# Genetics: A Study Coming Soon to You!

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ACCELERATING RESEARCH. IMPROVING HEALTH.

# My Study Doesn't Include Genetics, Why Should I Care?

i. Currently ubiquitous in studies; expect explosive expansion

ii. Challenges, cautions and considerations in consenting research participants

iii. Implications and use of genetic samples and data for sharing and dbGaP

iv. Cautionary considerations for risks and return of genetic results

v. Keeping things real: managing participants' expectations

# Published Conditions Found to Have Inherited Influence

## Your environment changes your IQ on a genetic level

Kaminski, JA, et al Epigenetic variance in dopamine D2 receptor: a marker of IQ malleability? Translational Psychiatry 8/2018 volume 8, Article number, 169.

## Fondness for napping could be your genes

Honda, T, et al. A single phosphorylation site of SIK3 regulates daily sleep amounts and sleep need in mice. Proceedings of the National Academy of Sciences,PNAS 25, 2018 10.1073/pnas.1810823115.

## Genes responsible for Periodic Limb Movements

Stefansson, H. et al. Genetic Risk Factor for Periodic Limb Movement in sleep. N Engl J Med 2017; 357:639-647.

## Genetic link between schizophrenia and cannabis use

Joelle A. Pasman, et al. GWAS of lifetime cannabis use reveals new risk loci, genetic overlap with psychiatric traits, and a causal influence of schizophrenia. Nature Neuroscience volume 21, pages1161–1170 (2018).

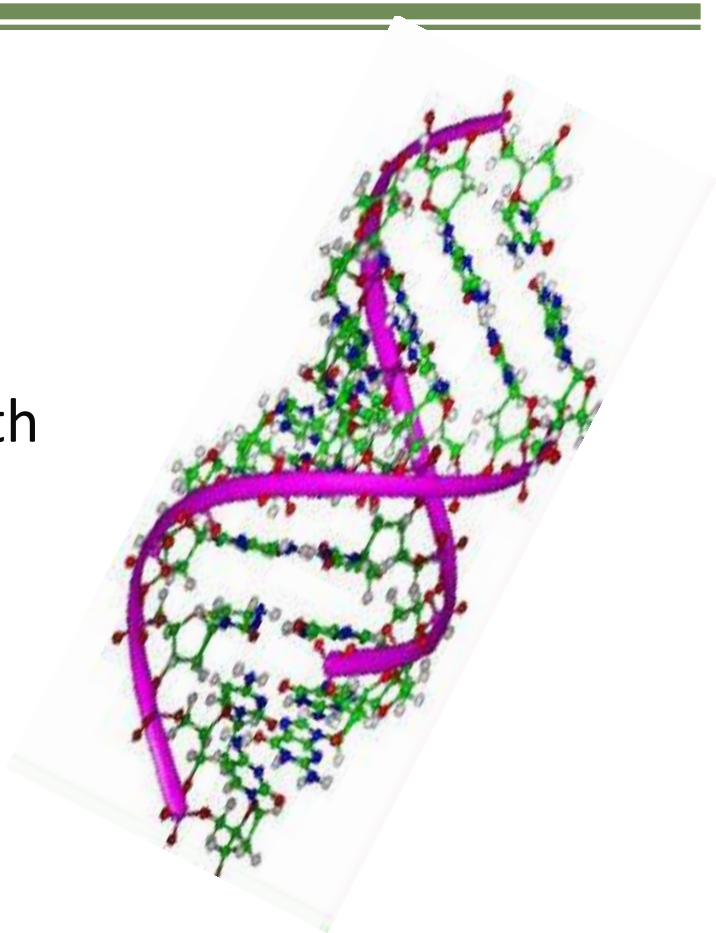
# Topics Currently Studied at UW Thought to Have Inherited Influences

Who would have guessed…….?

- Autistic attention getters
- Laziness, levels of self-control
- Visits to the ER, number of car crashes
- Ability to play a musical instrument
- Adaption to prosthetic limbs
- Sneezing at bright light
- Tolerance to pain, spicy foods
- Age of first sexual encounter

# Poll

- How many are working on a study involving genetics?
- How many are working on a study with no genetic involvement?
- What research target is your study investigating?



# Genetic Cliff Notes

**DNA** Inherited material that directs growth, development, functioning and reproduction for all living organism

**RNA** directs the assembly of proteins

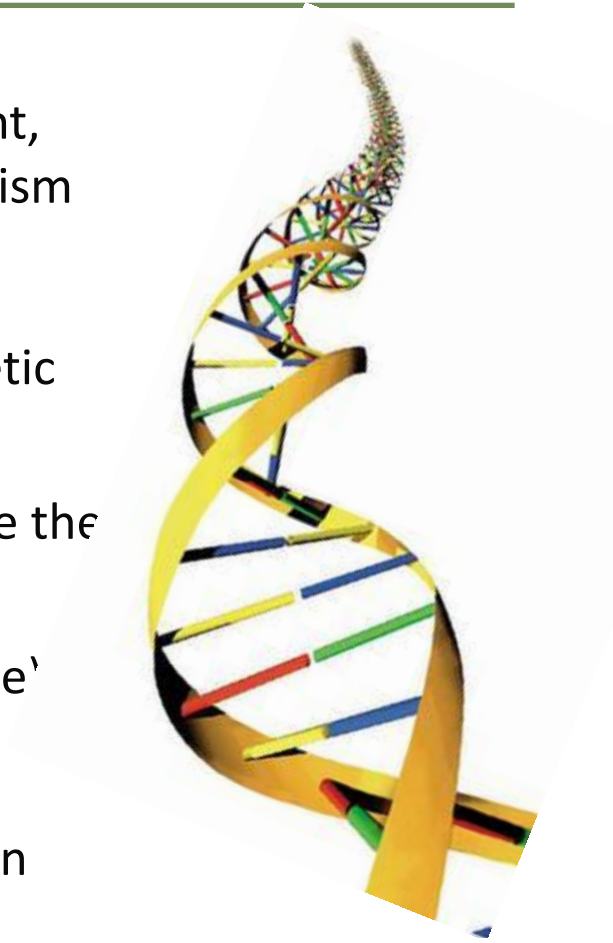
**Chromosome** 23 pairs of DNA molecules storing all genetic material of an organism (46 total)

**Nucleotide** "A,T,G,C" molecules when linked together are the building blocks of DNA or RNA

**Base pairs** A (adenine) pairs with T (thymine); G (Guanine) Pairs with C (cytosine)

**SNP** (Single Nucleotide Polymorphism) single variation on a gene

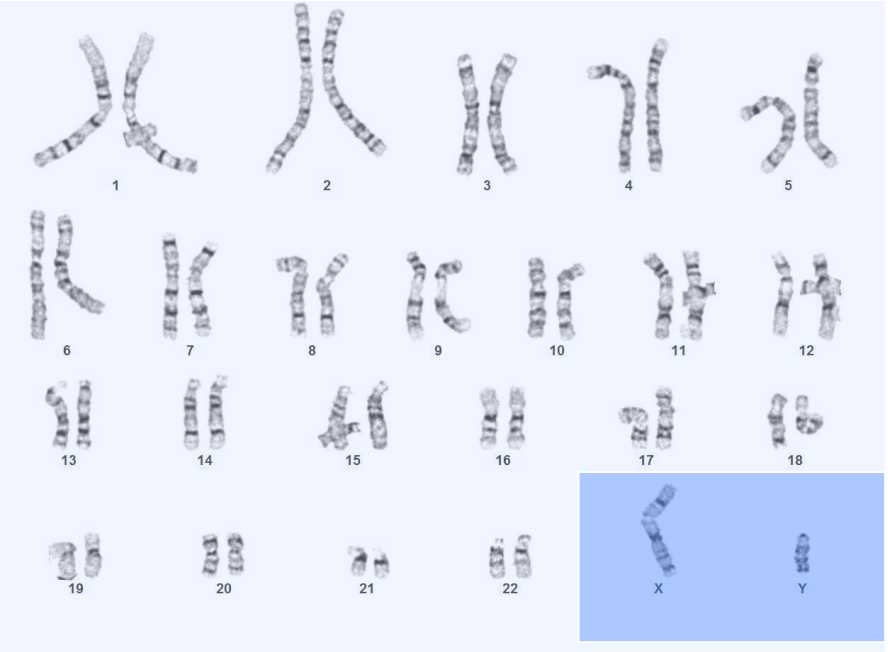
**Allele** Generally, 2 or more variations on a gene



# Genetic Testing Timeline: The Past

The Past

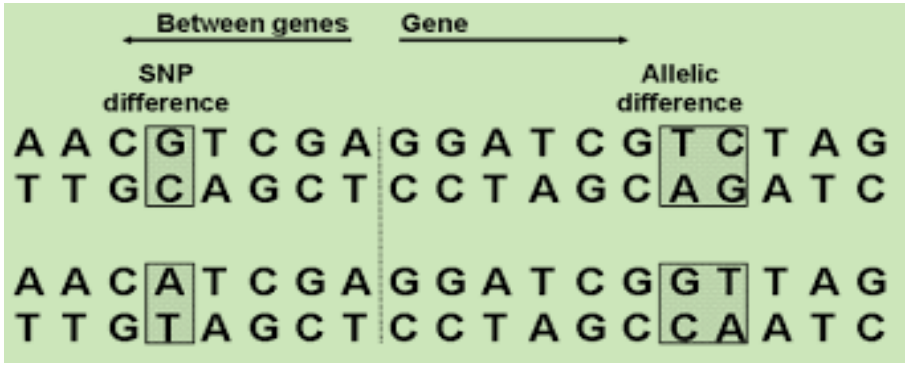
- Late 1800s; Chromosomes discovered
- Early 1900s; inherited disease linked to chromosome
- Early 1950s; develop genetic tests for Down, CF, MD
- Early 1960; testing used to confirm diagnosis (PKU)



# Genetic Testing Timeline: The Present

The Present

- Tests for >2000 rare and common conditions
- Tests currently available;
  - Diagnostic
  - Predictive (pre-symptomatic)
  - Carrier Status
  - Prenatal
  - Pre-implantation
  - Pharmacogenomics
  - Research genetic testing*

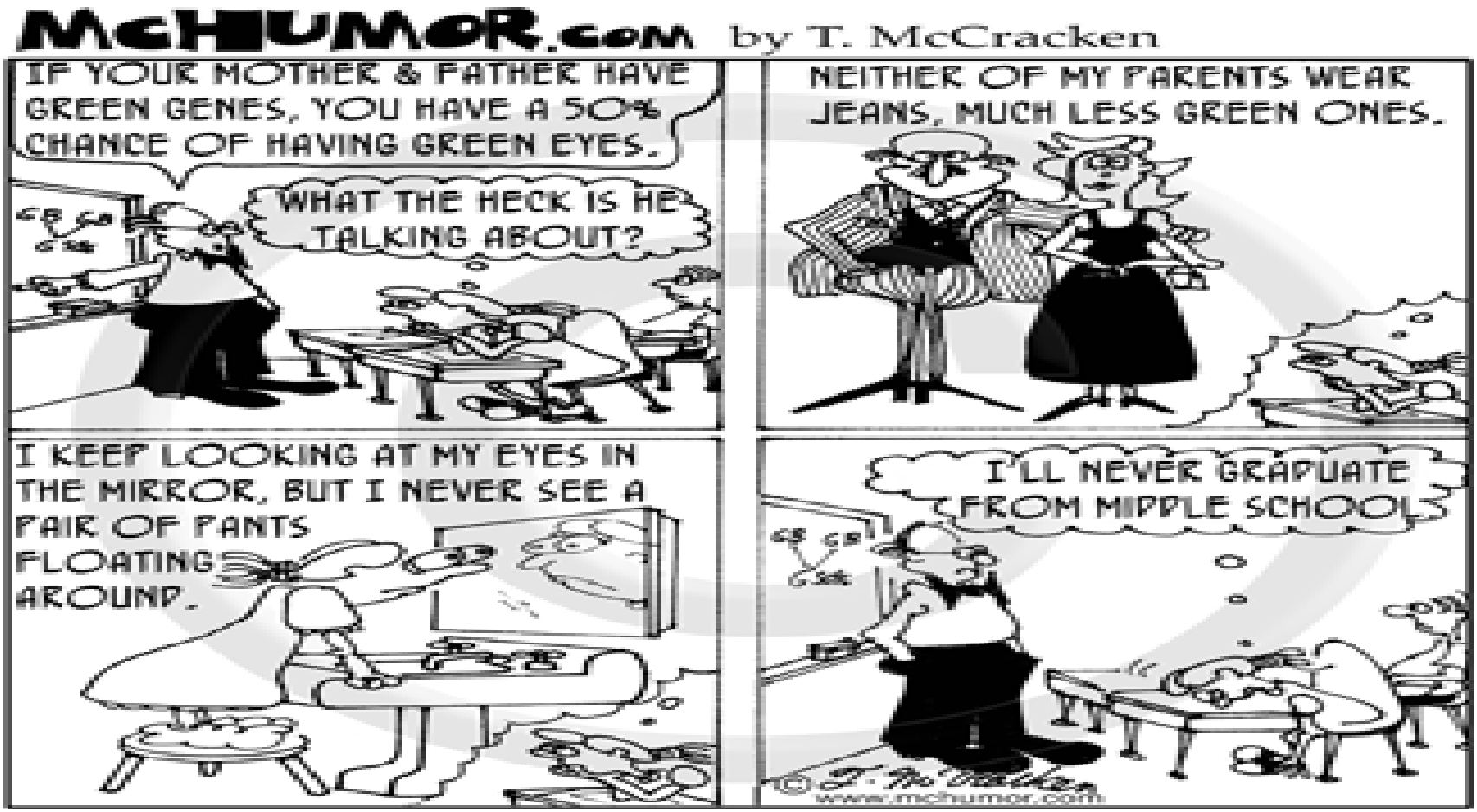


# Genetic Testing Timeline: The Present

The Future

- Greatly reduced cost of sequencing
- Greatly reduced amount of sample needed
- Greater disease risk predictions
- Increased behavioral/personality predictions
- Personalized medicine therapies

# Now you Want to Study my Genes? DNA? What?



# Talk to your neighbor

- Explain what genes are without using the words “genes or genetic”
- Name 3 uses for genetic testing
- Why are more studies using genetic testing?
- How many chromosomes are in DNA?
  - Can humans live with more?
  - Can humans live with less?

# Cautions and Considerations in Consenting Genetic Research Participants

Your DNA (inherited material) *may* be studied to help explain why some people have certain *disease, disorder, condition, behavior* and other people don't. Researchers want to search your unique genetic code (genes) to discover how human disease is affected by inherited materials.

# The Challenge is in Defining Disease Risks

# Challenge in Defining Terms

Is sequencing, sequencing, sequencing?

- Targeted gene sequencing
- Whole exome sequencing
- Whole genome sequencing
- RNA functional studies

If you have IRB approval for sequencing, do you have umbrella approval for all sequencing? That depends…..

# Suggested Consent Language Targeted Gene Sequencing

We *may* study your DNA from the blood sample you give us. Your DNA may contain **genes that are already known** to be associated with a (*disease, disorder, condition, behavior).* This is called targeted gene sequencing. We *may* also be searching for new genes to examine that may help to explain why some people develop (*disease, disorder, condition, behavior).*

# Suggested Consent Language Whole Exome Gene Sequencing

Normally, researchers look for genes known or suspected to be associated with *(disease, disorder, condition, behavior).* This is called targeted gene sequencing. In whole exome gene sequencing, **we look at all protein coding areas of the DNA**. This is a much larger portion of your DNA than a single gene, but is **still only about 2% of the total DNA.** It is possible that we will find some unexpected genetic findings from the larger gene search. We will not give you any results unless it is deemed important for your medical health.

# Suggested Consent Language Whole Genome Sequencing

Normally, researchers look for genes known or suspected to be associated with *(disease, disorder, condition, behavior).* This is called targeted gene sequencing. In whole genome gene sequencing, we look at all protein coding areas of the DNA. **If we conduct whole genome sequencing, 100% of your genes are available to view.** It is possible that we will find some unexpected genetic findings from this expansive gene search. We will not give you any results unless it is deemed necessary for your medical health.

# Questions So Far?

# Implications and Use of Samples and Data for Sharing

Think ahead, add template language *in the event of:*

- Collaborations(i.e. sharing) of data or samples in the future
- Requirements, now or in the future, to participate in large databases such as dbGaP, dbSNP, ClinVar, etc.
  - dbGaP stands for **d**ata**b**ase for **G**enotype **and P**henotype
  - Required for NIH funded studies collecting genetic information
- Future genetic protocols such as creation of permanent cell lines, iPSCs

*Are your data retrospective or prospective? Both?*

# Risks Involved in Genetic Research are Almost Never Physical

- We cannot ever promise complete confidentiality or guarantee no breaches in data security will occur; *what harm can come?*
  - Medical Health insurance consequences harm to family relationships?
- What scientists think are "genetic truths" today may not be true tomorrow; *how does that feel?*
  - How will you handle an evolving science without firm answers?
  - What about the discovery of "cheater", "risk taker" gene?
  - What else is will be discovered?

*Some people should be "encouraged" <u>not</u> to join a genetic study*

# Return of Genetic Results; Do No Harm!

- Genetic research results are currently returned only under strict conditions and are rarely termed a benefit
- Must be interpreted and disseminated by genetic professionals
- Result are what is known today
- What about?
  - Incidental Findings (IF)
  - Variants of Unknown Significance (VUS)

# Keeping Things Real: Managing Participant's Perceptions and Expectations

# Be Aware of Common Misconceptions

- Participant's expectations of genetic research are often distorted, unrealistically optimistic or pessimistic
- Genetic research is not forensics
  - Be ready to answer questions about cloning
  - Know the difference, and never confuse the differences between clinical and research information
- genetic samples and data do not require standard security
- Negative genetic result does not mean DNA is perfect
- Genetic results are based on what is known <u>today</u>

# Case studies

1. The baby gender reveal party

   Lesson: A bit of skepticism is healthy

2. Normal result, not normal individual

   Lesson: accurate medical records informs correct test

3. Religion vs Genetics

   Lesson: Respect for persons

# What's new in genetic technology?

Cheap sequencing

RNA functional analysis

Cell free DNA

Single cell DNA

Single nucleotide

Gene therapy; successes and failures

Direct to Consumer genetic testing