The Genetic Basis of Obesity

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DNA and Genes

AGCTACCCTATTCCCATGCGCGAGCTATTA

A

C

G

T

Wikimedia users: Mikael Häggström, GAThrawn22, cacycle
Genome (All of your DNA)

Gene

DNA

Protein

Chocolate Chip Cookie Recipe
There are different versions of genes

The proteins may function differently, but not necessarily
Simple Example: ABO Blood Type
One gene controls blood type. There are 3 versions (A, B, O).
Recap

• Genes are sections of DNA that spell out the recipe for proteins
• There are different versions of genes
• Each person has two copies of each gene
  – One from Mom
  – One from Dad
Questions?
Why do we think genes play a role in obesity?

Obesity tends to ‘run’ in families
- Obese parents tend to have children that grow up to be obese

But this could also be environmental (the food that the family eats, amount that family exercises)
Why do we think genes play a role in obesity?

Identical twins are much more likely to have the same body size than siblings

- Environment is the same for both twins and siblings
- Identical twins share all of their genes, where siblings only share roughly half of their genes
SCIENCE LIKES TO MAKE THINGS BLACK AND WHITE WHEN POSSIBLE
Is there a version of a single gene that explains why some people are obese?

YES!*
In 1949, researchers found mice that were born a normal size, but quickly became very obese.

They traced the problem to ONE gene, the one that makes leptin.
Leptin is important in appetite control. When leptin levels are high, the brain signals to stop eating and feel full. When leptin levels are low, the brain signals to eat more. This process helps regulate food intake and body weight.
No Leptin is Made in the Obese Mice

These mice are always eating because they never feel full
No Leptin is Made in the Obese Mice
Only found a few people in the world that were unable to make leptin

This doesn’t explain why most people are obese
Complicating Genetic Factors

• More than one gene is involved

Leptin → Obesity → MC4R → LEPR → Obesity
POMC → Obesity
Complicating Genetic Factors

• More than one gene is involved
• There are genes that increase your chance of becoming obese

Those with 2 copies of this version are 6.6 lbs heavier than those with no copies of this version of FTO

Those with 1 copy of this version are 2.6 lbs heavier than those with no copies of this version of FTO

Those with no copies of this version are 1.67 times more likely to be obese than those with no copies of this version of FTO
Complicating Genetic Factors

- More than one gene is involved
- There are genes that increase your *chance* of becoming obese

→ Evidence that it is both of these combined

There are a lot of genes that each have a small effect on body size
Questions?
There are also non-genetic factors!
The Environment Plays a Role

• Your diet matters!
  – Balance of the calorie equation

• The filmmaker gained 24.5 pounds in one month while only eating fast food
Most people fall on the scale between completely environmental and completely genetic.

Genes have been estimated to explain 40-70% of the variability in body size.
Looking for General Body Size Genes

Scientists decided to look for the genes that affect variation in body size and not just those that cause obesity.
Looking for General Body Size Genes

Analyzed across the genome in a large number of people (>200,000) to find regions that seem to be associated with variation in body size

→ Found 32 different potential locations

Association analyses of 249,796 individuals reveal 18 new loci associated with body mass index

*NATURE GENETICS VOLUME 42 | NUMBER 11 | NOVEMBER 2010*
We Still Don’t Have the Whole Picture

45% Environmental
55% Genetic

Variance in BMI

Genetic variance important in BMI

The 32 locations only explain 1.45% of the total variance in BMI

List from Speliotes et al. 2010
Unexpected Directions: New Avenues for Research

- Nervous system
- Immune system
- Gastrointestinal system

Wikimedia user: Mikael Häggström
Summary

• Genes are regions of DNA that contain the recipe for proteins

• A single gene can cause obesity, but this is very rare

• Obesity is due to a play between environmental factors and a number of genes that each have a small effect
Thanks!

Questions?