

Lets do a quick survey...

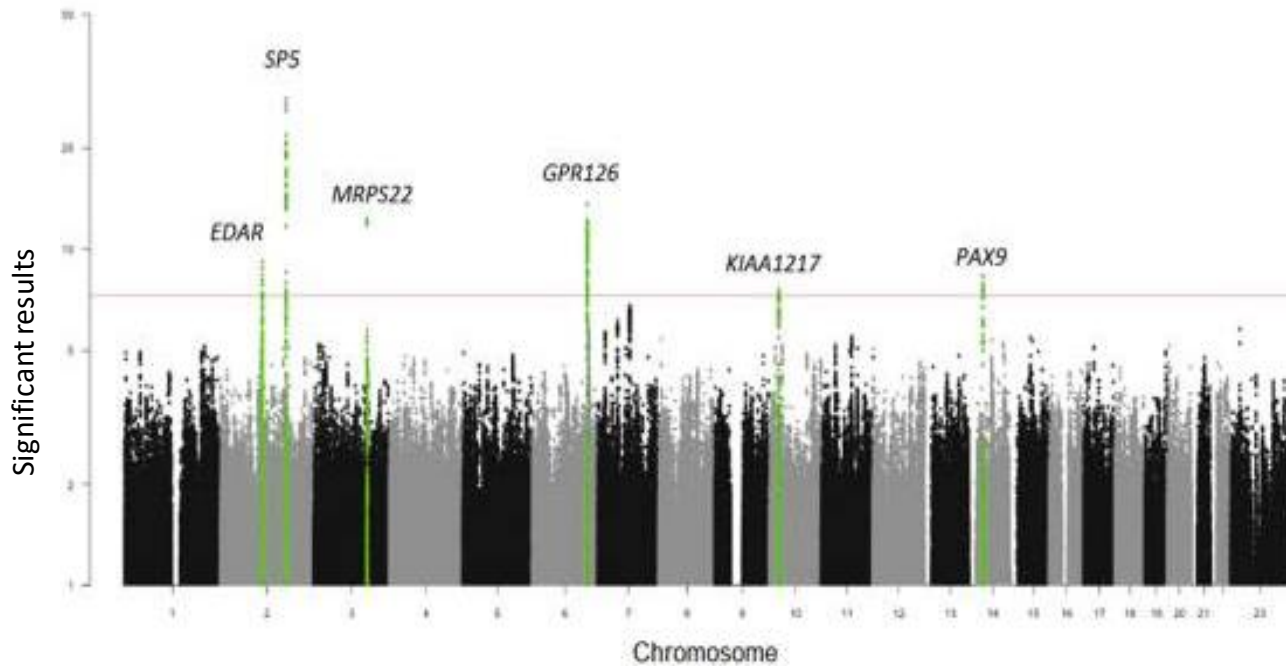
Do you have an attached earlobe?

- Feel your earlobes... are they dangling or are they attached to the ear?



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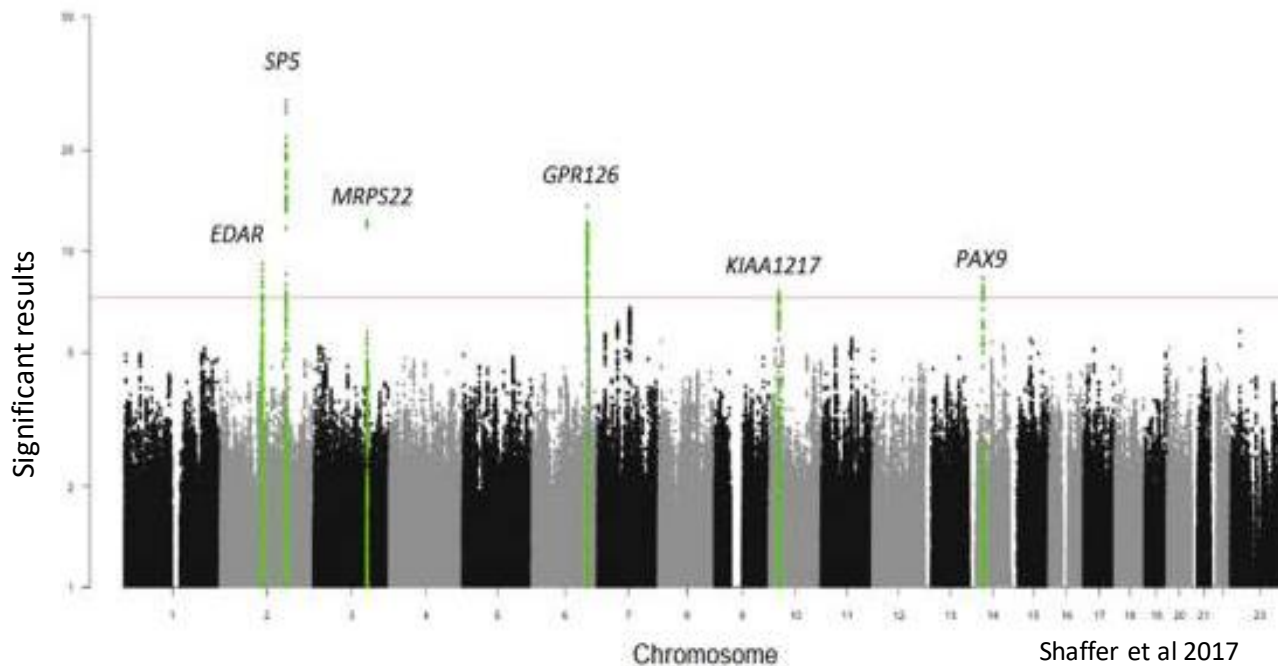


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1. Combination of genes, working together are involved in determining the structure of our ears



Shaffer et al 2017

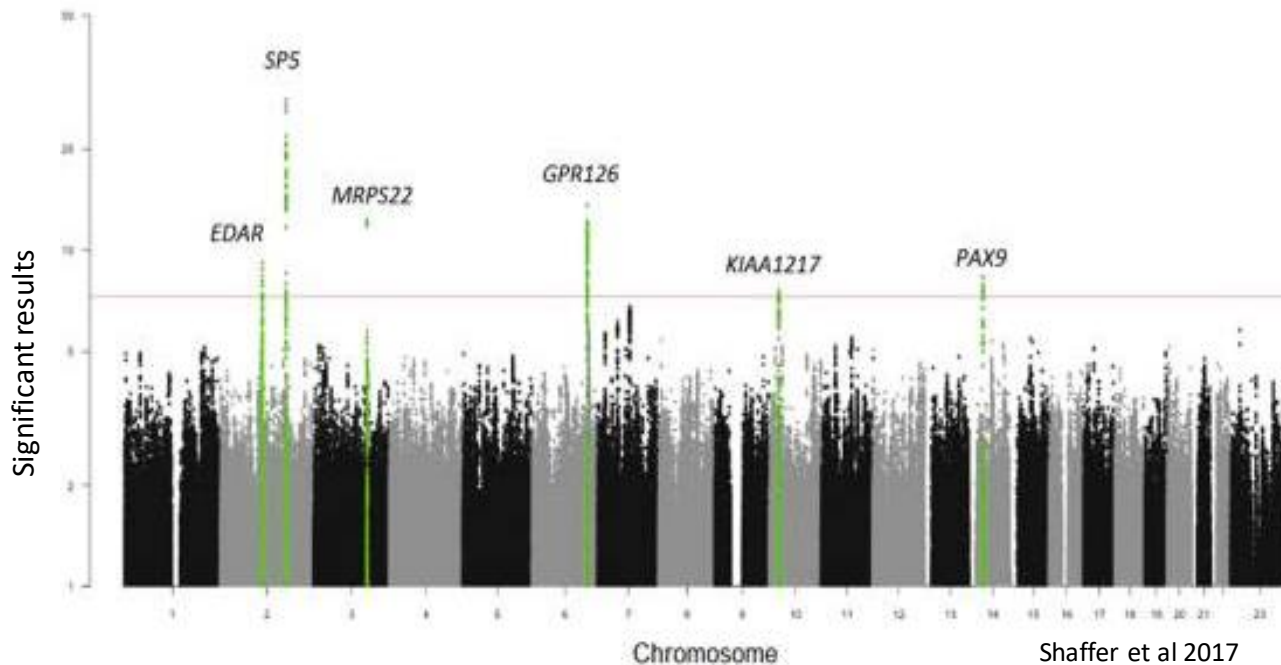
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Q: Are both of your earlobes the same?



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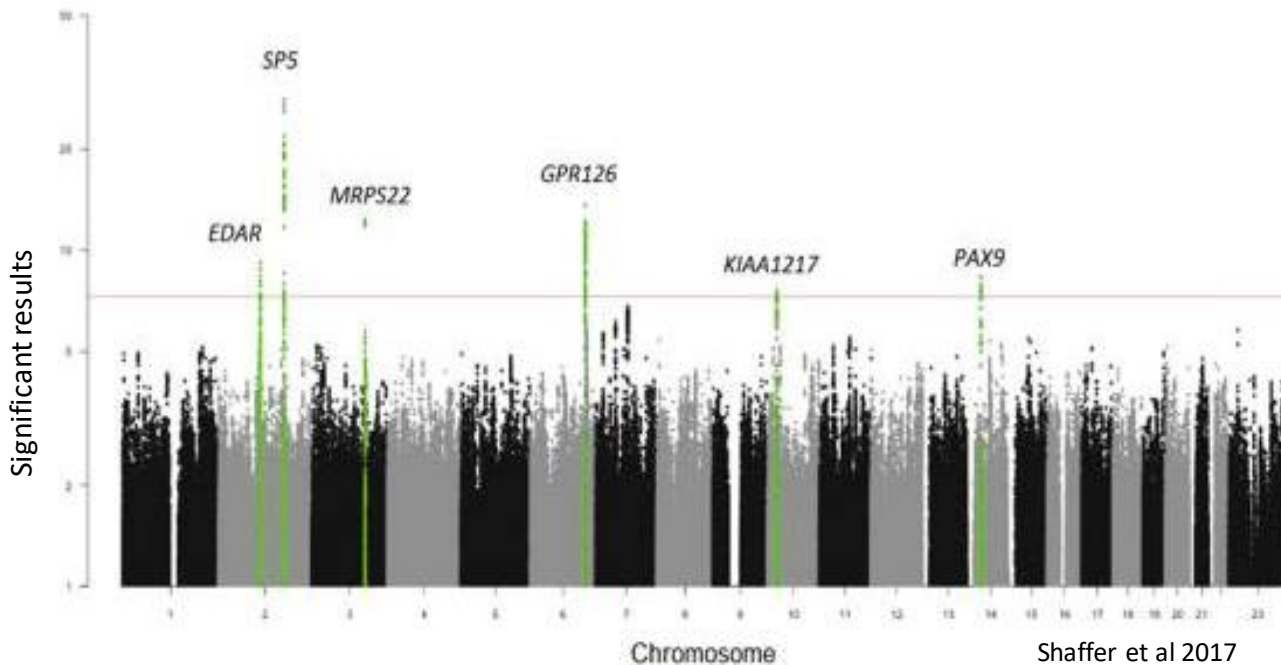
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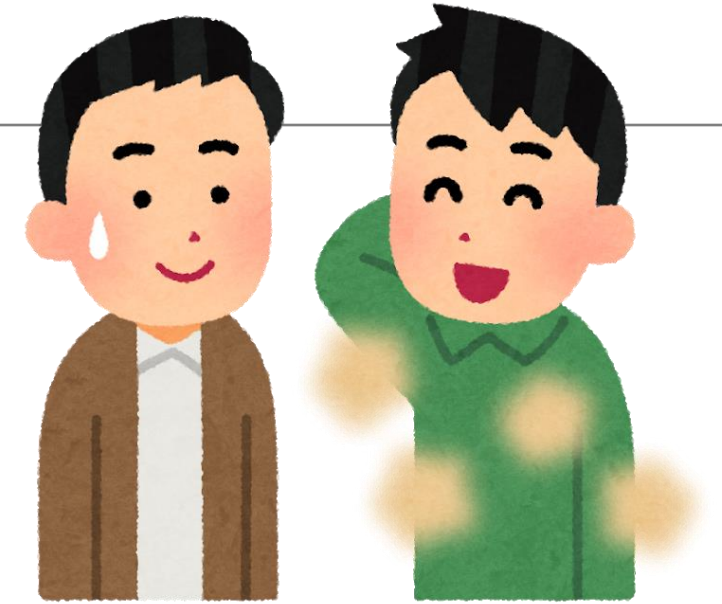
2. Both our ears are exactly the same because all our cells carry the same blueprint (i.e. DNA)!



Shaffer et al 2017

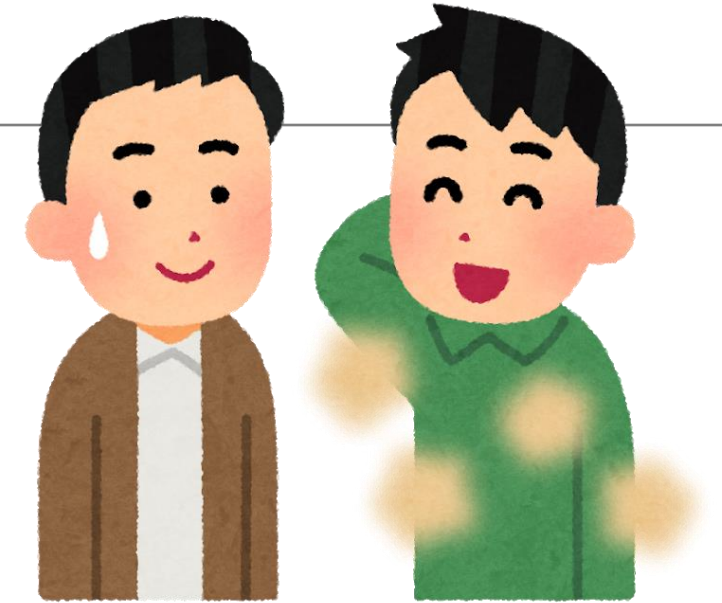
Do you have a body odor?

- Do you often feel the need to use deodorant / perfume?



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- The ABCC11 expressed in our sweat glands is the cause of body odor
- People who have the gene 'turned off' actually don't have any body odor

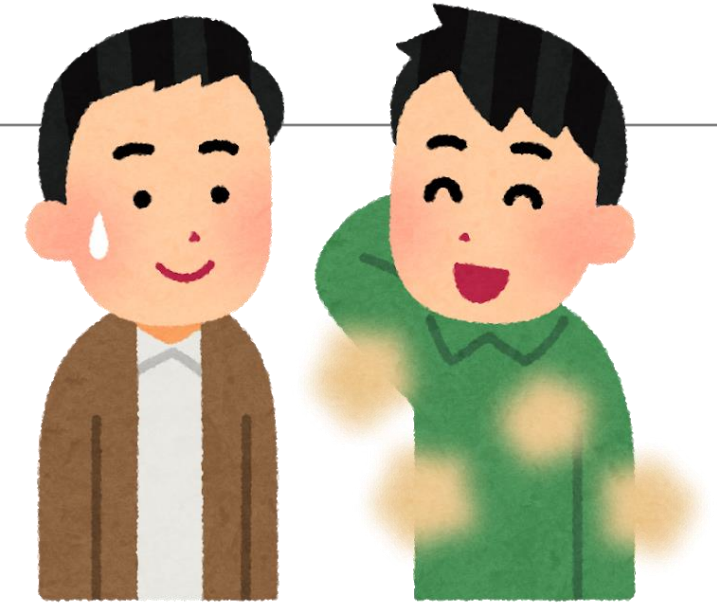


Gene Activity	% of ppl
100% on	49%
Partially on	42%
100% Off	9%

9% of the world doesn't need a deodorant

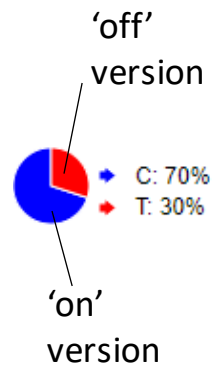
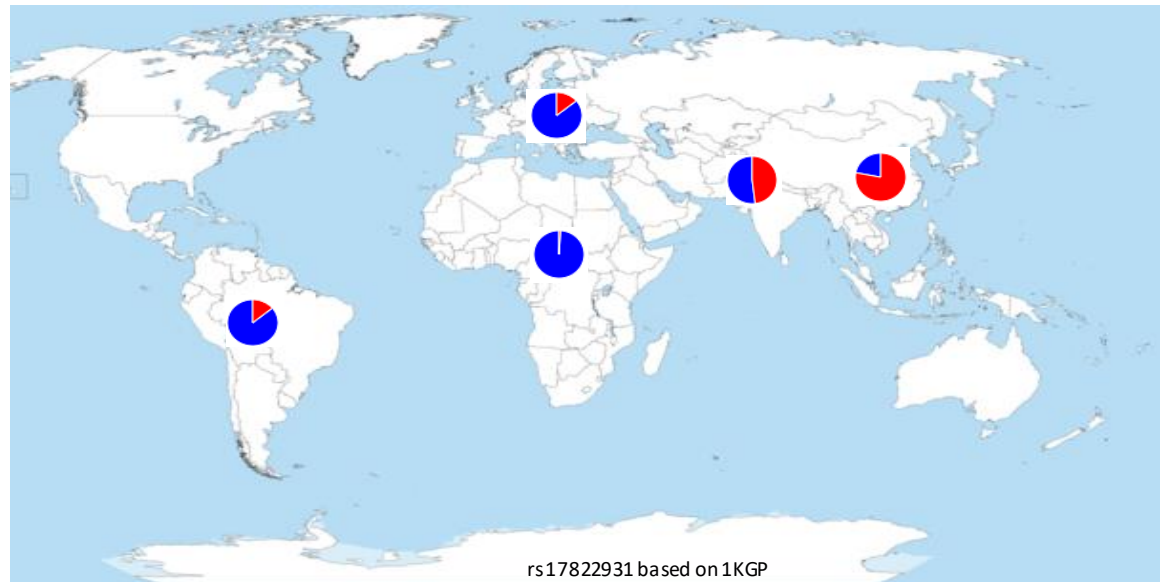
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rs17822931 based on 1KGP

Does Genetics determine everything?

Can you guess if the following traits are genetic?

Eye-color

Skin Color

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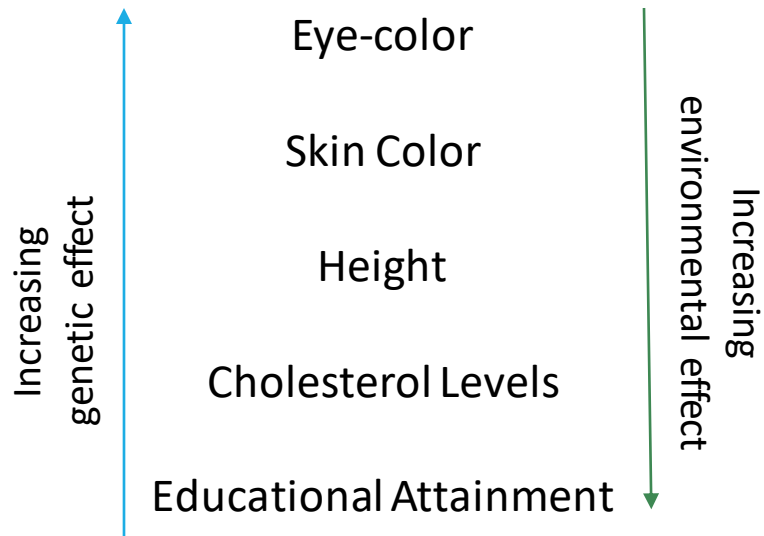
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Educational Attainment

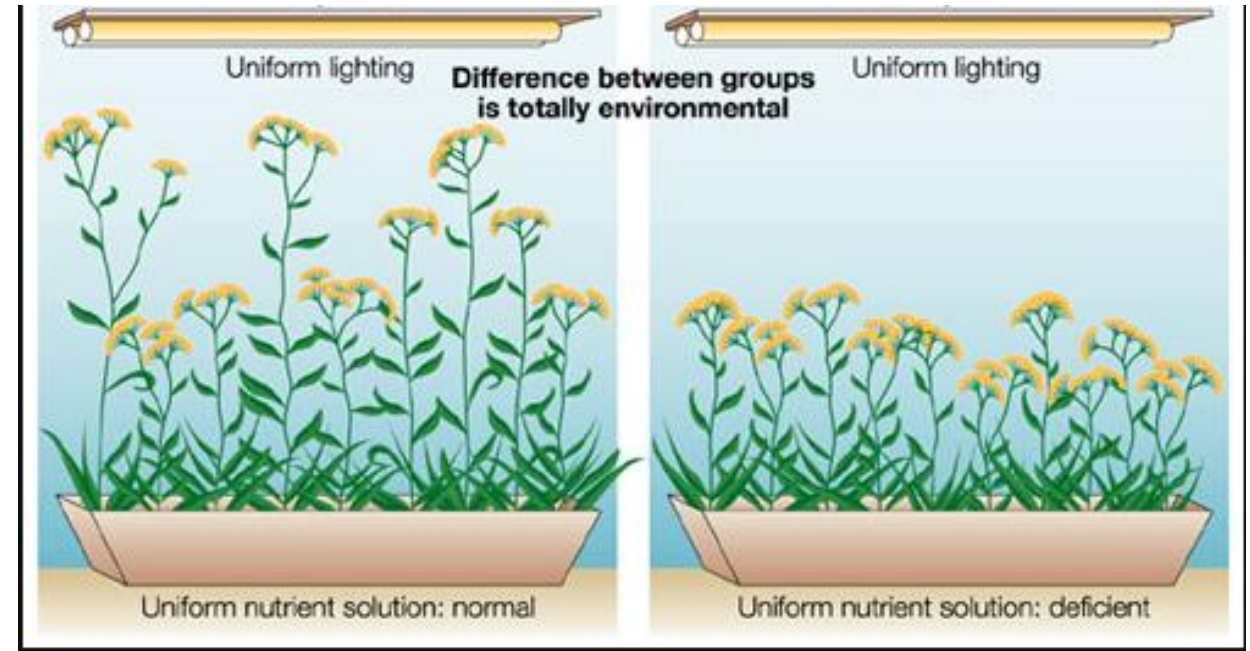
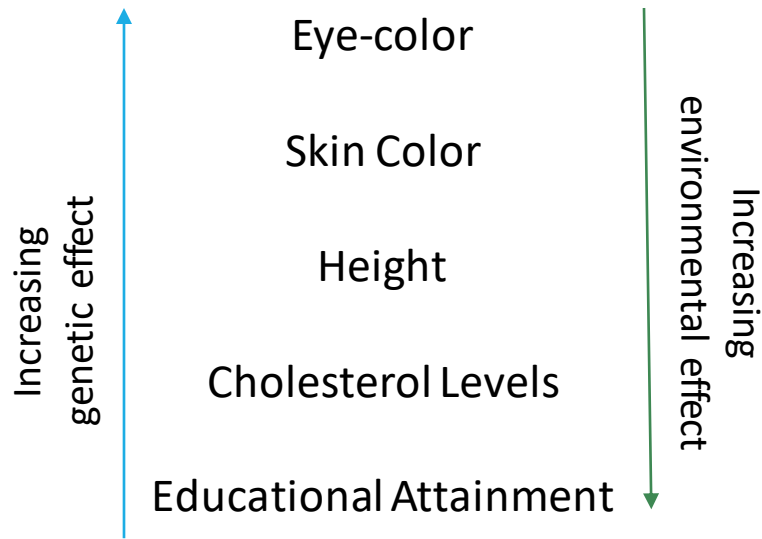
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Does Genetics determine everything? – Not really

Can you guess if the following traits are genetic?



Why is studying this important?

Surah Ar-Rum: Ayat 23

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And among His Signs is the creation of the heavens and the earth, and the diversity of your tongues and colors.
In that surely are Signs for those who possess knowledge

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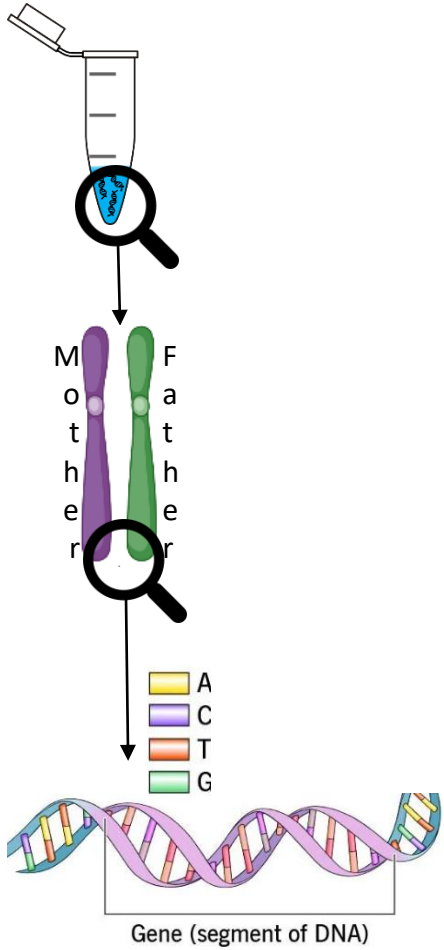
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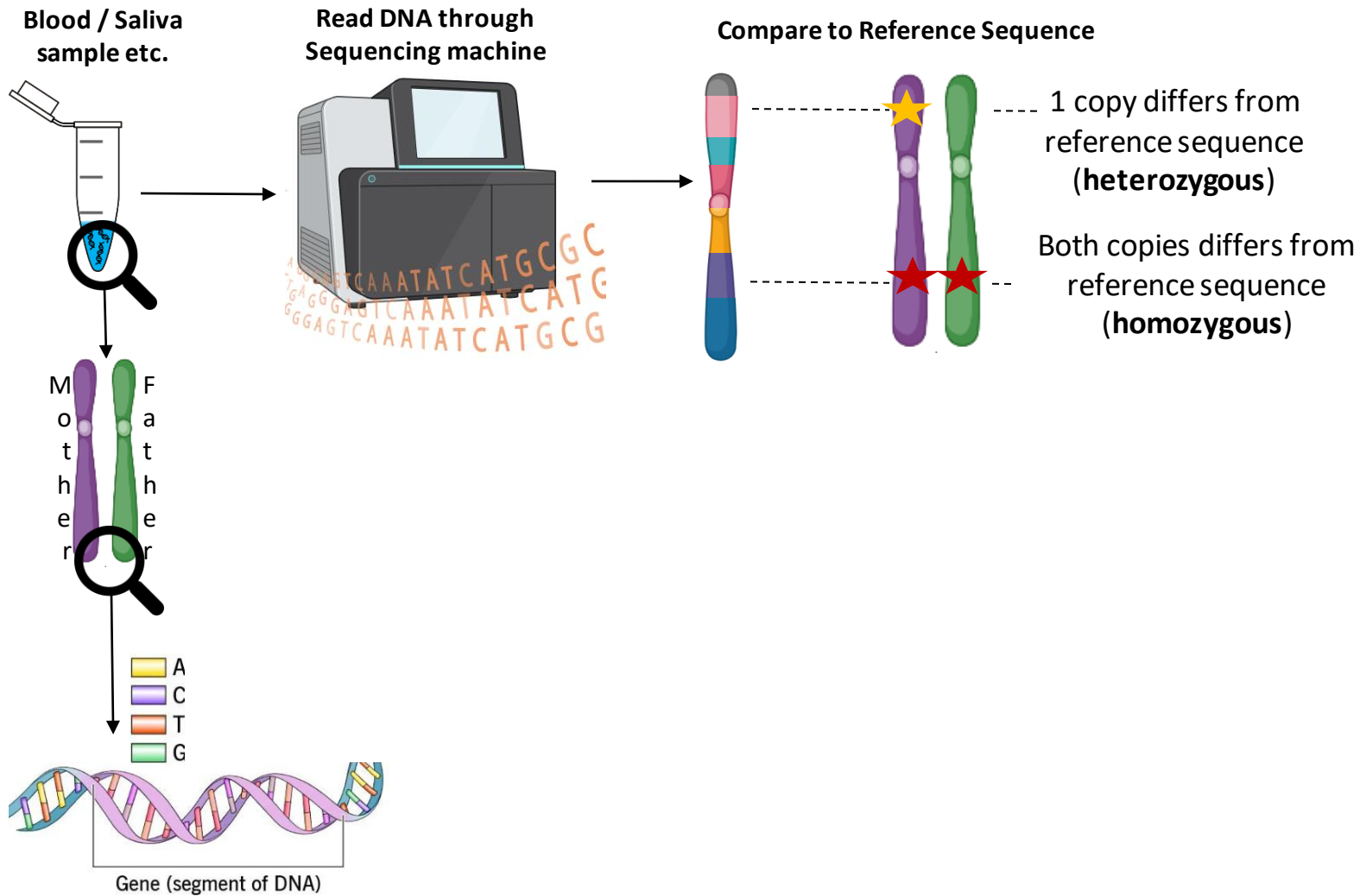
1. Understand the function of our genes
2. Diagnose Genetic Diseases
3. Help Develop cures for Disease

How do we read DNA?

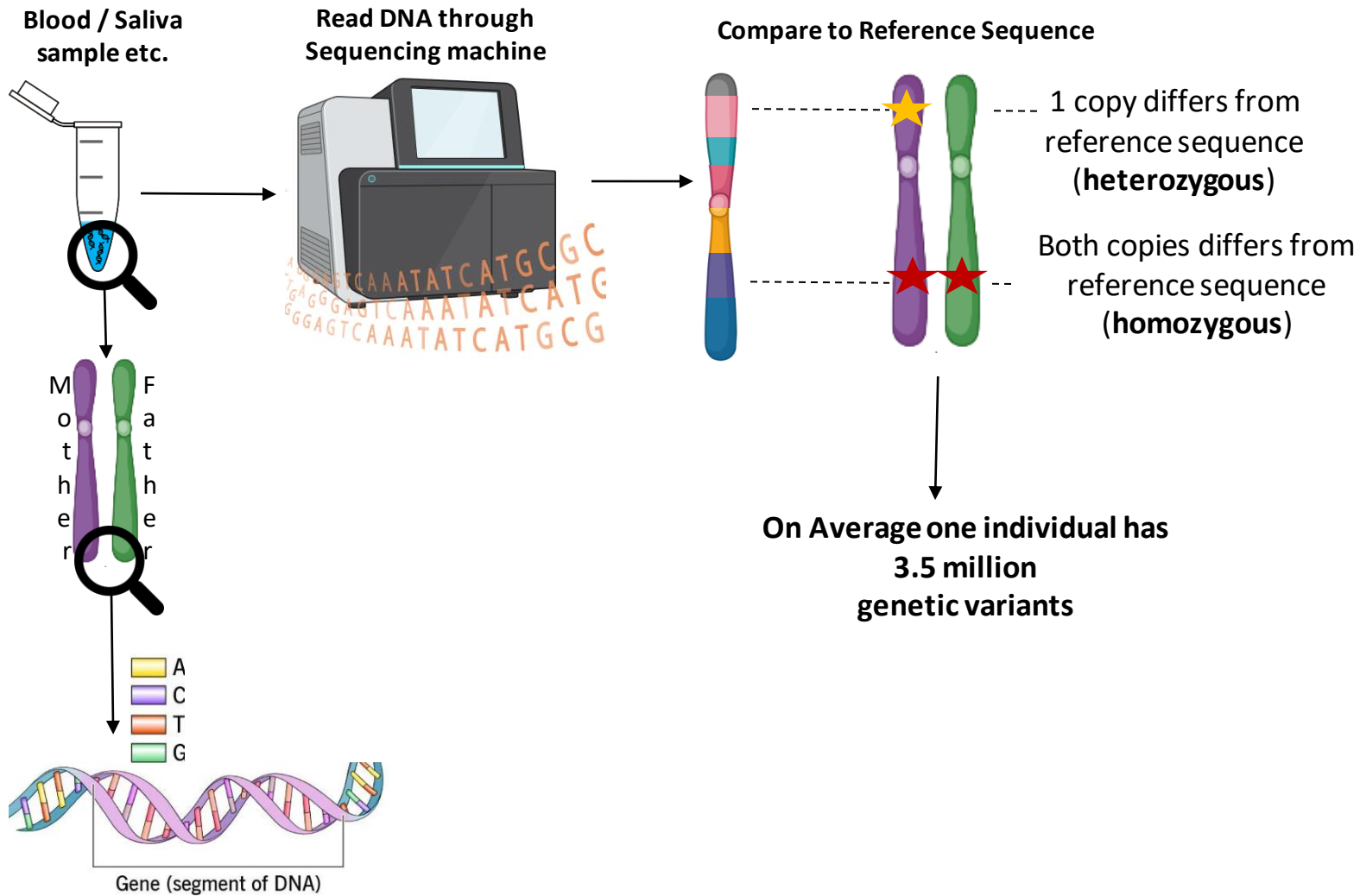
Blood / Saliva
sample etc.



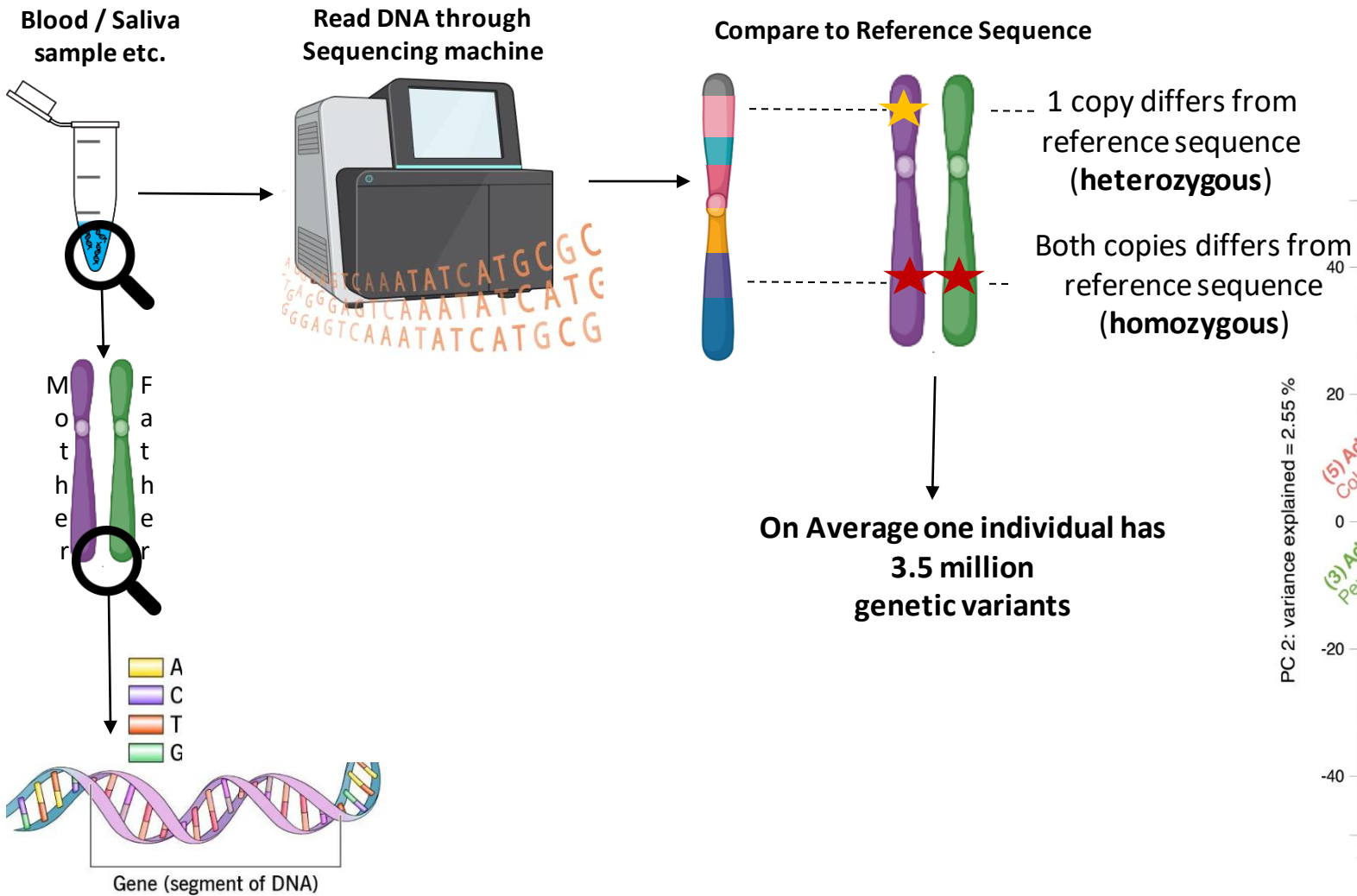
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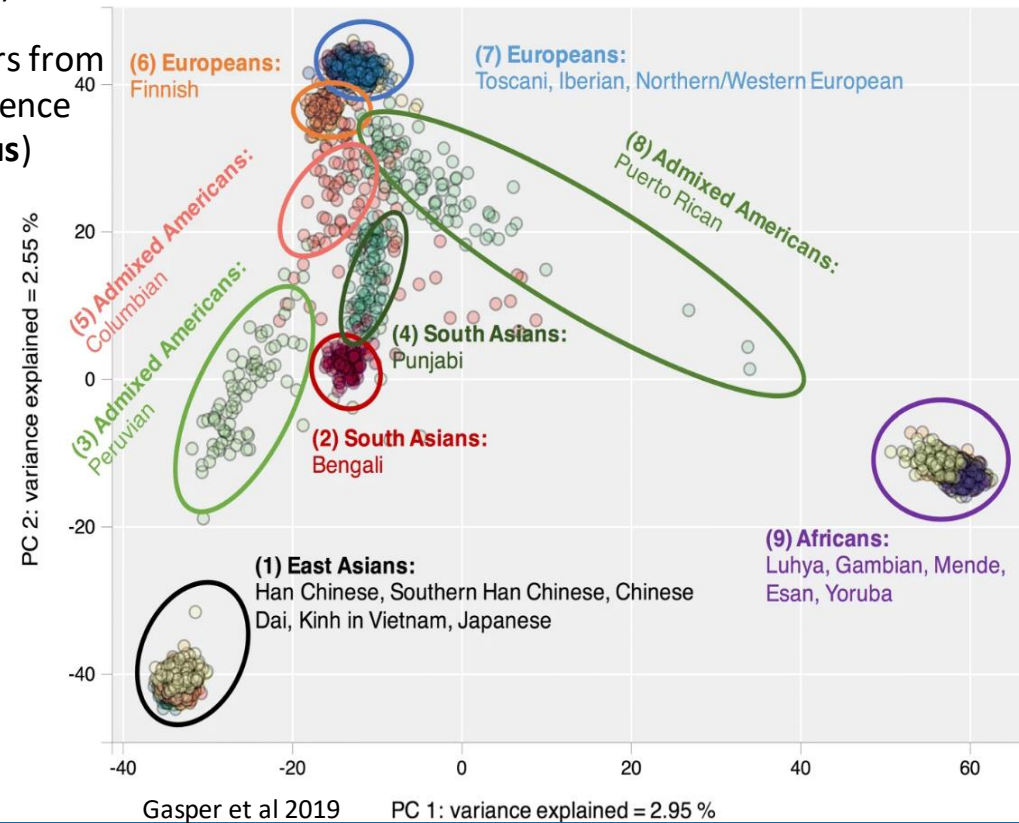
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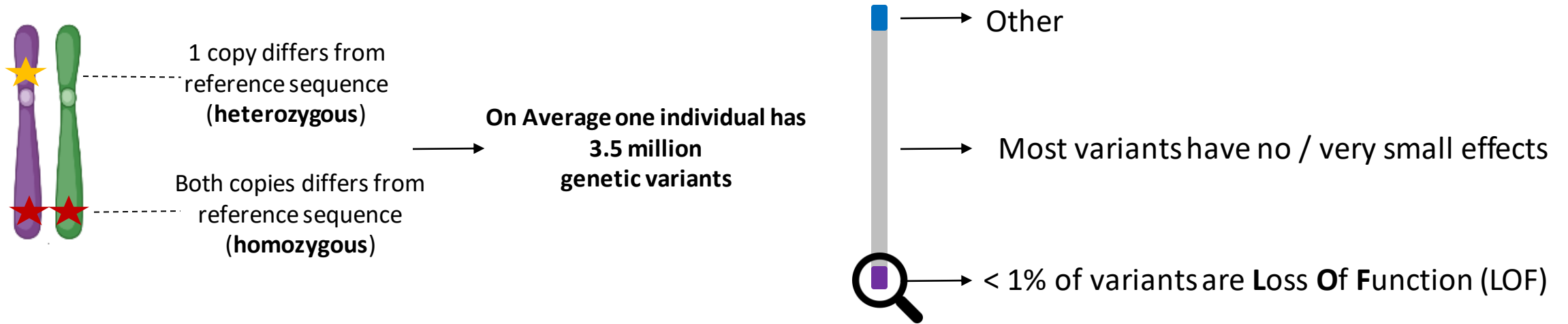
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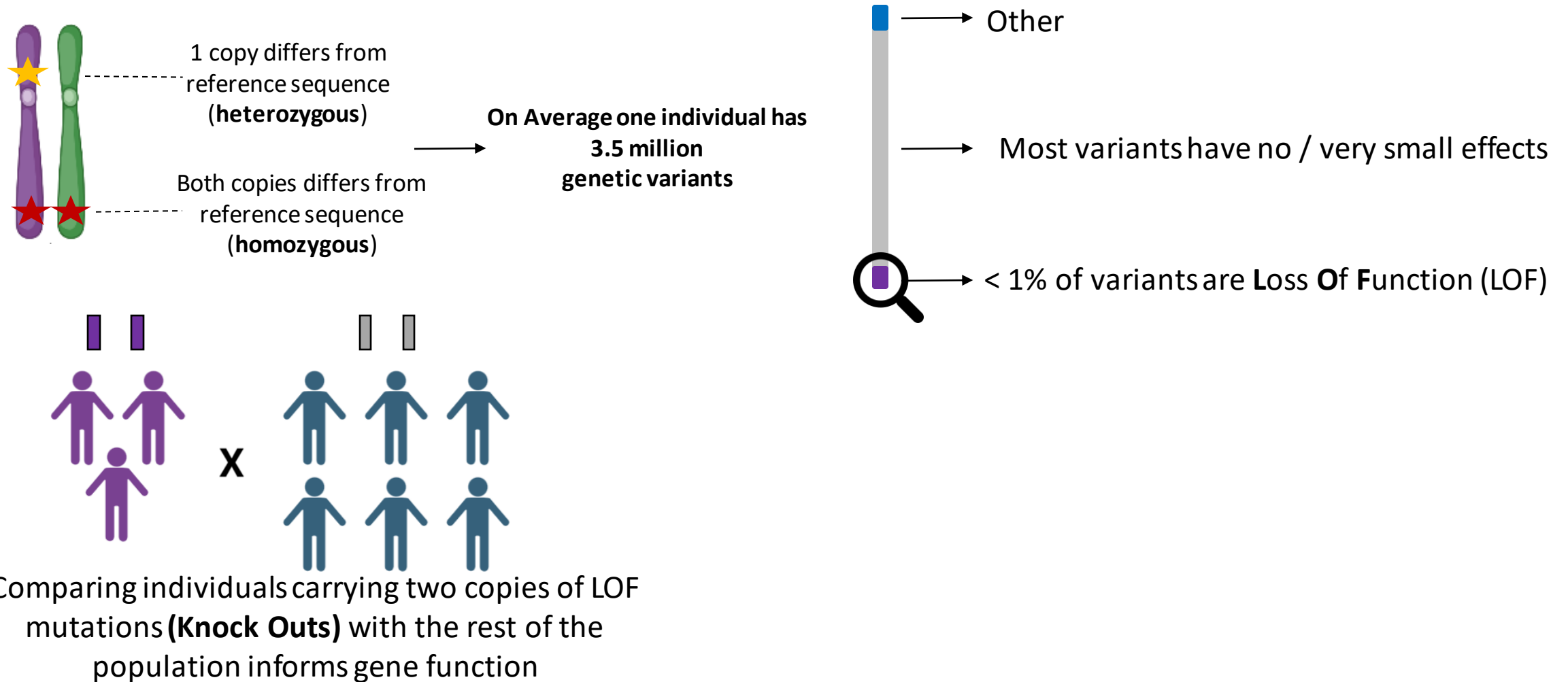
Underlying *diversity of colors* is our genetic diversity



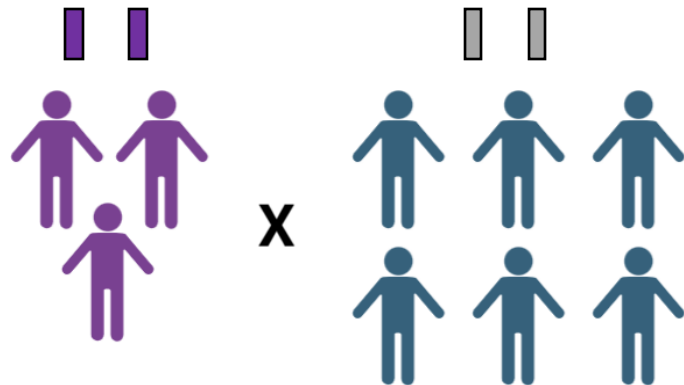
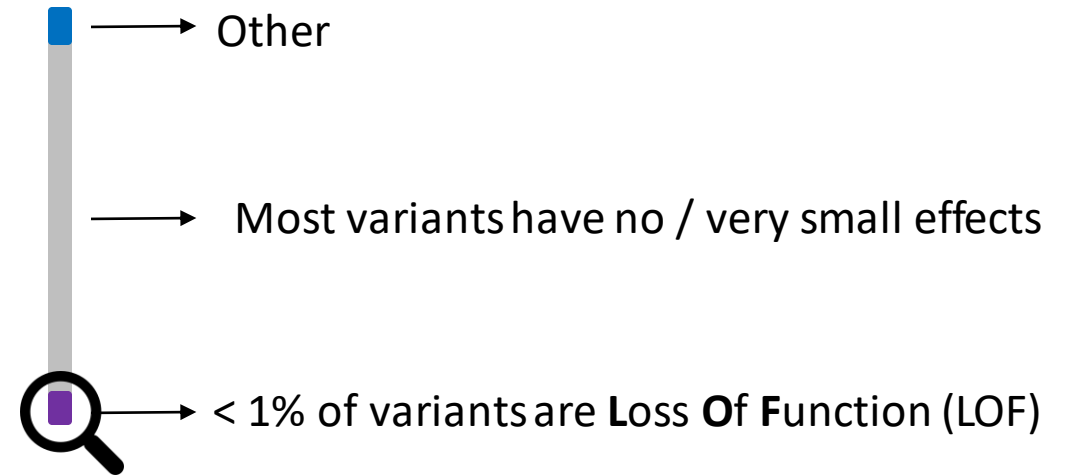
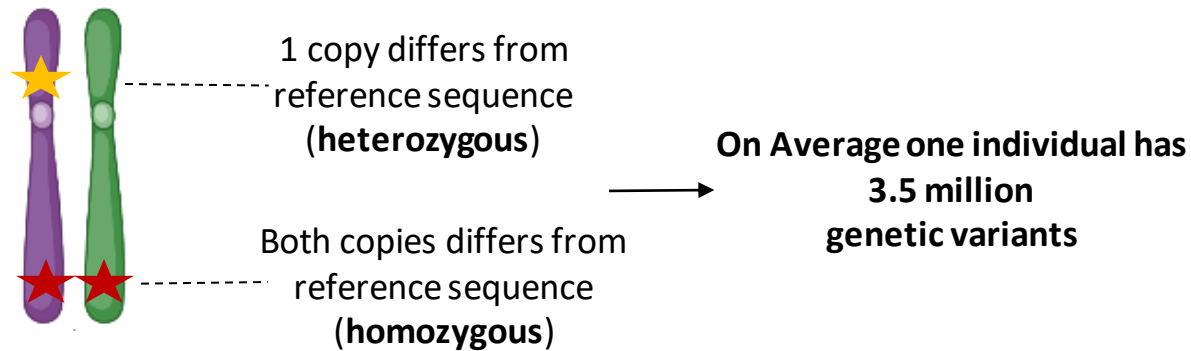
Genetics to Therapies



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Comparing individuals carrying two copies of LOF mutations (**Knock Outs**) with the rest of the population informs gene function

- The most famous example of this is PCSK9, where knock outs have lower LDL Cholesterol levels
- Multiple therapies developed targeting PCSK9 including CRSPR based therapies to artificially knock out PCSK9 in the body

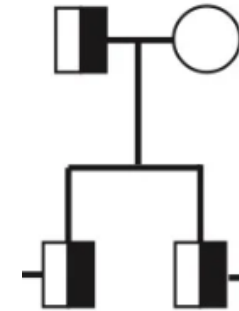
LOFs are rare, 2 copies of LOFs are rarer

Data across ~200,000 individuals from the UK

	% of Genes
Genes with at least 1 knock out	7.8%
Genes with multiple (+5) knockouts	2.8%

Stutzwoski et al 2021

Reason %age is low is because it's rare for two carriers to be married and pass down the LOF mutations



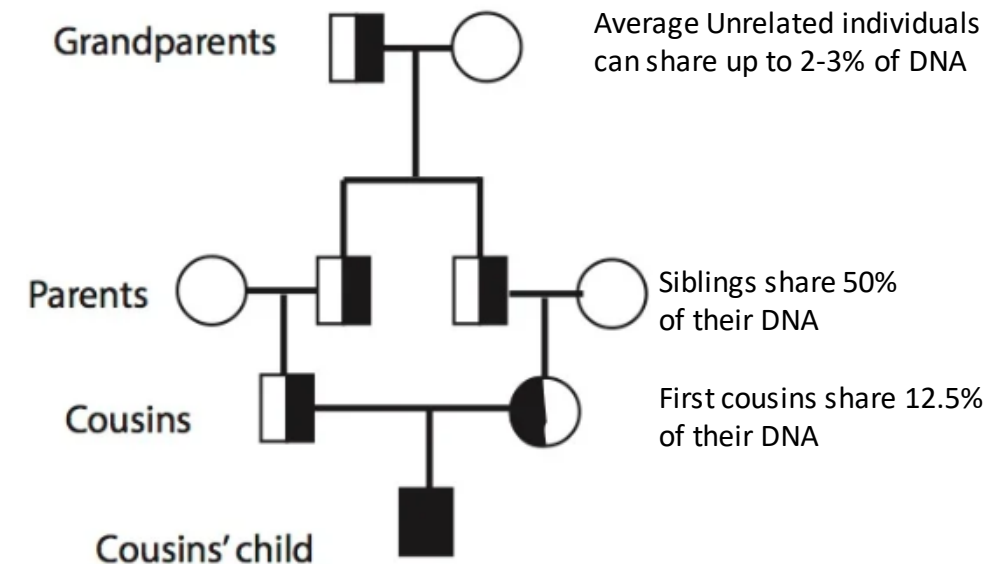
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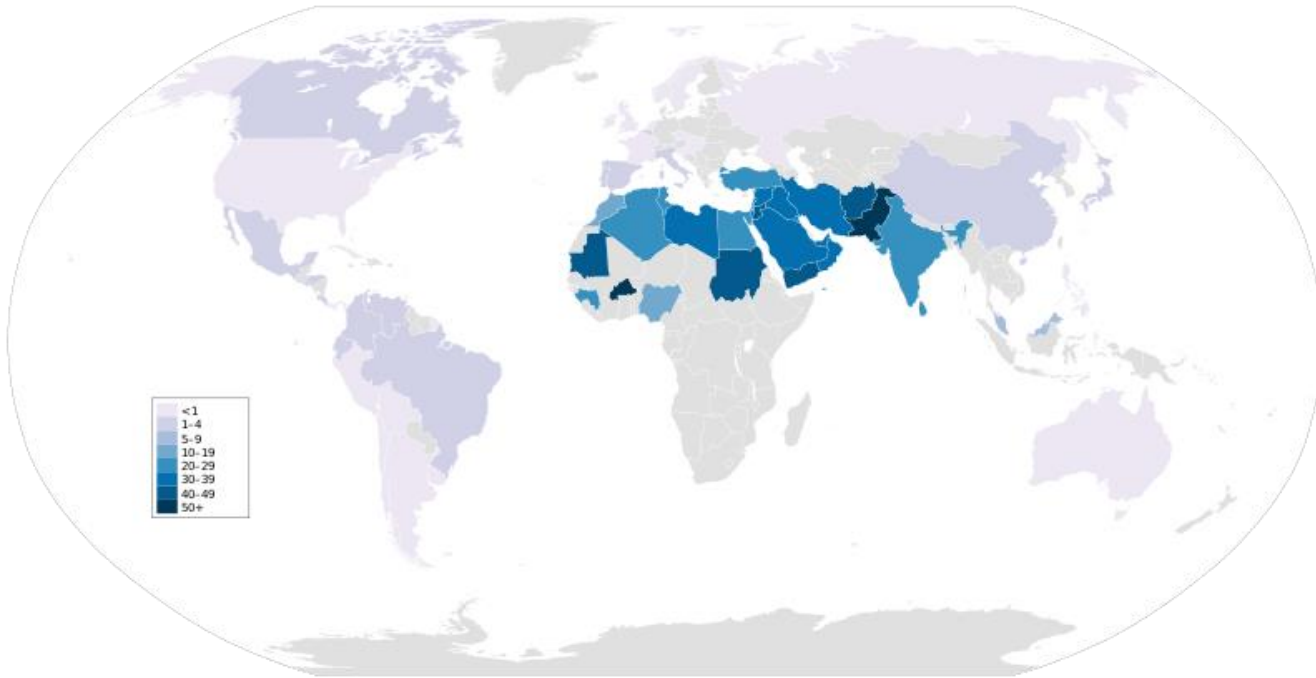
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Chances can more than double in the case of cousin marriages

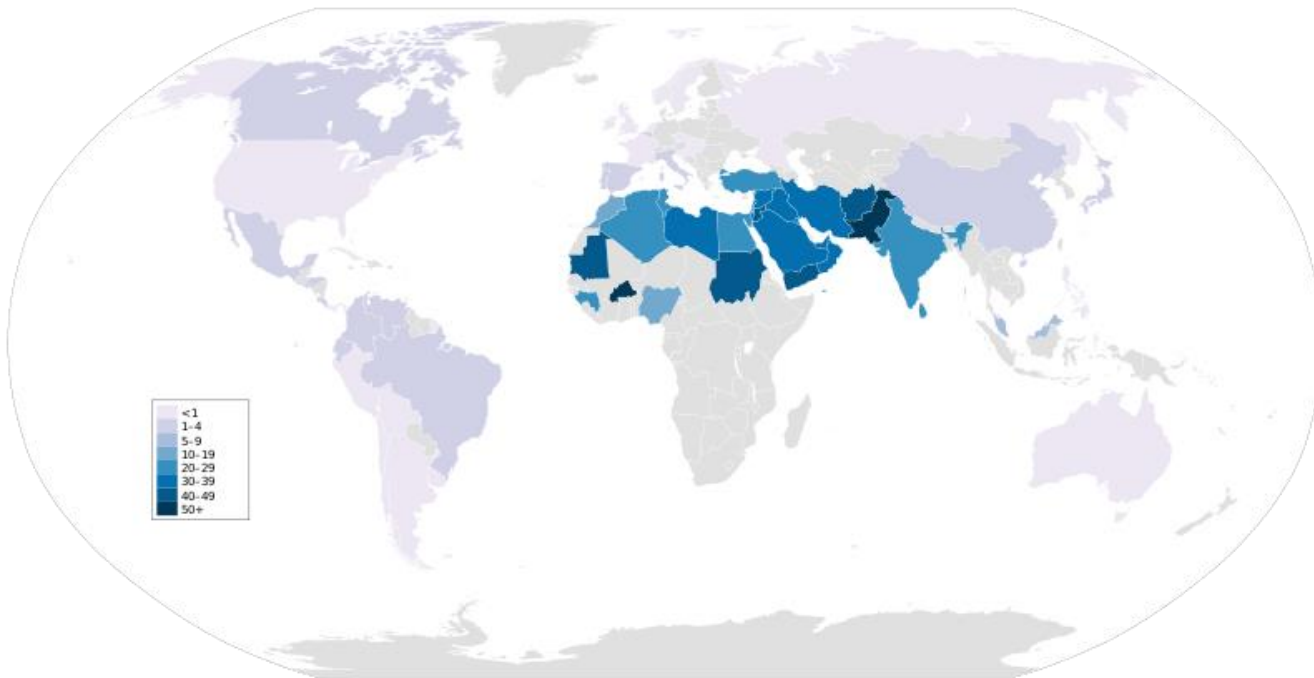
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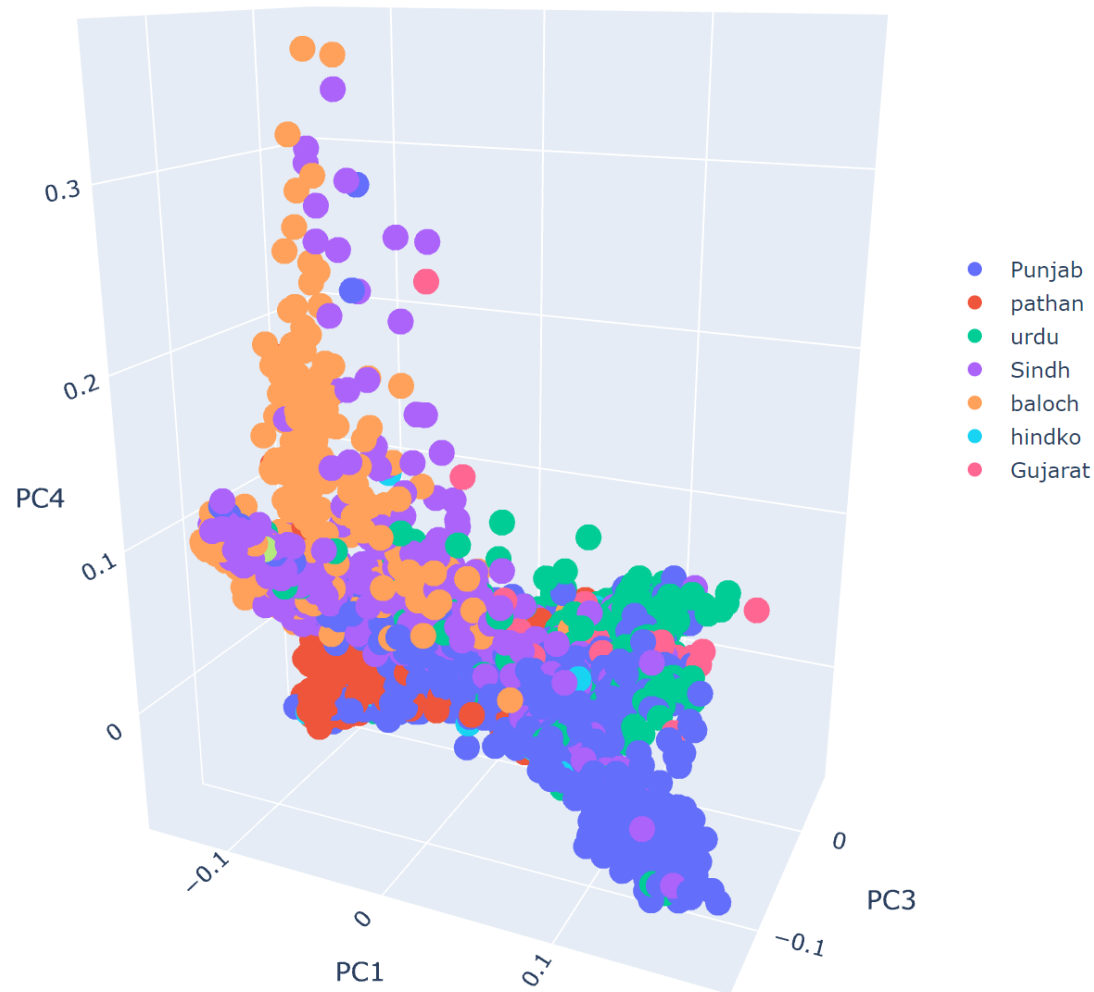
Pakistan has the highest rates of consanguinity



DNA sequencing data from major cities in Pakistan of up to 76,000 individuals

	% of Genes
Genes with at > 1 knock out in Pakistan	27%
Genes with > 1 knock out in Europe	6%

Consanguinity and Diversity



Similar to what we saw for the worldwide population, within Pakistan we see a lot of genetic structure as a result of marriage patterns

The Boy Who Felt No Pain...

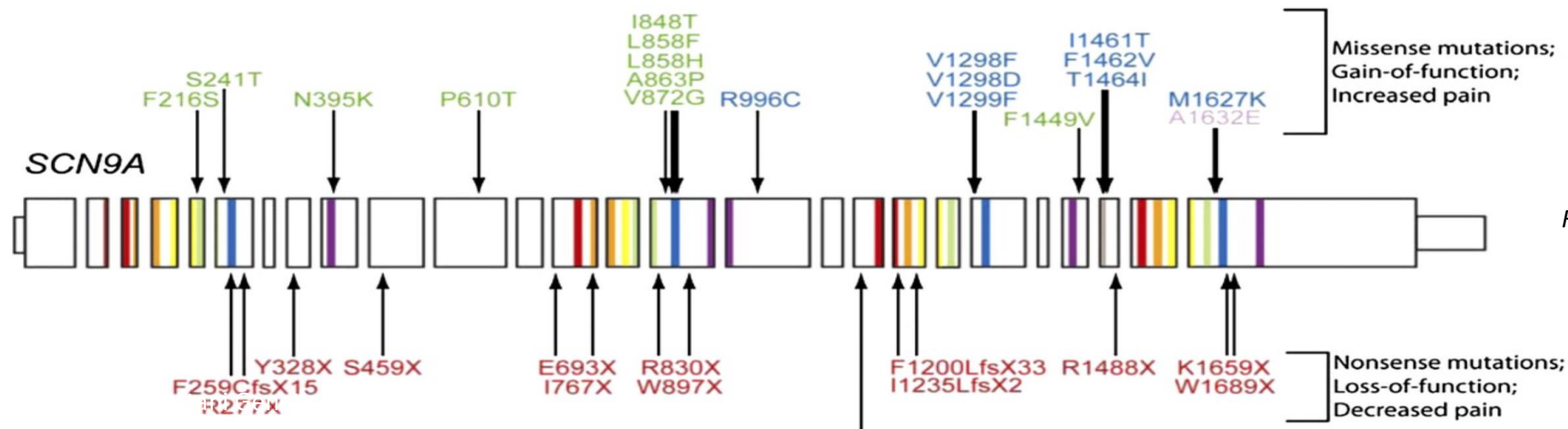
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- *'The index patient was a ten-year-old child, well known to the medical service after regularly performing 'street theatre'. He placed knives through his arms and walked on burning coals, but experienced no pain.'*



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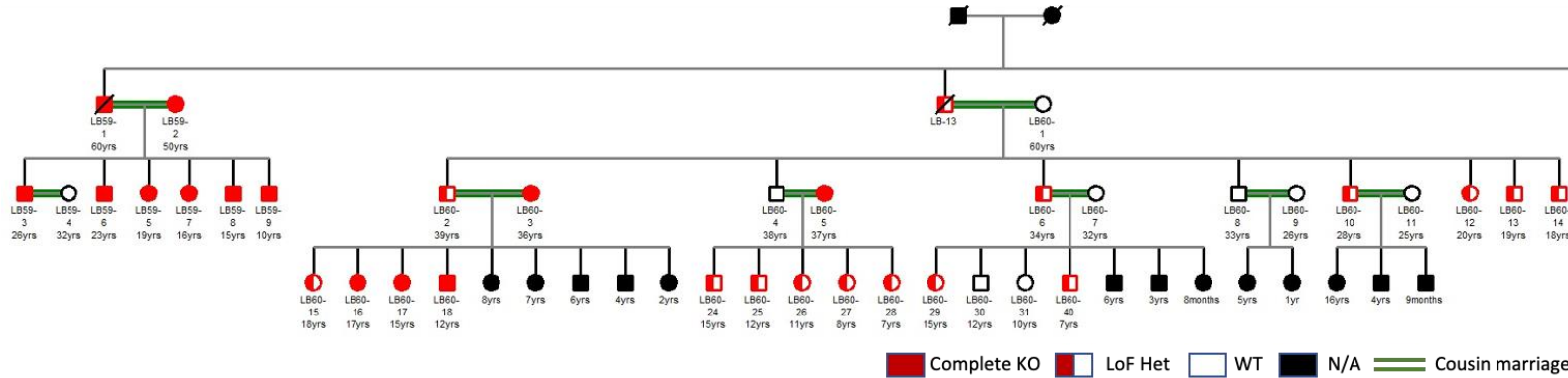
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- These individuals were identified to be carriers of LoF variants in SCN9A which codes for a sodium ion channel Nav1.7 highly expressed in pain specific neurons



Reimen et al PNAS 2010

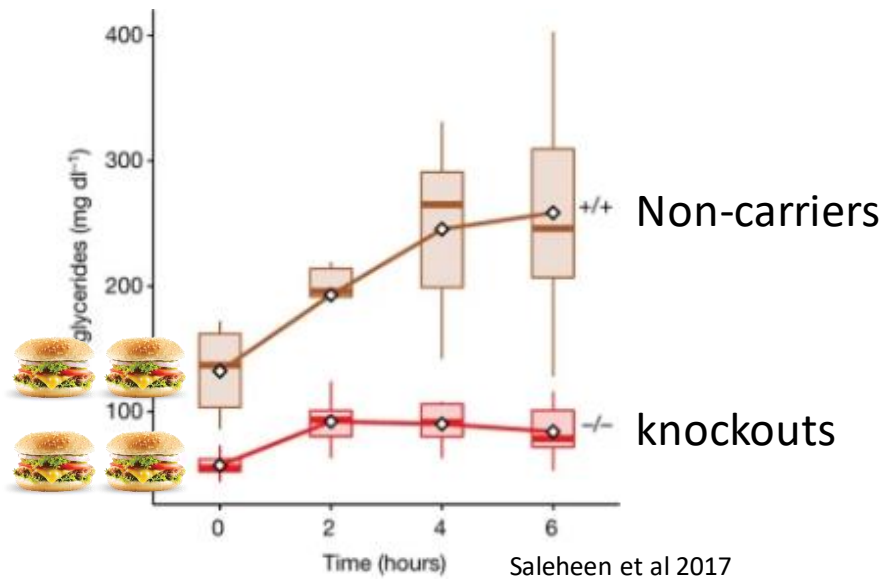
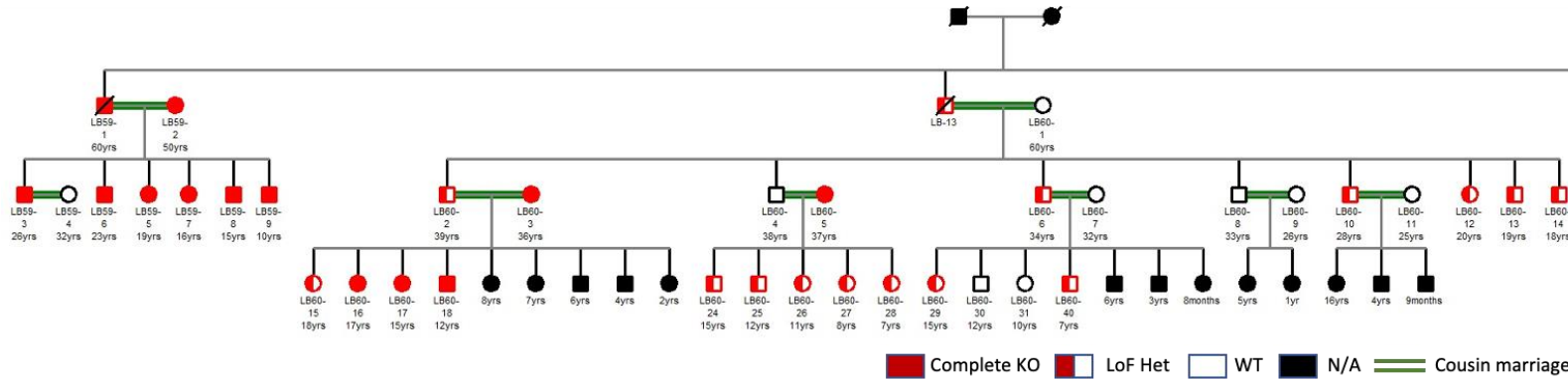
Super Fat Metabolizers

- Identified knock outs for the Gene APOC3 near Karachi

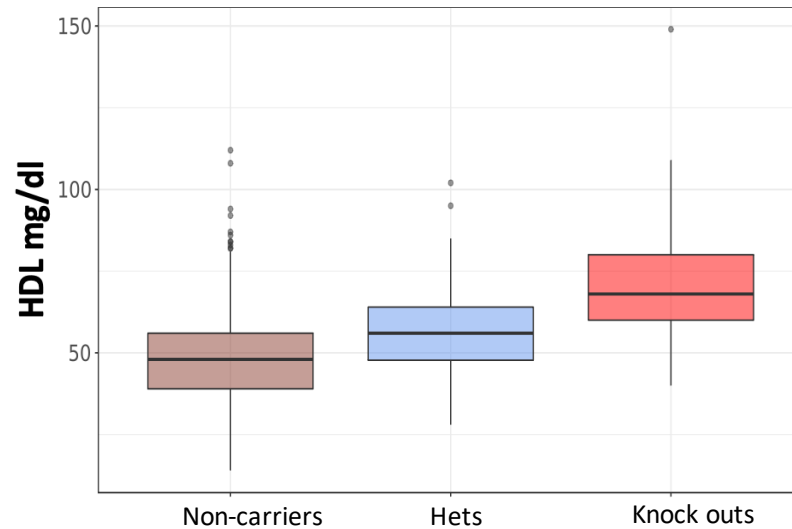


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Saleheen et al 2017



Khalid et al 2021

Showed to researchers that knocking out APOC3 is an effective way to lower Triglycerides

NHGRI's 10 Bold Predictions for 2030

With hope and anticipation, the NHGRI *boldly* predicts that by 2030:

1. Genome sequencing will be commonplace.
2. The role of *all* human genes will be known.
3. The impact of environmental factors on our genome and disease risk will be understood.
4. Genomics will move away from using social constructs like race in human research studies.
5. Hands-on genomic research will begin in elementary school.
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