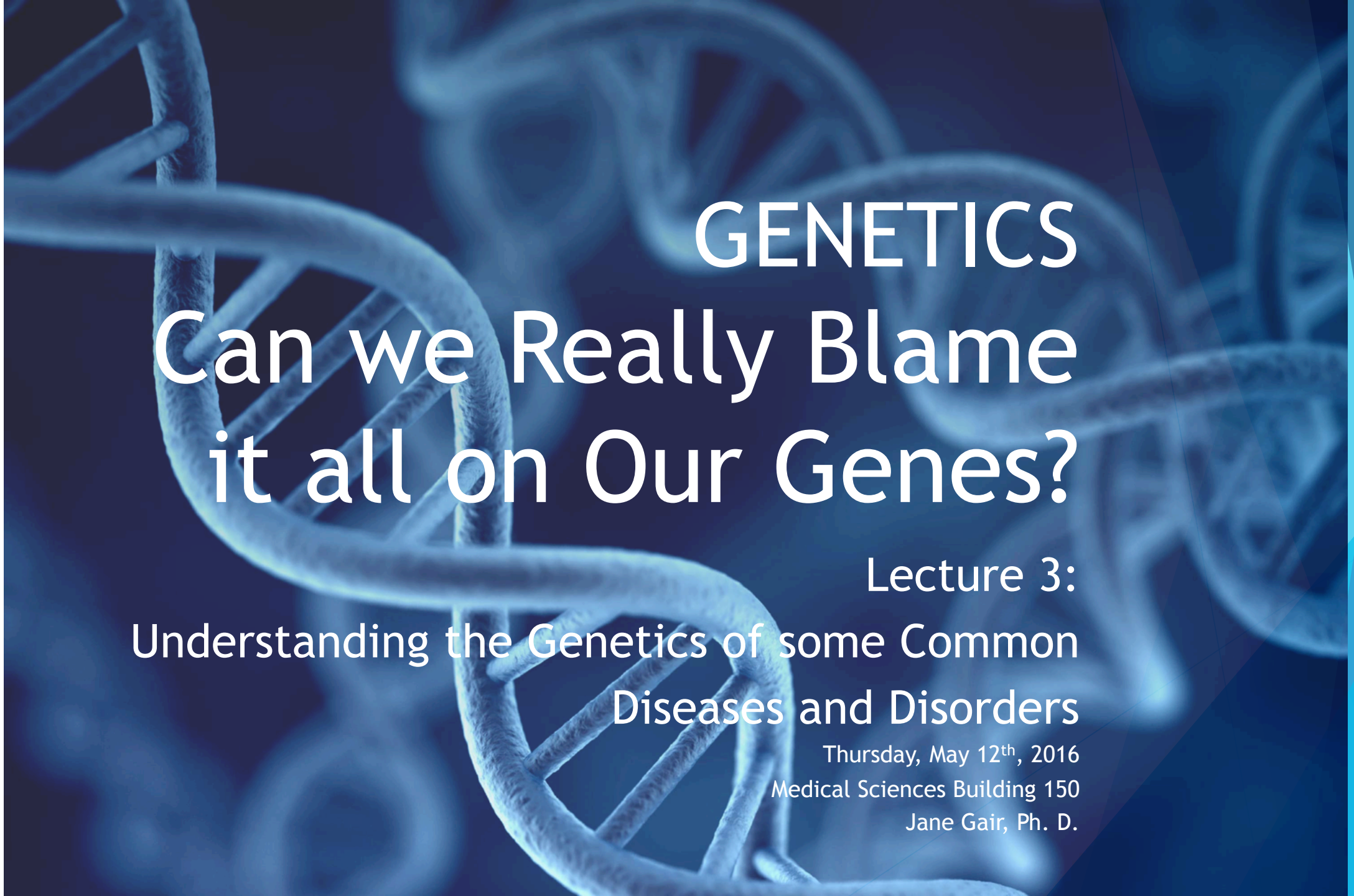


GENETICS
Can we Really Blame it all on Our Genes?

Lecture 3:
Understanding the Genetics of some Common Diseases and Disorders

Thursday, May 12th, 2016

Medical Sciences Building 150

Jane Gair, Ph. D.

Upcoming Let's Talk Science MEDS Seminar

LIVE AND LET DIE:
An explanation of physician-assisted suicide in Canada

Let's talk science with med students at UVic

- What does the Supreme Court of Canada 2015 ruling say?
- What does the current proposed legislation say?
- Which other countries have a physician assisted suicide law?

Join first-year Island Medical Program students **Sergiy Shatenko, Samuel Harder** and **Andrew Watters** to learn the answers to these questions.

Tuesday, May 17 @ 7:00 pm
Medical Sciences Building Room 150

Refreshments available | This is the latest in a series of medical student presentations
More information: Dr. Jane Gair - jgair@uvic.ca

a place of mind THE UNIVERSITY OF BRITISH COLUMBIA Faculty of Medicine | University of Victoria | let's talk science

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

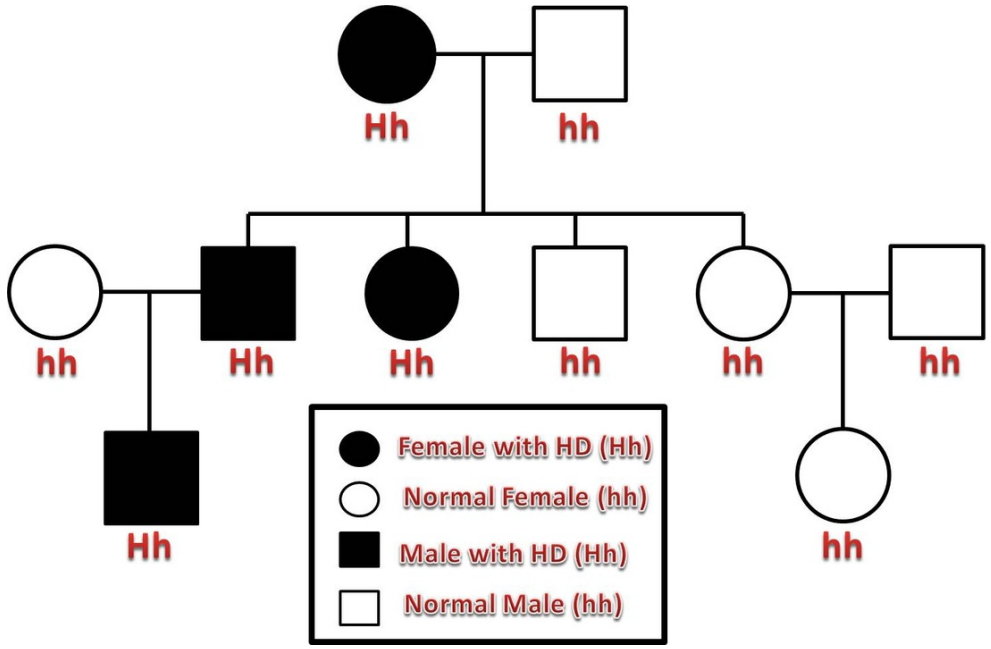
- Continuation from last week
- Genetics of diabetes
- Cancer
- Genetics of Alzheimer's and Huntington Disease
- Depression
- Anxiety

How is Genetics Important for your Health? (Lecture 2)

HUNTINGTON DISEASE - Video **(2:10 mins)**

https://www.youtube.com/watch?v=JL9Y3P870jU

PEDIGREE:



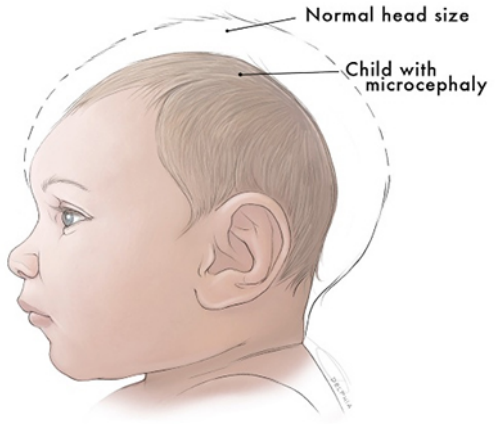
Huntington Disease (Continued)

- Results from a dominant mutation
- All heterozygotes develop the neurological disease (50% Probability Risk)
- Affects patients in their middle age
- Offspring have 50% probability of inheriting disease allele
- Block of huntingtin cleavage by caspase IX will treat Huntington disease (cleaved peptides are highly neurotoxic)

How is Genetics Important for your Health? (Lecture 2)

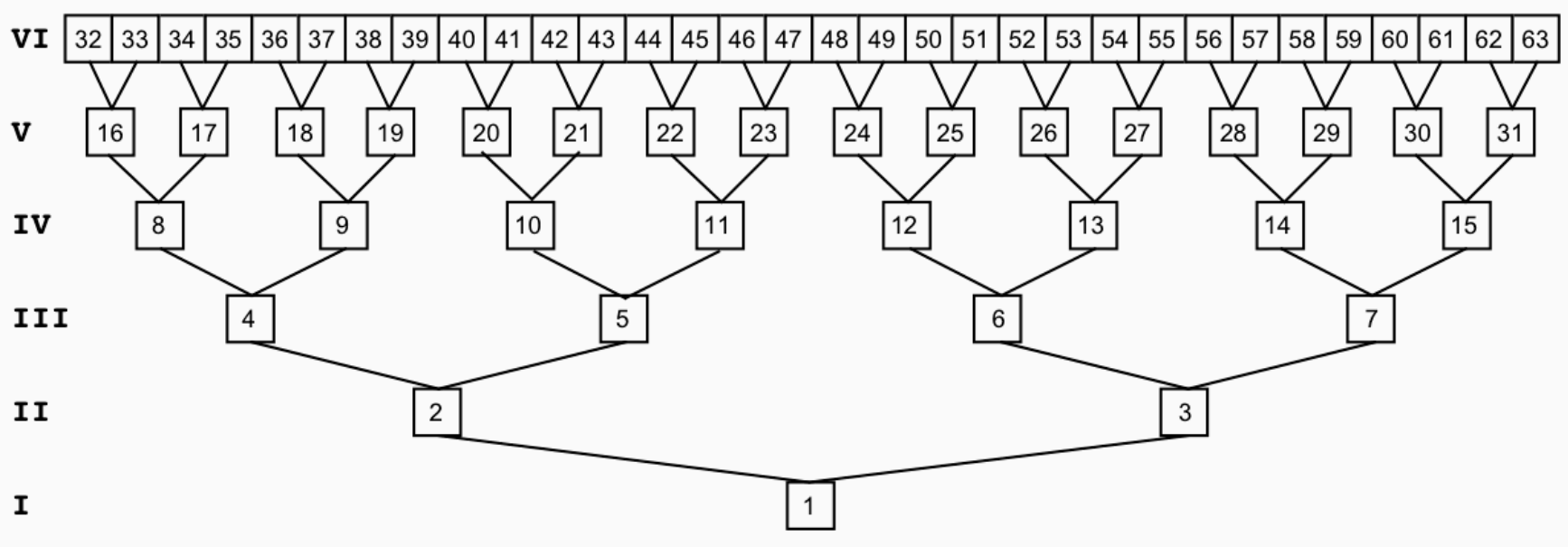
Inheritance of Zika Virus- Present day disease concerns

- Heritability of Zika virus not fully understood yet
- Known to cause disruptions in fetal development
- Instances of Microcephaly reported
- http://www.bbc.com/news/world-latin-america-36184799



How is Genetics Important for your Health? (Lecture 2)

[Understanding Pedigrees – Video (6 mins) https://www.youtube.com/watch?v=Ir1t9awmUl4]



How is Genetics Important for your Health? (Lecture 2)

- **Importance of Family Medical History Records**
  - **Powerful screening tool**
  - **Allows for faster diagnosis of genetic diseases**
  - **Should be updated each visit**
  - **Family History for Prenatal Providers**
    - **Address family history**
    - **Improved health for female patient, fetus and family**
  - **Helps investigate genetic predisposing factors that are associated with the health of the individual**

- **Importance of Family Medical History Records**
  - **Should include at least three generations**
  - **Questions include:**
    1. **General information (names and birthdates)**
    2. **Family's origin or racial/ethnic background**
    3. **Health Status**
    4. **Age at death and cause of death of each member**
    5. **Pregnancy outcomes of the patient and relatives**
  - **Formation of Pedigrees to analyze possible risk factors (certain characteristics of the individual that ↑ likelihood of disease)**

How is Risk Calculated?

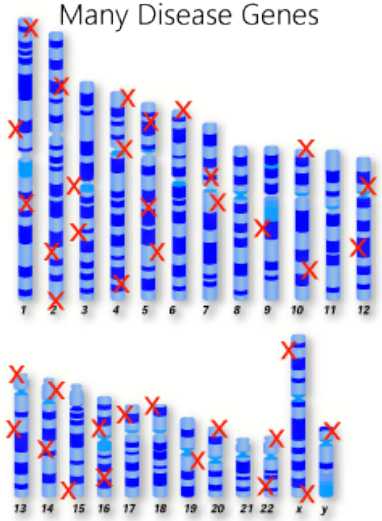
Simple Disease

Risk is easy to calculate for rare disorders caused by a single gene.

Single Disease Gene

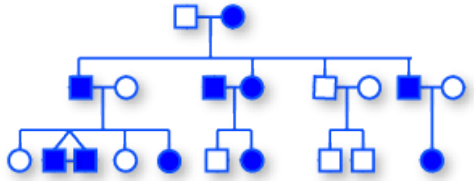
Complex Disease

Many Disease Genes



But for complex diseases that are influenced by multiple genes, risk is much more difficult to calculate.

Complex Disease Family Pedigree



Risk must be estimated based on observation of data collected from large families affected by these diseases.

How is Genetics Important for your Health? (Lecture 2)

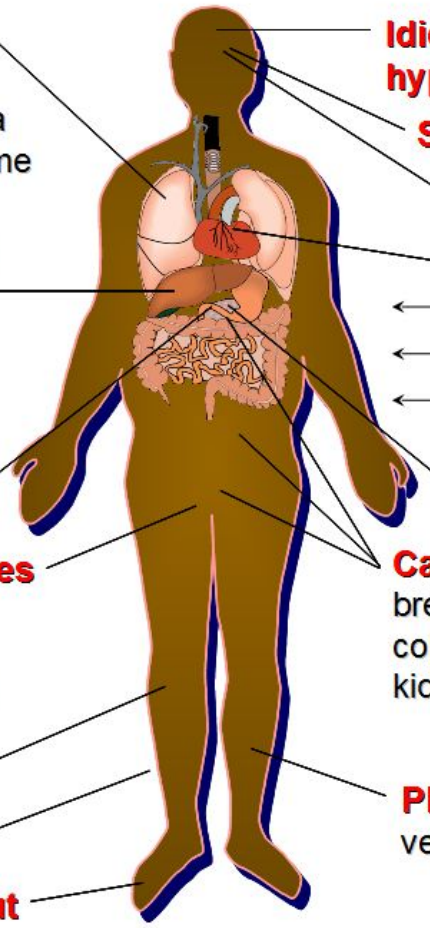
- **Record-keeping strategies are becoming more advanced**
  - **23andMe project reports genetic health, traits and ancestry for individuals for less that $300 CAD**

  - **The Genographic project by National Geographic is tracing human history**
    - https://www.youtube.com/watch?v=MdTCj9tC1Pw

How is Genetics Important for your Health? (Lecture 2)

- Diseases are not only caused by genetics
  - DIET can alter predisposition to impair health
    - Provides nutrients that the body requires
    - Lack of well-nourishing diet leads to increased risk from chronic disease
  - EXERCISE
    - Works synergistically with poor diet
    - Sedentary lifestyle in combination with diet and high stress are the main causes for obesity and type 2 diabetes in North America

Medical Complications of Obesity



Pulmonary disease
abnormal function
obstructive sleep apnea
hypoventilation syndrome

Nonalcoholic fatty liver disease
steatosis
steatohepatitis
cirrhosis

Gall bladder disease

Gynecologic abnormalities
abnormal menses
infertility
polycystic ovarian syndrome

Osteoarthritis

Skin

Gout

Idiopathic intracranial hypertension

Stroke

Cataracts

Coronary heart disease

Diabetes

Dyslipidemia

Hypertension

Severe pancreatitis

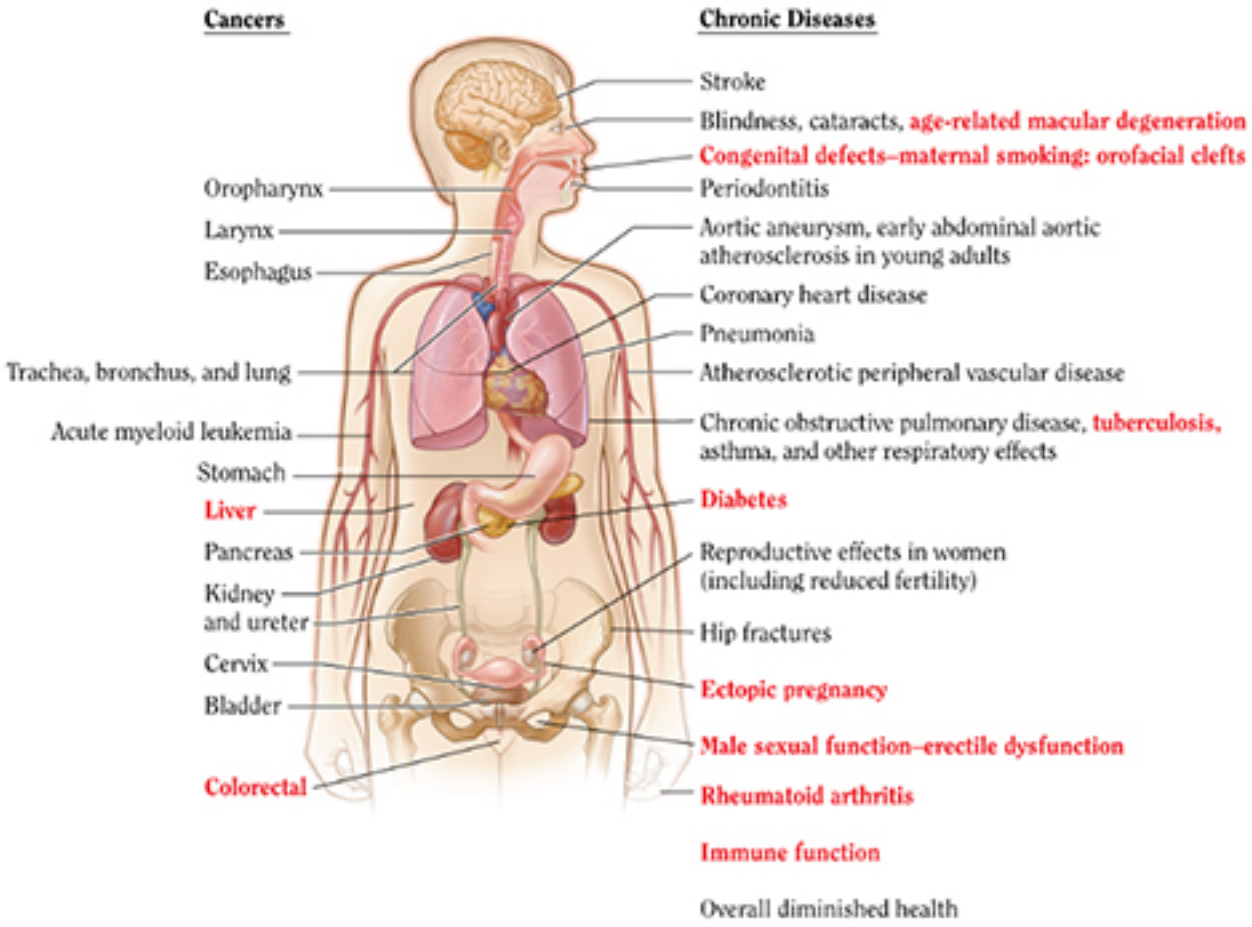
Cancer
breast, uterus, cervix
colon, esophagus, pancreas
kidney, prostate

Phlebitis
venous stasis

How is Genetics Important for your Health? (Lecture 2)

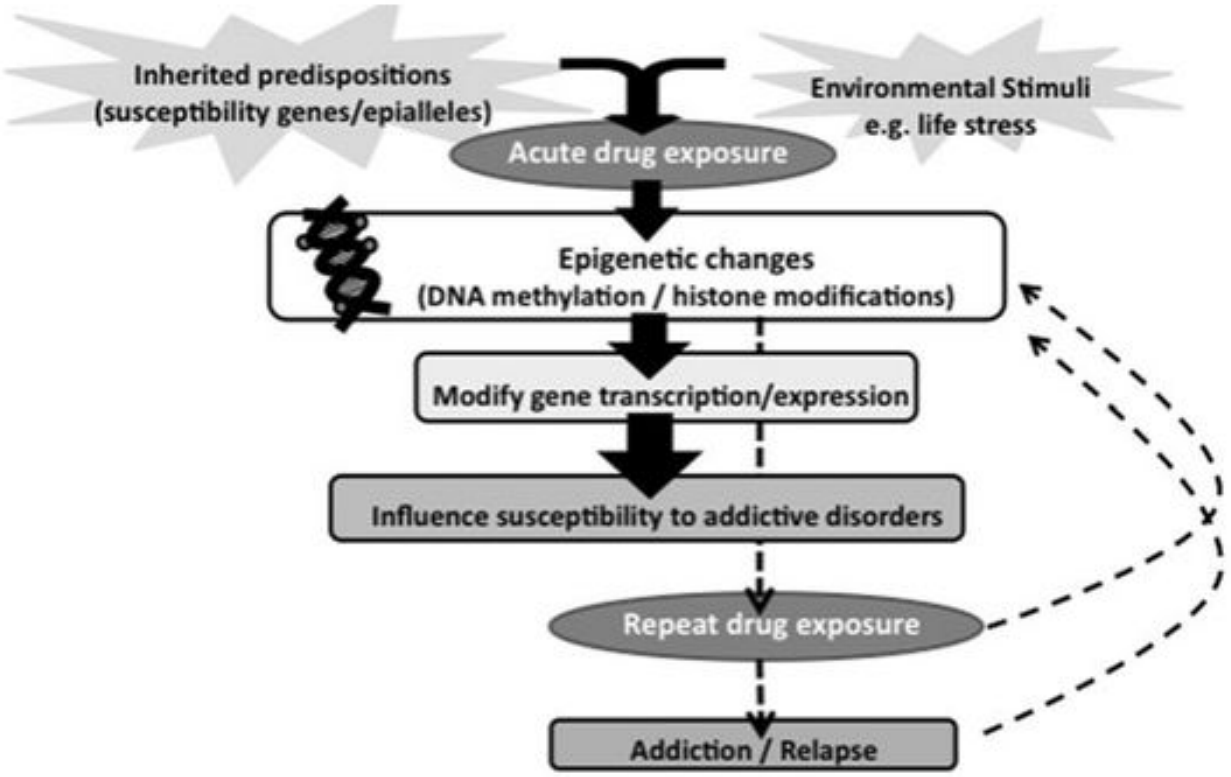
- **LIFESTYLE CHOICES**
  - **Proper diet and exercise are crucial for good health, but other factors also influence health**
  - **Introducing substances into your system can drastically impact health**
    - **Smoking ↑ risk of many fatal diseases**
    - **LACK OF SLEEP can lead to obesity, diabetes, heart disease and hypertension**

Impact of Smoking on Health



How is Genetics Important for your Health? (Lecture 2)

- **ADDICTION INHERITANCE**
  - https://www.youtube.com/watch?v=dvnJhtw15HA

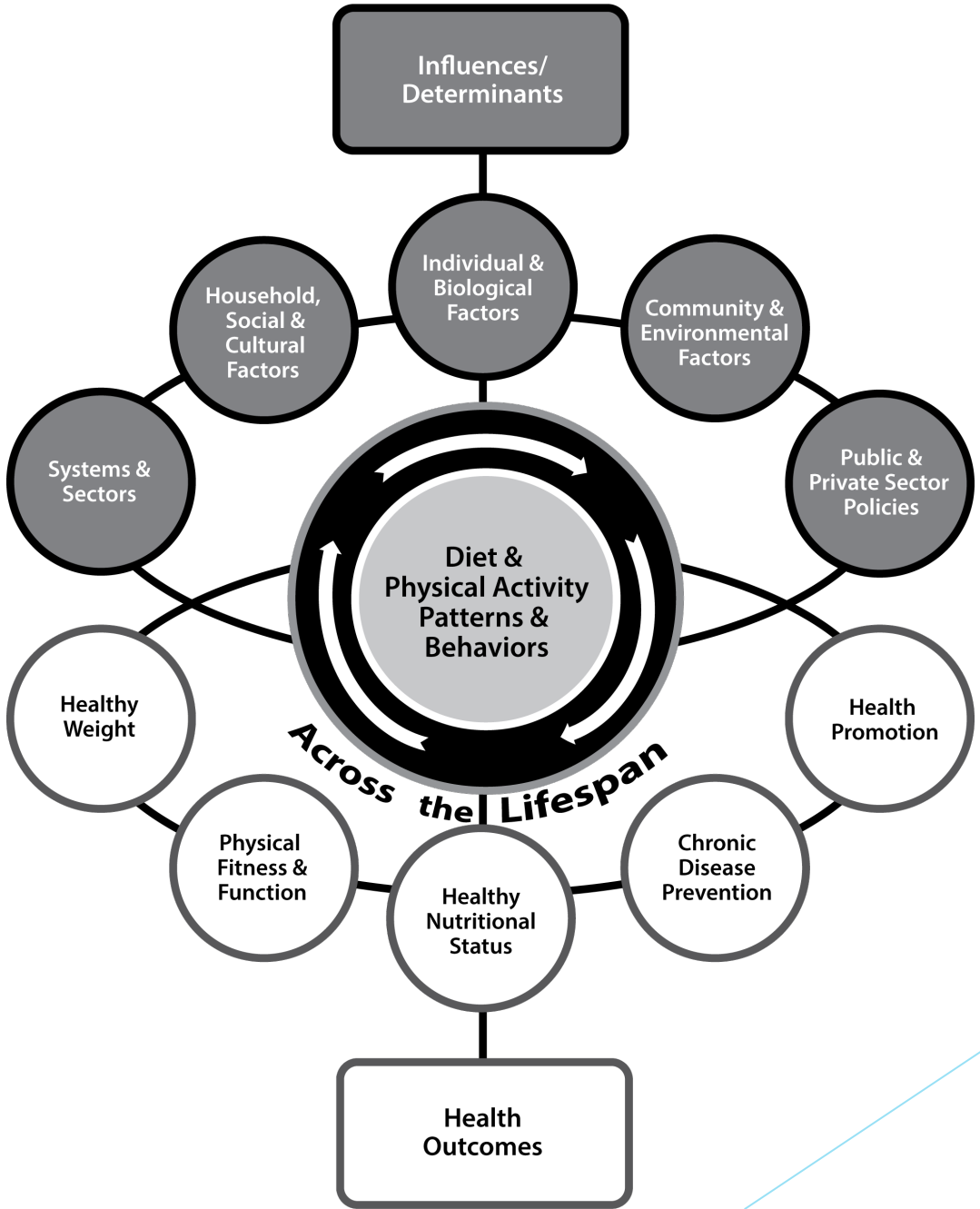


How is Genetics Important for your Health? (Lecture 2)

- **A healthy life involves all factors discussed (exercise, diet and lifestyle choices)**

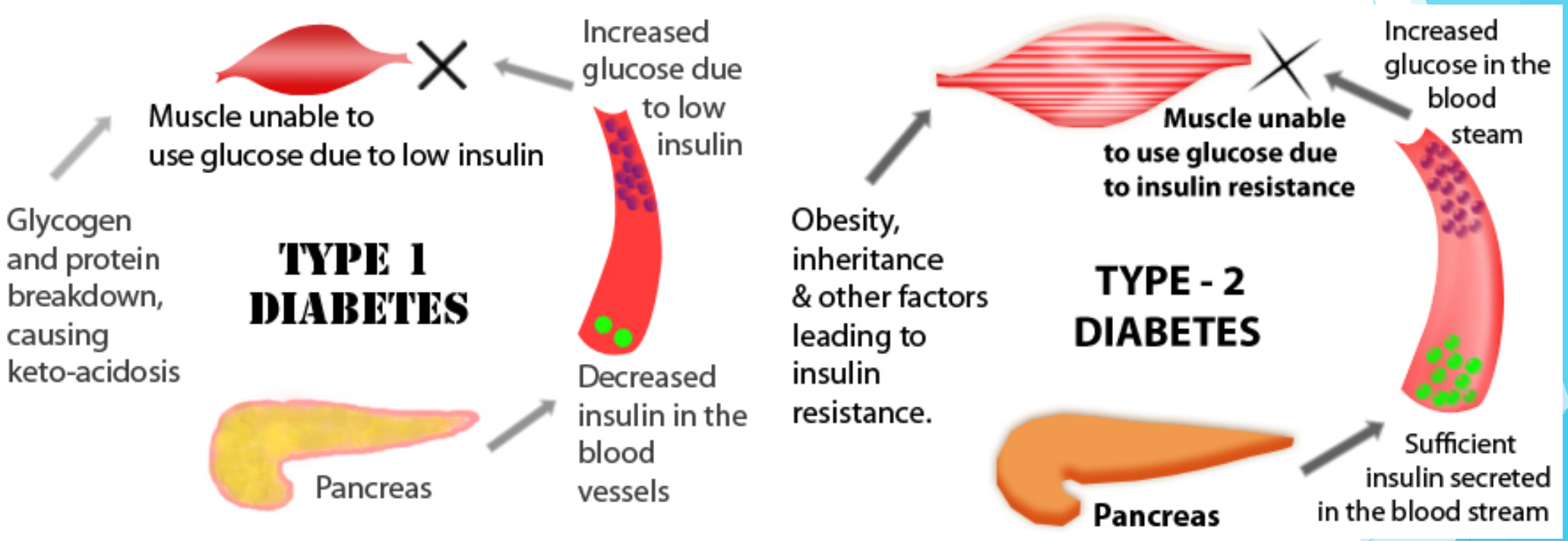
- **Also requires a balance of nourishing aspects: physical, social, emotional, mental and spiritual engagements.**

Diet and Physical Activity, Health Promotion and Disease Prevention at Individual and Population Levels across the Lifespan



- SUMMARY
  - Mutations can be beneficial for an organism, but can also cause changes that lead to abnormalities and disease
  - Family history and formation of pedigrees allows for an analysis of possible risk factors
  - Genetic, as well as environmental factors contribute to the alteration of genes and overall health
  - Different forms of inheritance results in disease phenotype but sometimes traits are silenced in some generations (reiterates the importance of family history-taking)

- Genetics of Diabetes Mellitus
  - Two types of Diabetes:
    - Type 1: Insulin-dependent diabetes
      - Pancreas produces little to no insulin
      - Factors contributing include **genetics** or exposure to viruses
    - Type 2: Insulin-resistant diabetes
      - Body becomes resistant to insulin or does mot make enough
      - Usually caused by lack of physical activity and obesity
      - Even MORE likely to have a **genetic** component

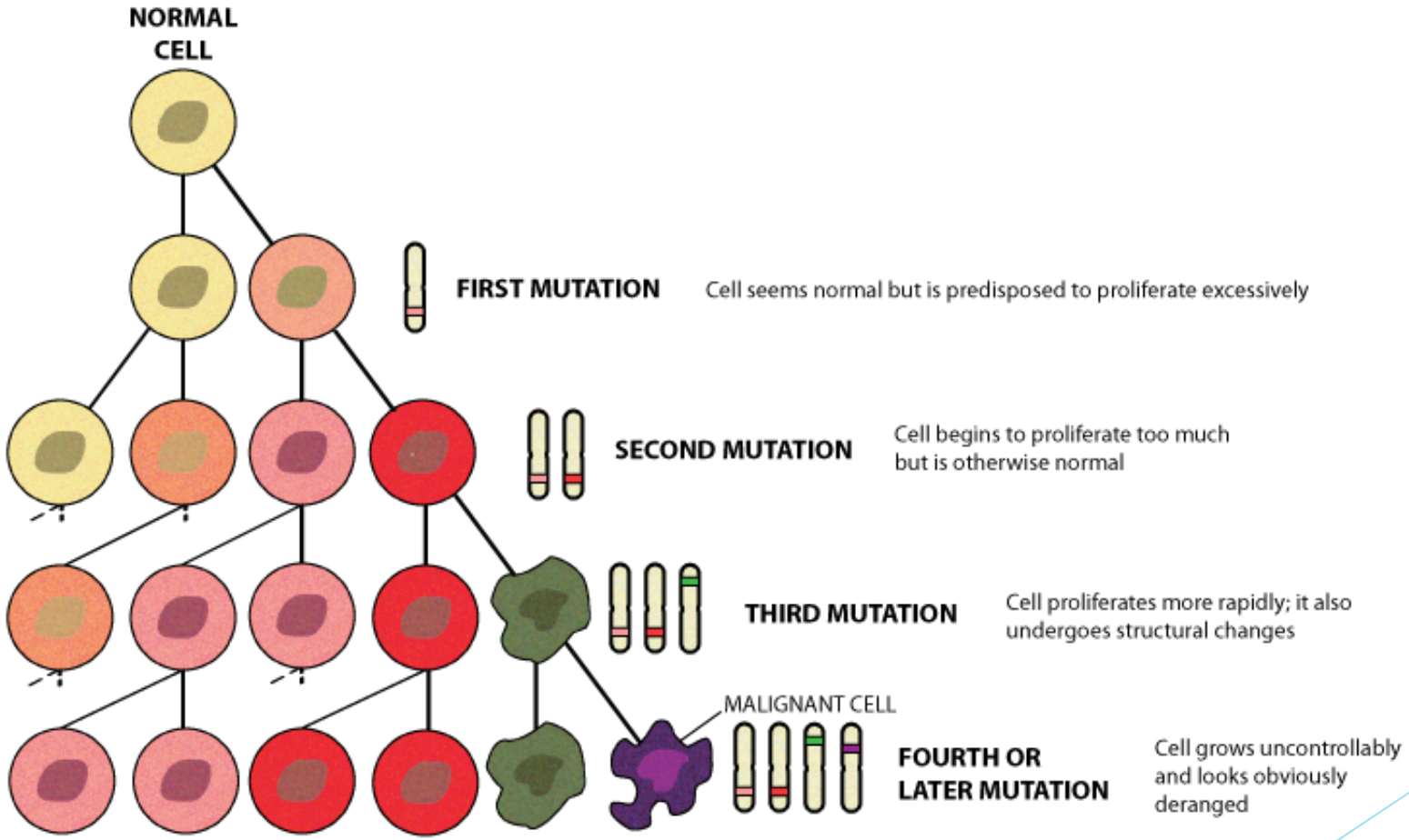

Muscle unable to
use glucose due to low insulin
Increased
glucose due
to low
insulin
Glycogen
and protein
breakdown,
causing
keto-acidosis
TYPE 1
DIABETES
Pancreas
Decreased
insulin in the
blood
vessels
Obesity,
inheritance
& other factors
leading to
insulin
resistance.
Muscle unable
to use glucose due
to insulin resistance
Increased
glucose in the
blood
steam
TYPE - 2
DIABETES
Pancreas
Sufficient
insulin secreted
in the blood stream

- Treatments for Diabetes
  - Mostly regulatory initiatives taken by most patients (administration of insulin)
  - Some treatments appearing
    - Pancreatic Islet transplants (leads to secretion of insulin from Beta cells in the Islet) for Type 1 Diabetes
    - Still expensive and not available to everyone, but progress in the right direction
  - https://www.youtube.com/watch?v=sRxqRU6CCJA

- Genetics of Cancer
  - Cancer is a disease caused by malignant tumour cells which spread to one or many parts of the body
  - Changes in DNA cause mutations and these mutations can lead to the formation of cancer cells
  - It is known that several oncogenes exist
    - Oncogene: gene that has the potential to cause cancer
    - Some common proto-oncogenes include Ras (rat sarcoma), WNT, MYC, ERK and TRK

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

- https://www.youtube.com/watch?v=zLRqu9HhVtA



- 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

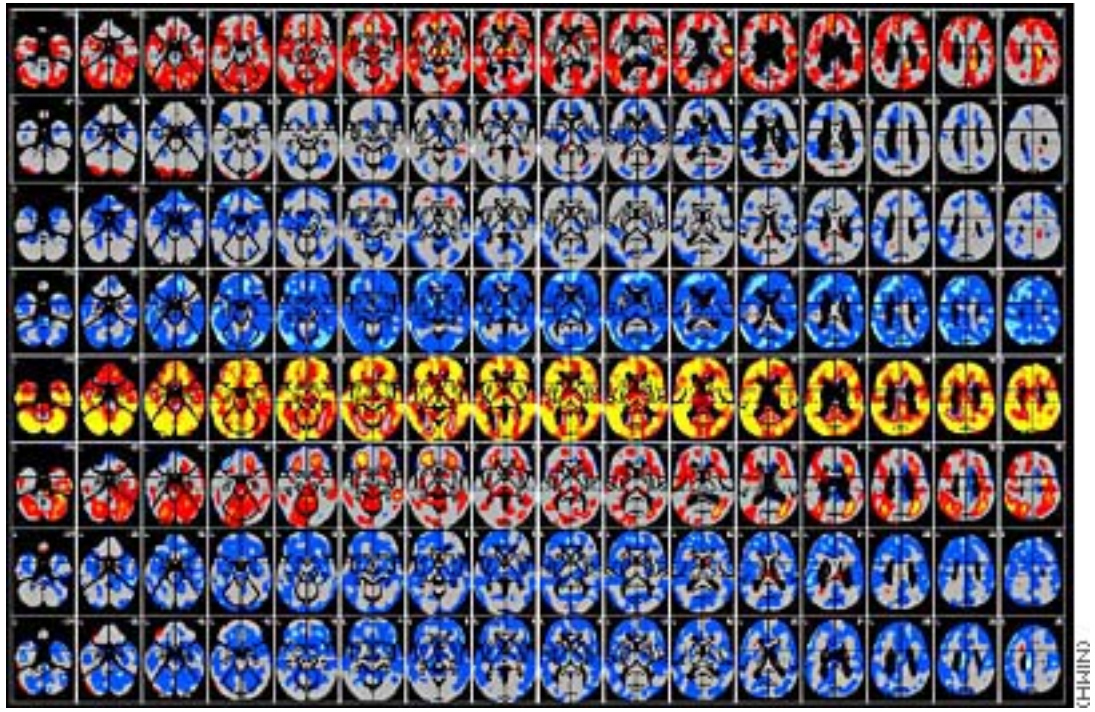
- Late-onset Alzheimer's Disease
  - Occurs at ages 60+(more common form)
  - Combination of genetic, environmental and lifestyle factors
  - APOE gene on chromosome 19 is a presumed risk factor
  - APOE has several forms (alleles)
    - APOE ε2 (rare). May provide protection against disease
    - APOE 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)

- 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

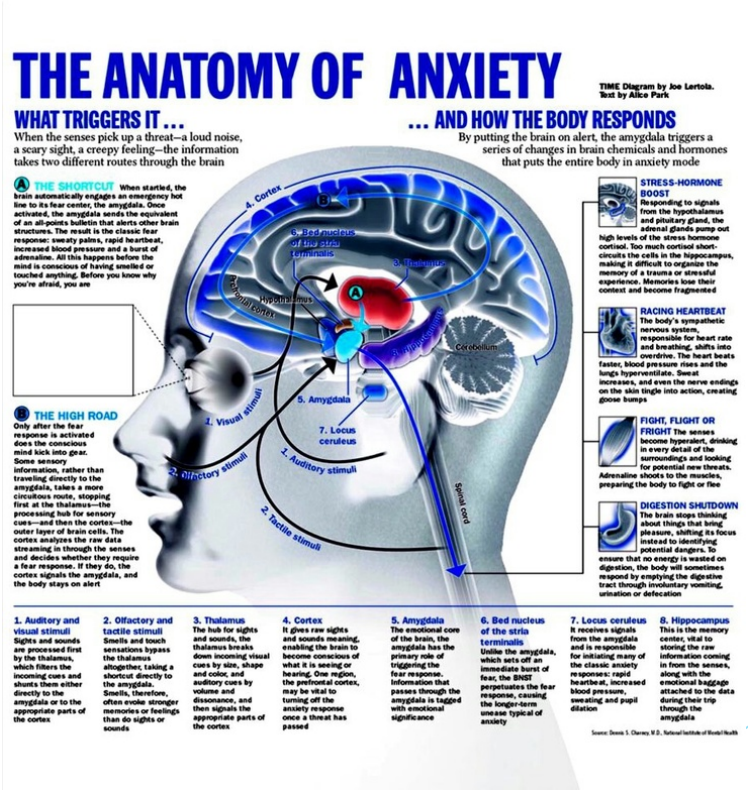
Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

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



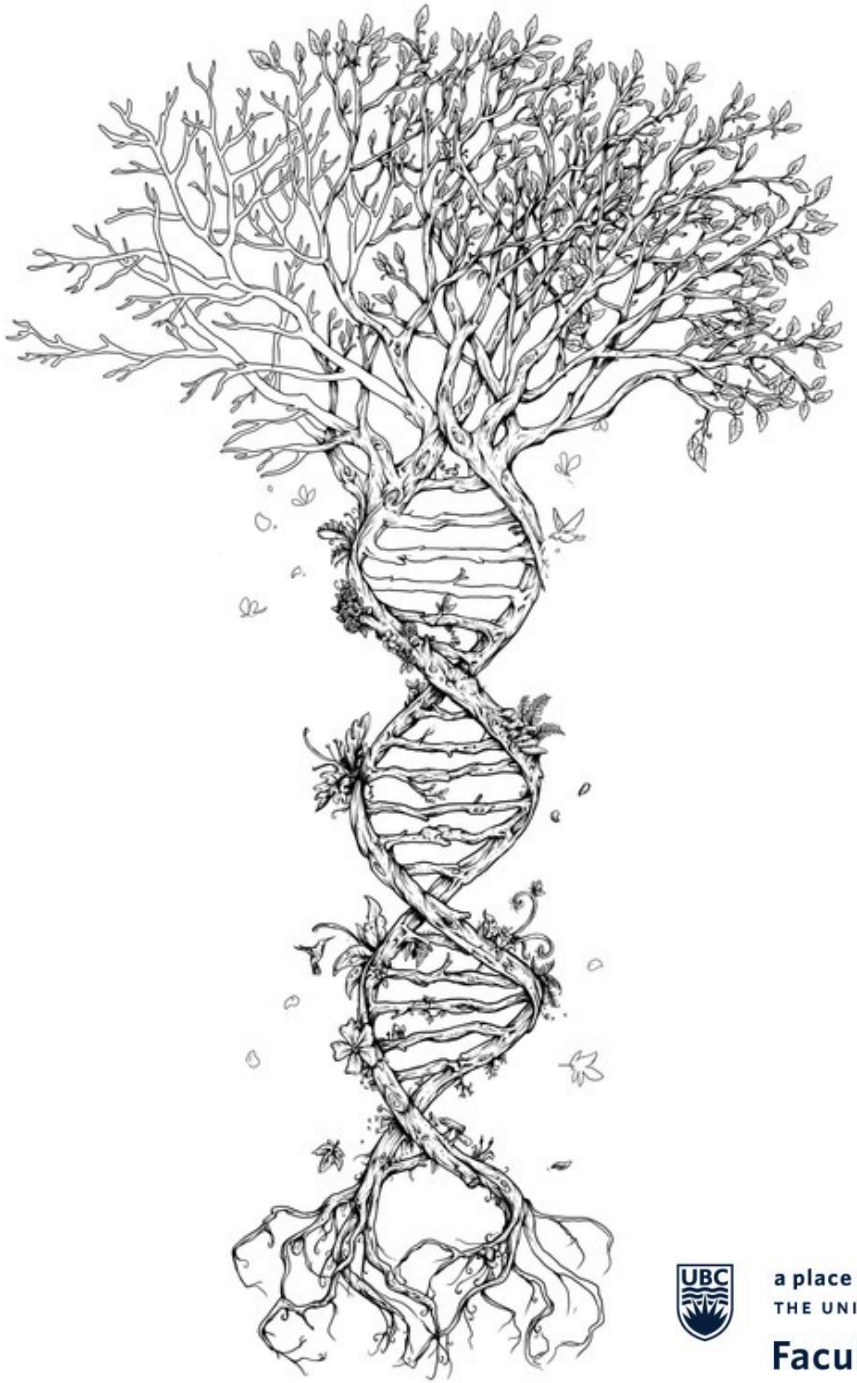
Understanding the Genetics of some Common Diseases and Disorders (Lecture 3)

- 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

QUESTIONS?



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