Genomics and our Health

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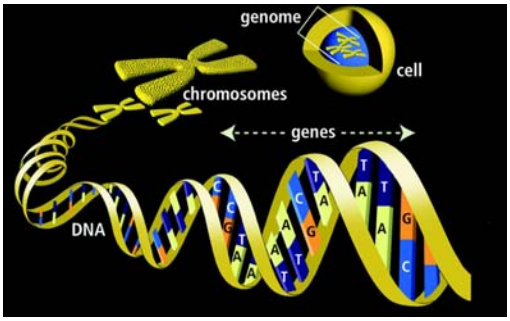
Overview

- Basics
- Genetics vs Genomics
- How does this impact newborn screening?
- Whole Genome Sequencing

- What do you want to know?

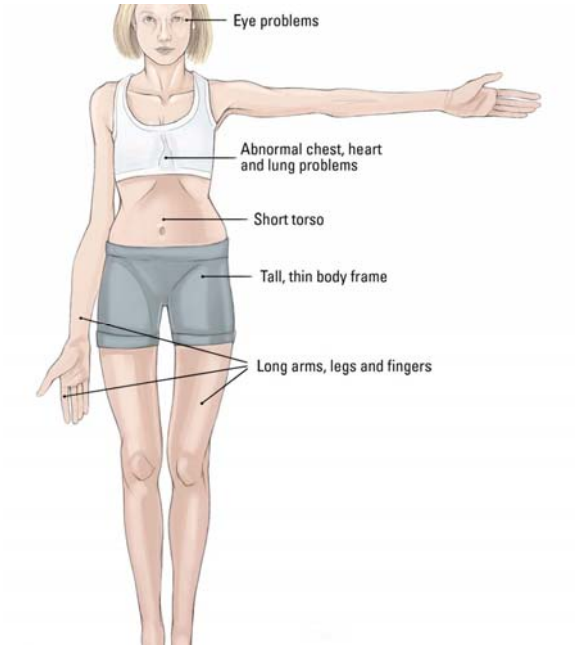
Some basics…

- Each human cell has a **genome** consisting of genetic material.
- The genetic material is packaged into **chromosomes**.
- Each chromosome is made up of **DNA**.
- DNA is made up of a code that tells our bodies how to grow and develop.
- **Genes** are units of heredity.
- Each gene codes for a particular set of body functions and/or structures.
- Humans have about 30,000 genes.
- If the code is altered/changed, the body may grow or develop differently.



What's the Difference?

Genetics	Genomics
a discipline of biology; the science of genes, heredity, and variation in living organisms	a discipline that attempts to sequence, assemble, and analyze the function and structure of genomes
the investigation of the roles and functions of single genes	genome = the complete set of DNA within a single cell of an organism



Genetics example

- The *FBN1* gene codes for the development of connective tissue (among other things).
- If the *FBN1* gene has a change (mutation), then the code is not read properly.
- diagnosis = Marfan syndrome
- Clinical signs and symptoms are present.
- In the genetics clinic, we can test for a change in the *FBN1* gene, and provide genetic counseling about inheritance and medical prognosis.

GENOMICS

- Whole Genome Sequencing (WGS) looks at a huge amount of data and compares it to genomic data from populations.
  - provides raw data on all six billion letters in a person's DNA
- WGS can identify:
  - many single gene conditions
  - DNA changes that can increase or decrease a person's risk for complex disease (like diabetes or heart disease)
  - variants of unknown significance
  - adult-onset conditions
  - carrier status

- Clinical signs and symptoms may or may not be present.
- In the genetics clinic, we can order WGS and provide genetic counseling about the meanings of the results.
  - We may not be able to provide evidence-based information about inheritance, risks, etc.

Genomics Example

- Nicholas Volker was a healthy boy until age 2, when his mother first noticed an abscess when changing his diaper.
- He developed more fistulas, or openings of his bowels.
- even surgeries (>100) to fix the fistulas created more
- feeding tube used because he could not eat food by mouth
  - when he ate, holes would open between his intestine and skin, causing feces to leak into a large wound in his abdomen
  - bony arms and distended belly of a famine victim
  - at age 4, he weighed less than 20 pounds
- >two years in the hospital

Genomics Example

- Pediatrician wanted to sequence Nic's genome
  - On the X chromosome, on the gene *XIAP*, humans usually have the amino acid sequence thymine-guanine-thymine.
  - Nic had thymine-adenine-thymine.
  - He has a "typo" in his genetic code: an A instead of a G.
- The XIAP protein has two jobs:
  - block a process that makes cells die
  - help prevent the immune system from attacking the intestine
- In Nic, the XIAP protein is not made correctly
  - his immune system is at war with his intestine

Genomics Example

- Exceeded his lifetime $2 million insurance benefit
  - $70,000 to sequence the protein-coding region of his genome (called the "exome")
- At seven, it has now been 2 years since a cord blood transplant and Nic is healthy.
- Since Nic's genes were sequenced, Children's Hospital has approved more than 20 children for DNA sequencing and completed reports for eight of them

Current Status of WGS

- WGS is currently offered clinically and as a direct-to-consumer (DTC) service.
  - DTC = an individual can order, receive, review, and share results with others without being required, at any stage in that process, to engage a healthcare professional (e.g., a physician or a genetic counselor)
- Important to remember that one's WGS interpretation could change based on new research results
- Not all DTC companies offer genetic counseling as a part of their testing – so what to do with all that data?
- The $1000 genome, the $1,000,000 interpretation!

Implications for Newborn Screening

- Currently, newborn screening (NBS) identifies specific conditions based (mostly) on biochemical test results.
  - Note: cystic fibrosis is now on many state NBS panels, and some states report carrier status
- American Academy of Pediatrics and the American College of Medical Genetics recently published a joint statement on genetic testing in children
  - firmly advised against genetic testing in children to determine future risk of disease
- If NBS were to include WGS, results would be more complex, comprehensive, expensive….

Considerations

- How much does WGS cost?
  - 2008 - $350,000
  - 2013 - $6000 (at least one company that offers WGS at this price says "data analysis is not included")
  - Compared to $1500 for Chromosomal Microarray (CMA), a test commonly ordered in genetics clinics
    - CMA does not cover the entire genome
  - Each newborn screen currently costs about $50-$100
- Who will interpret the data?
- Duty to re-contact
- Implications for insurance
- Adult-onset conditions, carrier status
- Opting out of certain information
- Informed consent

Conclusion

- **Personalized medicine** = the customization of healthcare; medical decisions, practices, and/or products tailored to the individual patient
- Are clinical services moving from "genetics" to "genomics"?
- What do you want to know about genomics?
- What should your doctor know about genomics?