GENETICS
Can we Really Blame it all on Our Genes?

Lecture 4:
How Medicine can work with your Genetics to Improve your Care

Thursday, May 19th, 2016

Medical Sciences Building 150

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GENETICS: Can we Really Blame it all on Our Genes? Series Overview

- WEEK 1 (April 28th, 2016):
  Introduction to Genetics

- WEEK 2 (May 5th, 2016):
  How is Genetics Important for your Health?

- WEEK 3 (May 12th, 2016):
  Understanding the Genetics of some Common Diseases and Disorders

- **WEEK 4 (May 19th, 2016):**
  How Medicine can work with your Genetics to Improve your Care

OVERVIEW: How Medicine can work with your Genetics to Improve your Care (Lecture 4)

- Continuation from last week
- Stem cell treatments for Alzheimer's and Parkinson’s Diseases
- Genes Associated with Obesity and Over-eating
- Personalized medicine
- Human Genome Project
- Pharmacogenetics
- Questions

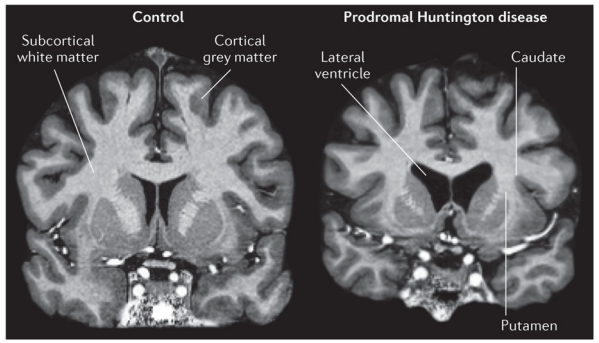
- Alzheimer's Disease
  - Characterized by
    - development of amyloid plaques and neurofibrillary (tau) tangles
    - Loss of connections between neurons in brain
    - Death of nerve cells
  - Both early and late-onset Alzheimer's have genetic components
  - Several Risk genes implicated
    - Apolipoprotein E-e4 (APOE-e4) has the strongest influence (thought to contribute to 20-25% of Alzheimer cases)

- Early- onset familial Alzheimer's Disease (FAD)
  - Occurs at ages 30-60 (less than 5% of Alzheimer's Patients)
  - Child of a carrier parent have 50/50 chance of inheriting mutation
  - Caused by single-gene mutations on chromosome 21, 14 and 1
    - Chromosome 21: formation of abnormal amyloid precursor protein (APP)
    - Chromosome 14: abnormal presenilin 1
    - Chromosome 1: abnormal presenilin 2
  - Mutations breakdown APP (function of protein not fully understood) but generates the harmful amyloid plaques

- Late-onset Alzheimer's Disease
  - Occurs at ages 60+(more common form)
  - Combination of genetic, environmental and lifestyle factors
  - APOE gene on chromosome 19 is a presumed risk factor
  - APOE has several forms (alleles)
    - APOE ε2 (rare). May provide protection against disease
    - APOE ε3 (most common allele). Neutral role , neither increase or decreasing risk.
    - **APOE ε4.** increased risk for Alzheimer's disease and associated with earlier onset of the disease. Person can have 0,1, or 2 APOE4 alleles (more leads to increased Alzheimer's risk)

Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

- Late-onset of Huntington Disease
  - Neurons normally do not replicate
  - Huntington Disease is characterized by accumulation of Huntington protein due to mutation in the gene
  - The overexpression of Huntington protein leads to neurodegeneration



Nature Reviews | Disease Primers

Note:
-Enlarged ventricles

-Atrophy of the basal ganglia and nerve tissue

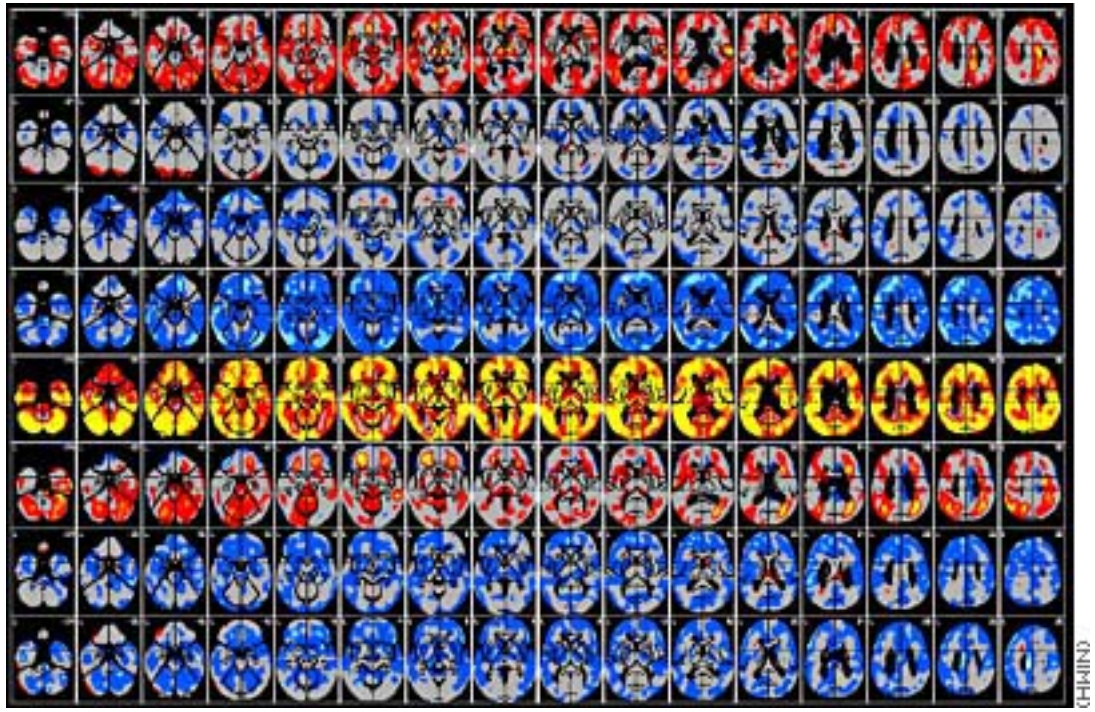
- Stem cell treatment for Alzheimer's and Parkinson's Disease
  - https://www.youtube.com/watch?v=1yCgLythe00
  - Early stages in research but some successful trials on mice
  - Stem cells can be made from patient's skin cells which undergo a chemical transformation
  - Currently Stem Cell research is quite controversial
    - Stem-Cell Challenges in the Treatment of Alzheimer's Disease: A Long Way from Bench to Bedside - Paper

Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

- Genetics of Depression
  - 40% of Depression thought to have a genetic link
  - Parents or siblings with depression are 3X more likely to have the condition

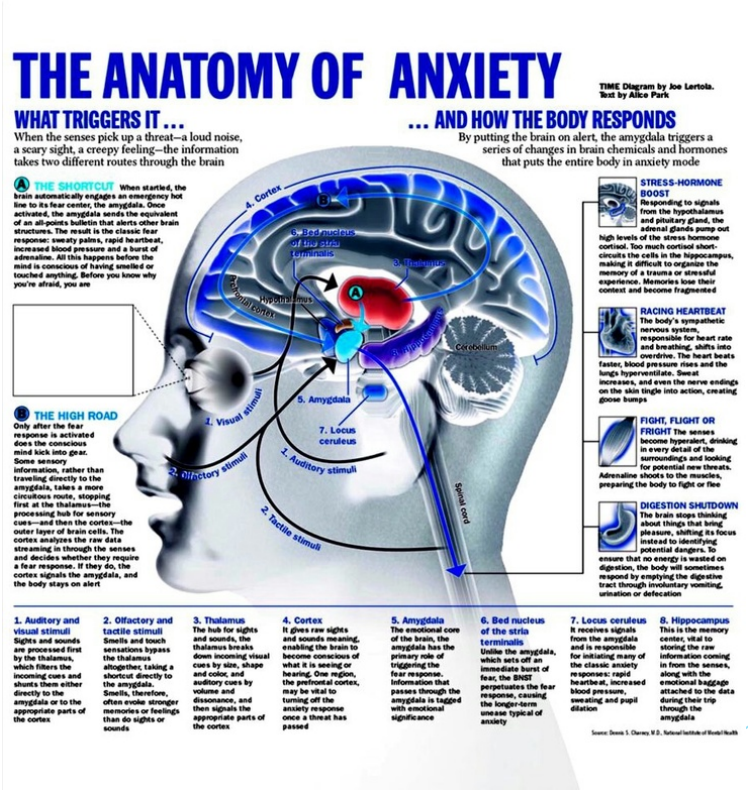
Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

- https://www.youtube.com/watch?v=oREhaoXP8uI



Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

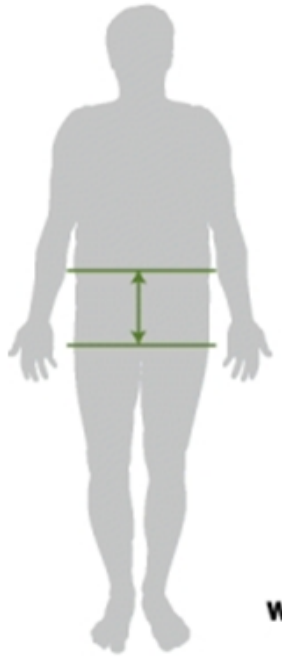
- Genetics of Anxiety
  - Like Depression, some genetic causes but also environmental and lifestyle influences too
  - Around 30-40% of variability related to genetic factors



- SUMMARY
  - Alterations to genes can cause mutations which can lead to dysfunction in the body
  - Variation in both elimination or resistance to certain factors can play a role with disease in organisms
  - Disease and disorders are preventable by supplementation/ bringing the body back to homeostasis
  - There are many diseases and disorders that have a genetic influence, but environmental and lifestyle choices are also implicated

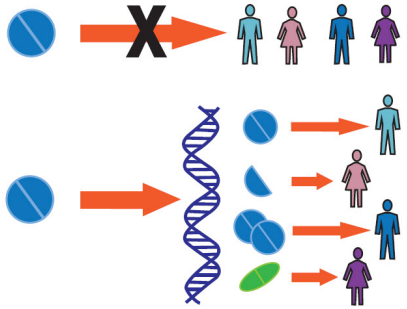
Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

- Genetics of Obesity and Over Eating
  - https://www.youtube.com/watch?v=Ts2qo44aNi4



Gene name	Position	Study
NEGR1	1p31	[36••, 37••]
SEC16B, RASAL2	1q25	[37••]
LYPLAL1, ZC3H11B	1q41	[17••]
SDCCAG8	1q43–q44	[39]
TMEM18	2p25	[36••, 37••, 39]
Near ETV5	3q27	[37••]
Near GNPDA2	4p13	[36••]
TFAP2B	6p12	[17••]
NCR3, AIF1, and BAT2	6p21	[37••]
PRL	6p22.2–p21.3	[38••]
MSRA	8p23.1	[17, 39]
PTER	10p12	[38••]
MTCH2	11p11.2	[36••]
BDNF region	11p14	[37••]
C12orf51/PTPN11	12q24	[53••]
FAIM2, BCDIN3D	12q13	[37••]
NRXN3	14q31	[47]
SH2B1 region	16p11.2	[36••, 37••]
MAF	16q22–q23	[38••]
FTO[a]	16q22.2	[29••, 30, 35••–38••, 39]
NPC1	18q11.2	[38••]
MC4R[b]	18q22	[35••–38••, 39, 40••]
KCTD15	19q13.11	[36••, 37••]

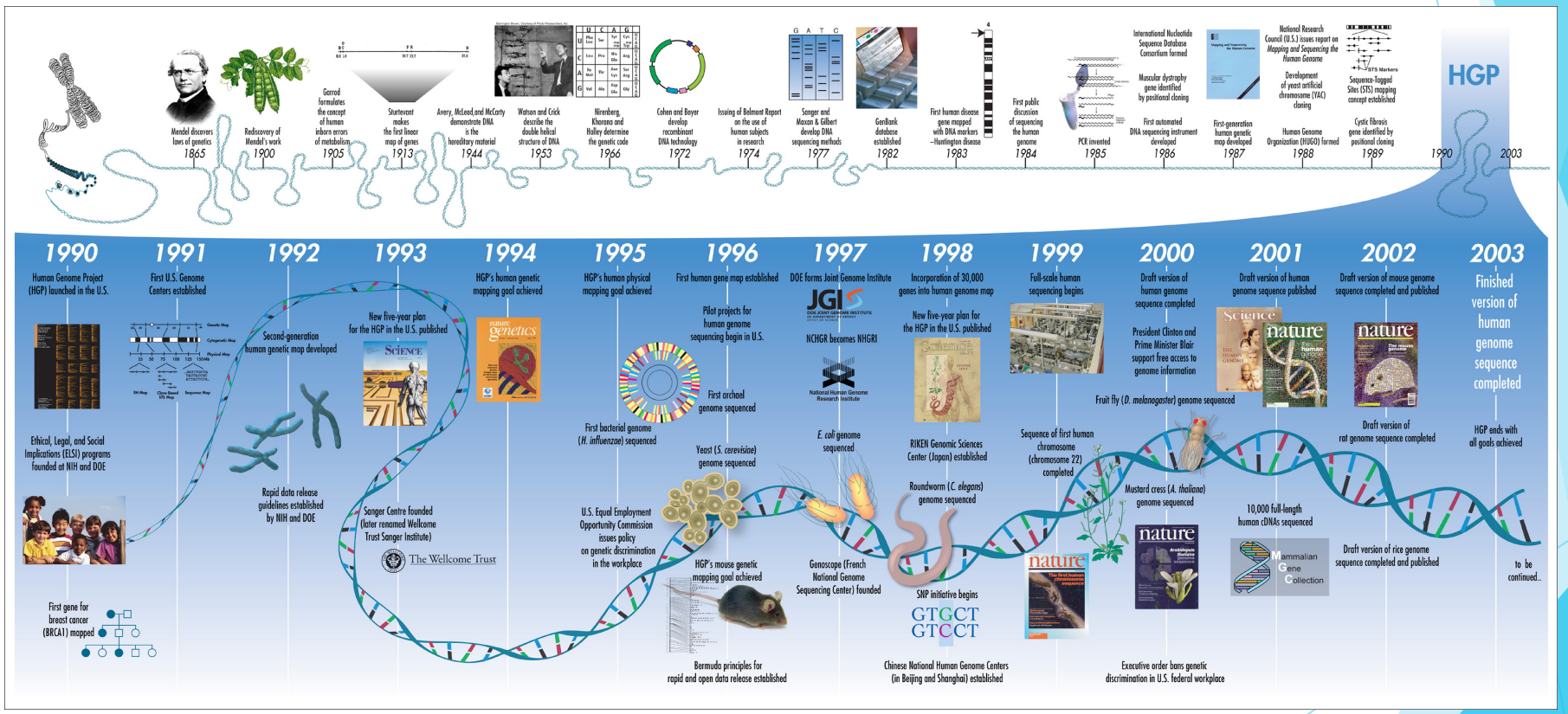
- Personalized Medicine
  - Definition: Separates patients into different groups
  - Medical practices are tailored to accommodate for the unique needs of the individual
  - based on their predicted response or risk of disease
  - Dates back as far as Hippocrates, where the professional was expected to treat the patient rather than the disease (create a remedy suitable for the person)



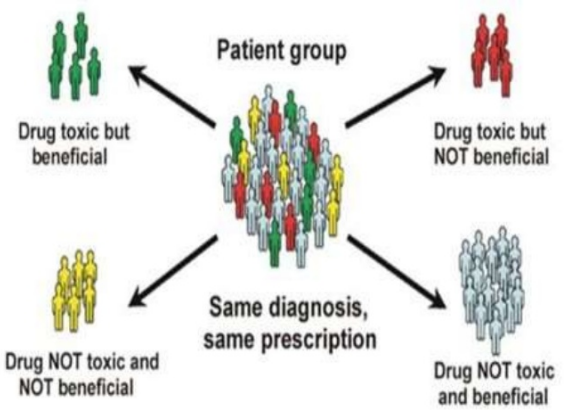
- The Human Genome Project
  - International research effort
    - Goal to sequence and map all the genes that comprise the complete genome of humans
  - Completed in April 2003
  - Allows comprehension of the human “blueprint”
    - Personalized medicine utilizes the data to highlight trends that occur throughout the species
    - Diagnosis and treatment of genetic diseases occurs more quickly and efficiently due to availability of information

Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

- https://www.youtube.com/watch?v=MvuYATh7Y74

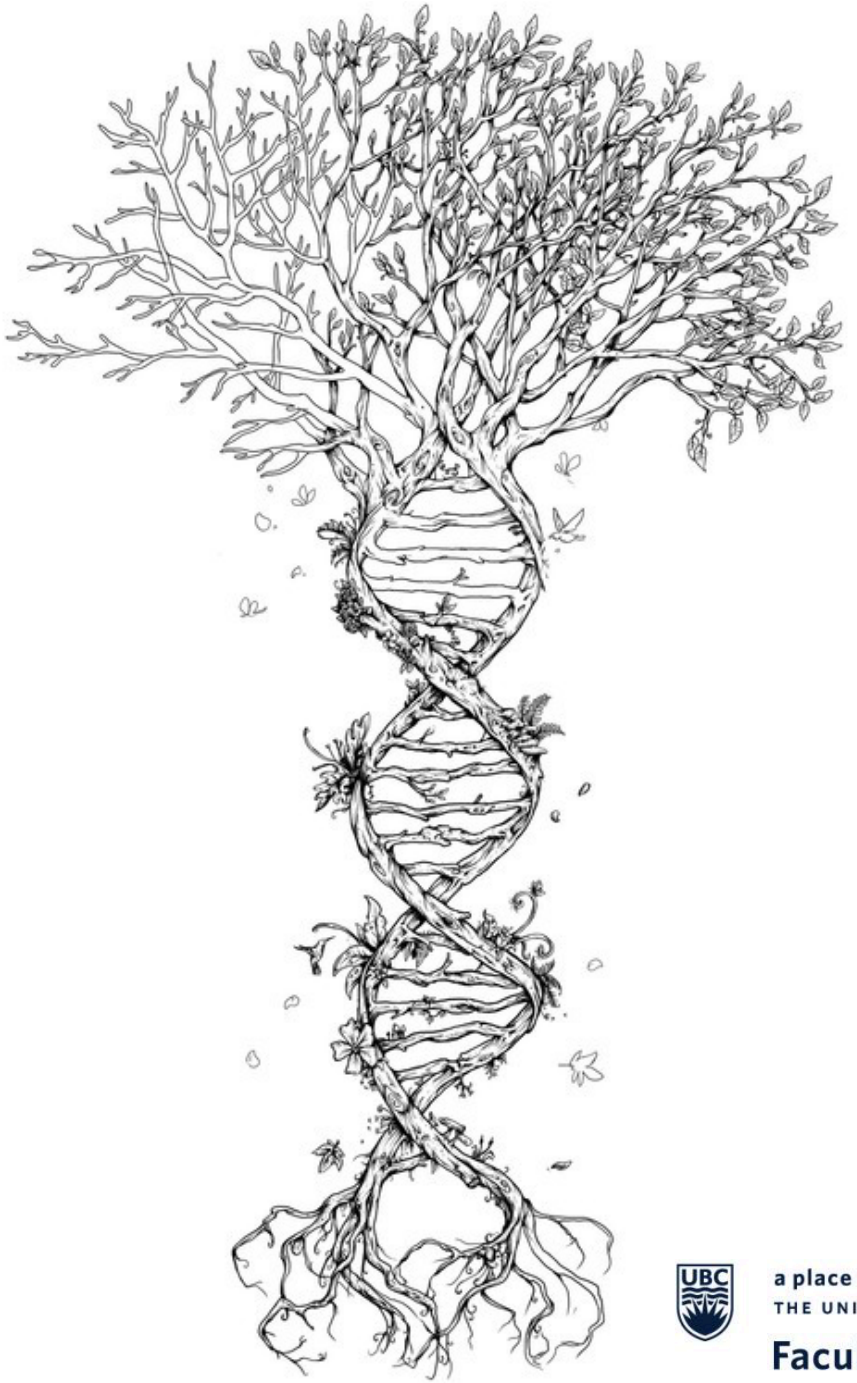


- Pharmacogenomics
  - Study of inherited genetic differences in drug metabolites and pathways affect patient's responses to drugs
  - Combines pharmacology (science of drugs) ad genomics (study of genes and their function)
  - Therapeutic effect: Consequence of the medical treatment, where the results are thought to be desirable
  - Adverse effect: Harmful or undesirable effect (Also known as side effect)
  - https://www.youtube.com/watch?v=fGjG_9EEeeA



- SUMMARY
  - Large variation seen in individuals due to genetic differences (as well as lifestyle and environmental factors)
  - Personalized medicine treats the PATIENT uniquely rather than the disease characteristics alone
  - Trends studied throughout the past, including the Human Genome Project, allow for correlation and a set point when helping an individual
  - Pharmacogenetics is the study of drugs used specifically for certain individuals and is used to predict the outcome of certain therapies and their effectiveness

QUESTIONS?



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