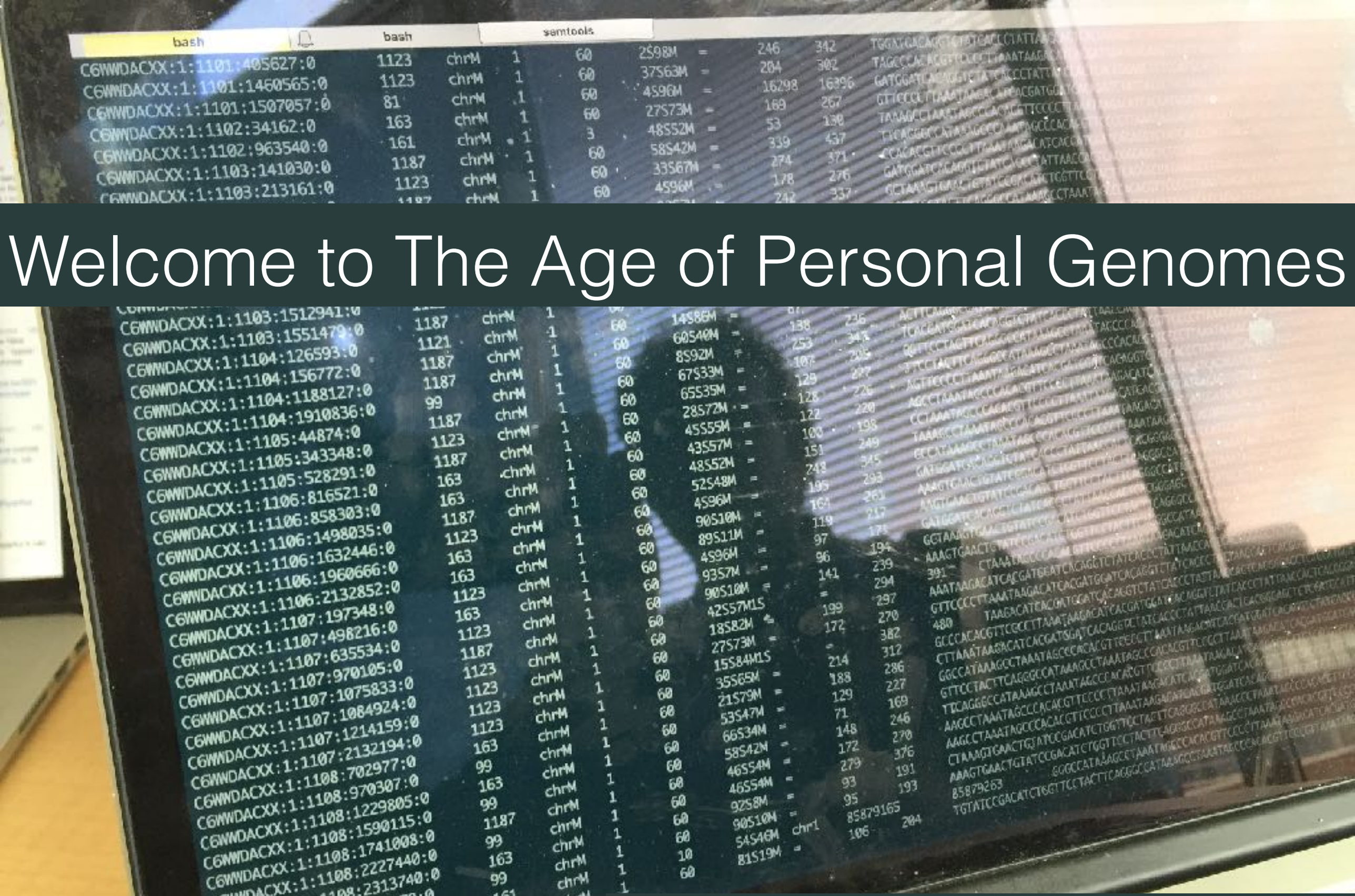


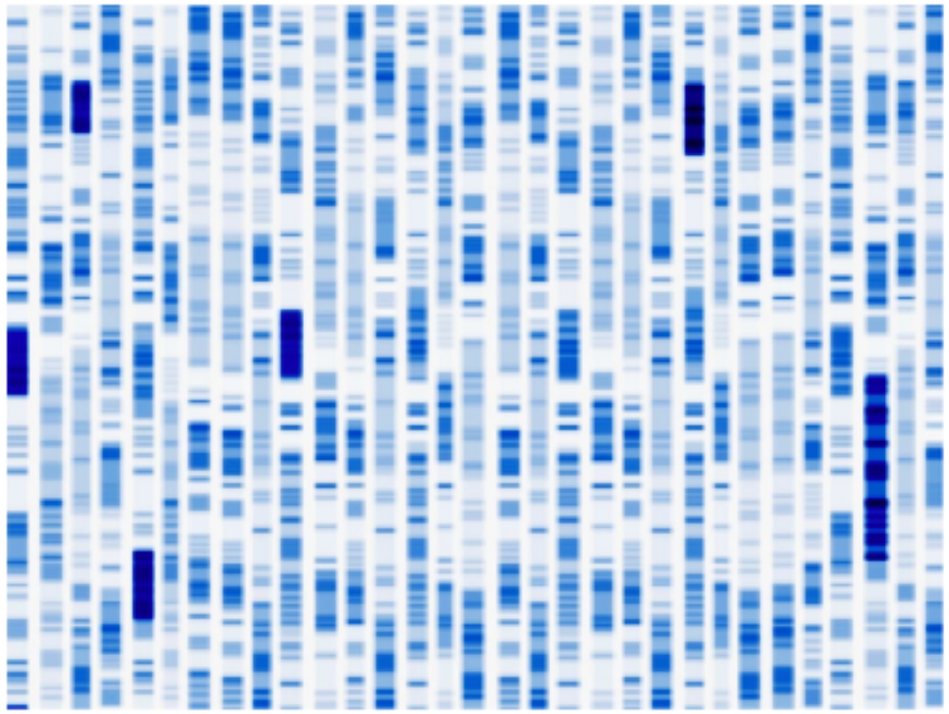
Welcome to The Age of Personal Genomes

Carl Zimmer

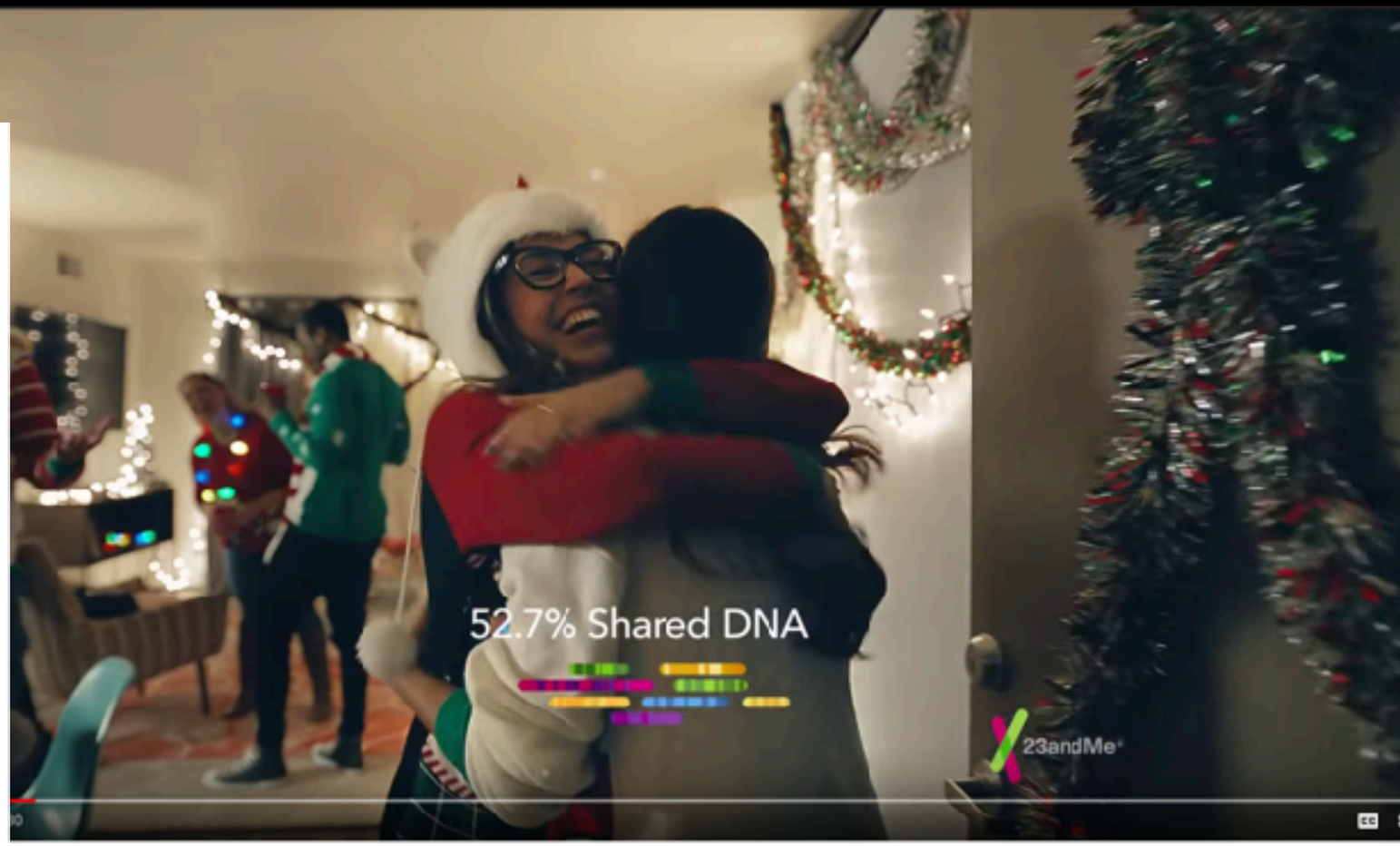
February 4, 2019, Yale MBB 452

MEGAN MOLTENI SCIENCE 12.01.17 07:00 AM

ANCESTRY'S GENETIC TESTING KITS ARE HEADING FOR YOUR STOCKING THIS YEAR

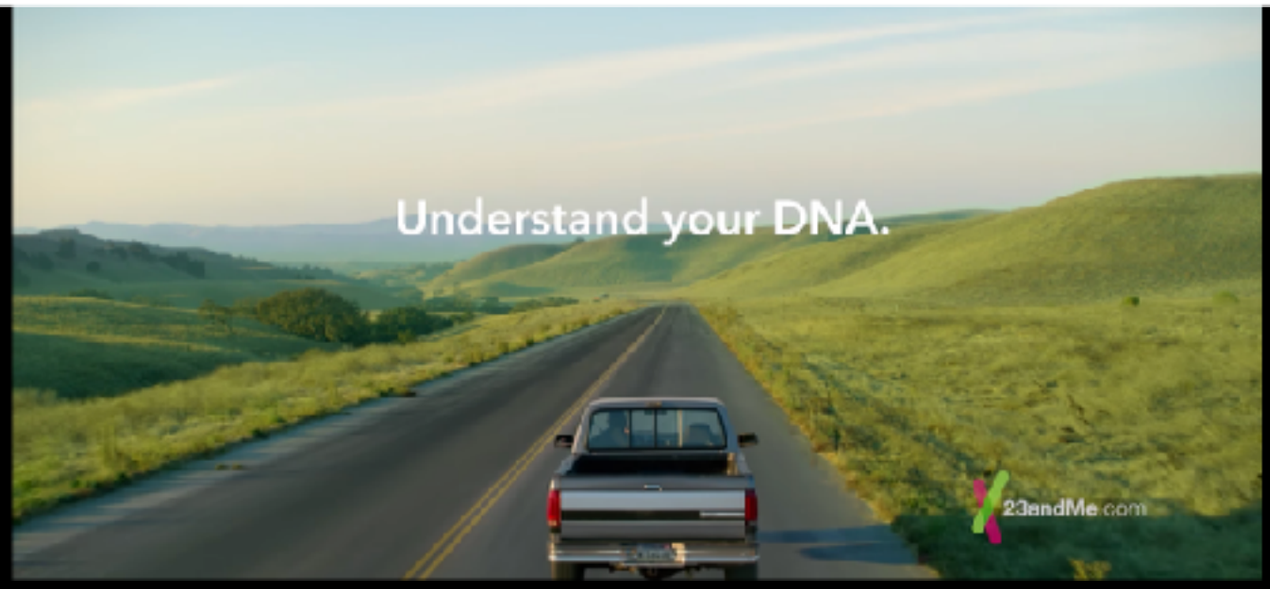


ALFRED PASIEKA/SCIENCE PHOTO LIBRARY/GETTY IMAGES



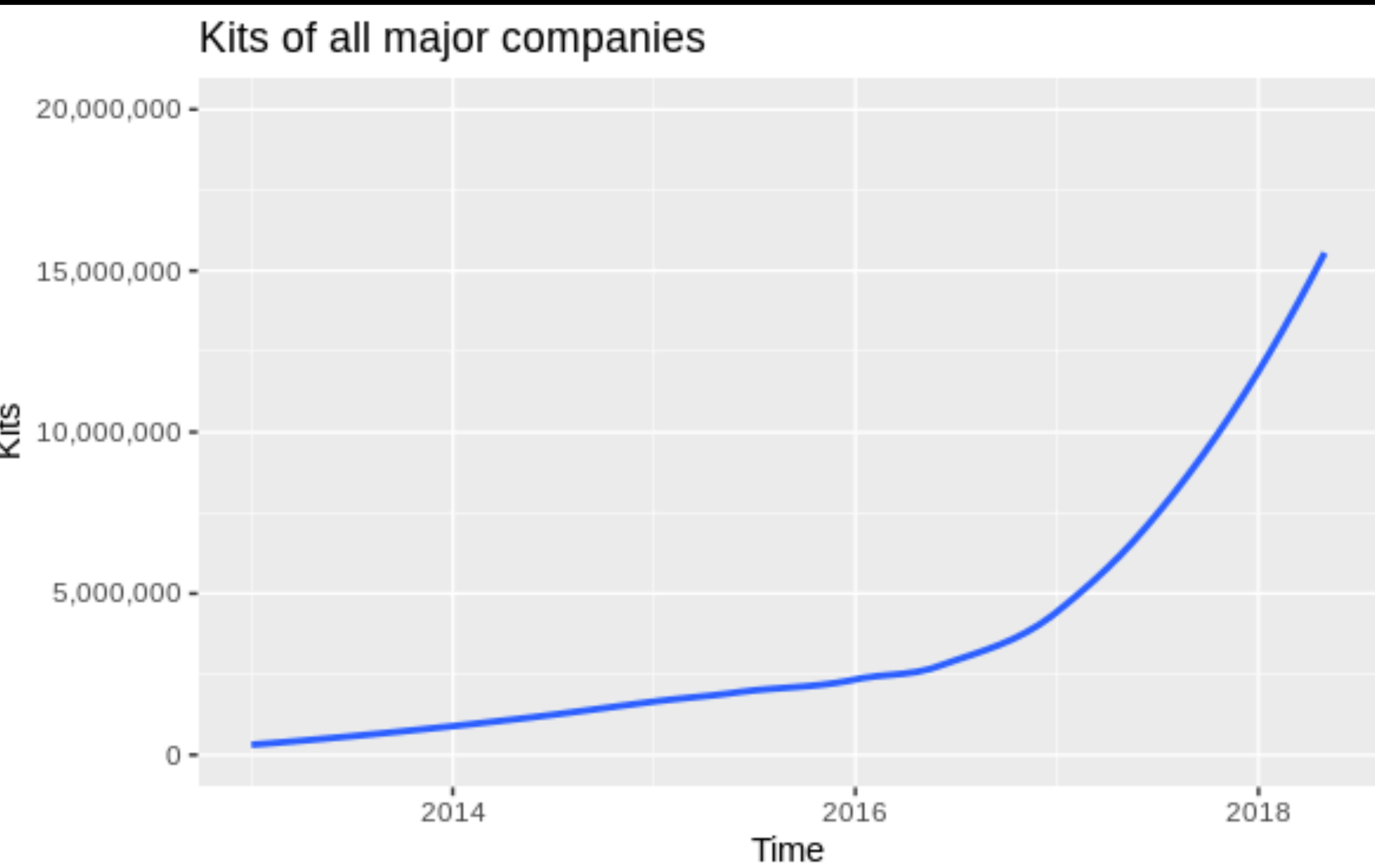
For Everyone You Love!

Up next



ispot.tv/ad/wHZ4/23andme-one-body-one-mind

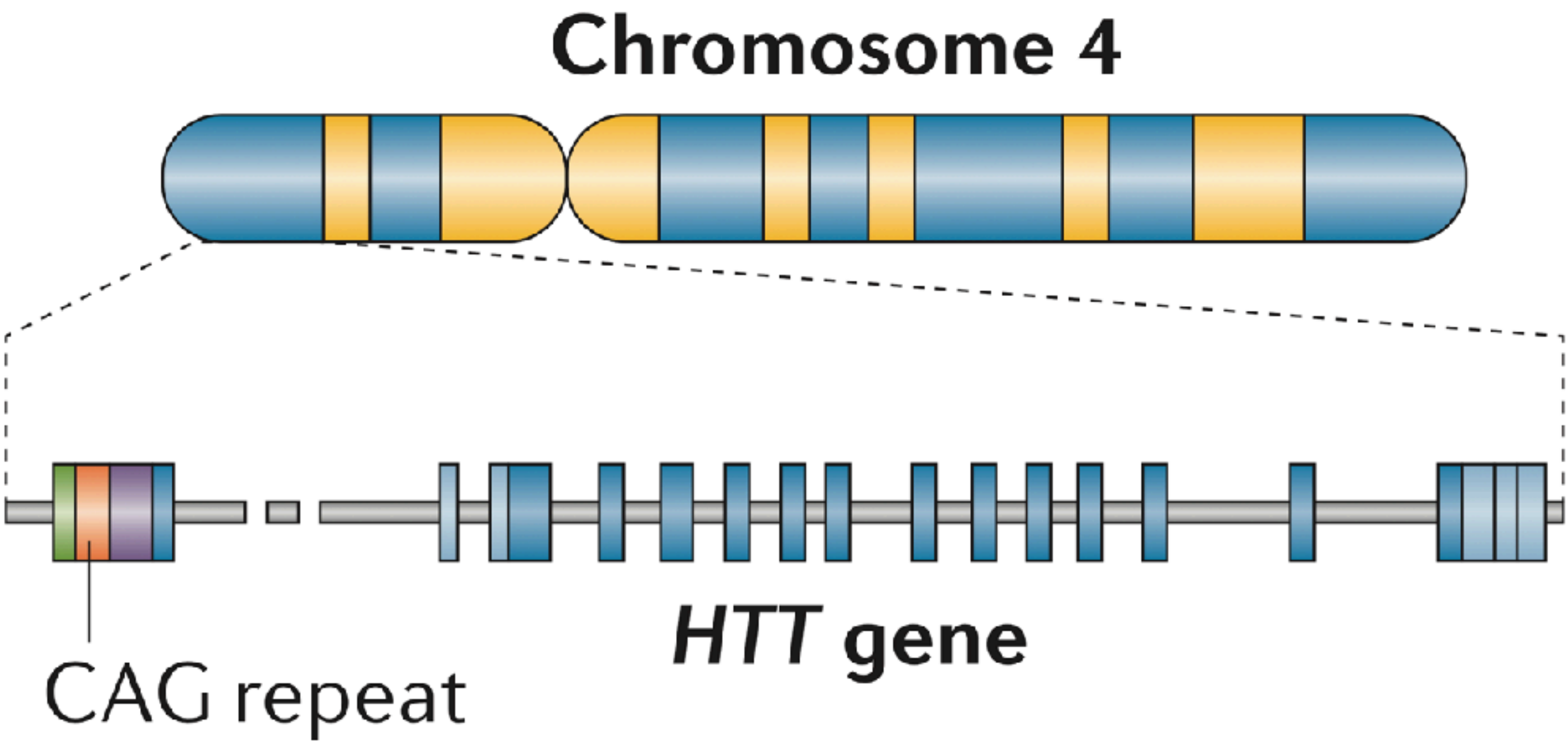
wired.com/story/ancestrys-genetic-testing-kits-are-heading-for-your-stocking-this-year/



gnxp.com/WordPress/2018/08/26/there-could-be-100-million-genotyping-kits-sold-by-january-1st-2020/

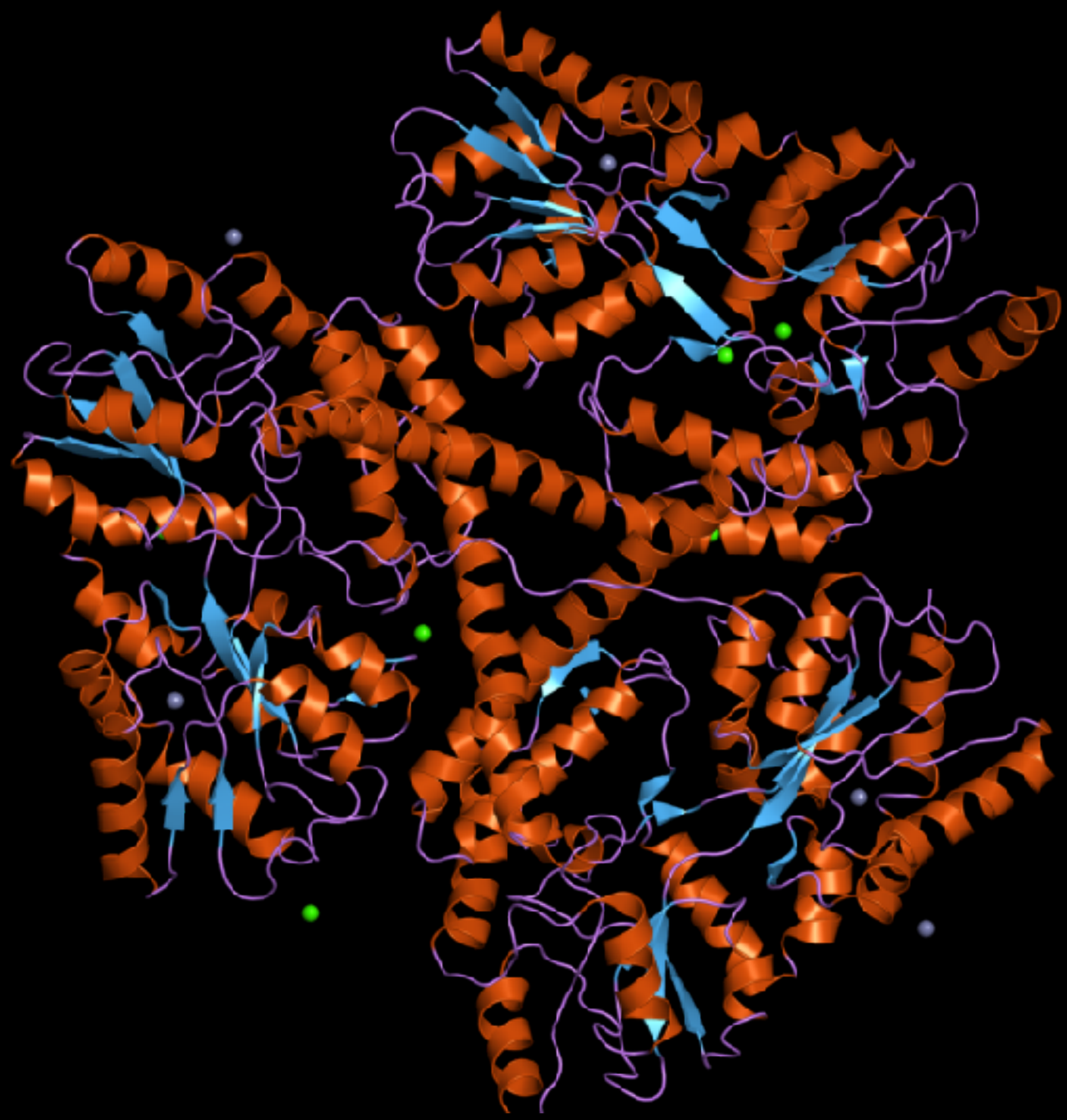
Woody Guthrie

Wikipedia



Bates et al, *Nature Reviews Disease Primers* 2015

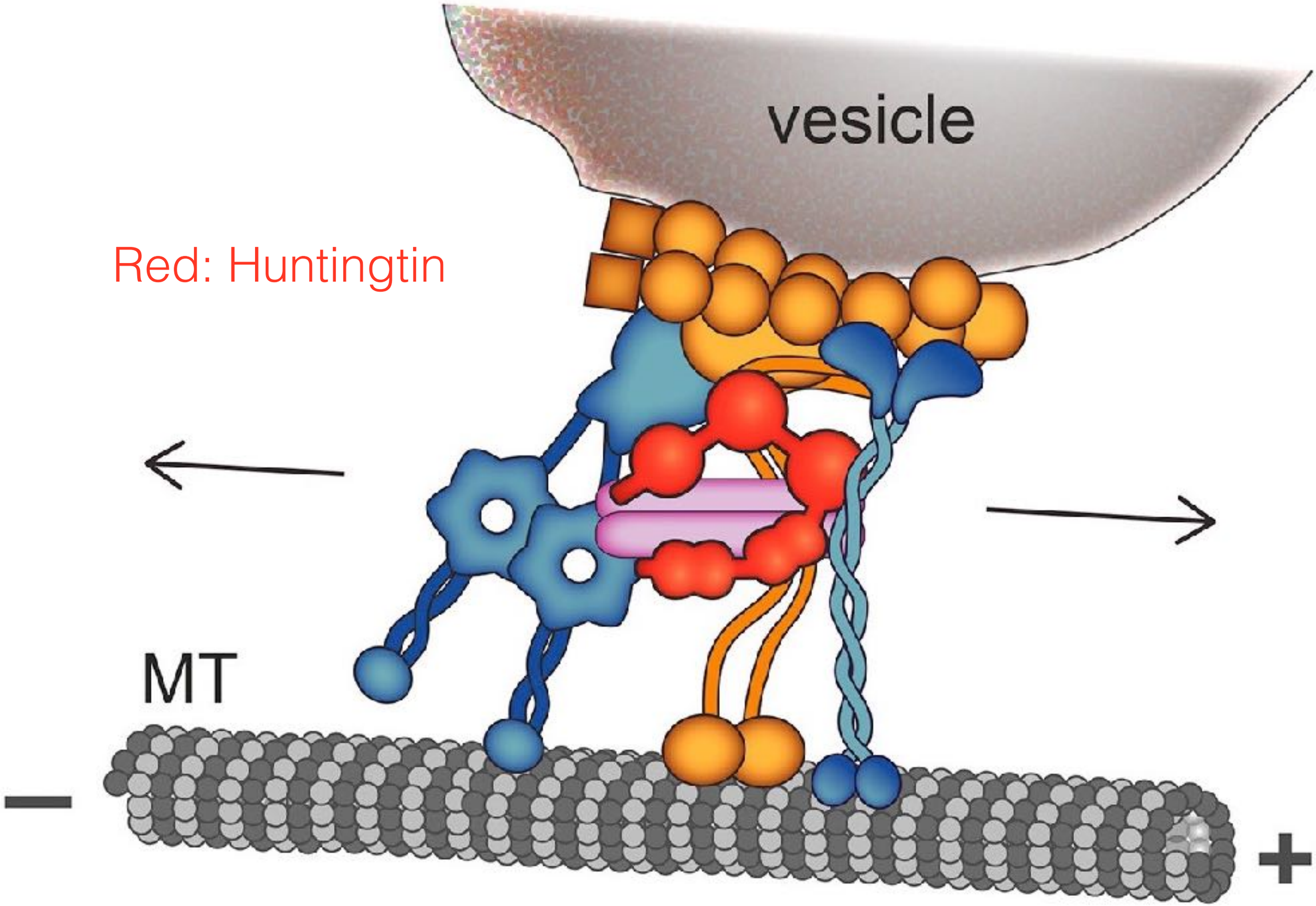
Huntingtin



Bates et al, *Nature Reviews Disease Primers* 2015

Wikipedia

Red: Huntingtin



Sadou & Humbert 2016 *Neuron* 89:910

Predictive Testing for HUNTINGTON DISEASE

Healthcare Provider Area Login

Search:

1. WHAT IS HD? | 2. TESTING FOR HD | 3. RESOURCES

How Is It Done? | Prenatal Testing | Deciding To Test | Alternatives | Interpreting Results | Undergo Testing

What is Predictive Testing?

This section is intended to help the individual considering testing for HD reflect on some of the issues involved in testing and in dealing with the test results.

Family, friends and professional support people may also find this material useful in supporting those considering testing.

In 1983, genetic markers closely linked to the Huntington disease (HD) gene were identified. This discovery, together with the identification of additional genetic markers, led to the development of predictive testing

HD Resources

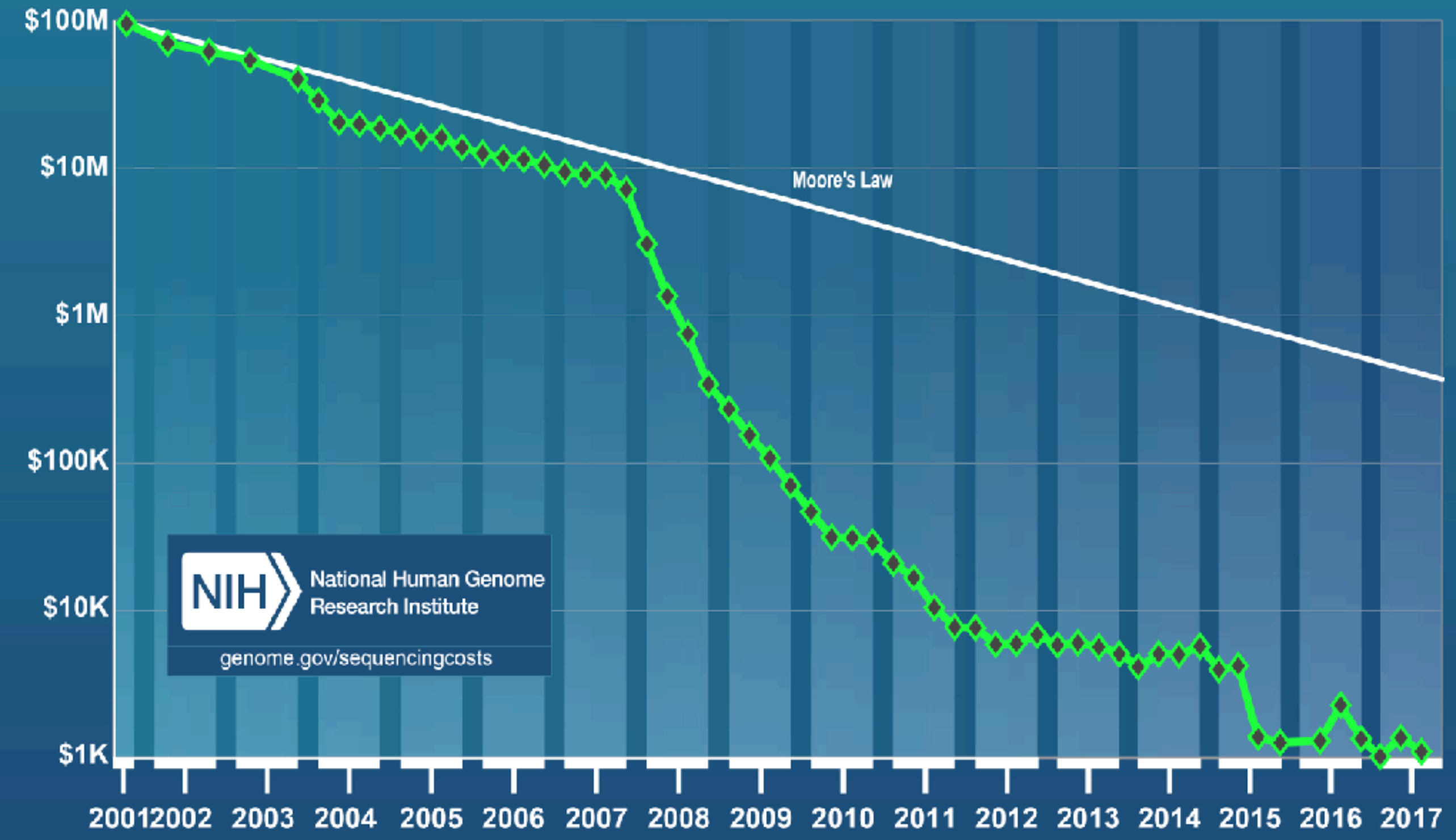
There are many other online websites and resources which provide information regarding HD in general, support groups in your area, research updates and opportunities to be involved in clinical trials.

Find out more

Our Stories

We understand that learning that someone in your family has HD can be devastating. It can leave you with questions, concerns, and no idea where to turn next. Find about more about what others have done in your situation – you are not alone.

Cost per Genome



CARL ZIMMER

The Powers, Perversions,

and Potential *of* Heredity

UNDERSTAND YOUR GENOME®

IT STARTS WITH YOU

THINK ME. THINK WE. *think* **BIG**

illumina

TruGenome Predisposition Screen

Clinical Report

illumina

TruGenome Predisposition Screen

Clinical Report

No pathogenic or likely pathogenic variants were found in the 1,691 genes evaluated that are expected to be clinically significant for the patient. However, this screen only detects single nucleotide substitutions and insertions and deletions of up to seven base pairs. Other types of genetic variants, including but not limited to larger insertions or deletions, copy number variants and trinucleotide repeats are not reported in this screening test. Further, the coverage of each gene is less than 100%. Therefore, clinically significant variants could exist in this genome that are not detected with this test. The coverage for each gene is provided in the Gene-Disease appendix.

illumina

TruGenome Predisposition Screen

Clinical Report

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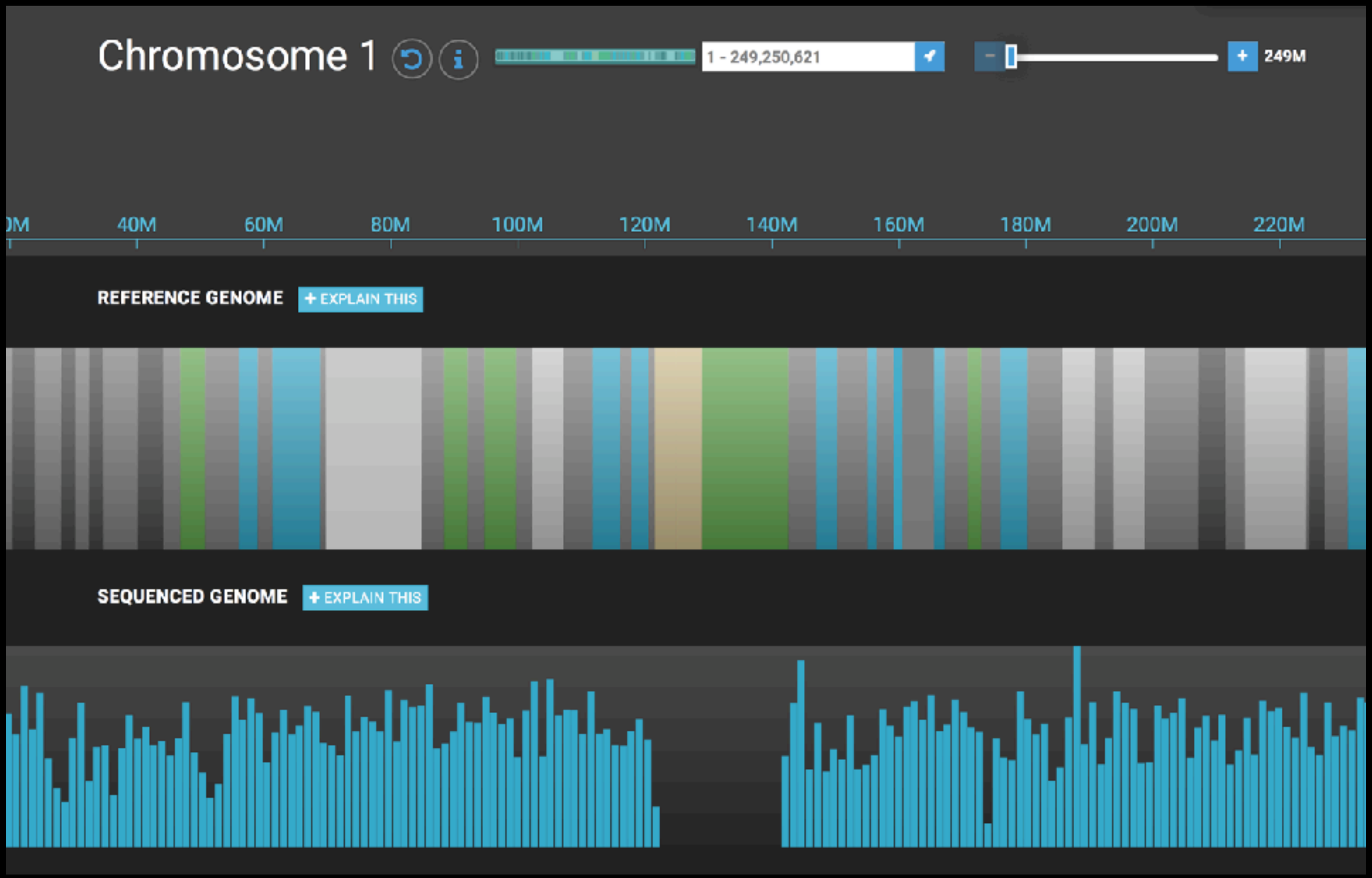
TruGenome Predisposition Screen

Clinical Report

Findings Regarding Carrier Status				
Variant	**Interpretation**	**Associated Condition**	**Mode of Inheritance**	**Zygosity**
MEFV c.2177T>C (p.Val726Ala)	Pathogenic	Familial Mediterranean Fever	Autosomal Recessive	Heterozygous
MBL2 c.154C>T (p.Arg52Cys)	Likely Pathogenic	Mannose-Binding Protein Deficiency	Autosomal Recessive	Heterozygous



understandyourgenome.com

Here is what we see in your DNA...

Your odds of developing male pattern baldness are increased if you are Caucasian.

You are less likely to have flush reaction if you drink alcohol.

Your muscle fibers are built for power.

You are likely to perceive bitter tastes.

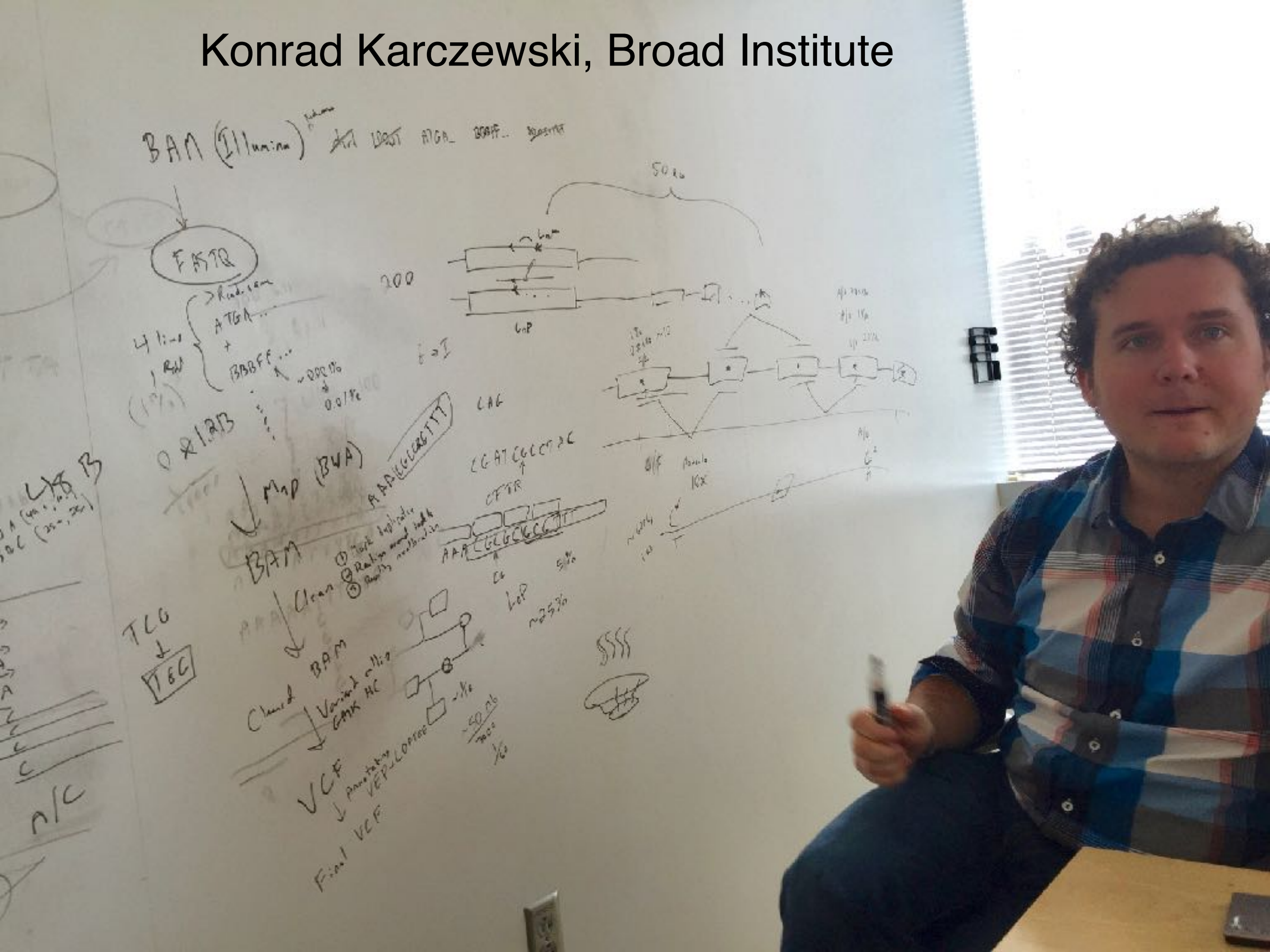
understandyourgenome.com

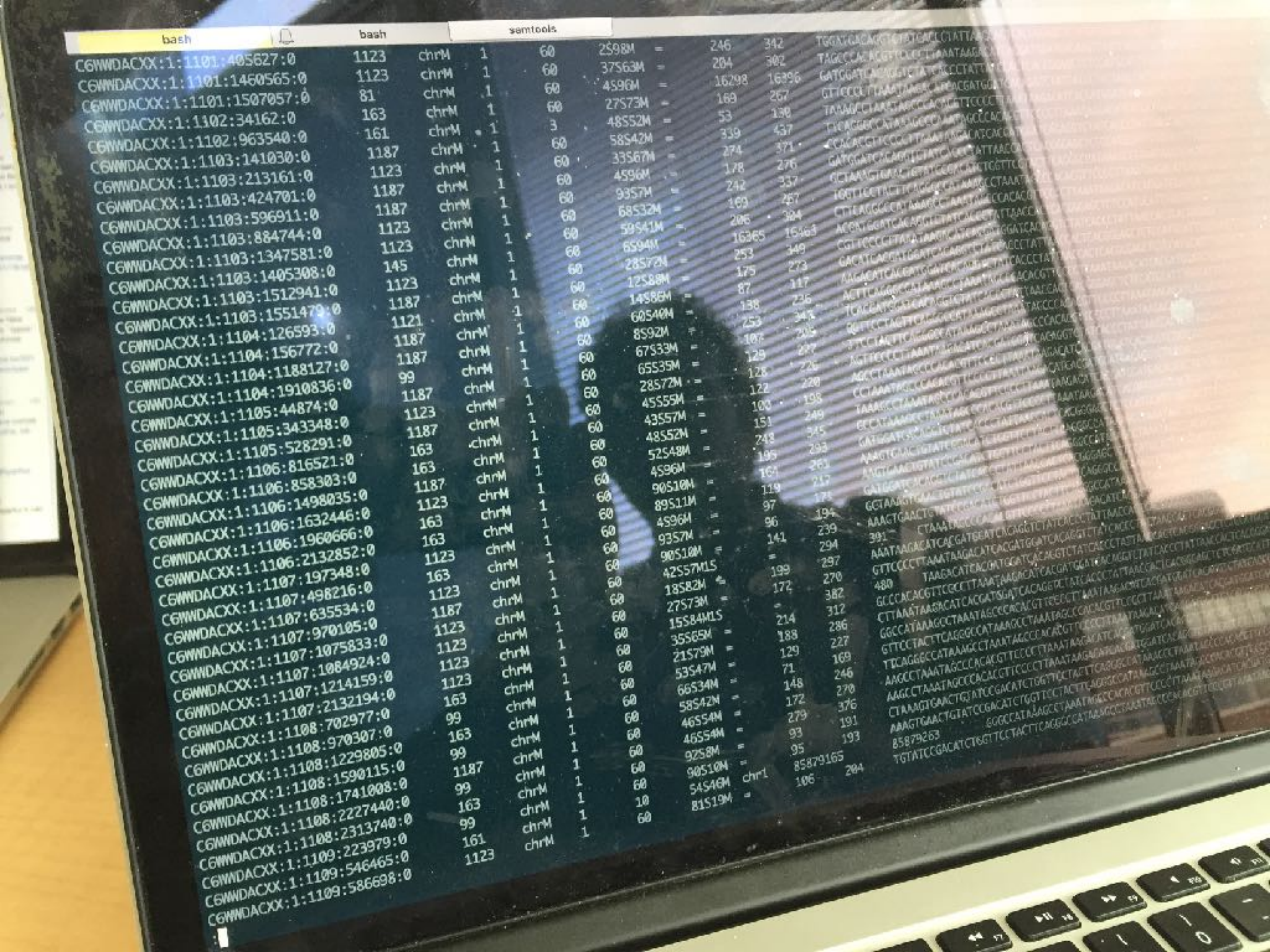

illumina


illumina


illumina

Konrad Karczewski, Broad Institute

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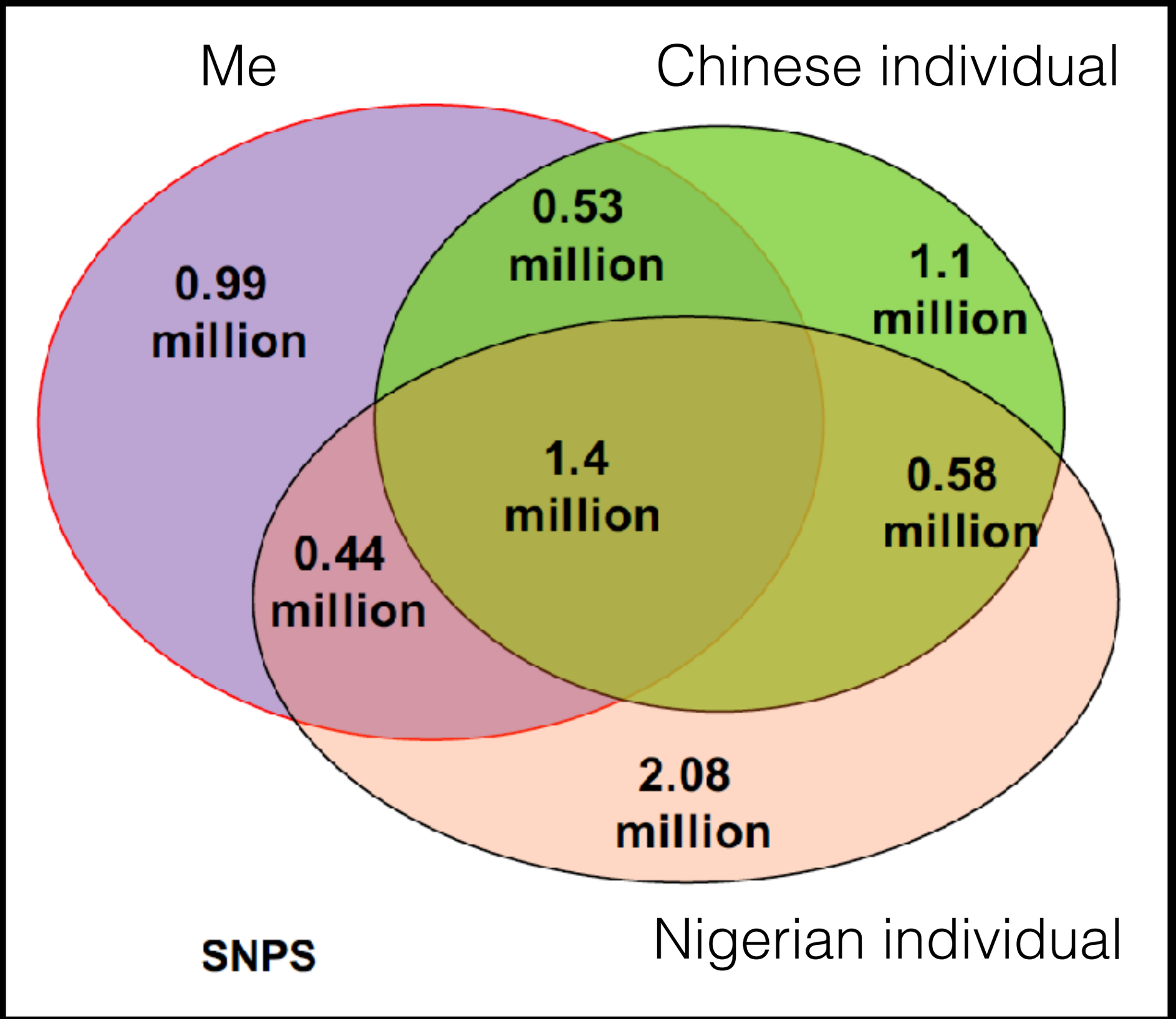
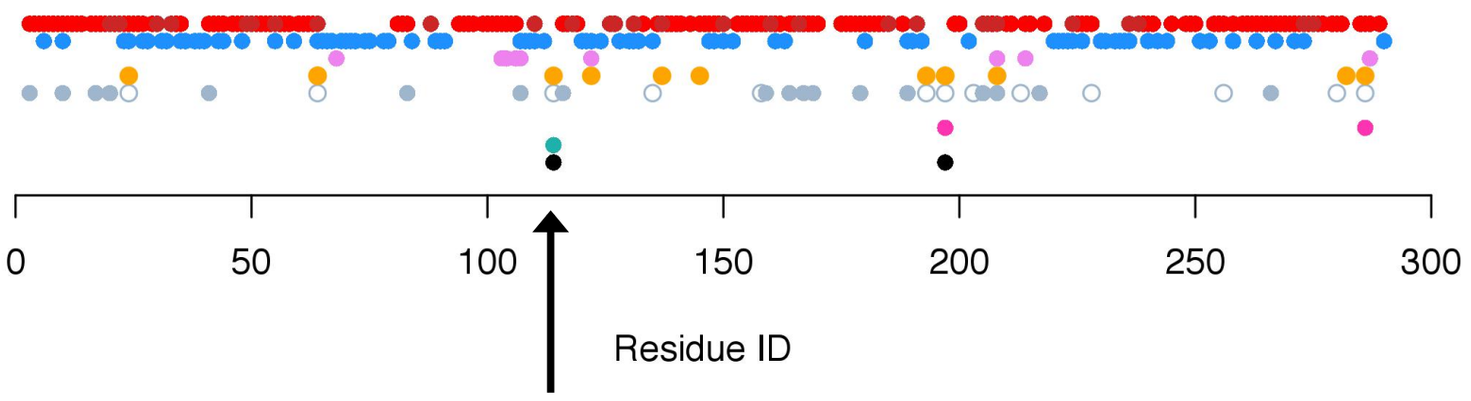
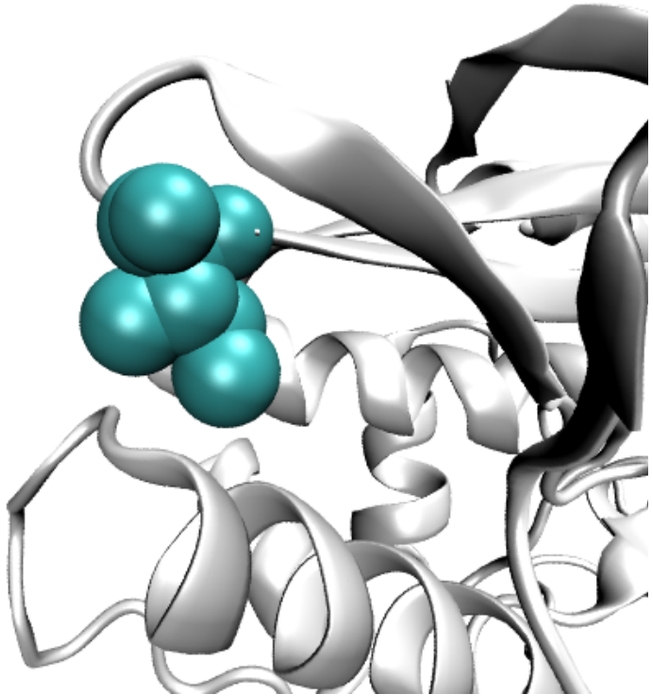


Analysis courtesy of Sushant Kumar, Yale University



114: I->T



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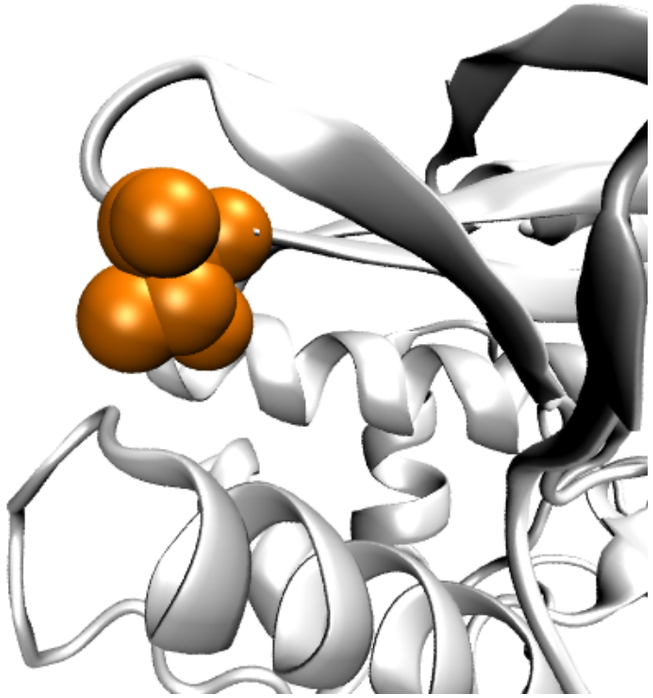

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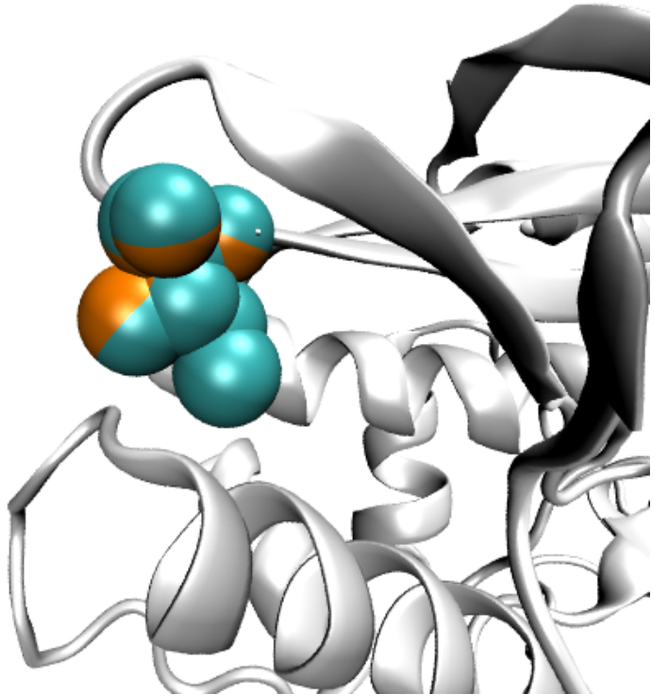
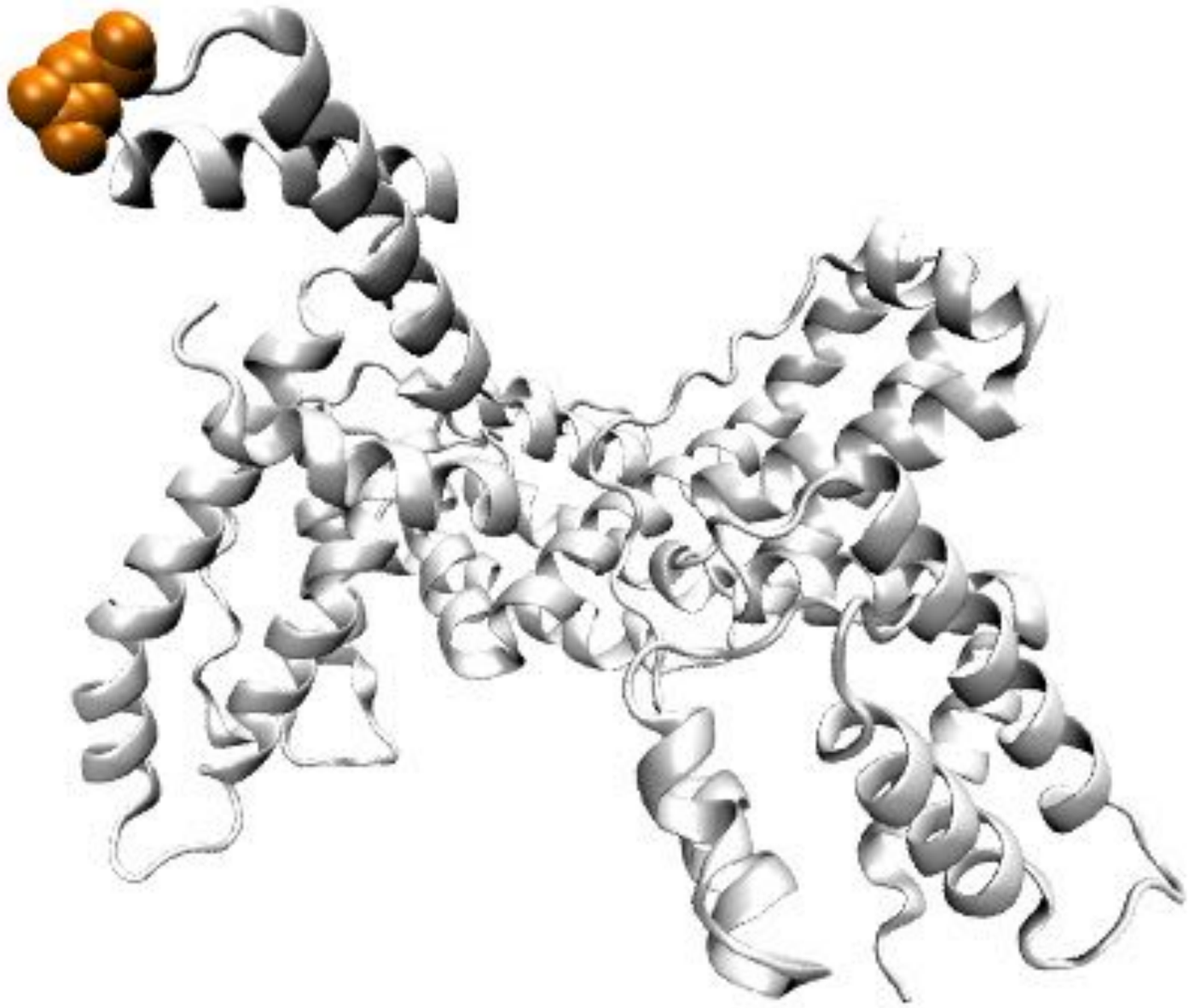


(superimposed)

Analysis courtesy of Declan Clarke, Yale University



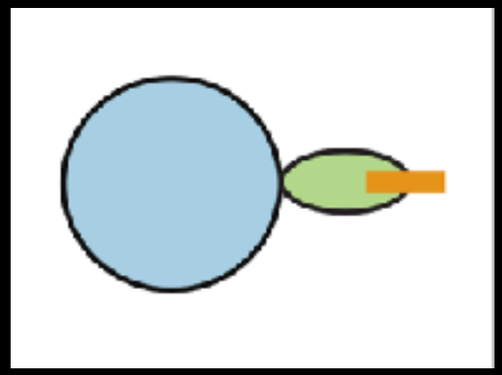
Ali Torkamani,
Scripps Translational
Science Institute

My variant: rs11209026
Gene: IL23R

Bob Handsaker,
Broad Institute

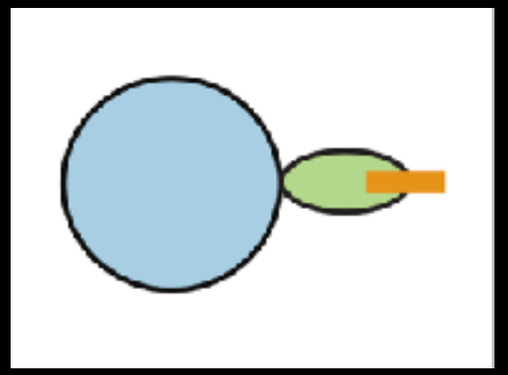
Haptoglobin

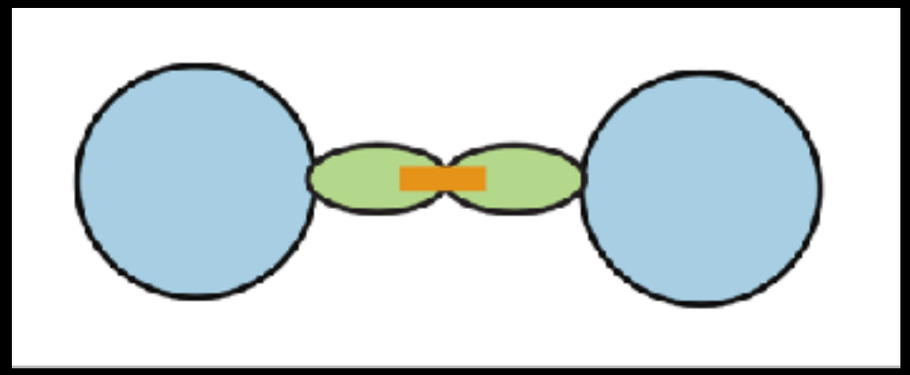
Boettger et al *Nature Genetics* 2016 48:359–366



Haptoglobin

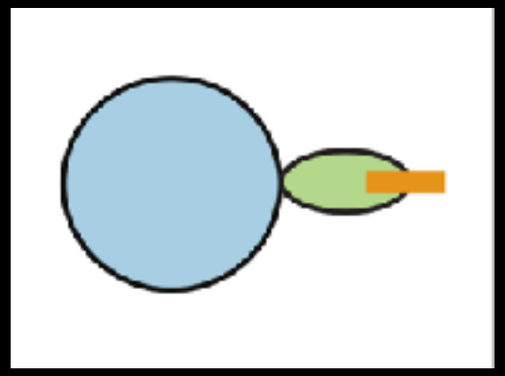
Boettger et al *Nature Genetics* 2016 48:359–366

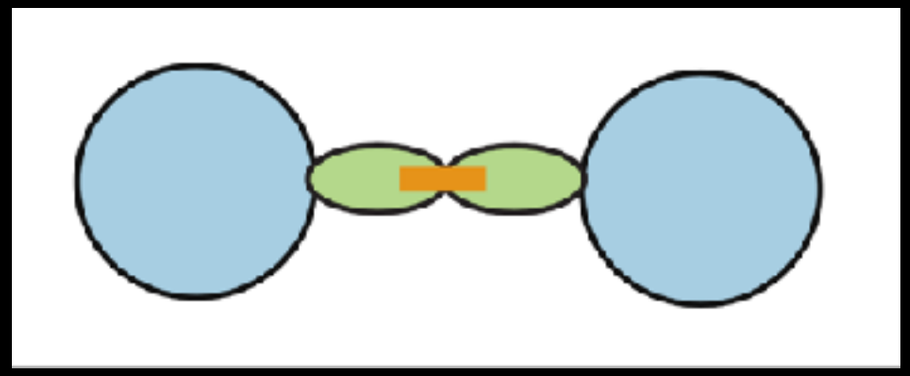




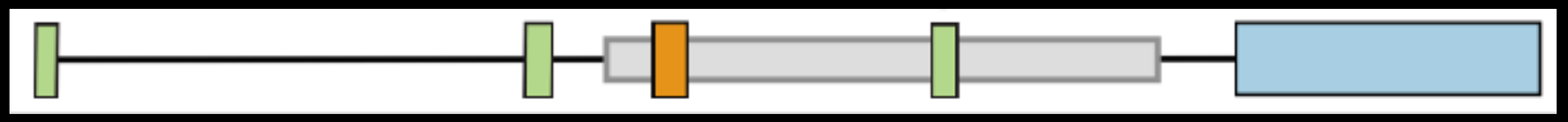
Haptoglobin

Boettger et al *Nature Genetics* 2016 48:359–366



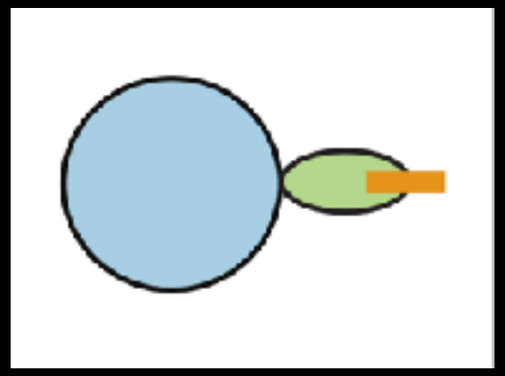


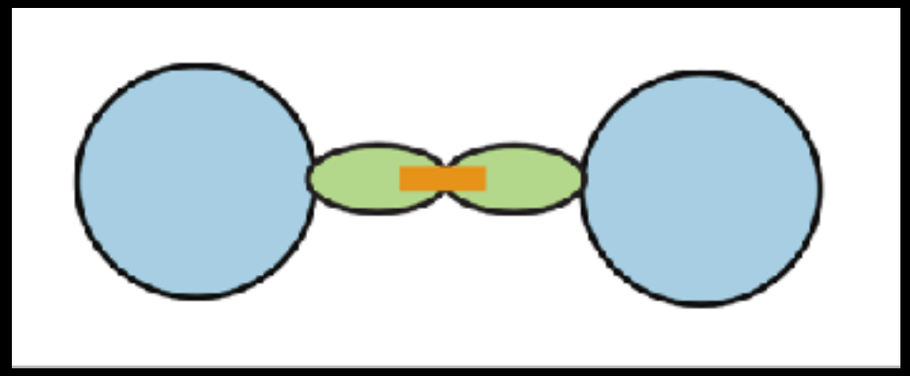
Lower cholesterol



Haptoglobin

Boettger et al *Nature Genetics* 2016 48:359–366

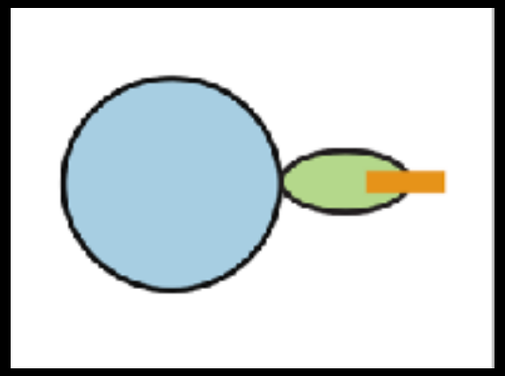


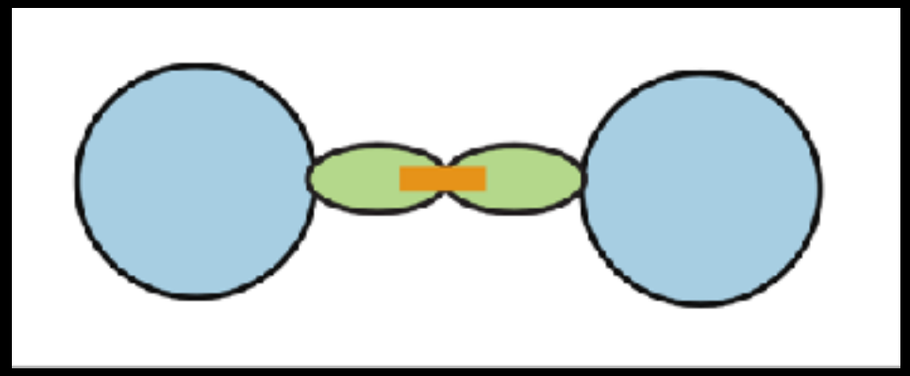


Lower cholesterol

Haptoglobin

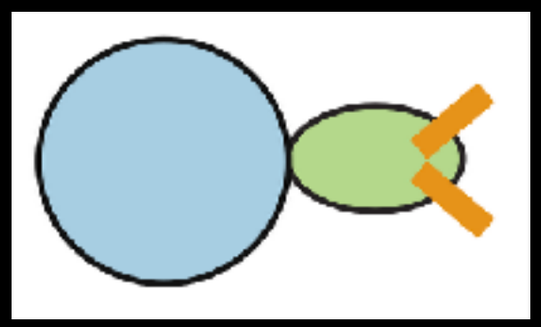
Boettger et al *Nature Genetics* 2016 48:359–366



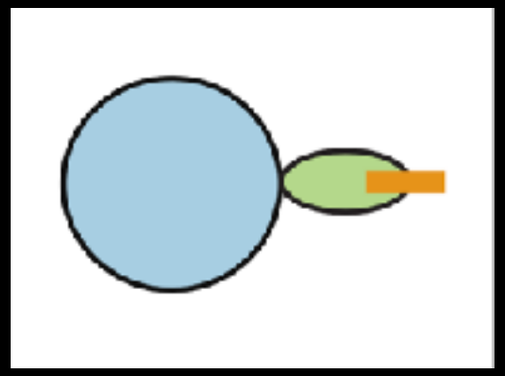


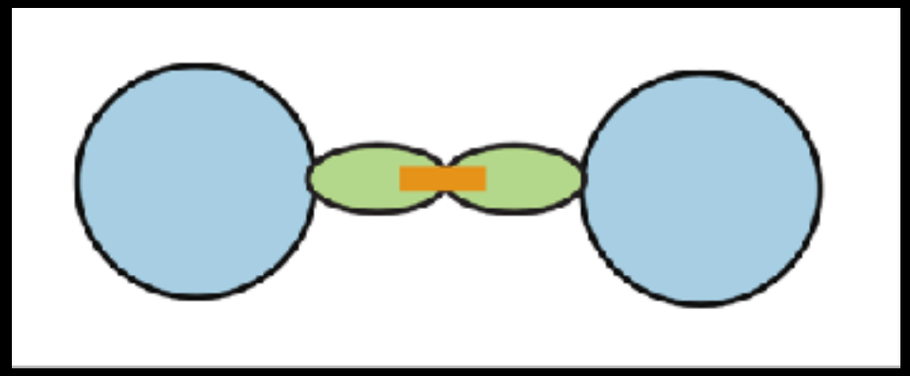
Lower cholesterol

Haptoglobin



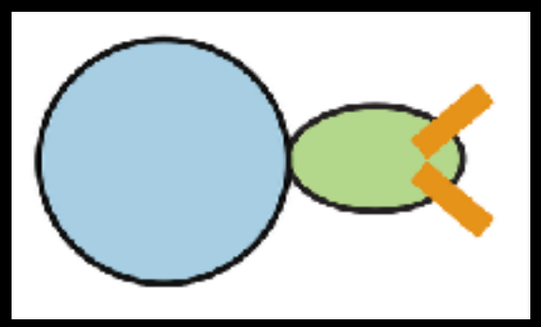
Boettger et al *Nature Genetics* 2016 48:359–366

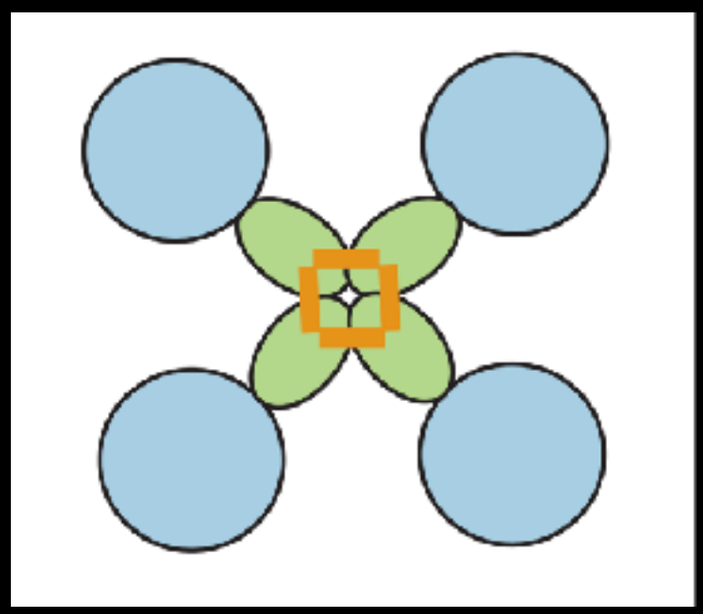




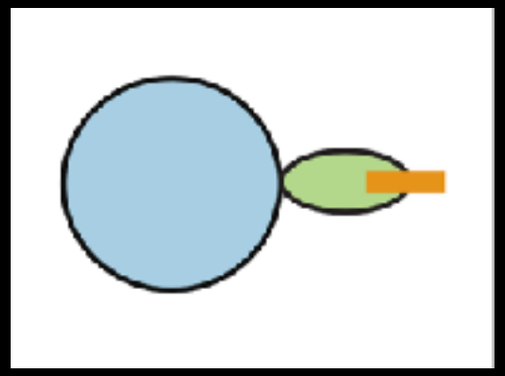
Lower cholesterol

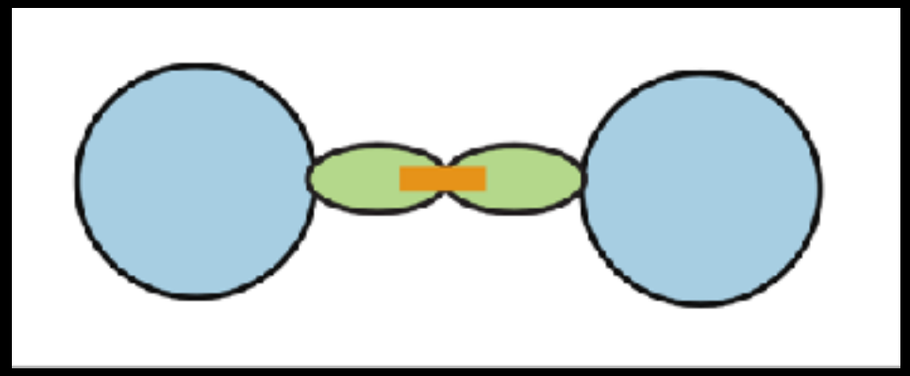
Haptoglobin





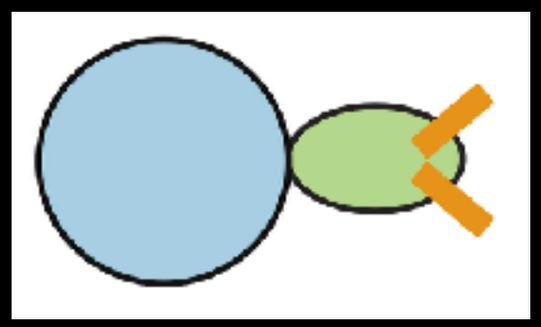
Boettger et al *Nature Genetics* 2016 48:359–366

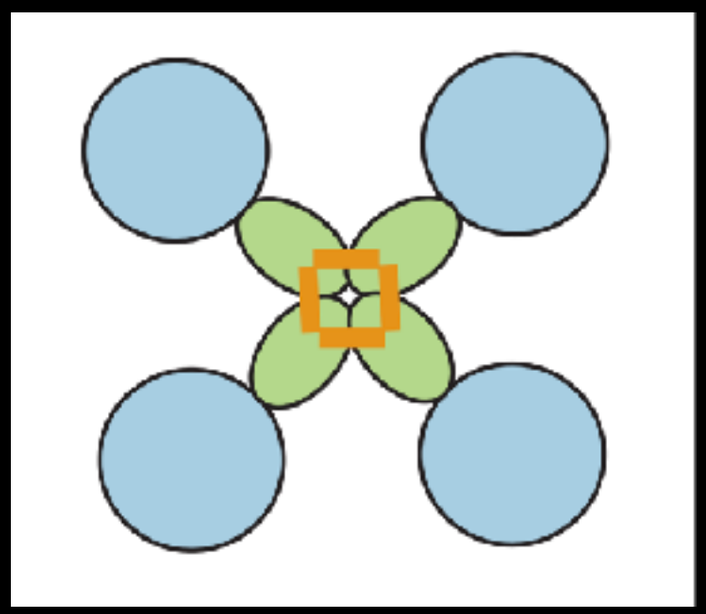




Lower cholesterol

Haptoglobin

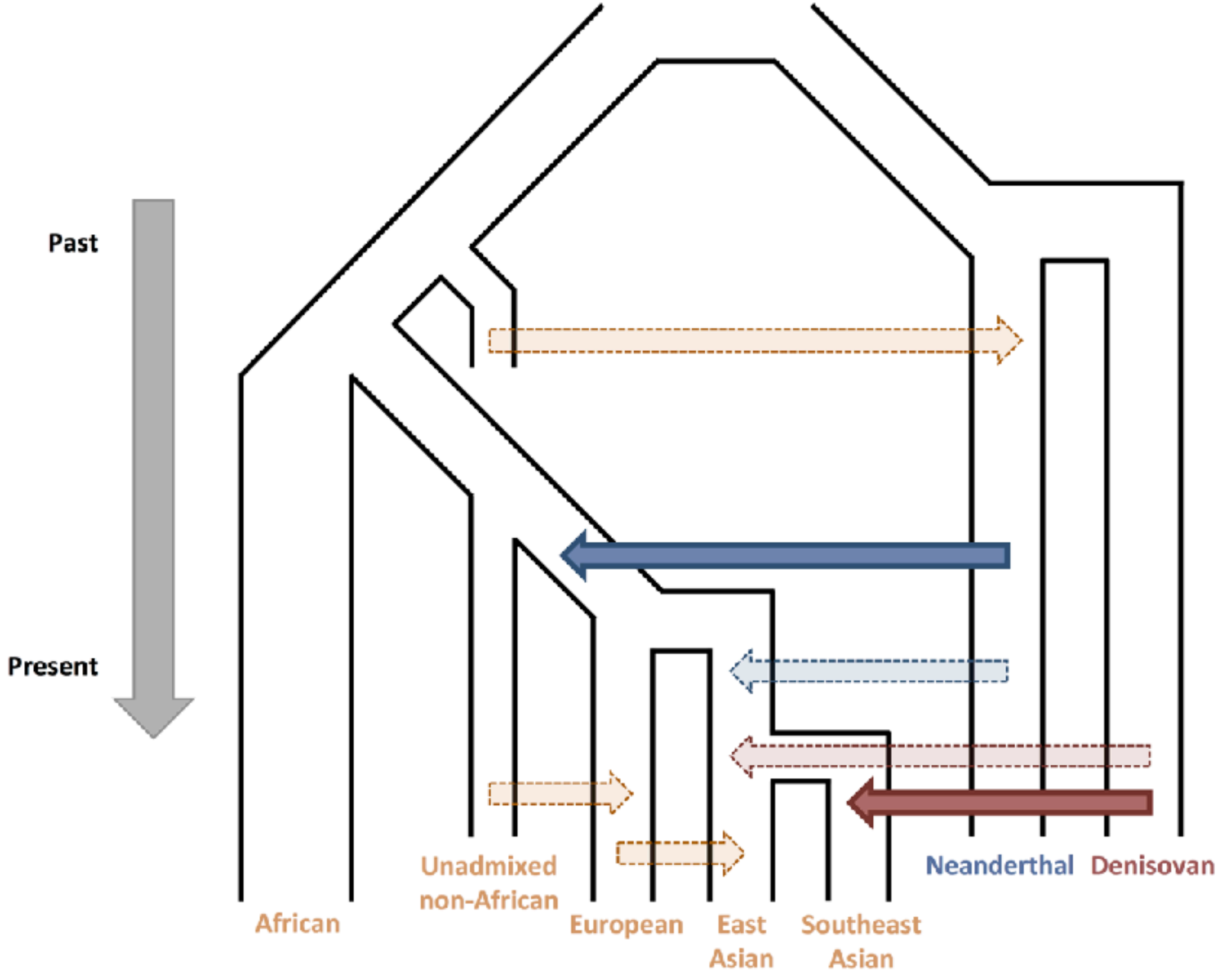




Higher cholesterol

Boettger et al *Nature Genetics* 2016 48:359–366

Image: Viktor Deak



Wolf, Aaron B., and Joshua M. Akey. "Outstanding questions in the study of archaic hominin admixture." *PLoS genetics* 14.5 (2018): e1007349.

Vertical lines=Neanderthal segments
Circles=centromeres

Analysis courtesy of Joshua Akey
& Selina Vattathil, Princeton

gene	chrom	gene_start	gene_end
MIR7846	chr1	12226999	12227095
MIR4632	chr1	12251769	12251830
TNFRSF1B	chr1	12227059	12269277
TNFRSF8	chr1	12123433	12204264
LRRC38	chr1	13801444	13840242
C1orf64	chr1	16330730	16333190
HSPB7	chr1	16340522	16345285
ZBTB17	chr1	16268363	16302627
CLCNKA	chr1	16348485	16360545
LDLRAD2	chr1	22138757	22151714
HSPG2	chr1	22148724	22263790
USP48	chr1	22004791	22109688
FGR	chr1	27938800	27961727
AKIRIN1	chr1	39456915	39471737
PABPC4	chr1	40026484	40042521
HEYL	chr1	40089102	40105348
OXCT2	chr1	40235196	40237020
PPIE	chr1	40204516	40229586
BMP8B	chr1	40223902	40254533
SMAP2	chr1	40839377	40888998
ZFP69B	chr1	40916336	40929390
C1orf168	chr1	57184476	57285369
LOC1019275	chr1	84041470	84326679
MIR548AP	chr1	84259597	84379059
LOC1019275	chr1	84267198	84326229
NTNG1	chr1	107682539	108027521
RPL31P11	chr1	161653494	161655042
FCGR2B	chr1	161632904	161648444
FCRLA	chr1	161676761	161684142
FCRLB	chr1	161691333	161697933
DUSP12	chr1	161719557	161726954
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ATF6	chr1	161736033	161933860
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LINC01142	chr1	170240545	170253349
FAM163A	chr1	179712297	179785333
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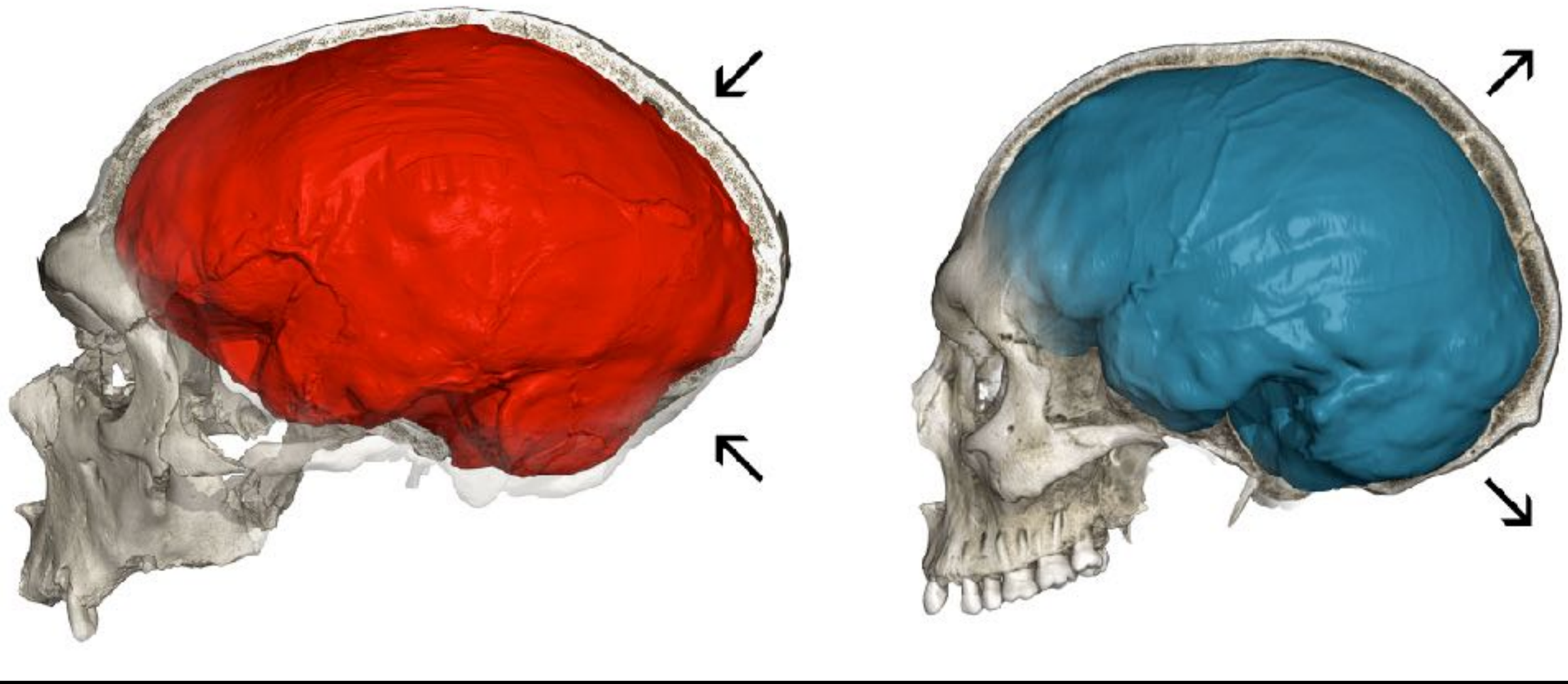
TOR1AIP2	chr1	179809101	179846941
CEP350	chr1	179923907	180084015
FLJ23867	chr1	180167143	180169859
QSOX1	chr1	180123967	180167169



Gunz et al.: “Neandertal introgression sheds light on modern human endocranial globularity”
cell.com/current-biology/fulltext/S0960-9822(18)31470-2

Promethease

Search

Main | Blood | PGx

rs12203592(C;T)

Primarily in Europeans; slightly lighter hair and eye color, less tanning ability

plus rs12203592 showed the largest allele frequency difference between the Irish individuals and those individuals of Northern, Central European and Eastern European descent associated with hair color rs12896399 rs12203592 rs12203592 for freckling was previously associated with hair color, eye color, and tanning response to sunlight A genome wide association scan in admixed Latin Americans identifies loci influencing facial and scalp hair features Squamous Cell Carcinoma [PharmGKB:Non-Curated GWAS Results: A Genome-Wide Association Study Identifies Novel Alleles Associated with Hair Color and Skin Pigmentation (Initial Sample Size: 2,287 women; Replication Sample Size: up to 8,465 individuals; Risk/trait Allele: rs12203592-T). This variant is associated with Black vs. red hair color.] [GW...

more info

2	Magnitude
Other	ClinVar Significance
26.5%	Frequency
0.05372	GMAF
22	References
IRF4	Gene
6	Chromosome
395321	Position
2	Max Magnitude
20150831	Rs time
plus	Stabilized
plus	Orientation

Topics Appearance | Eye color | Freckling

ClinVar Other Skin/hair/eye pigmentation

{'MLEAC': [1], 'AC': [1], 'BaseQRankSum': 0.996, 'MLEAF': [0.5], 'culprit': 'QD', 'AF': [0.5], 'VQSLOD': 1.94, 'POSITIVE_TRAIN_SITE': True, 'AN': 2, 'MQ0': 0, 'FS': 4.773, 'MQ': 59.45, 'ClippingRankSum': -0.159, 'MQRankSum': 2.439, 'PrometheaseInferredRsnum': True, 'ReadPosRankSum': 0.578, 'DP': 39, 'QD': 17.59}

rs8085664(A;C)

0.78x reduced risk of Male Pattern Baldness. Discovered by 23andMe based on customer surveys, and considered preliminary research.

This is the 23andMe discovery: 'Male Pattern Baldness: Preliminary Research'. It affects appearance.

more info

Good	Repute
2	Magnitude
40.7%	Frequency
0.3012	GMAF
SLC14A2	Gene
18	Chromosome
45234191	Position
2.1	Max Magnitude
20150106	Rs time

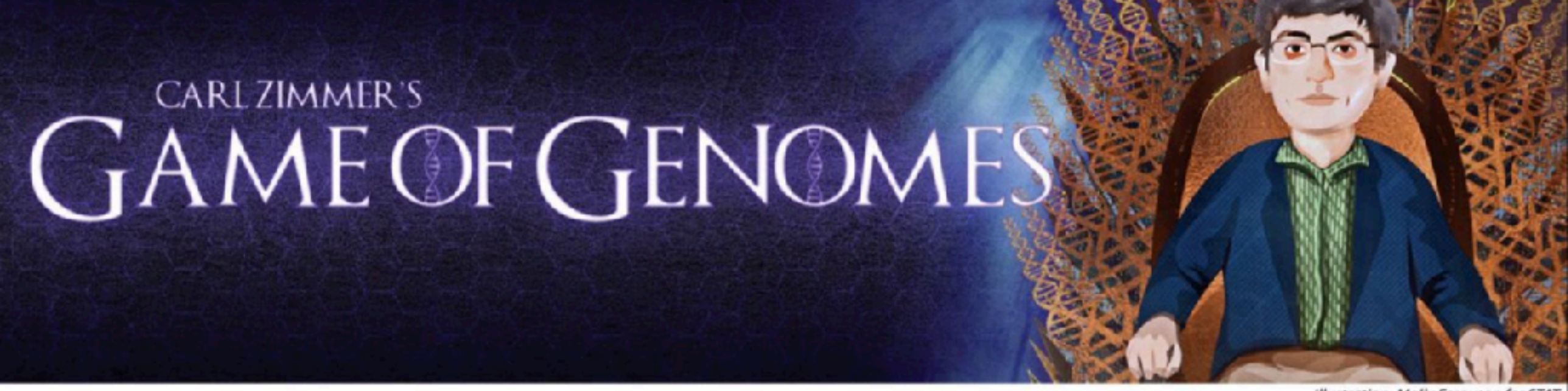


Illustration: Molly Ferguson for STAT;

Supplementary Materials

Welcome to the companion site for Carl Zimmer's "Game of Genomes" series on STAT. Here you will find data and analysis from some of the scientists who examined Zimmer's genome.

Part 1
Gerstein lab

Part 2
Torkamani lab

zimmerome.gersteinlab.org

Thank you

For more information, please visit carlzimmer.com & @carlzimmer