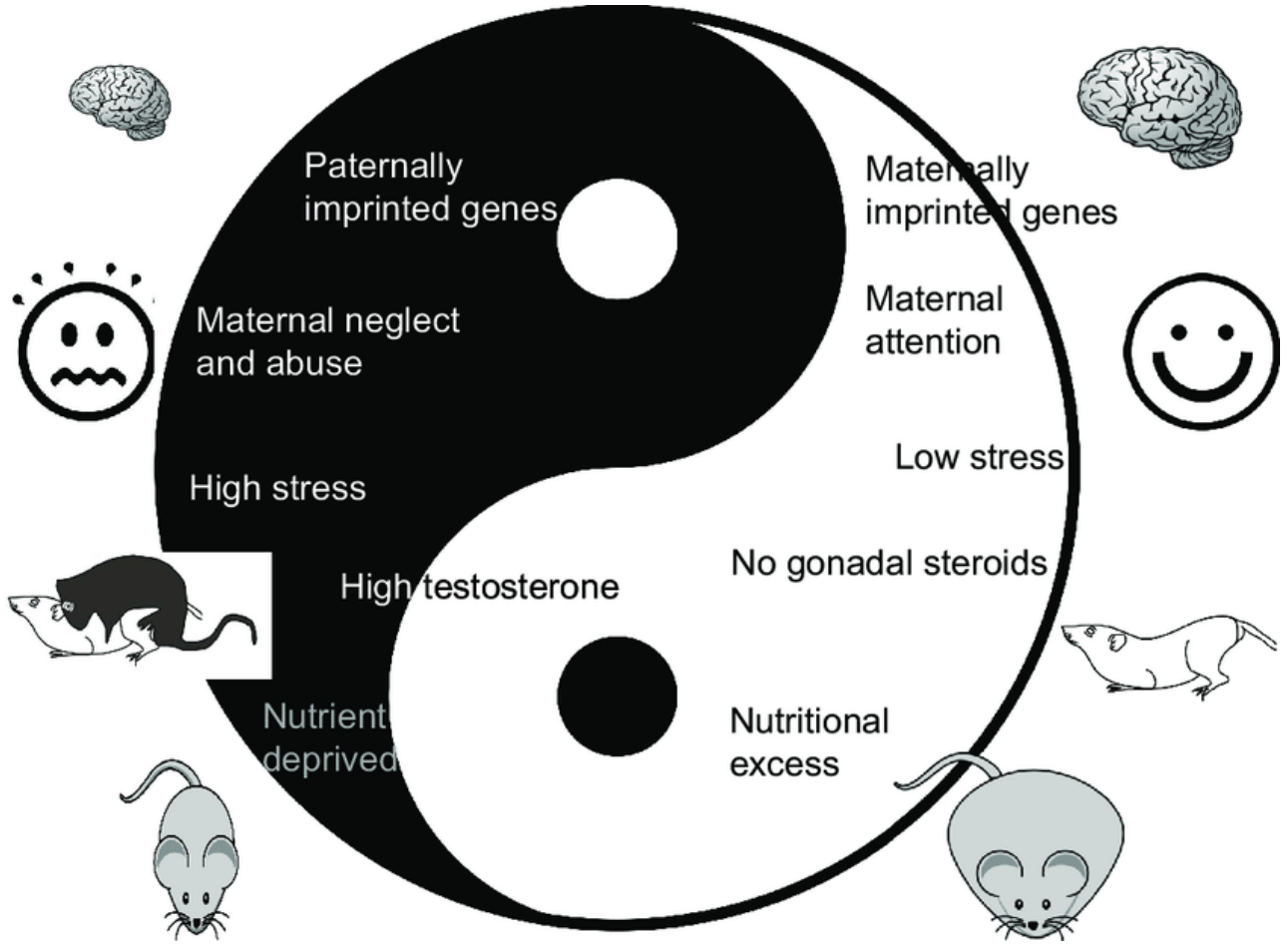




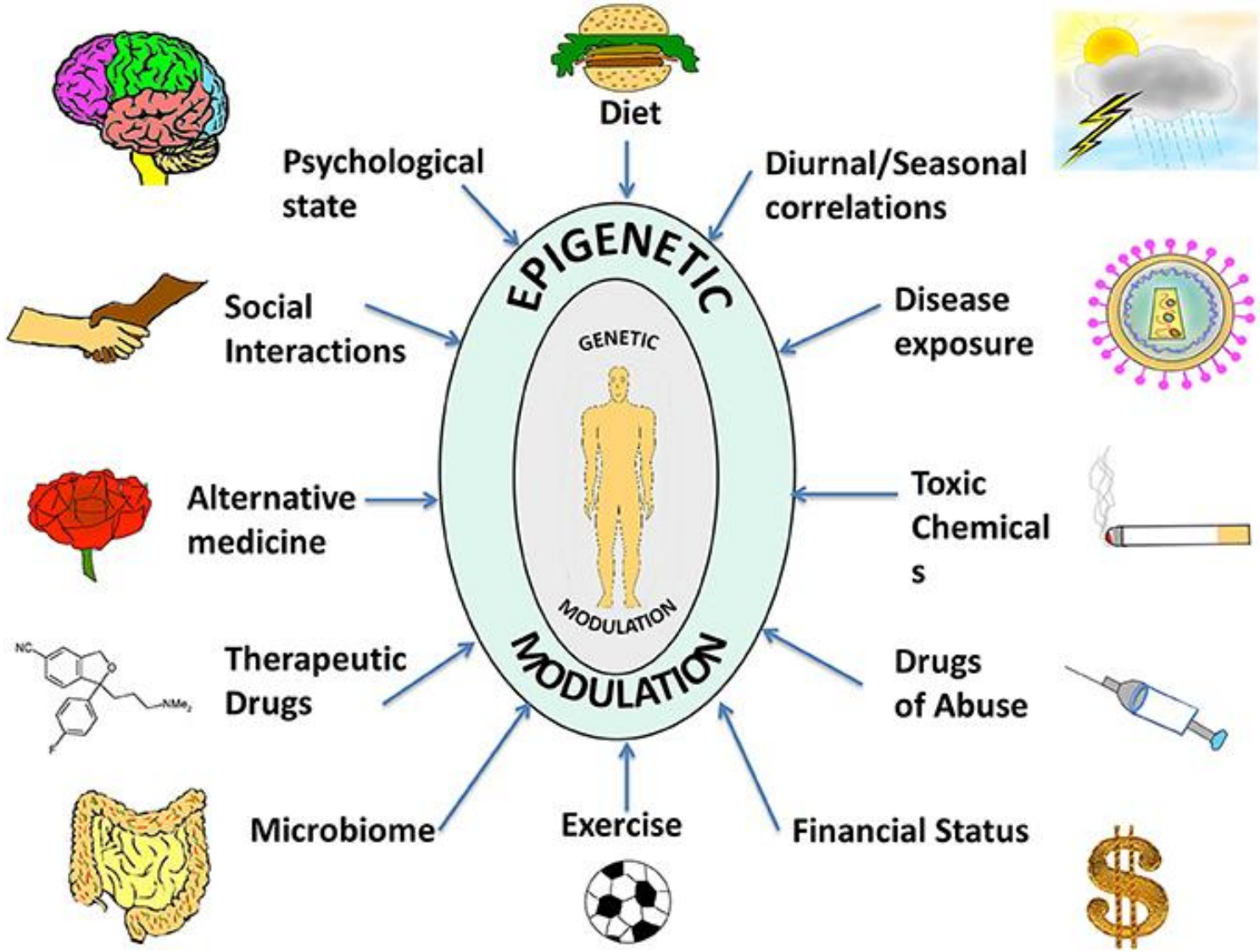
MENTAL HEALTH

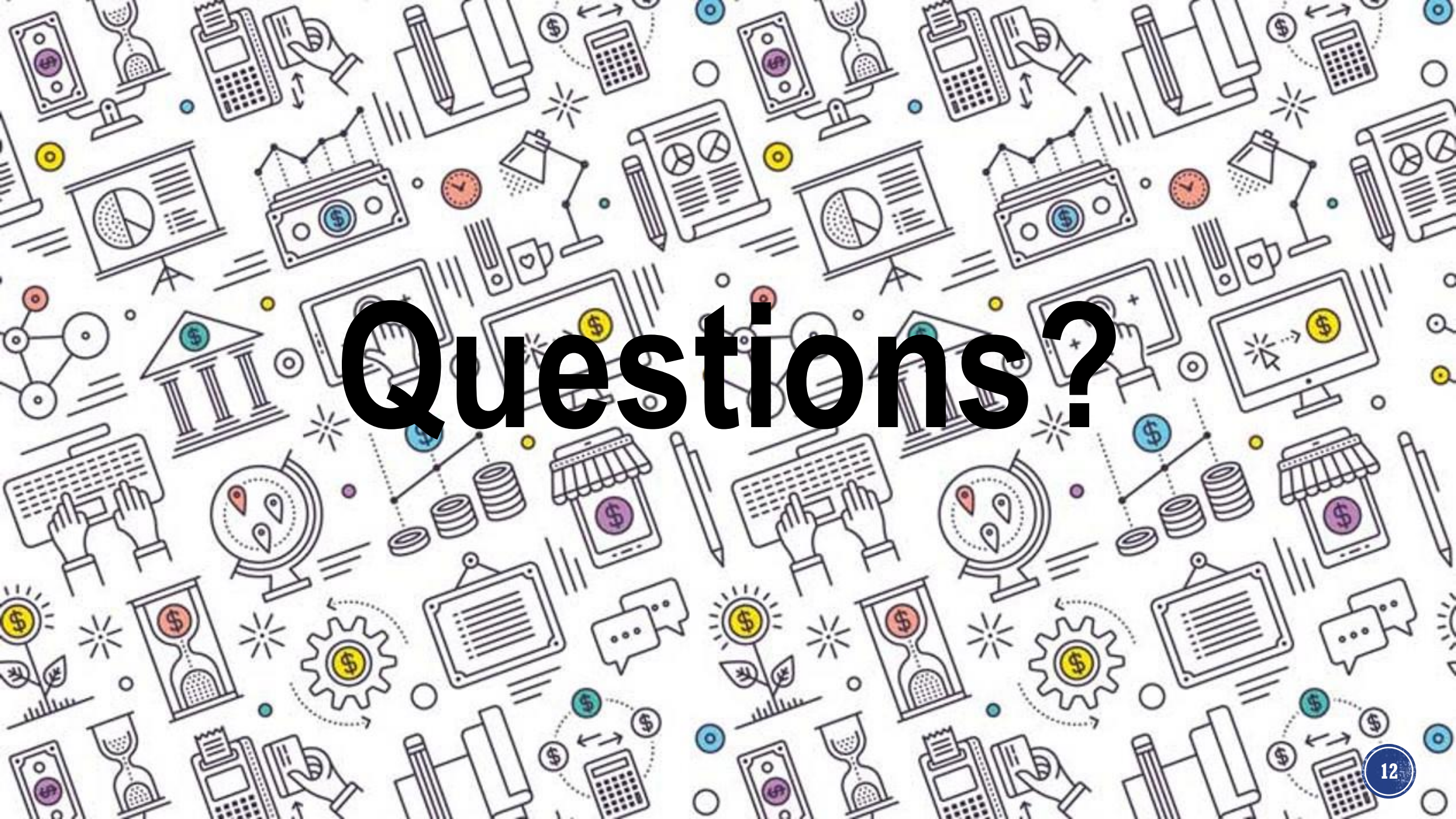


If stress is genetic, offspring will have same stress level as biological parent
If stress is environmental, offspring will have same stress level as foster parent



EPIGENETICS INFLUENCE ON HUMANS




Questions?