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Genes, Gene Panels & Cancer Risk: *Is Testing Right for Me?*

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BCC's 11th Annual Conference:
Sharing Knowledge ~ Creating Hope
Date: Saturday, November 1, 2014

Blueprint

- Genetics 101
- The Genetics of Cancer
- Genetic Tests / Gene Panels
- Q&A

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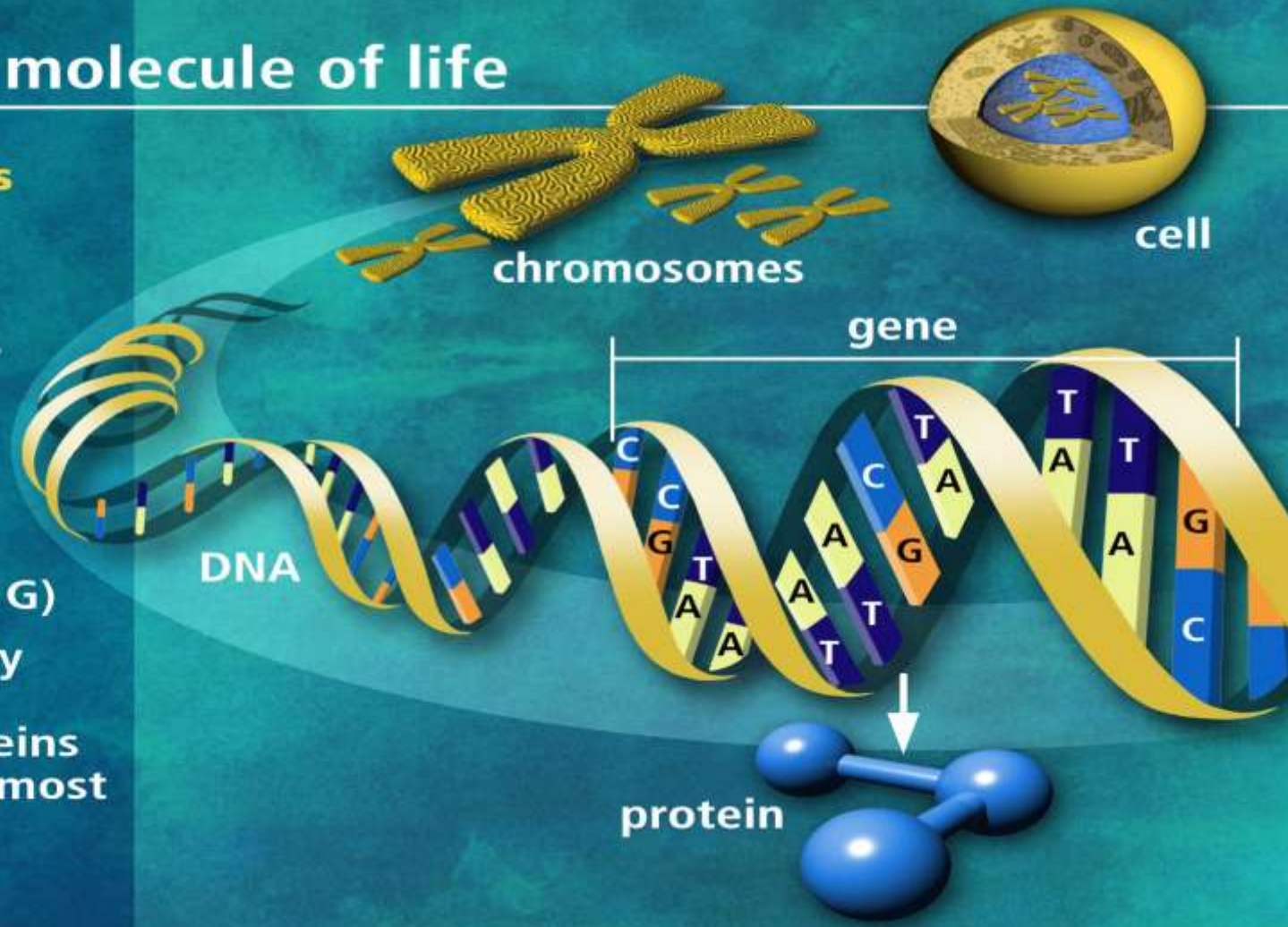
Genetics 101

DNA the molecule of life

Trillions of cells

Each cell:

- 46 human chromosomes
- 2 meters of DNA
- 3 billion DNA subunits (the bases: A, T, C, G)
- Approximately 30,000 genes code for proteins that perform most life functions



How do we inherit our genes?

- 23 chromosomes from each parent = 46 total
  - 44 identical in men & women
    - 2 copies of every gene here (autosomes)
  - + 2 sex chromosomes (X & Y)
    - Women inherit two X chromosomes
    - Men inherit one X from mother & one Y from father

What are genes?

- Sequence of bases = instructions for making a single protein
  - Enzymes, structural, signaling
- Additional bases that come before the gene = tell when each gene should be used
  - Hair protein: made only in certain skin cells, not the rest of the body

DNA Sequence Variation in a Gene Can Change the Protein Produced by the Genetic Code

Gene A from Person 1

GCA AGA GAT AAT TGT. . .

Ala (1) Arg (2) Asp (3) Asn (4) Cys (5) . . .

Protein Products

Gene A from Person 2

Codon change made no difference in amino acid sequence

GCG AGA GAT AAT TGT. . .

Ala (1) Arg (2) Asp (3) Asn (4) Cys (5) . . .

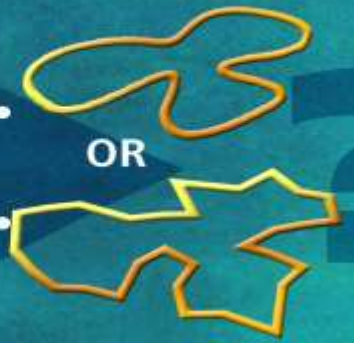
Gene A from Person 3

Codon change resulted in a different amino acid at position 2

GCA AAA GAT AAT TGT. . .

Ala (1) Lys (2) Asp (3) Asn (4) Cys (5) . . .

OR



Y-GA 98-649

Genetic Code Missteps -- analogy

THE BOY DID EAT ALL DAY

THE BAY DID EAT ALL DAY

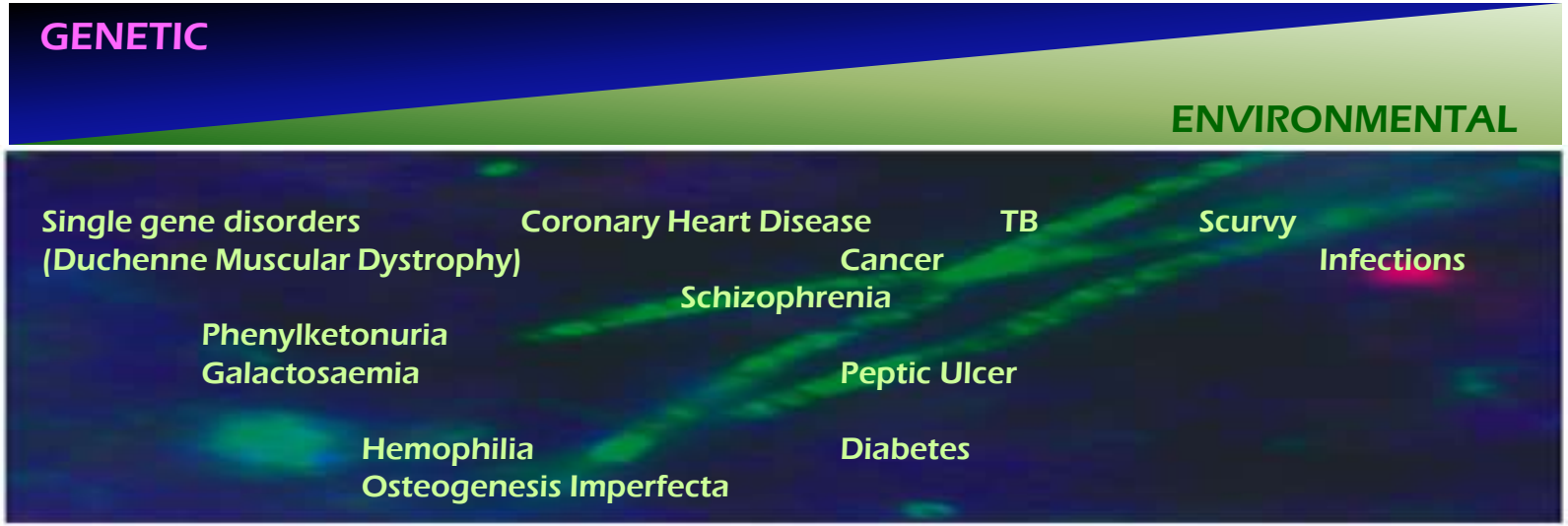
THE BYD IDE ATA LLD AY

What kind of problems can mutations cause?

- Altered function
  - Sickle cell anemia
- Lack of protein
  - Hemophilia
- Change how much protein is made
  - Cancer: proteins that prevent additional mutations from building up

Genetic Basis of Human Disease

Rare	Common
Genetics = simple	Genetics = complex
Unifactorial	Multifactorial



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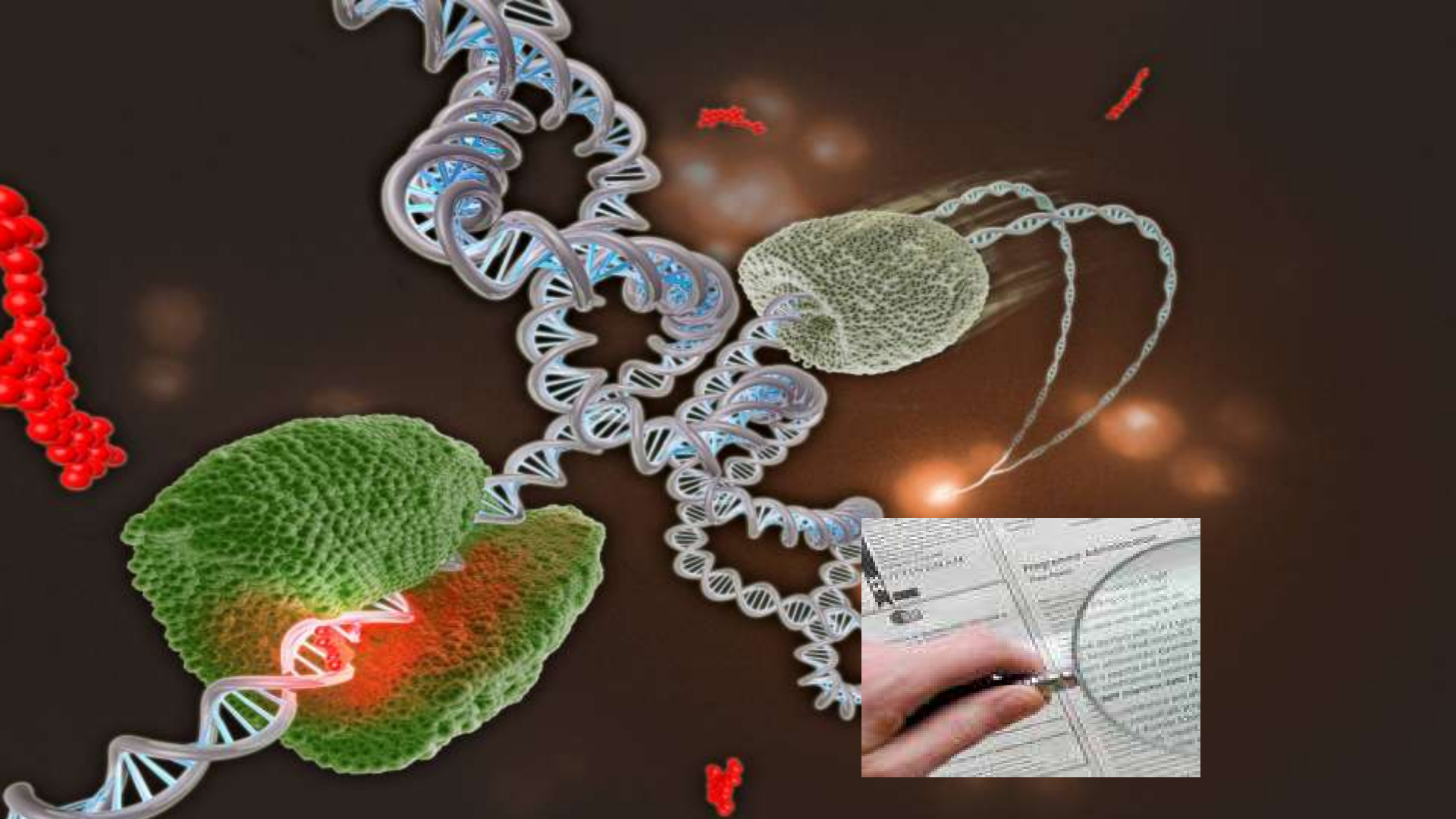
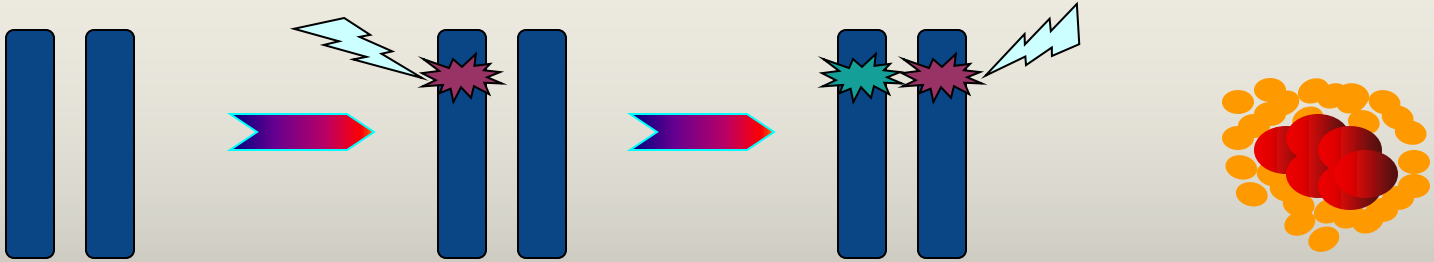
The Genetics of Cancer

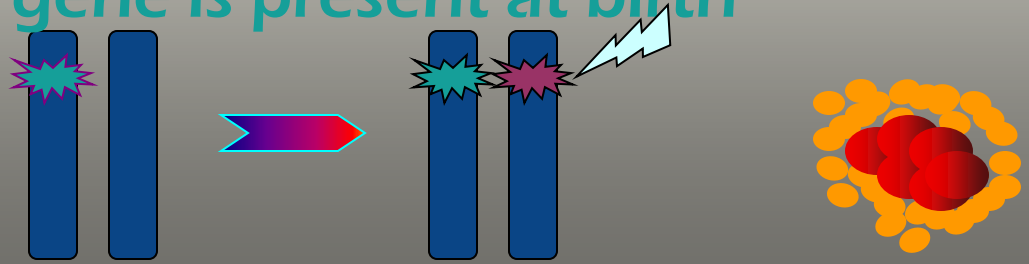


“Multi-Hit” Theory

- Sporadic Cancer



- **Hereditary Cancer**
  - **One damaged gene is present at birth**



“Multi-Hit” Theory

- Mutations happen frequently during normal cell division and/or due to environmental factors
- When genetic damage escapes the normal repair mechanisms of the body --
  - Mutations accumulate
  - Uncontrolled cell growth results
- Most cancer occurs because of multiple mutations

Genetic Testing…what does it mean?

- Diseases related to one gene = very rare
- Cancer is probably related to many genes interacting, plus environmental factors
- Genetic testing is usually an assessment of risk, not diagnostic

Common genetic tests in oncology

- BRCA1/2 + BART
- Lynch (MLH1, MSH2, MSH6, PMS2, EPCAM)
- Adenomatous Polyposis Syndromes (APC, MYH)

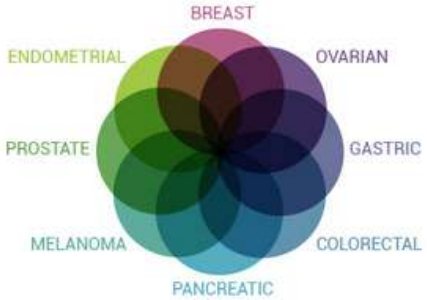
- Li-Fraumeni Syndrome (p53)
- Cowden Syndrome (PTEN)

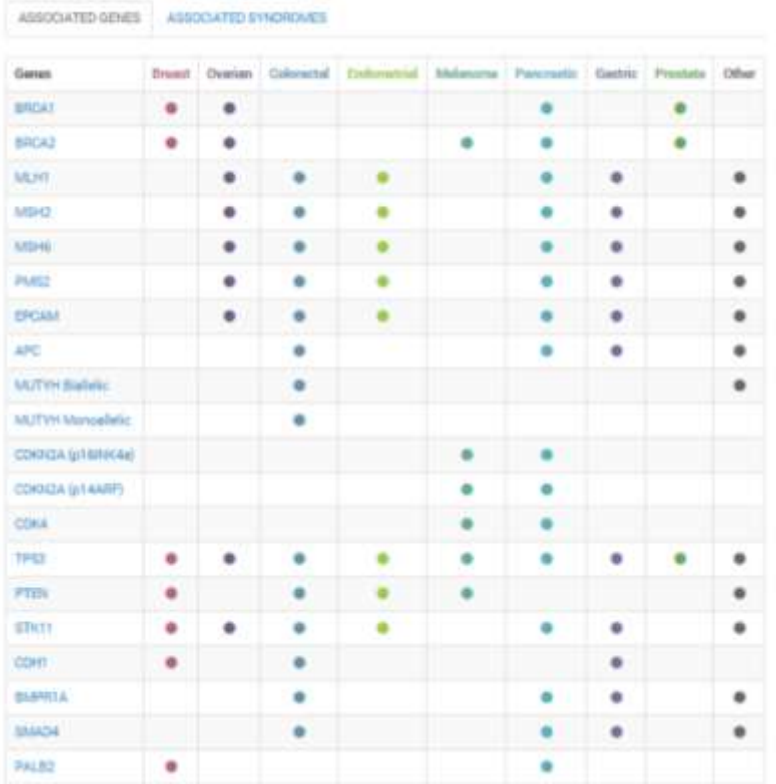
Multi-Gene Panels

- Next Generation Sequencing
  - Looks at multiple genes in one sample
- Highly penetrant genes are included, as well as intermediate penetrant genes
  - Unclear clinical actionability
  - May reveal variants of uncertain significance
- Currently offered by several clinical labs
- Covered by insurance in some cases

- **different from genomic panels done on tumor tissue*

Multi-Gene Panels





http://www.myriadpro.com/myrisk/why-myriad-myrisk/gene-selection/

Multi-Gene Panels

Why test? Things to consider…

- **To make a medical intervention.**
- **To relieve anxiety, especially in a family that knows that the cancer is due to a specific gene mutation.**
- **To relieve uncertainty.**

ASCO (2014)
Accessed online at:
http://www.cancer.net/navigating-cancer-care/cancer-basics/genetics/genetic-testing

Why test? Things to consider…

- **Testing may cause depression, anxiety, or guilt.**
- **Testing may cause family tension.**
- **Testing may provide a false sense of security.**
- **Testing may provide unclear results.**
- **Testing can be costly.**
- **Testing may cause confidentiality concerns.**

ASCO (2014)
Accessed online at:
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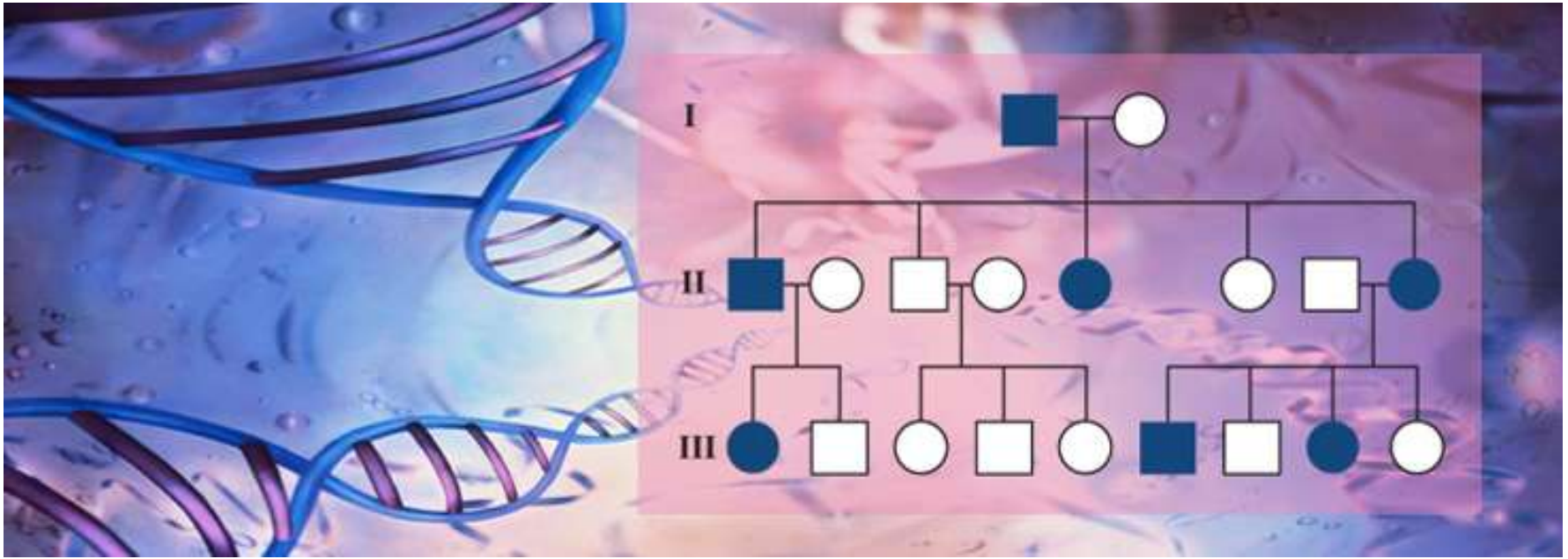
Can we overcome our genetics?

- Our risk for almost any medical condition is a function of both our genes and our environment
- Apply our knowledge of our family medical history to predict our risk for specific problems
- Focus on the things we can change — diet, lifestyle, screening, treatment — to ensure a long, healthy life.
- Genetic testing can identify mutations to help focus screening & prevention
- Choosing to have genetic testing requires “due diligence” – considering all the possibilities prior

Questions / Cases



Suggested Resources

- http://www.cancer.net/navigating-cancer-care/cancer-basics/genetics
- http://www.ncbi.nlm.nih.gov/sites/GeneTests/
- http://www.ginahelp.org/