



The Human Genome

And What We Do With It!

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22nd June 2016



Avon Longitudinal Study of Parents and Children

Supported by **wellcome**trust



Outline

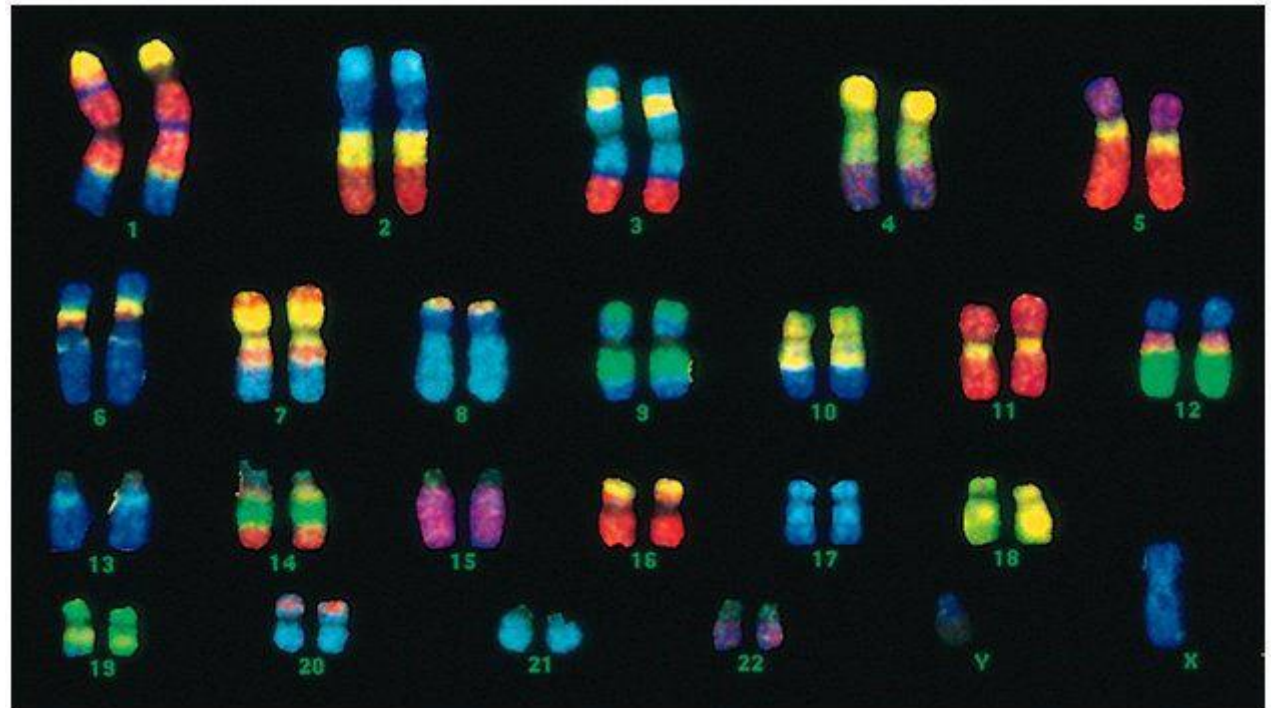
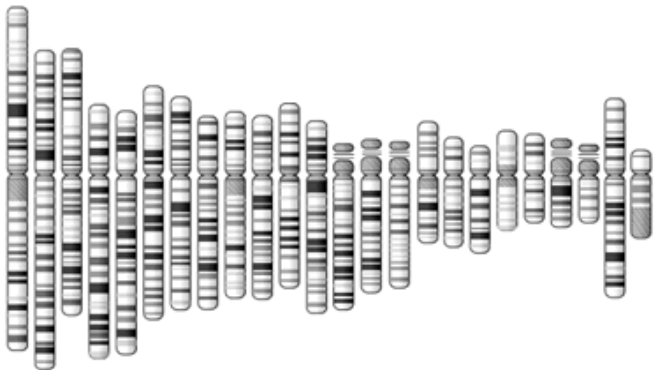
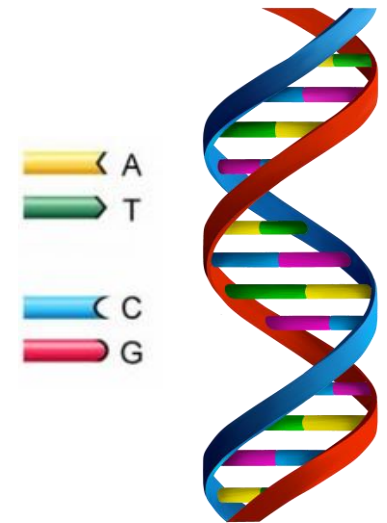
- DNA and the genome
 - What is it?
 - How **big** is it?
 - How is it organised?
 - What exactly is **in** the genome?
- Mutations
 - Within people
 - Within populations
- Genome-wide association studies



DNA and the genome

DNA and the genome

What do you know already?



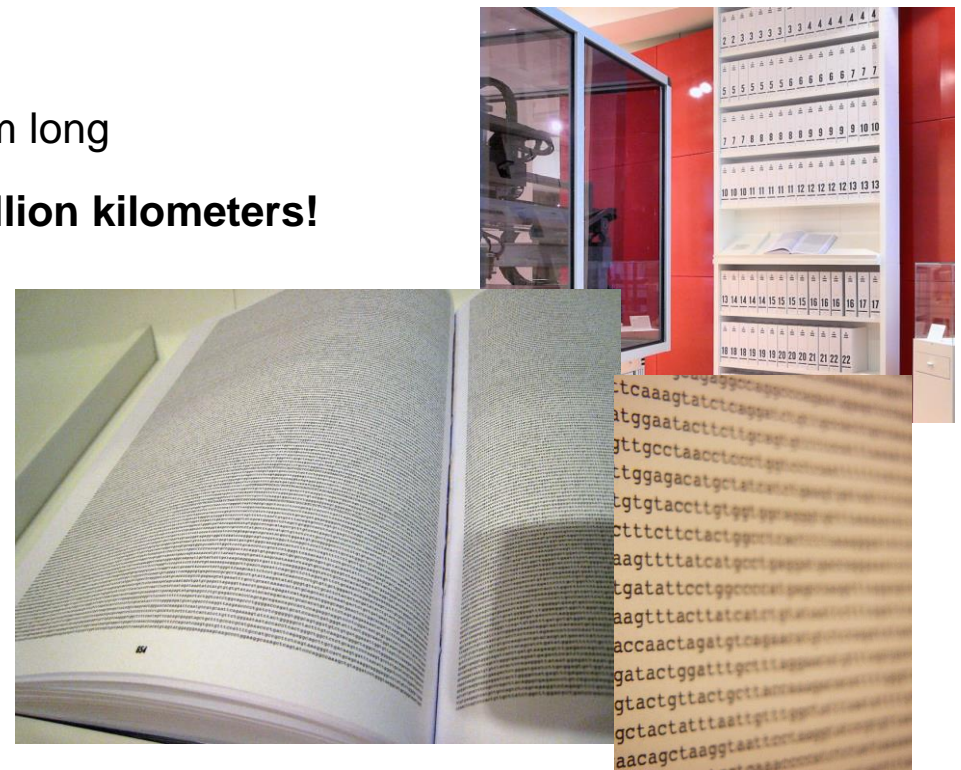
How big?

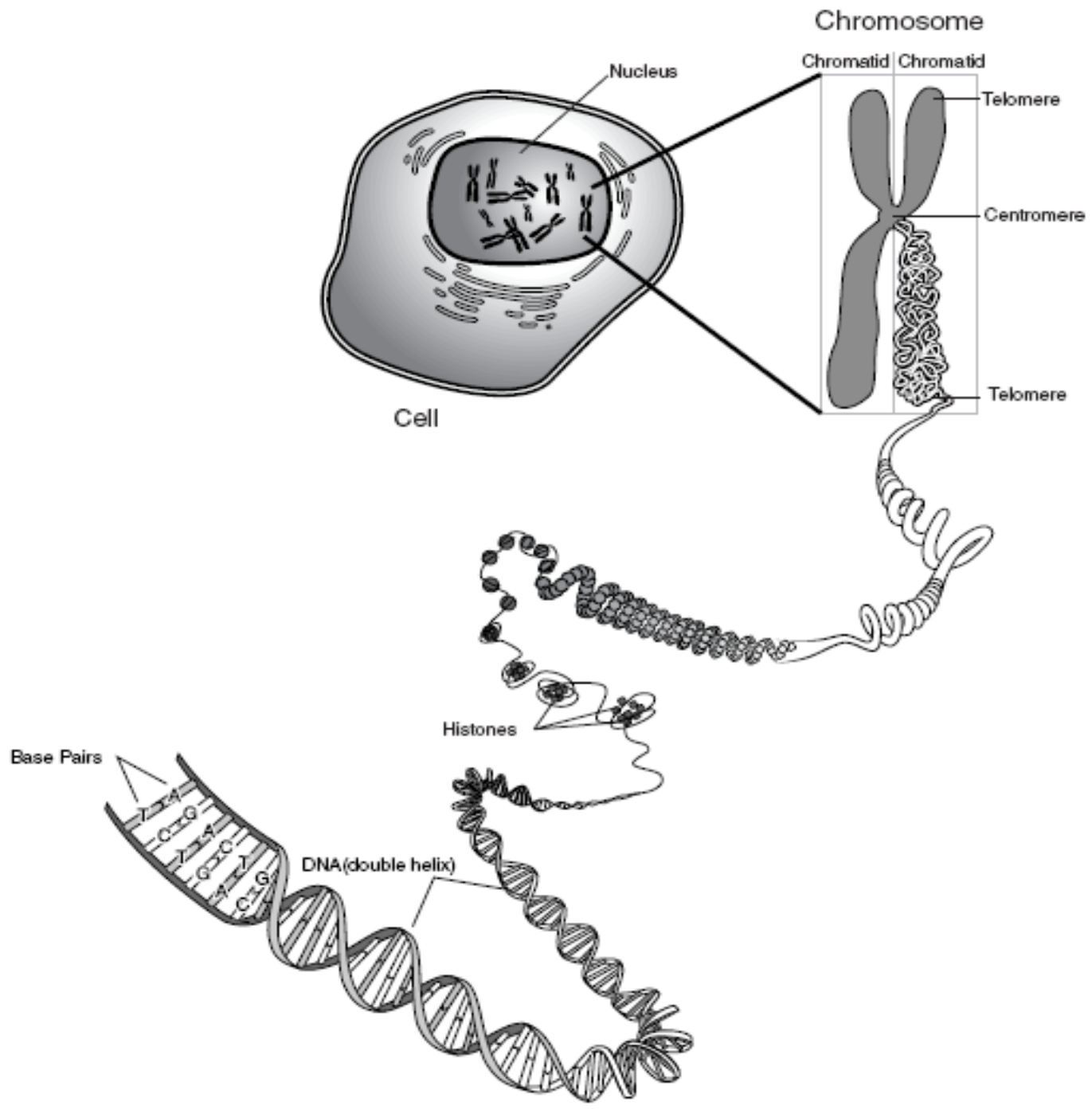
DNA. Base pairs. Genes.



How big is the genome?

- Base pairs
 - Each turn of the double helix is 10 base pairs (bp)
 - In one copy of DNA ~ **3,200,000,000 bp!**
- Centimeters
 - One chromosome ~ 5cm
 - One copy of the whole genome is ~ 2m long
 - All the DNA in your cells ~ **60 billion kilometers!**
- Books
 - One copy of the genome ~ >100 books
 - Entire genome ~ **1 million pages**
 - 5,000 books stacked 200 feet
 - 200 telephone directories





How much data is in genome?

...ATGCTAACTGACTAAGTAGCCAATGACAGAGCG...

- DNA per chromosome ~ 48-249Mb
 - Basic sequence of information for one individual ~ **700Mb**
- All the technical information ~ 200Gb
 - Encyclopedia Britannica ~ 130Mb
 - Wikipedia text ~ 8.8Gb
 - Windows 10 ~ 10Gb



Genes

- Protein-coding regions
- Separated into exons (protein-coding) and introns (non-protein coding)
 - Average number of exons per gene ~ 10 (1-363)
- Average length of a gene ~ 54,000bp (200-24,000,000bp)
 - Average exon size ~ 288bp (10-180bp)
 - Intron size range ~ 30-11,000,000bp

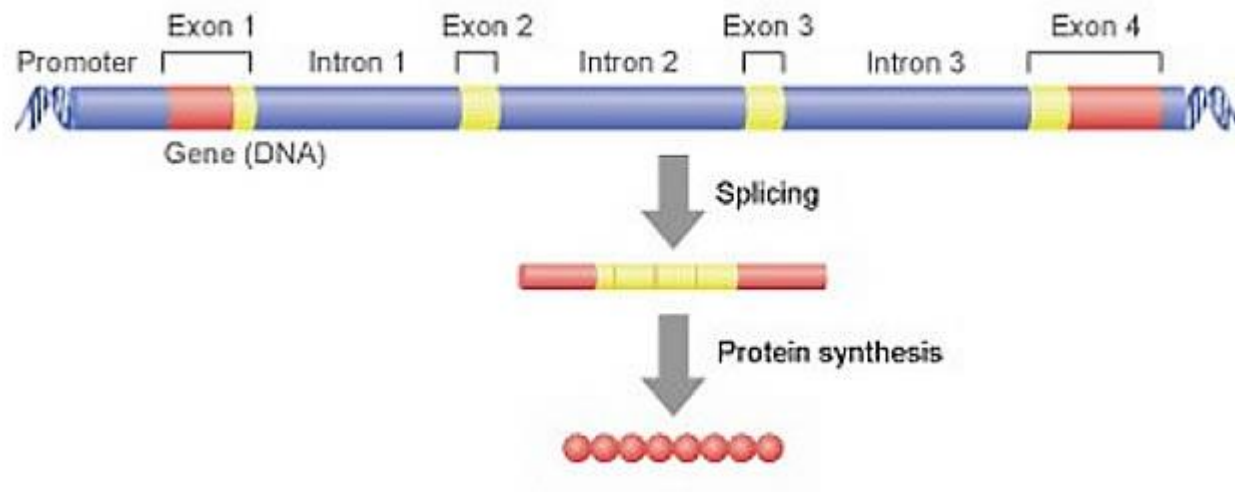


How many genes in the genome?

- Gene Sweepstake – bets on the size of the human genome (\$1 in 200, \$5 in 2001, \$20 in 2002)
 - Average 61,710 with range: 27,462 – 153,478

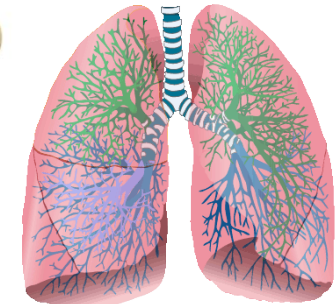
20,000 – 25,000

2% of the genome is made of genes!



What else is in the genome?

- The set of genes in your genome is always the same
 - Different cells types, tissues, organs
 - During development, childhood, puberty, adulthood
 - Before and after disease
 - When it's hot and cold
 - When you're hungry or you've eaten
 - During exercise, on a diet, taking medication, sleeping

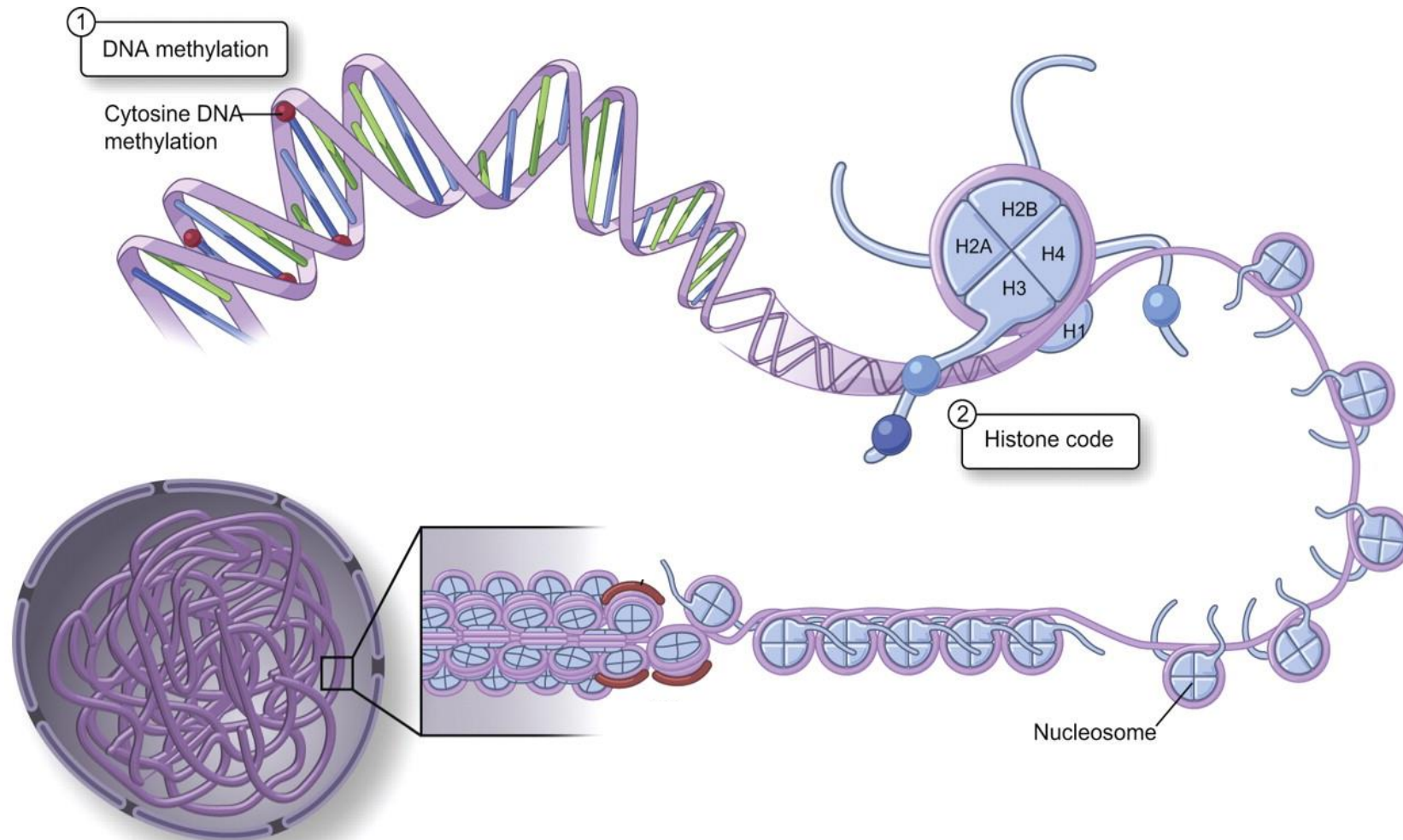


BABIES TOGETHER NURTURE INTERNATIONAL EXCITING GENERATIONS GROWING UNIQUE SUPPORT DN



LIFE BABIES TOGETHER NURTURE INTERNATIONAL EXCITING GENERATIONS GROWING UNIQUE SUPPORT
FRIENDLY BIRTH LIVING ME PARENTS FAMILY COMMITMENT BRISTOL YOU PERSONAL MOTHER DEVEL

What else is in the genome?



ANY QUESTIONS SO FAR??

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Mutations

Person 1	Maternal	AAT TAG GTC CCT TGA
	Paternal	AAT TAG GTC CCT TGA
Person 2	Maternal	AAT TAG GTA CCT TGA
	Paternal	AAT TAG GTC CCT TGA
Person 3	Maternal	AAT TAG GTA CCT TGA
	Paternal	AAT TAG GTA CCT TGA

SNP – pronounced ‘snip’

Mutations

- 1 in 110,000,000 base pairs
- ~60 new mutations in every new born
 - 134 million births last year
 - Every base pair mutated ~3 times per year
 - HUGE amount of genetic variation in the population
- The natural genetic variation is like a HUGE natural experiment
 - Sequence people to try and understand the consequences of mutations in a gene



Phenome

Psychological traits

Daily fluctuations

Physical traits

Tissue differences

Disease status

Gut microbial flora

Cell type differences

Life course changes

Personality

Behaviour

Chemical DNA modifications

Environmental exposures

Protein levels

Emotional

Transcription factors

DNA expression

Metabolite levels



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- Our commitment to you
- Newsletters and leaflets

Researchers

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Children of the 90s is a long-term health research project that started in the early 1990s. It recruited more than 14,000 pregnant women, and these women and their families have been involved ever since. The Children of the 90s project works with researchers all over the world.

Our participants

Our participants range from mums and their children to fathers, grandparents, brothers and sisters, and a new generation of 'children of the children of the 90s'



Young people



Children of the Children of the 90s

“ Children of the 90s has just been fantastic in so many ways. It has revealed some really profound insights into the way we grow and develop as humans. It's revealing important information not just for medics, for medicine, but for all of us ”

Dr Alice Roberts

What is Children of the 90s?

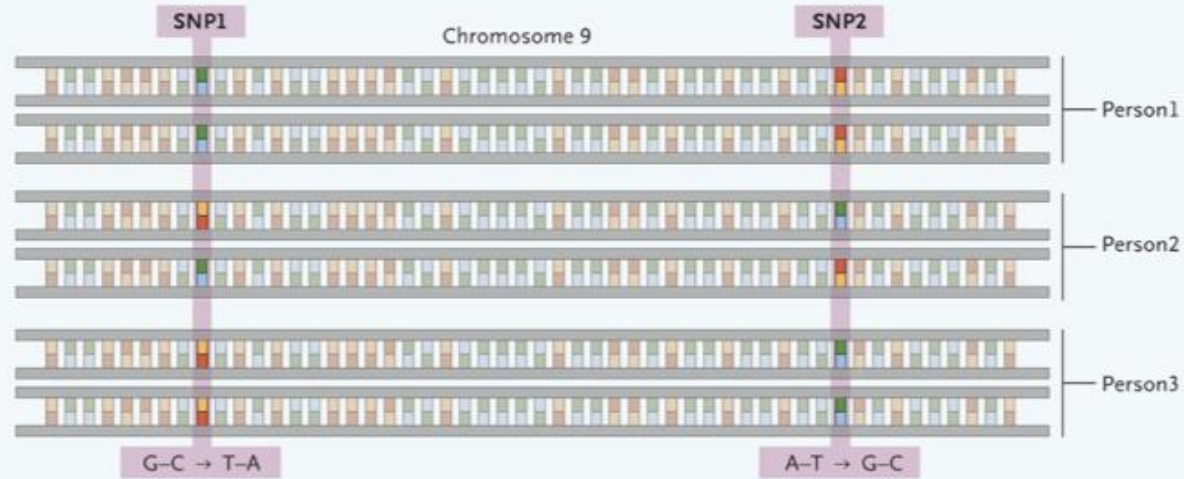
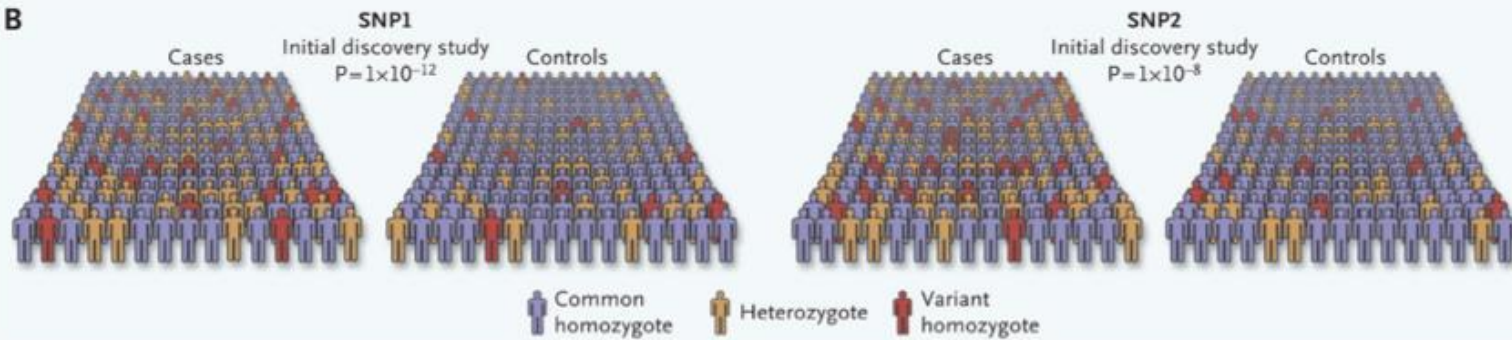
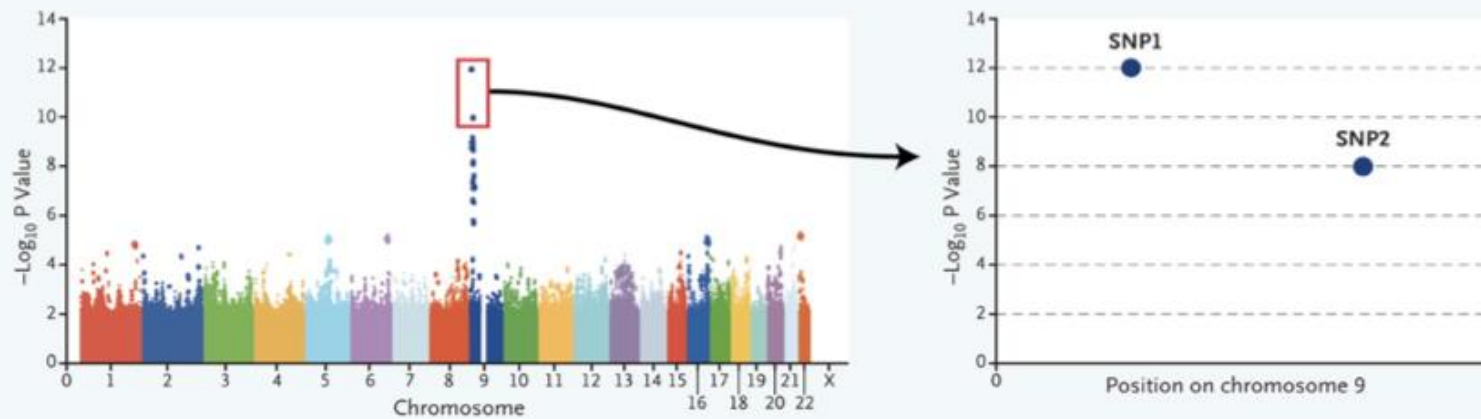
A film by the Wellcome Trust

Our discoveries





**Linking genome to
phenome**

A**B****C**

Outline

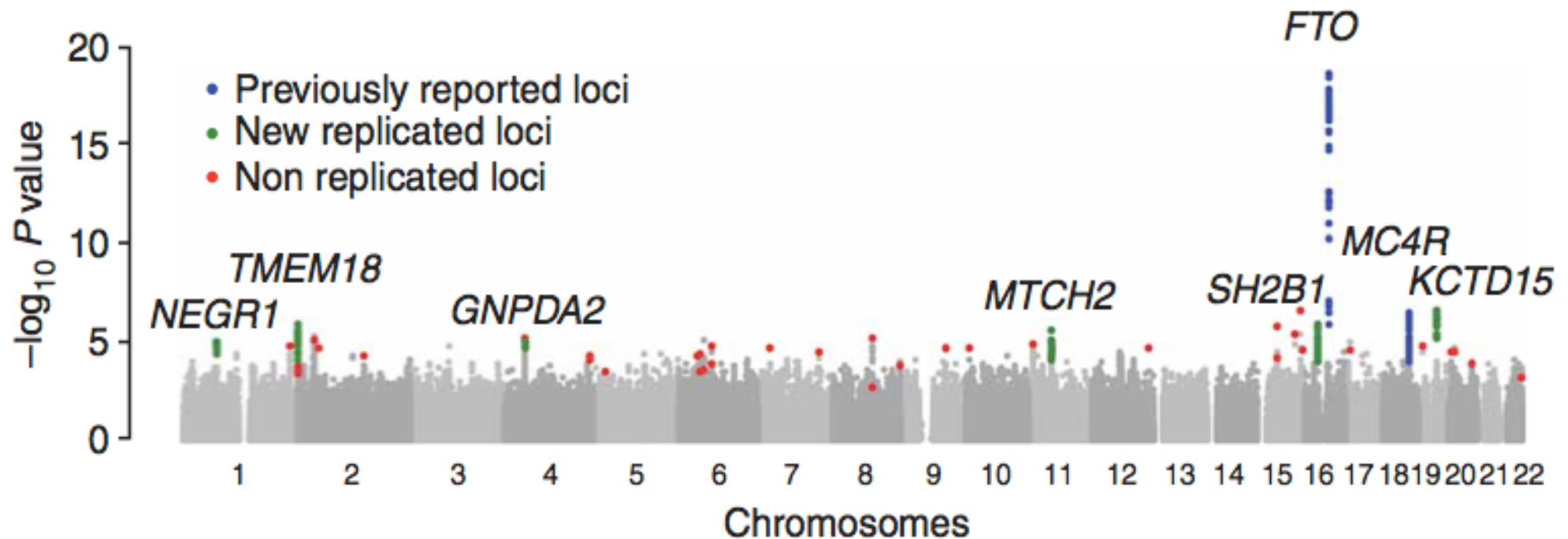
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Genome-wide association studies

- Over 2,500 GWAS in the past decade
- Identifying ~17,000 unique SNP-trait associations
 - **Body characteristics**
 - BMI, weight, height, waist and hip circumference, blood pressure, heart rate, baldness, puberty, organ function, aging, birthweight, hair colour...
 - **Blood contents**
 - Cholesterol, metabolites, calcium, glucose, insulin, vitamins, lipids, iron...
 - **Behaviours**
 - Smoking, alcohol intake, emotion recognition, response to drugs, coffee consumption, diet, anger, bitter taste response...
 - **Diseases**
 - Diabetes, asthma, eczema, cardiovascular disease, coronary heart disease, schizophrenia, gout, Alzheimer's, dementia, AIDS, autism and various cancers...

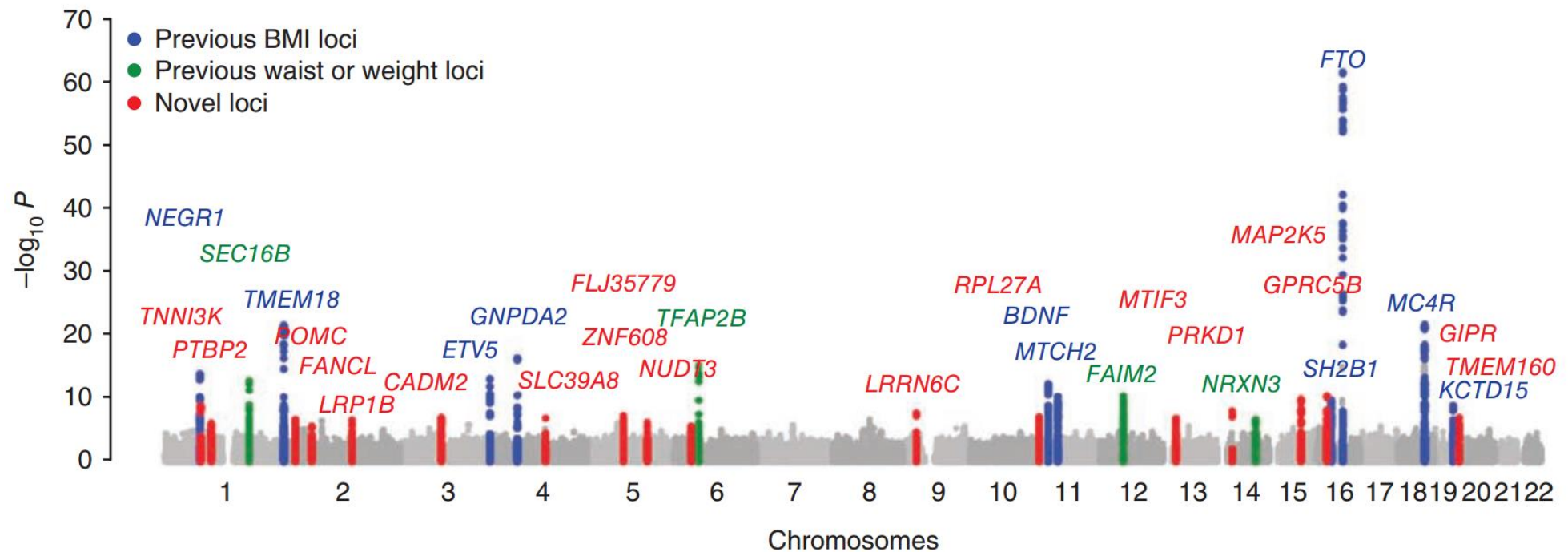
Genome-wide association studies

- Body mass index (2000 in 91,000 individuals)



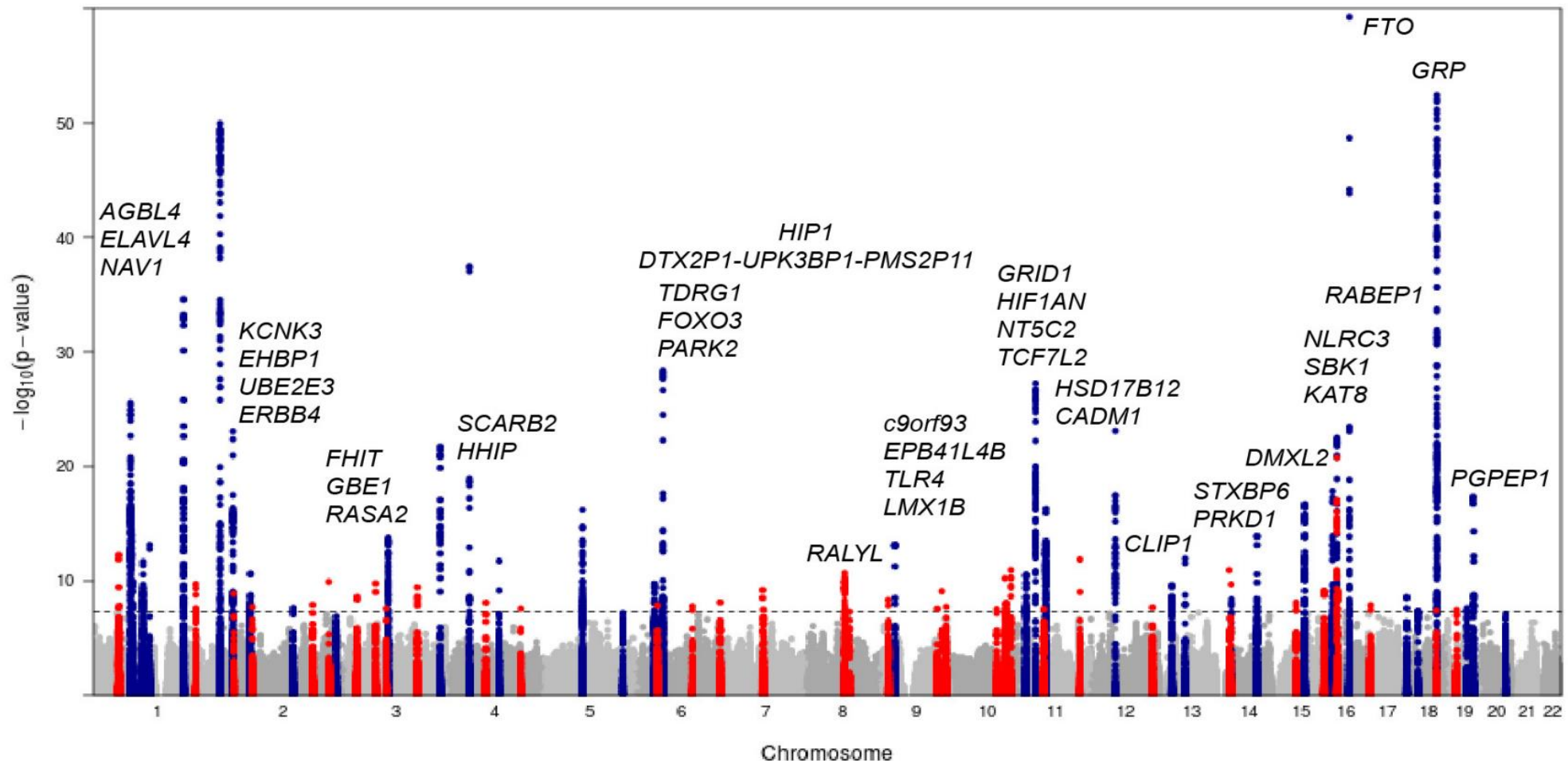
Genome-wide association studies

- Body mass index (2010 in 250,000 individuals)



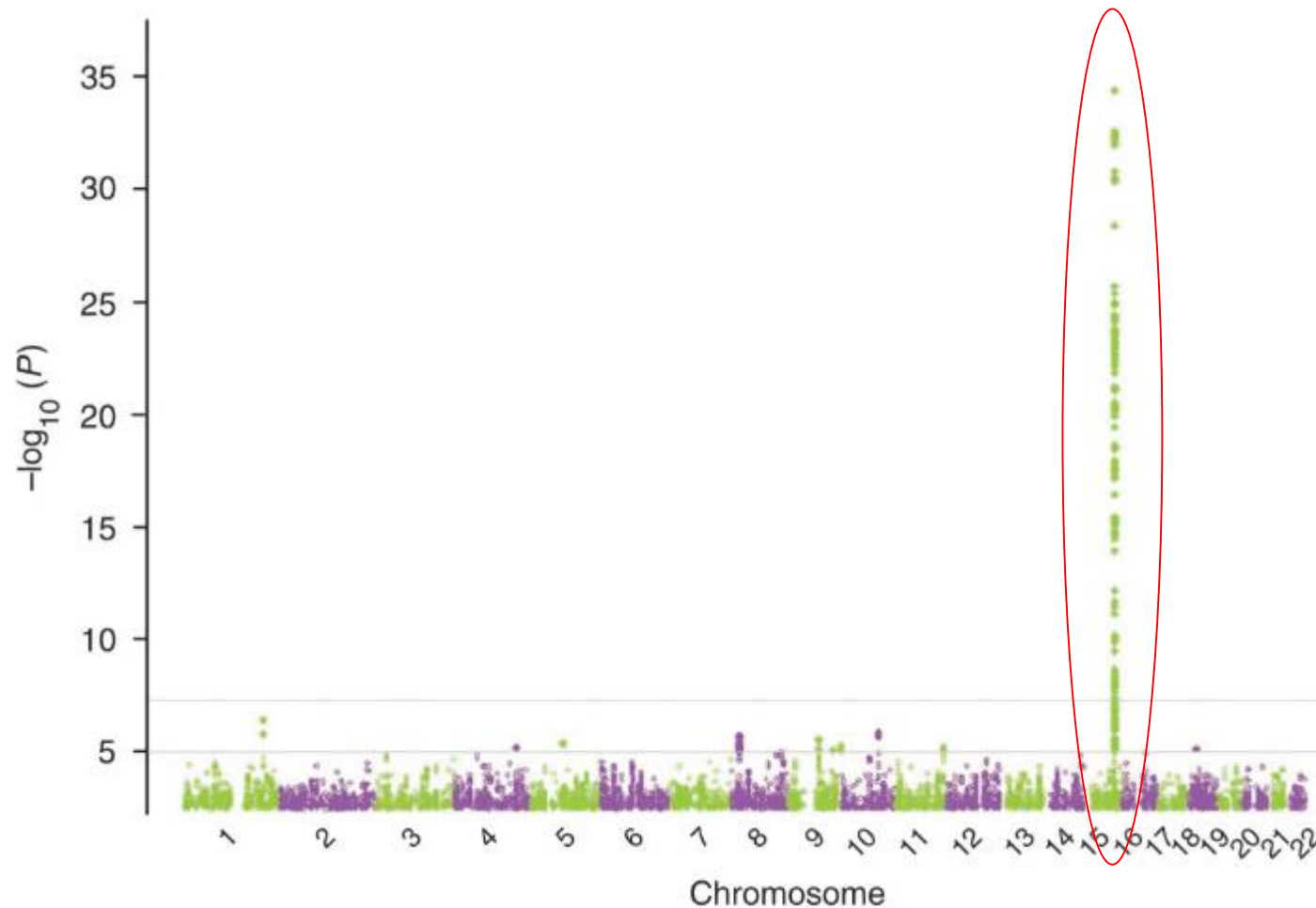
Genome-wide association studies

- Body mass index (2015 in 339,000 individuals)



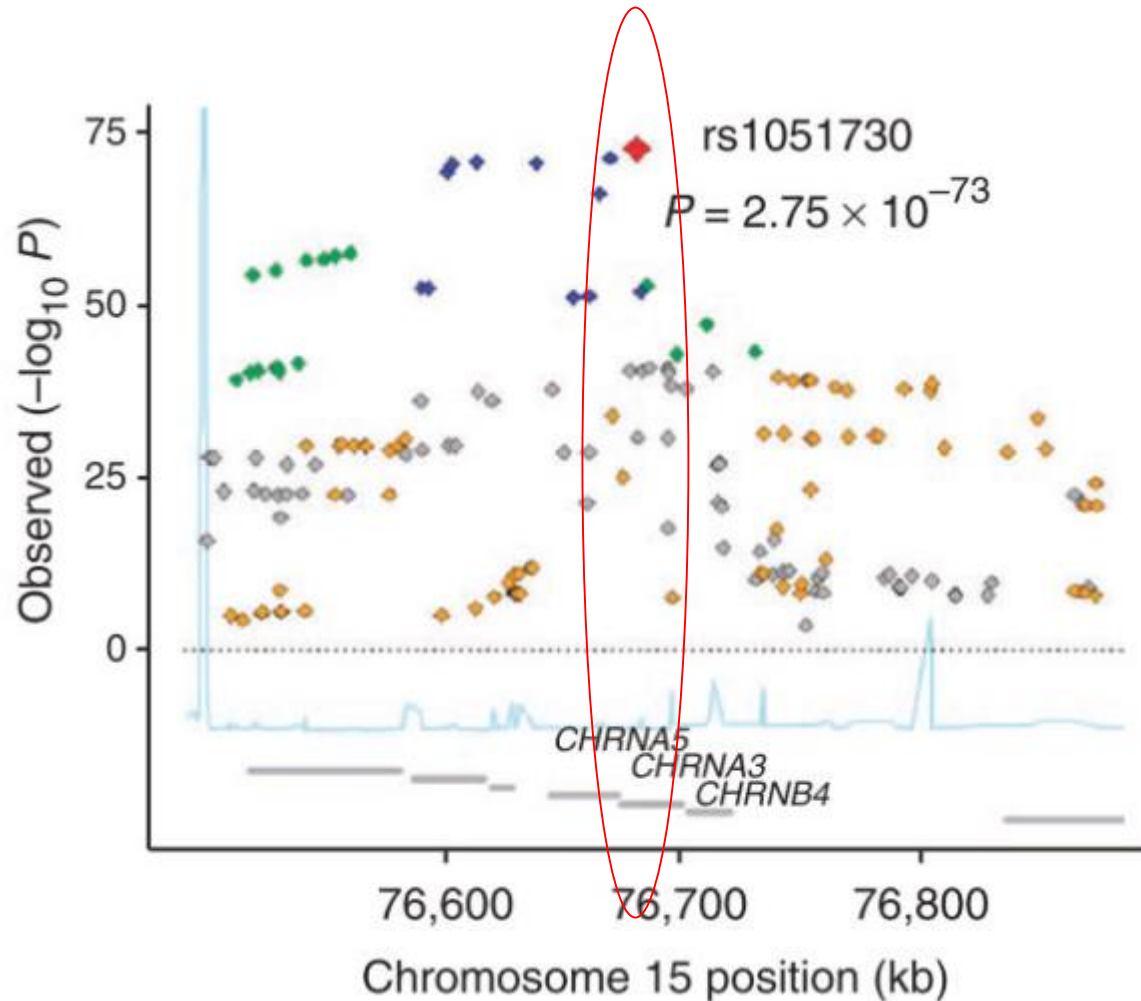
Genome-wide association studies

- Smoking (cigarettes per day)

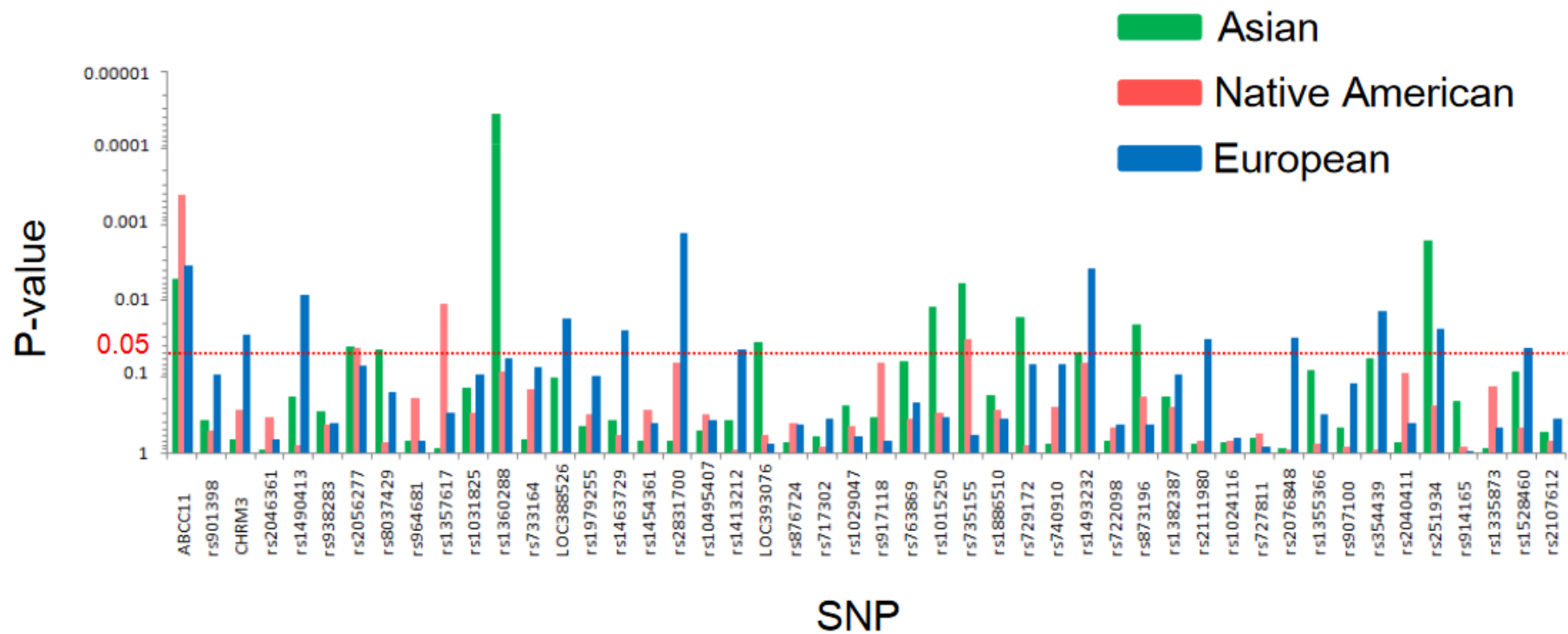


Genome-wide association studies

- Smoking (cigarettes per day) combining 2 consortium

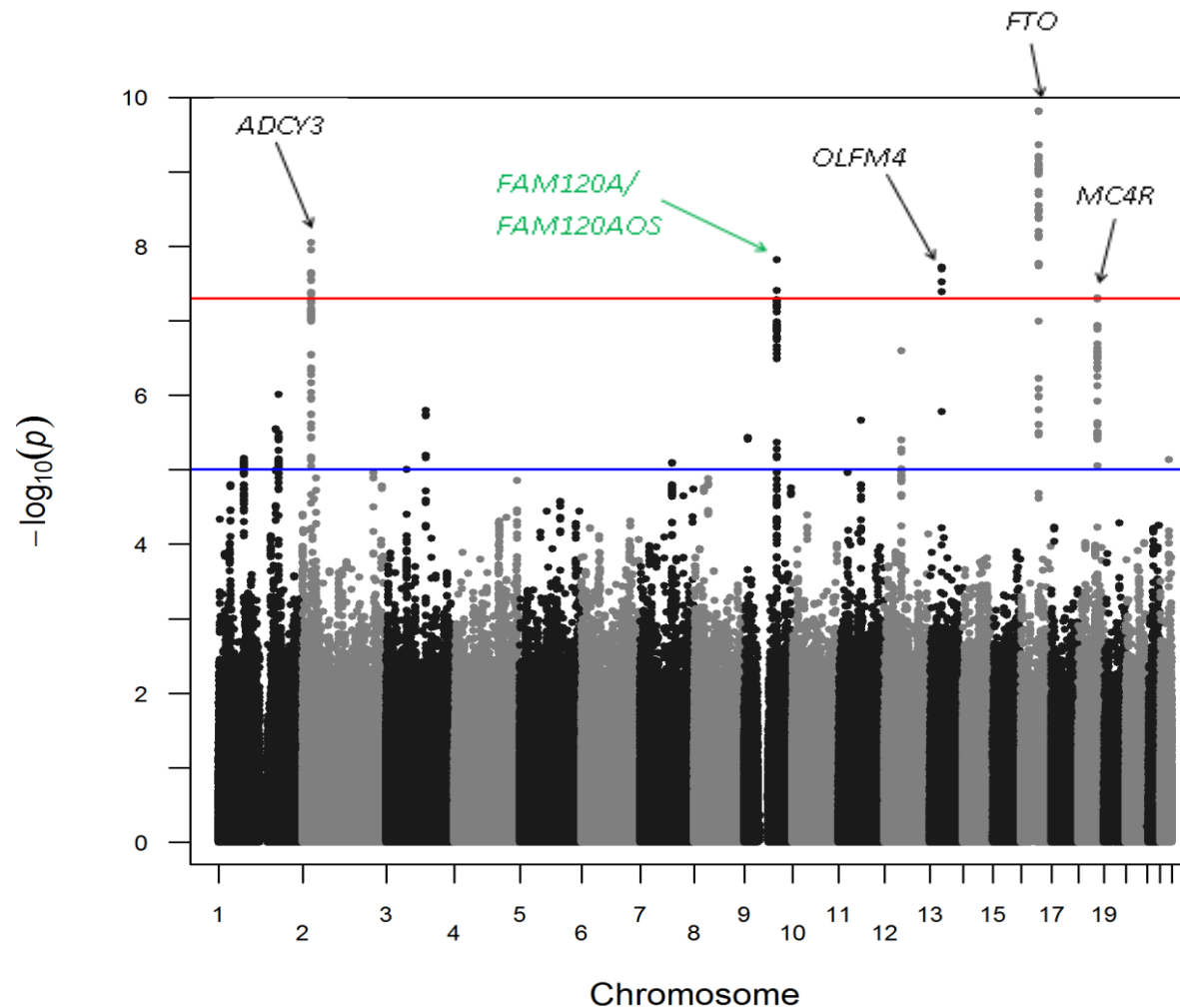


Genome-wide association studies

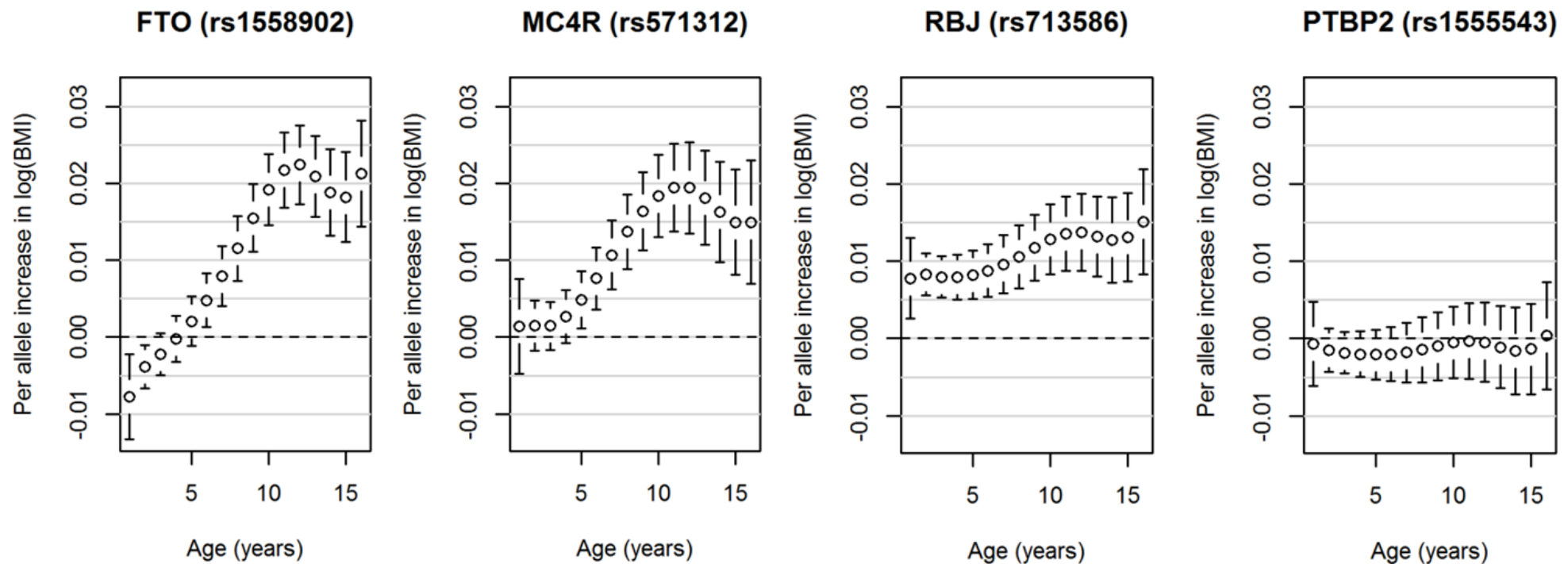


Genome-wide association studies

- Body mass index in Children of the 90s (green only found in early life)



Genome-wide association studies

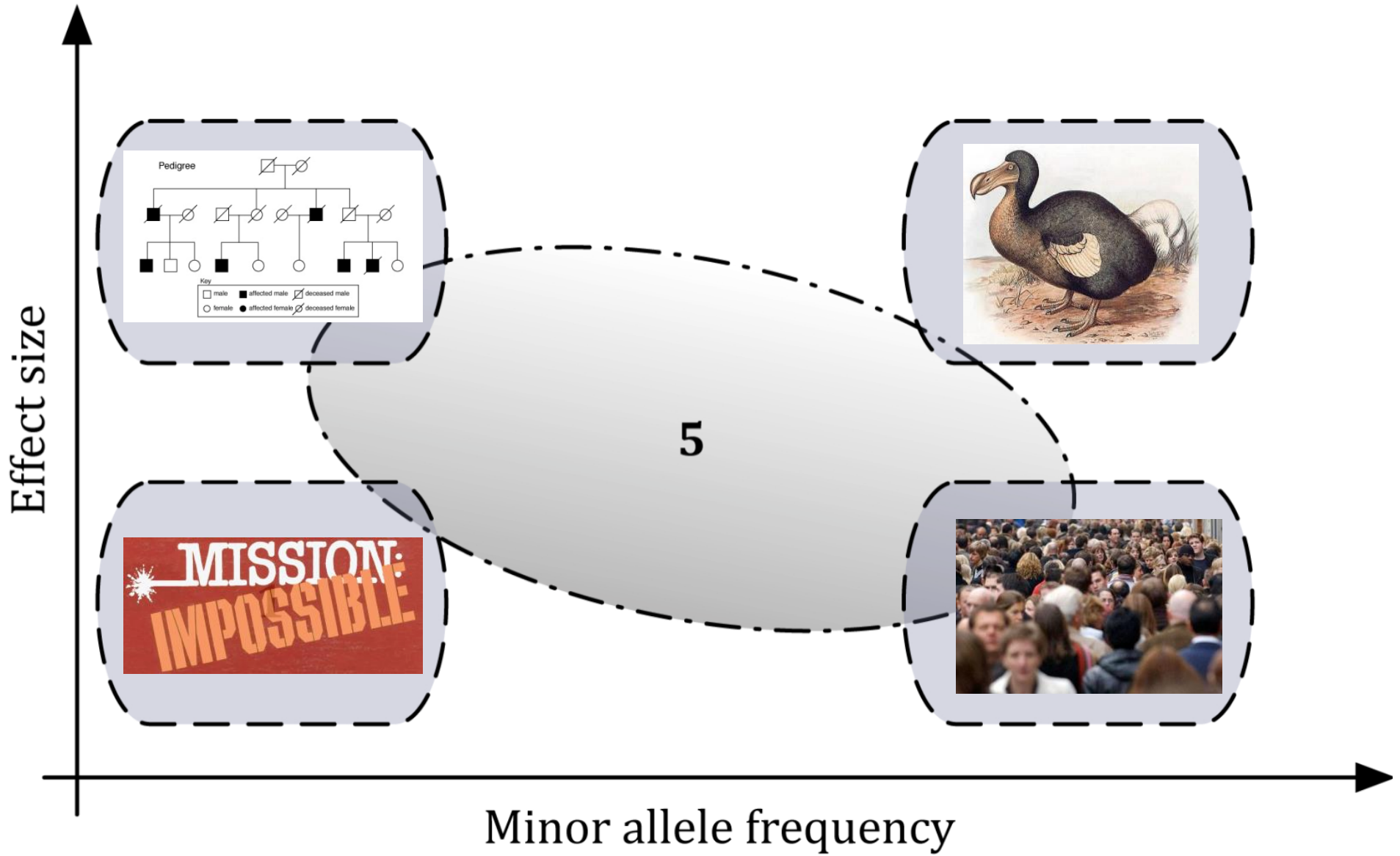


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What else?

- Genetics
 - Mendelian randomization (causal analysis)
 - Recall by Genotype
 - Rare vs. common variants



What else?

- Genetics
 - Mendelian randomization (causal analysis)
 - Recall by Genotype
 - Rare vs. common variants
 - Gene – environment interaction
- Epigenetics
 - Epigenome-wide association studies (“regulome”)
- Observational epidemiology
 - From childhood – adulthood

Game time!



THANK YOU



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ANY QUESTIONS?



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Feel free to contact me:

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