‘The Age of Genomic Medicine’

Action Duchenne Conference, 2019

Structure

Brief Introduction

What is a genome and what is genomics?

How do we sequence DNA?

Genomics in the UK

Why is genomics relevant for Duchenne?

The future of medicine is **patient-centric** and data-driven

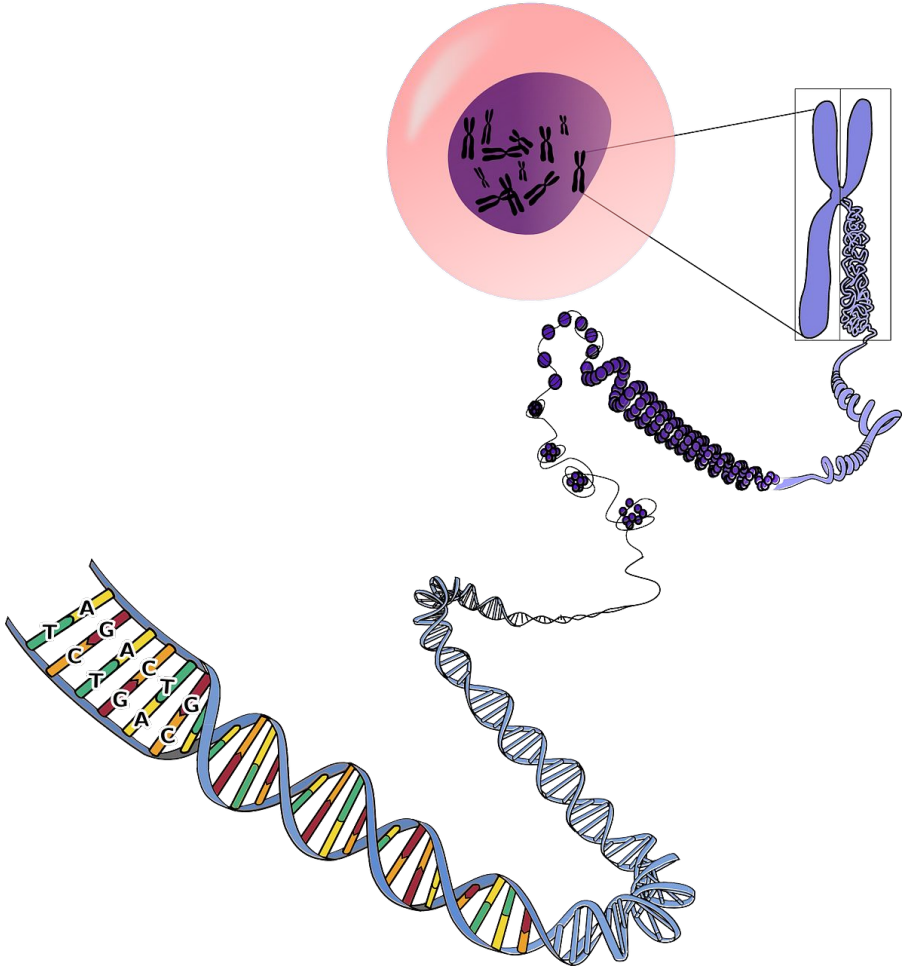
A copy of the ‘recipe for life’ in every cell

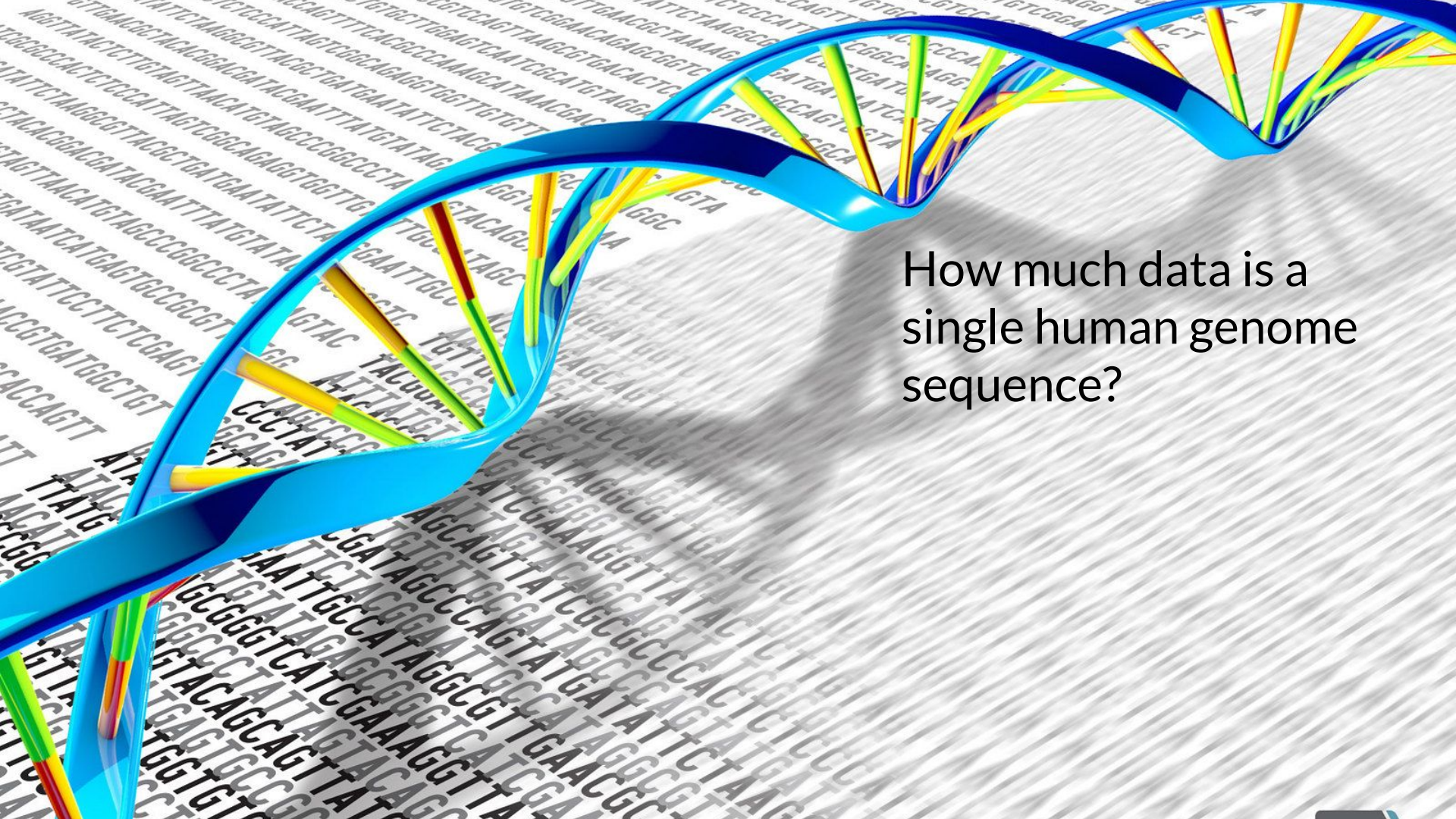
Our bodies have:

trillions of cells

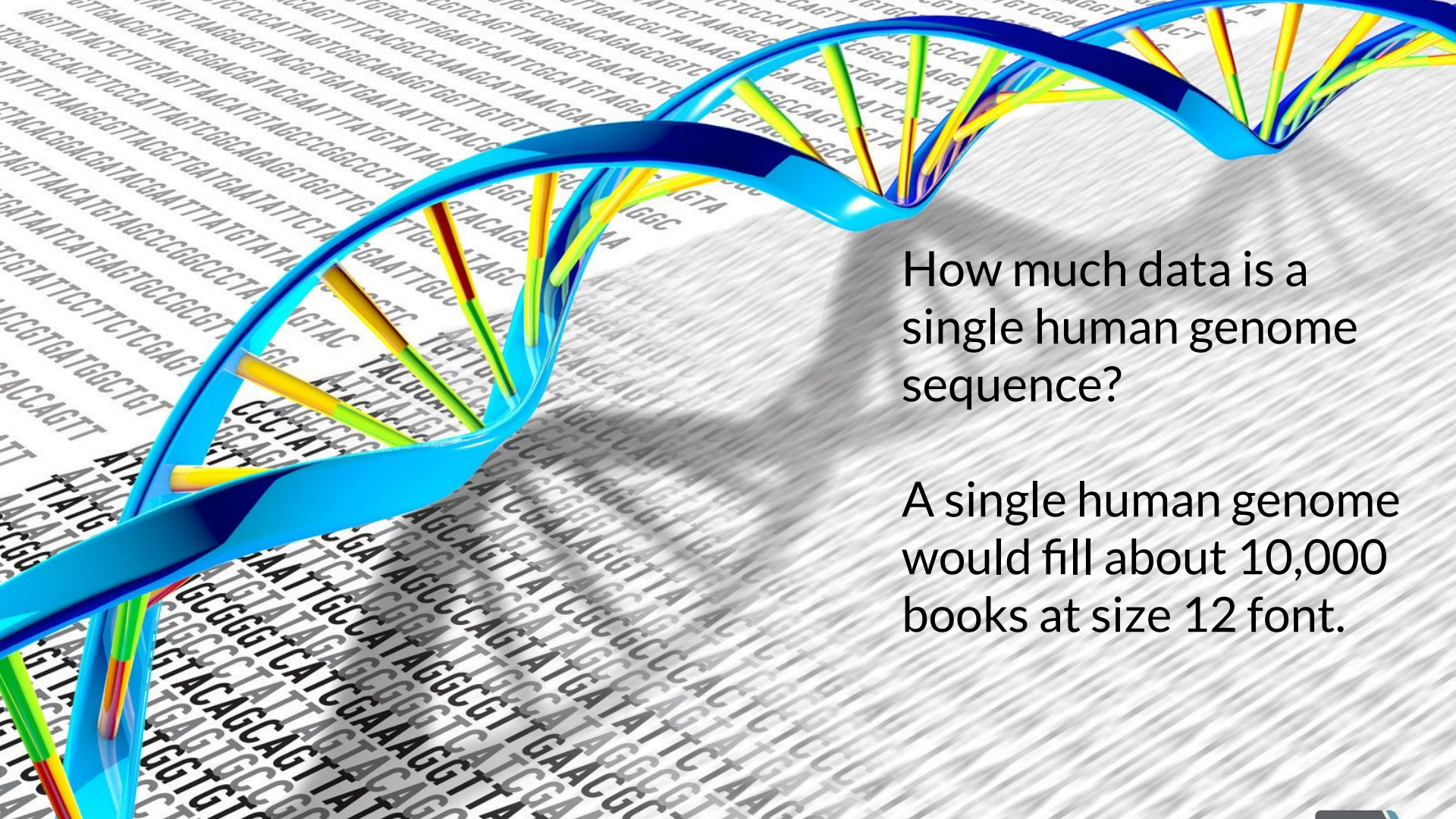
6.2 billion bases of DNA in every cell

Packaged into 23 chromosomes



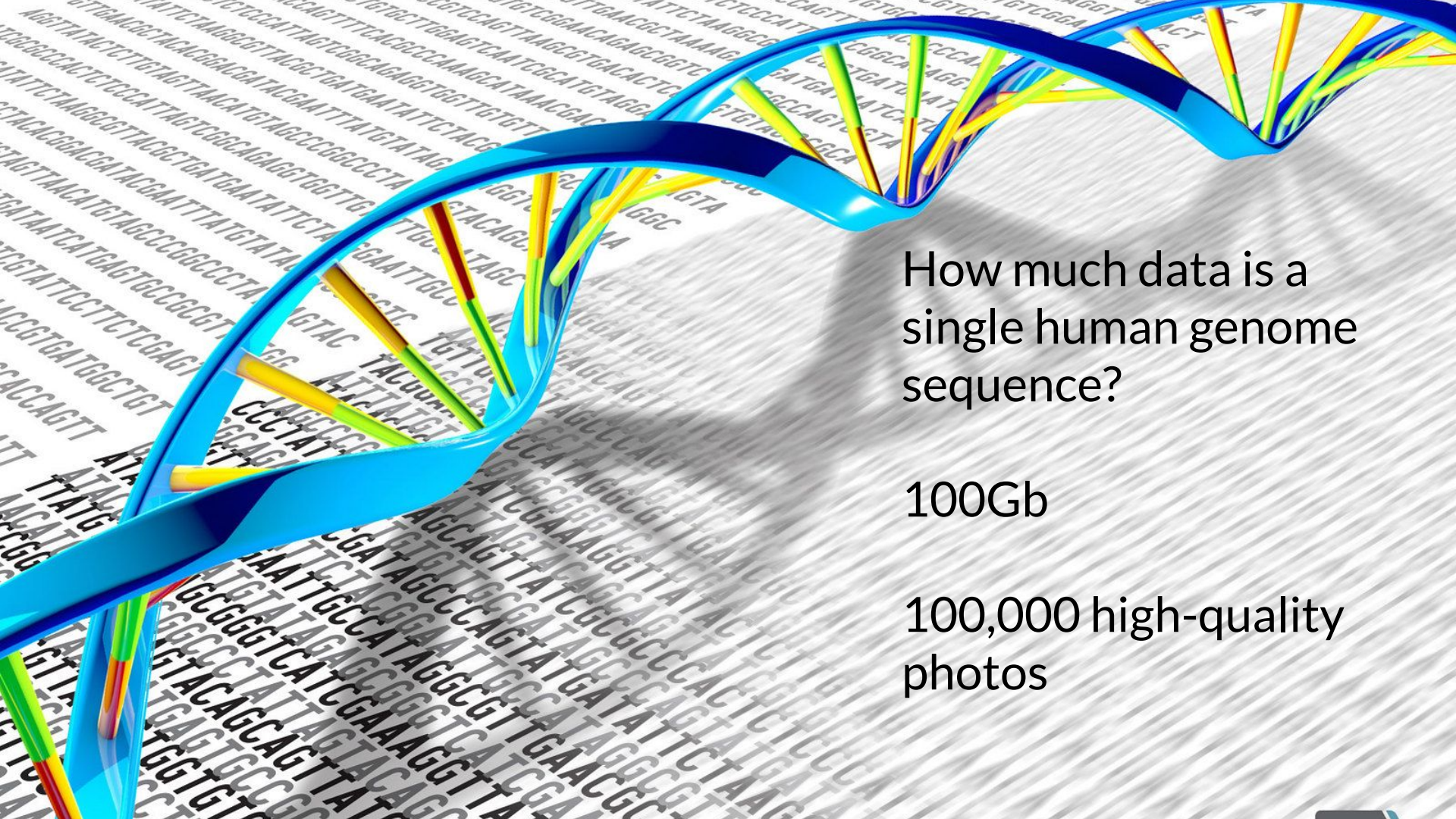


How much data is a single human genome sequence?



How much data is a single human genome sequence?

A single human genome would fill about 10,000 books at size 12 font.



How much data is a single human genome sequence?

100Gb

100,000 high-quality photos

If you stretched out all of your DNA end-to-end

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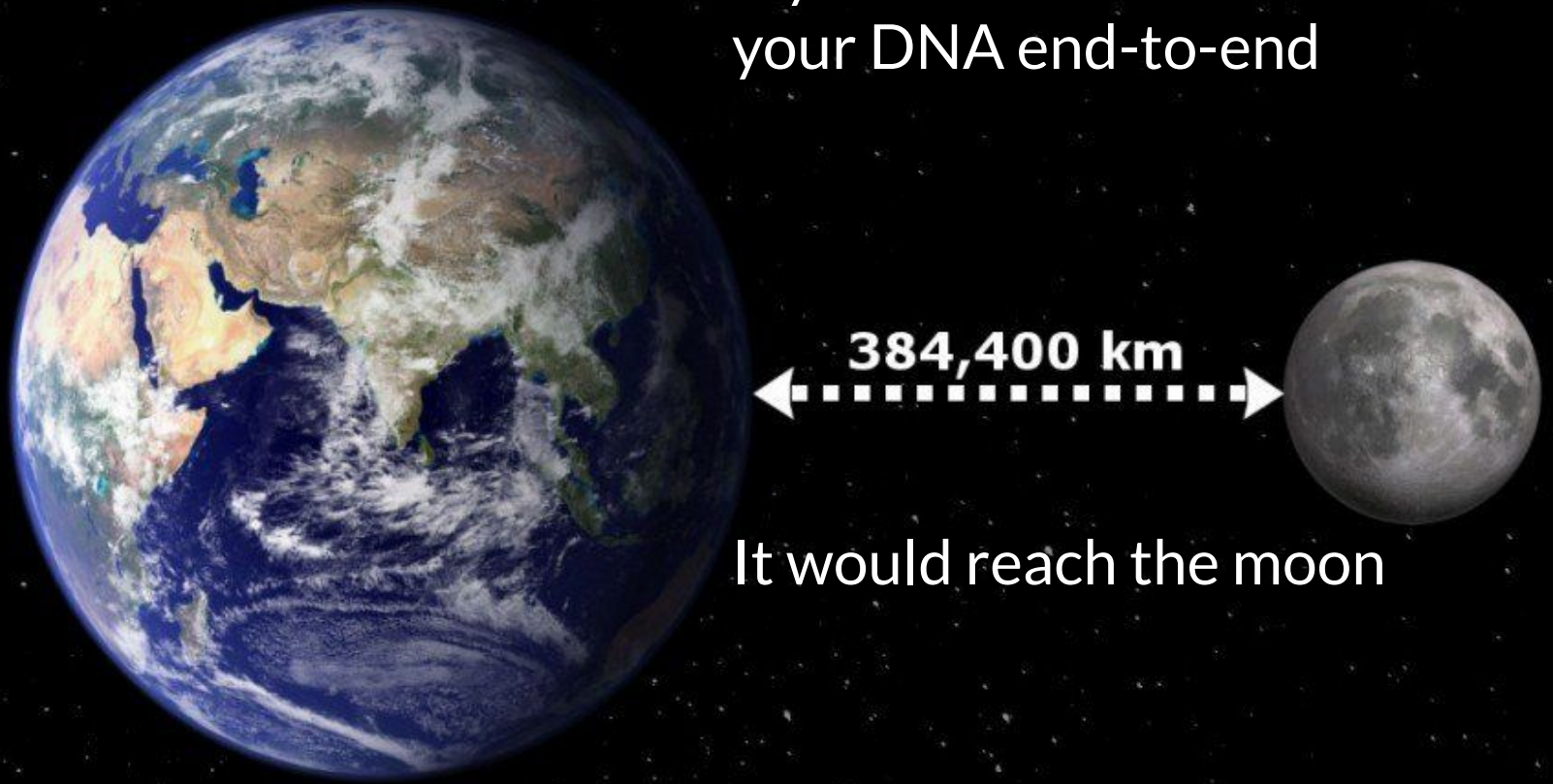

It would reach the moon

If you stretched out all of your DNA end-to-end

It would reach the moon

and back

If you stretched out all of your DNA end-to-end

It would reach the moon

and back

1500 times

DNA is in every cell, but only DNA in the sperm or eggs gets passed on to the next generation.

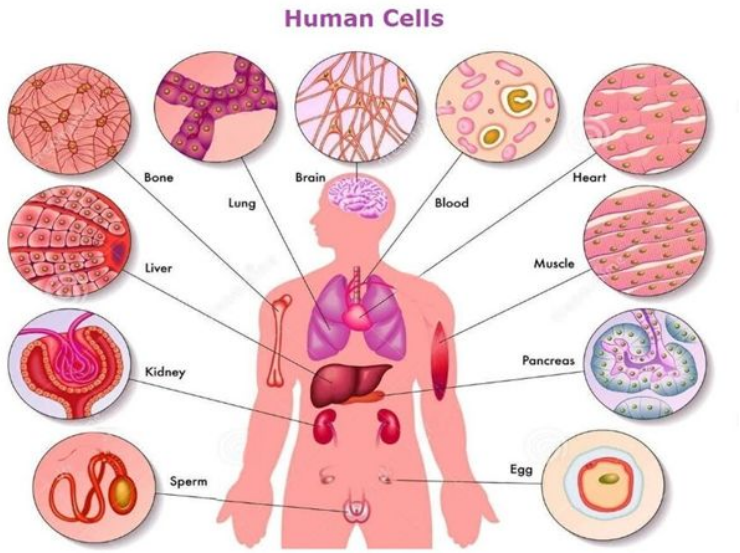

Image source: https://www.quora.com/How-many-cells-are-there-in-the-human-body

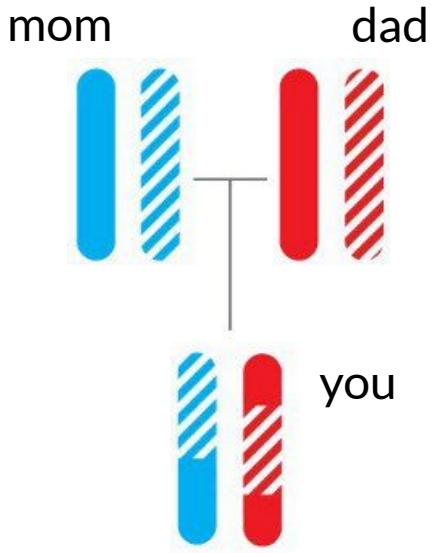

Image source: https://genetics.thetech.org/ask-a-geneticist/

Only 2% of human DNA is genes

About 2% of our DNA is genes, which turn into proteins. Proteins are the building blocks of cells, and they are different in every cell of our body.

10-20% of our DNA is regulatory, which turns genes on and off in different types of cells

The rest is more than likely doing nothing!

Genes turn into proteins, which determine how our cells work

DNA encodes a ‘recipe’ for creating proteins

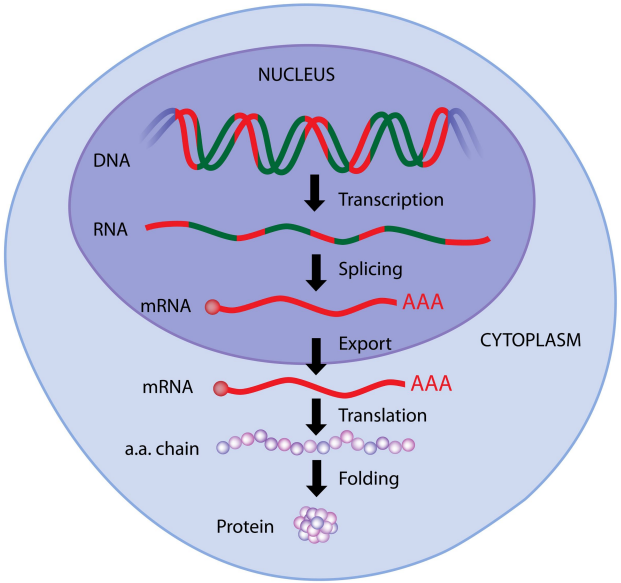

Image source: www.healio.com

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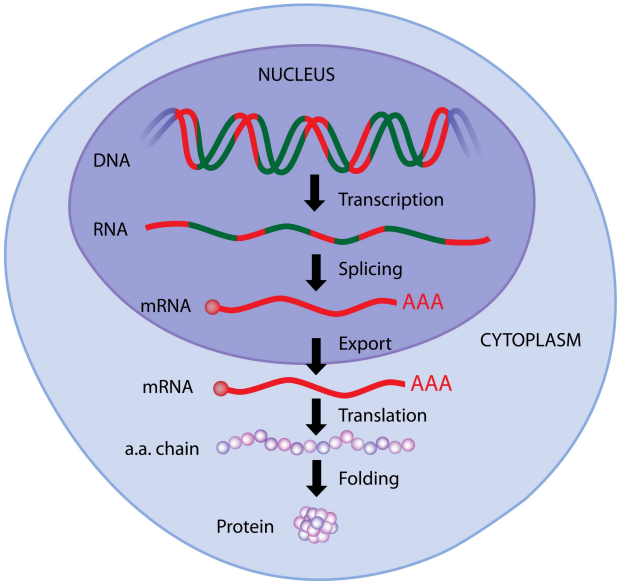


Image source: www.healio.com

	Muscles	Heart	Neuron
Gene A	✓	✓	✓
Gene B	✗	✗	✓
Gene C	✗	✓	✗
Gene D	✓	✗	✗

Humans have about 20,000 genes!

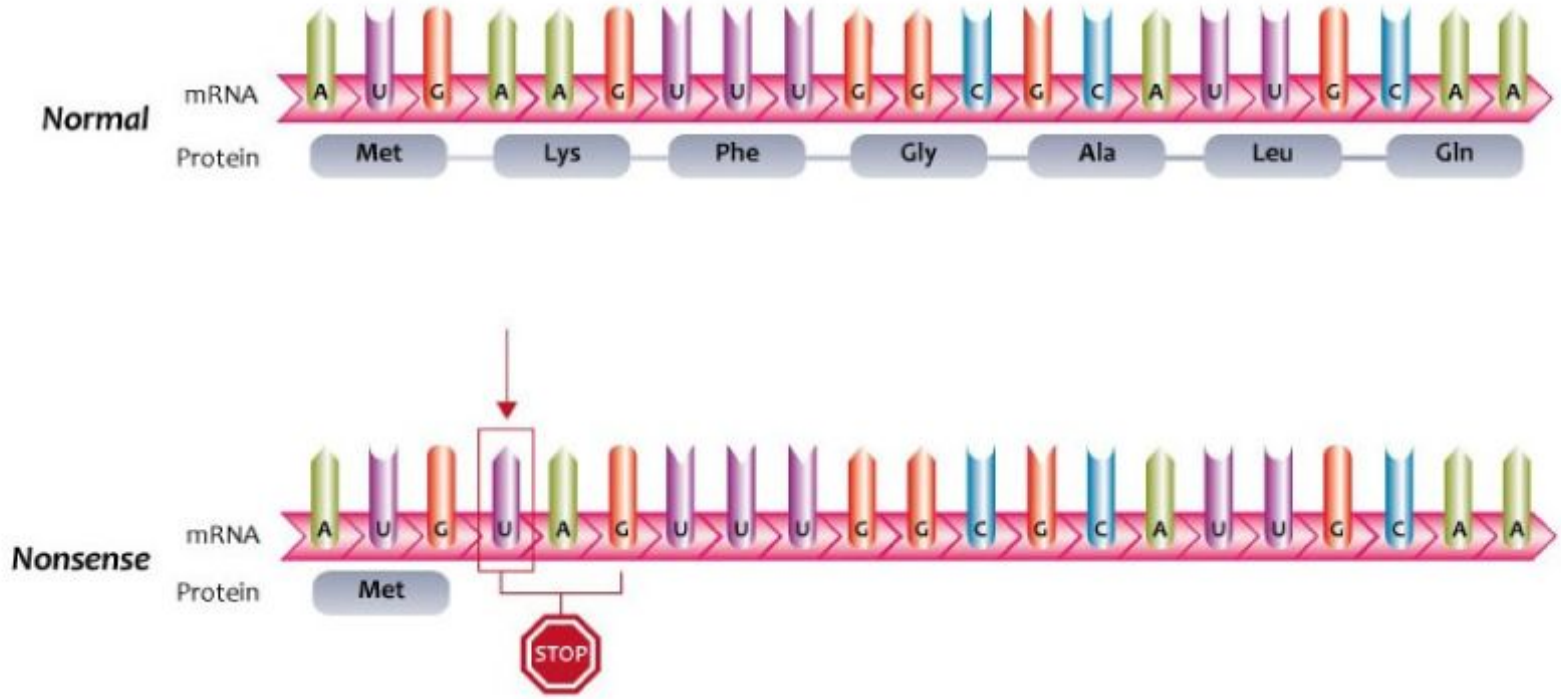
Small changes to our DNA can have a big impact

Small changes to the DNA can:

- Change amount of protein produced
- Change the shape of protein
- Destroy the protein

These small changes can change traits (like eye color) or risk of disorders (like DMD).

Single letter change can have a large impact



Adapted from Campbell NA (ed). Biology, 2nd ed, 1990

How do we read DNA?

ATCGCTAGCTAGCTCGCCCCCTAGCTAAACGATCGATCGTTAAGCTCCGACCCTTT

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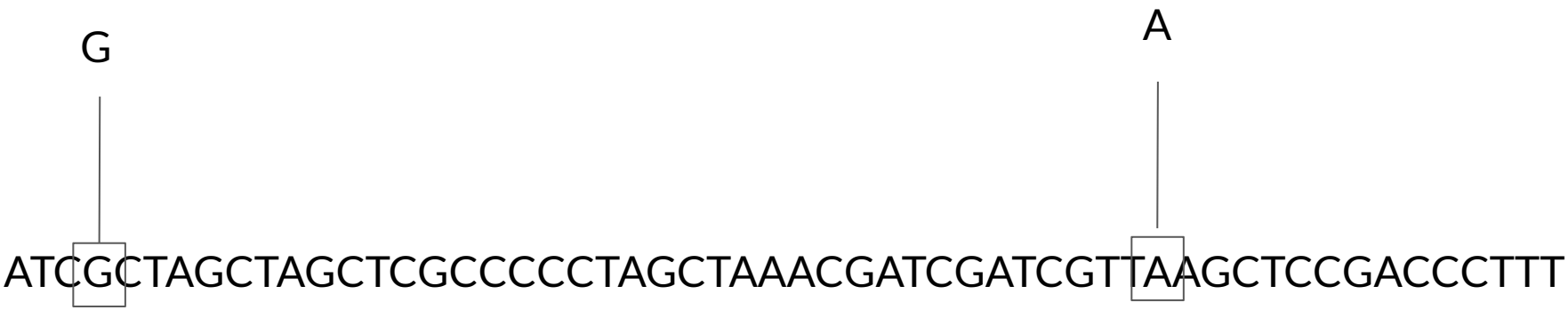

Genotyping, used by nearly all consumer DNA companies measures about 1 million pre-selected letters about 0.02% of the total DNA.

How do we read DNA? - Genotyping

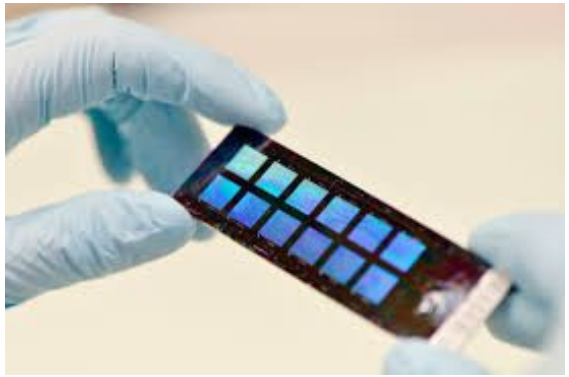

Image source: www.fimm.fi

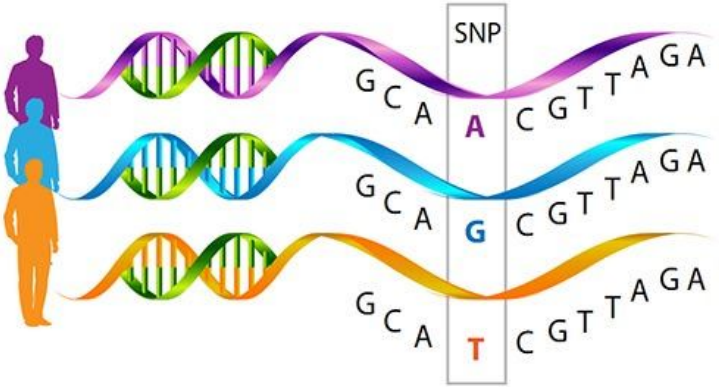

Image source: www.cincinattichildrens.org

This technology tests between 500k and a few million locations in the DNA that commonly vary in humans. These are called single nucleotide polymorphisms (SNPs)

Pro: low-cost ($20 - $70 per person)
Con: incomplete and misses rare genetic variation

This is the technology used by 23andMe, AncestryDNA, etc.

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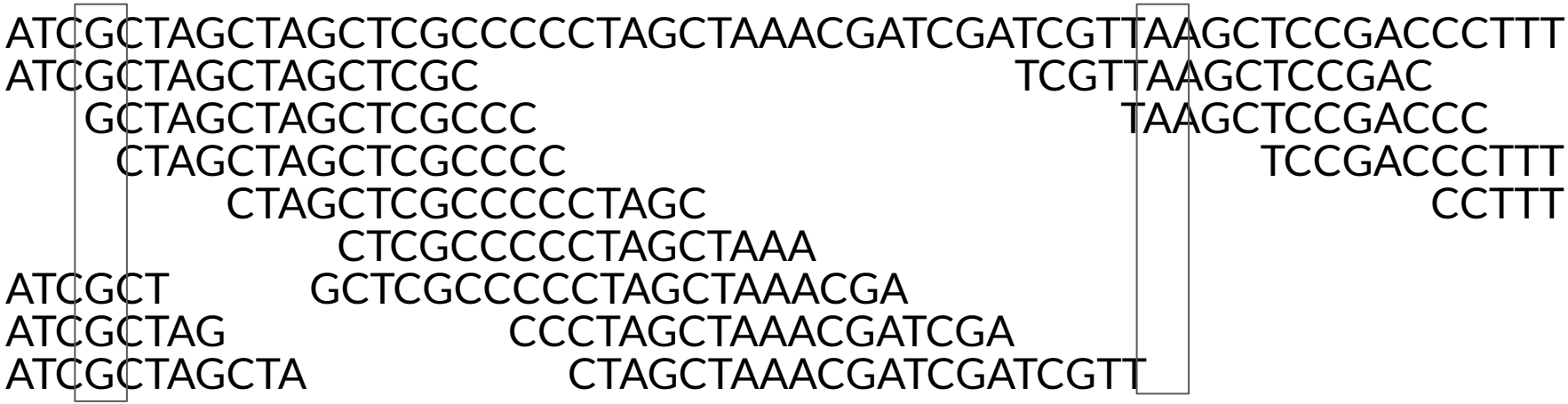
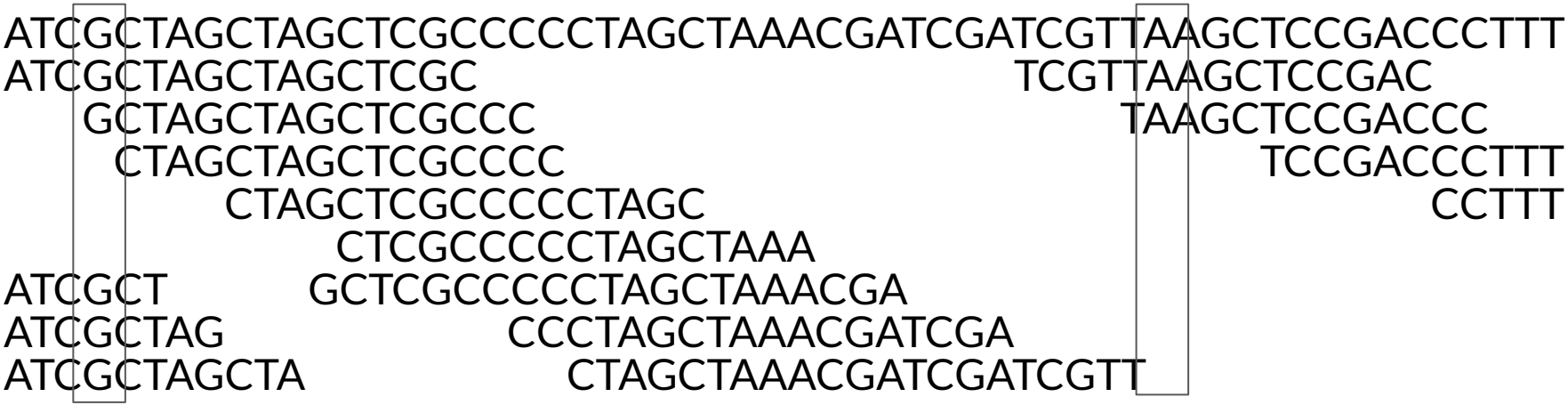


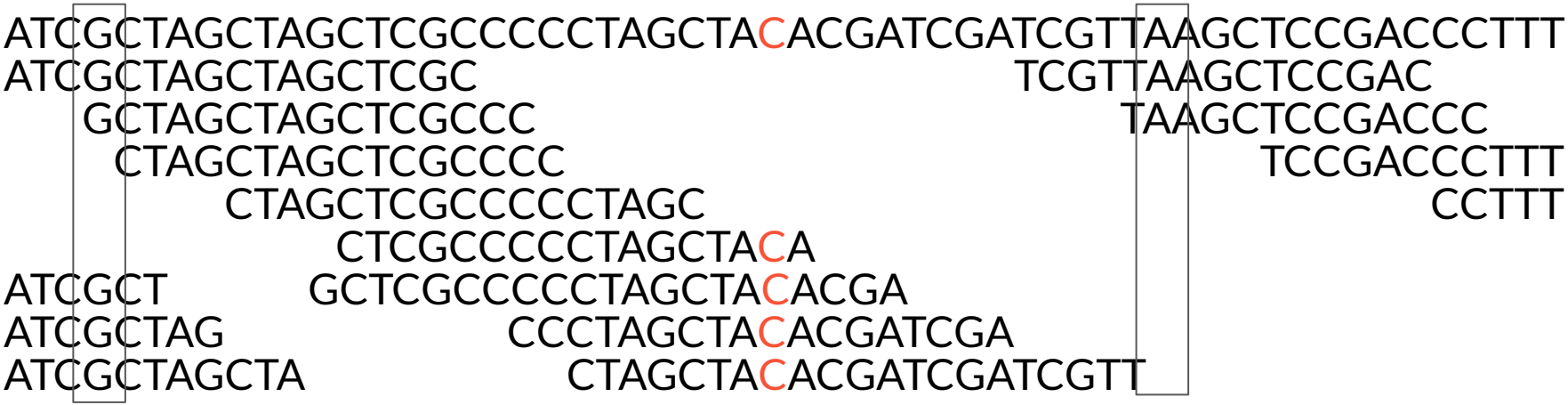
How do we read DNA?

Next generation sequencing allows us to read every letter tens or hundreds of times.



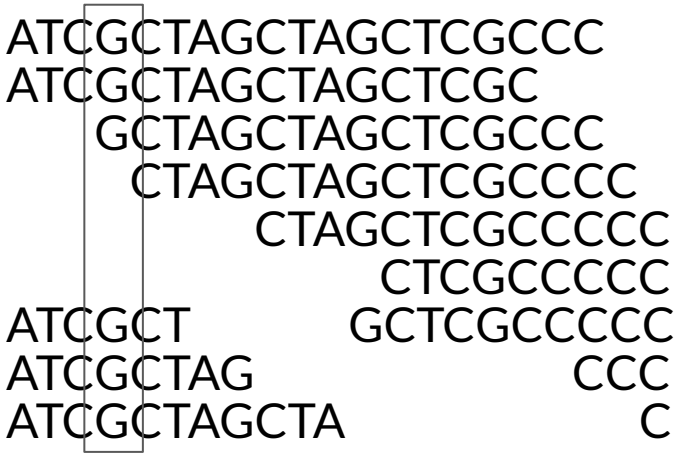
How do we read DNA?

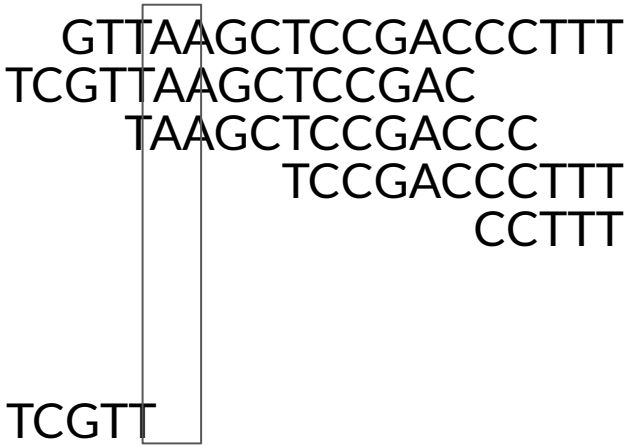
Sequencing can help us identify single letter changes



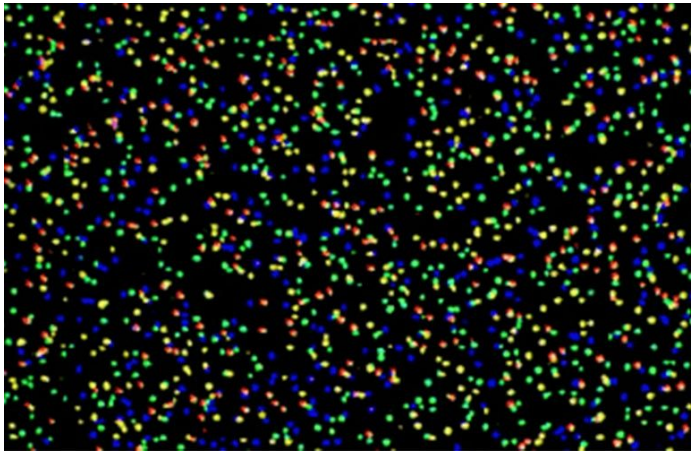
How do we read DNA?

As well as deletions and duplications





How does sequencing work?

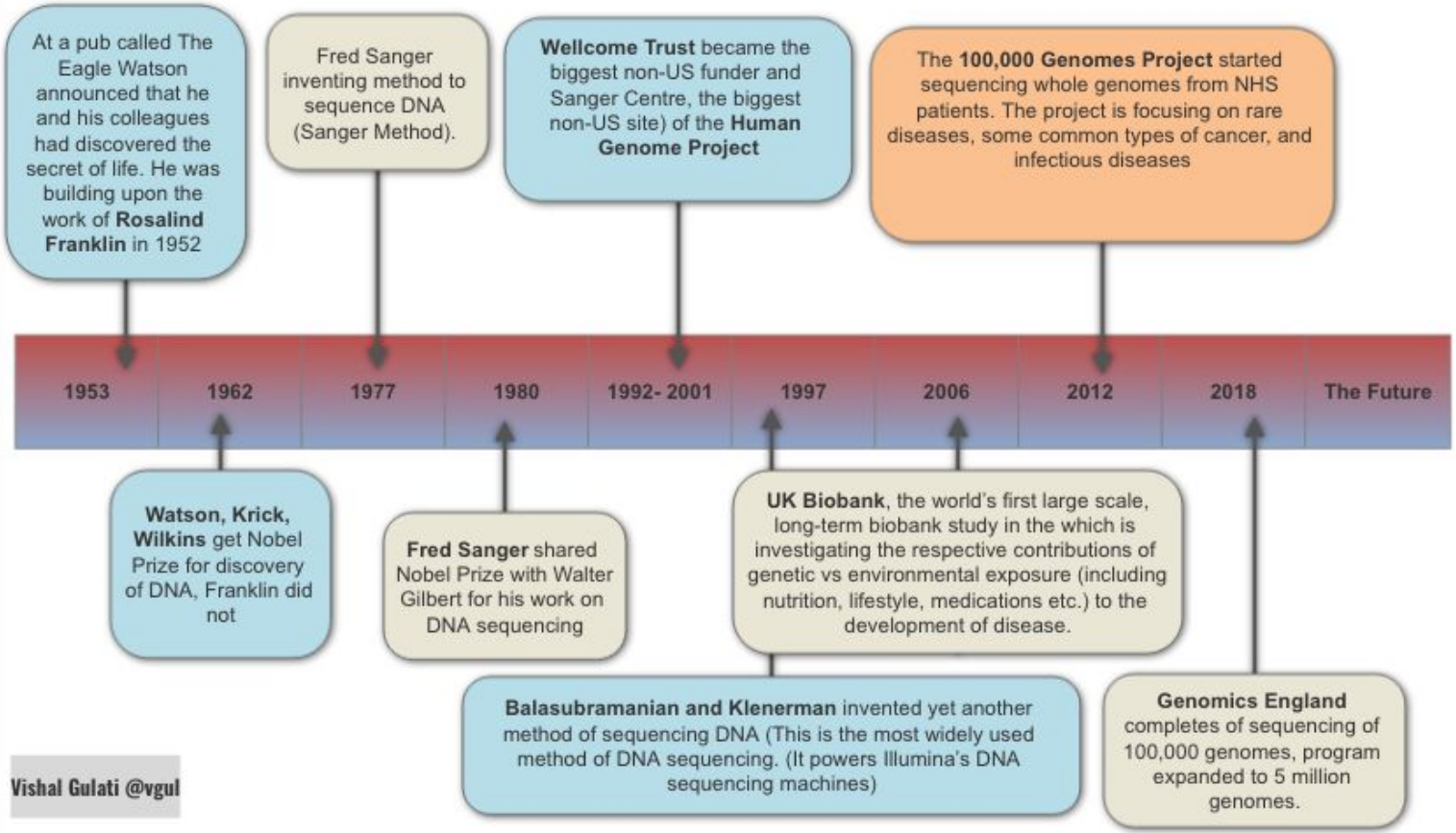


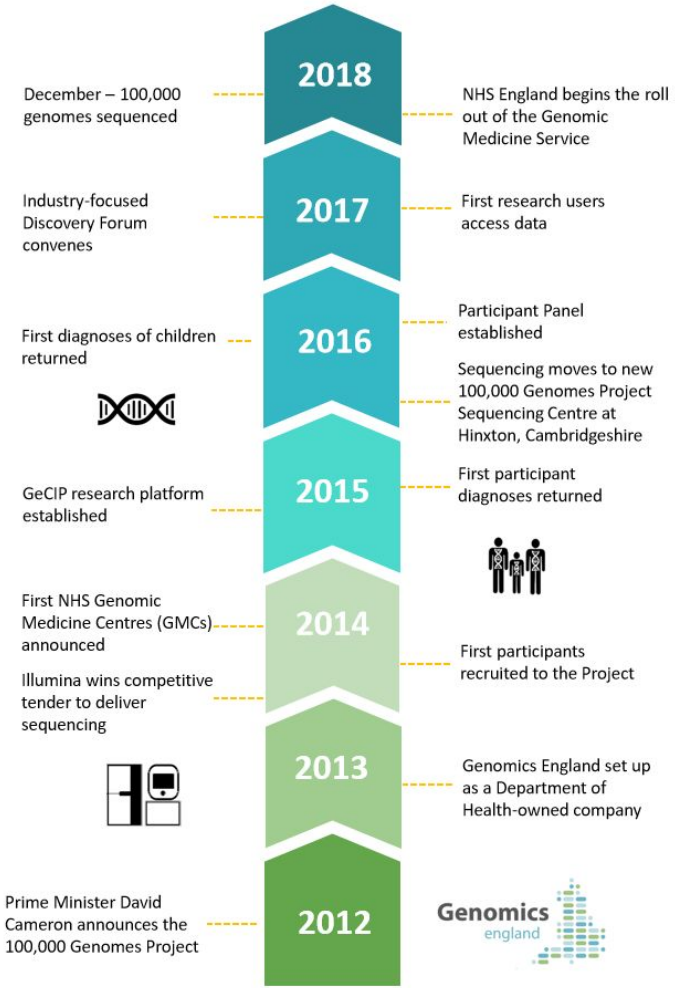
This technology tests specific genes in great detail, or the whole genome.

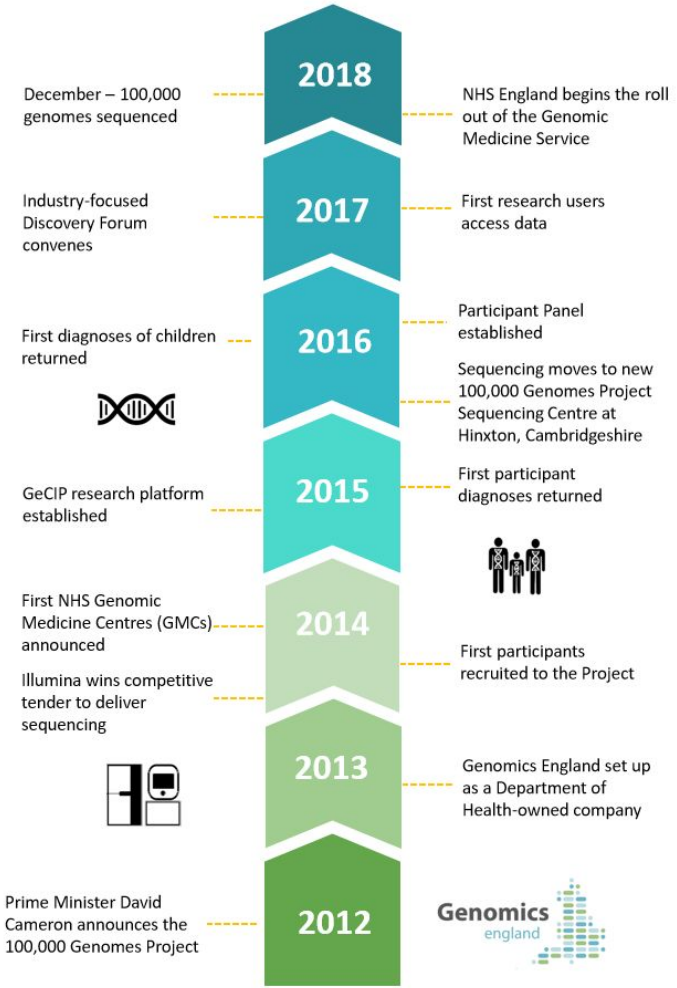
Pro: covers both rare and common variation
Con: more expensive - £300 - £1000

Next-generation is primarily used in research, but now offered by some direct-to-consumer companies.

HOW THE UK BECAME A GENOMICS SUPERPOWER




2018
December – 100,000 genomes sequenced
NHS England begins the roll out of the Genomic Medicine Service
2017
Industry-focused Discovery Forum convenes
First research users access data
2016
First diagnoses of children returned
Participant Panel established
Sequencing moves to new 100,000 Genomes Project Sequencing Centre at Hinxton, Cambridgeshire
2015
GeCIP research platform established
First participant diagnoses returned
2014
First NHS Genomic Medicine Centres (GMCs) announced
Illumina wins competitive tender to deliver sequencing
First participants recruited to the Project
2013
Genomics England set up as a Department of Health-owned company
2012
Prime Minister David Cameron announces the 100,000 Genomes Project
Genomics england



This new initiative means:

- Faster diagnoses using better technology
- National rare disease strategy with genomics as an integral part

Why is genomics relevant for DMD? Don’t we know the gene?

Review

Dystrophin and mutations: one gene, several proteins, multiple phenotypes

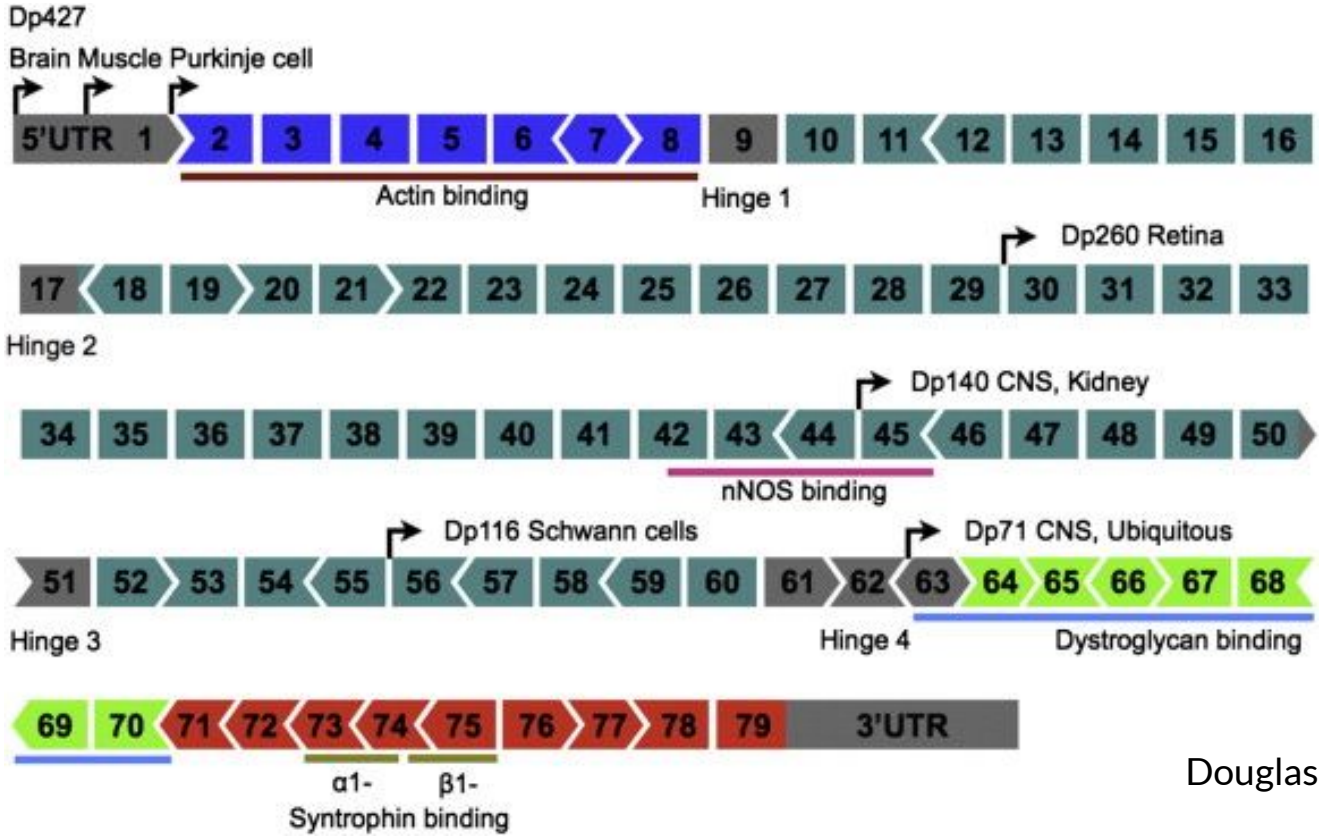
Prof Francesco Muntoni [a], Silvia Torelli [a], Alessandra Ferlini [b]

Show more

https://doi.org/10.1016/S1474-4422(03)00585-4

Muntoni et. al, 2003

The Dystrophin gene is longest in the genome, with a complex set of genetic changes



Douglas et. al

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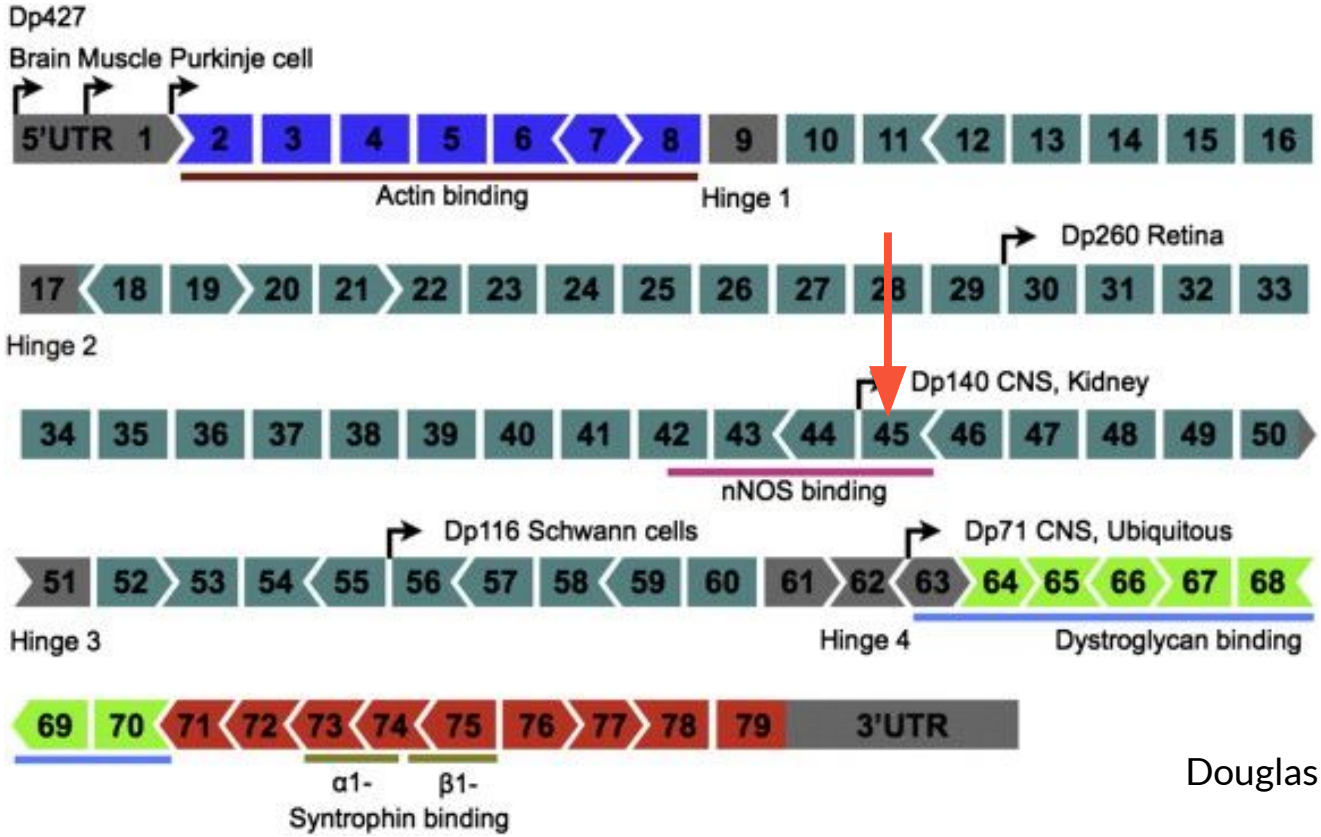

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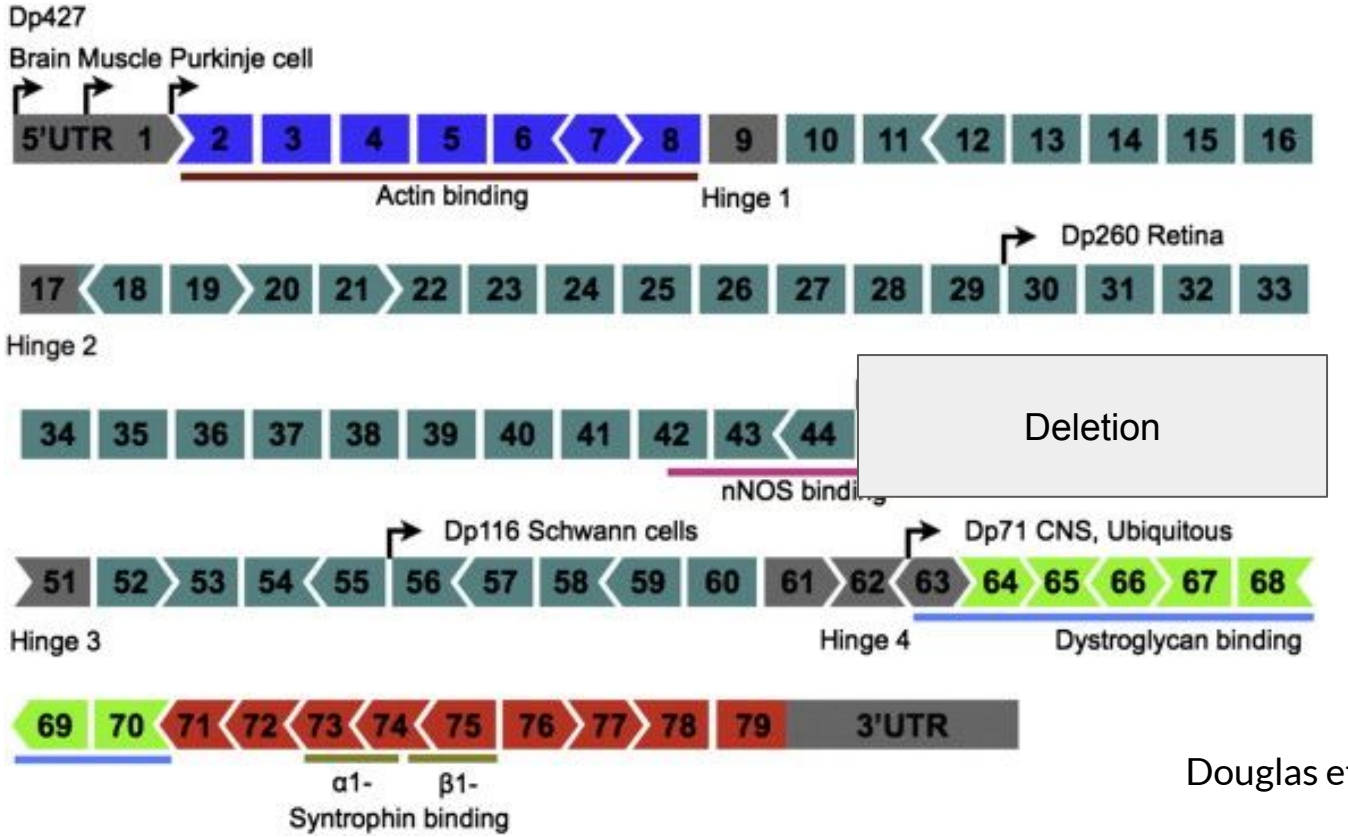

Douglas et. al

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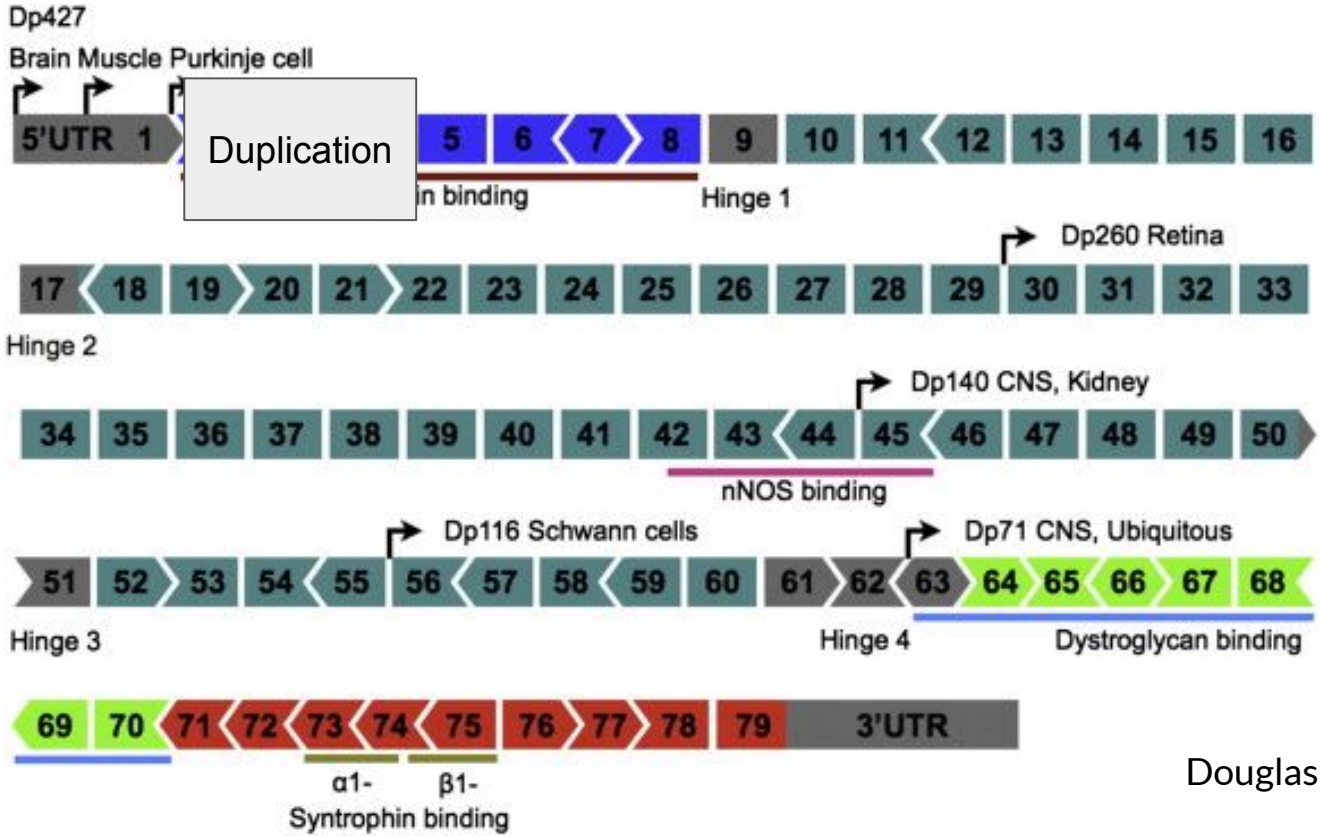
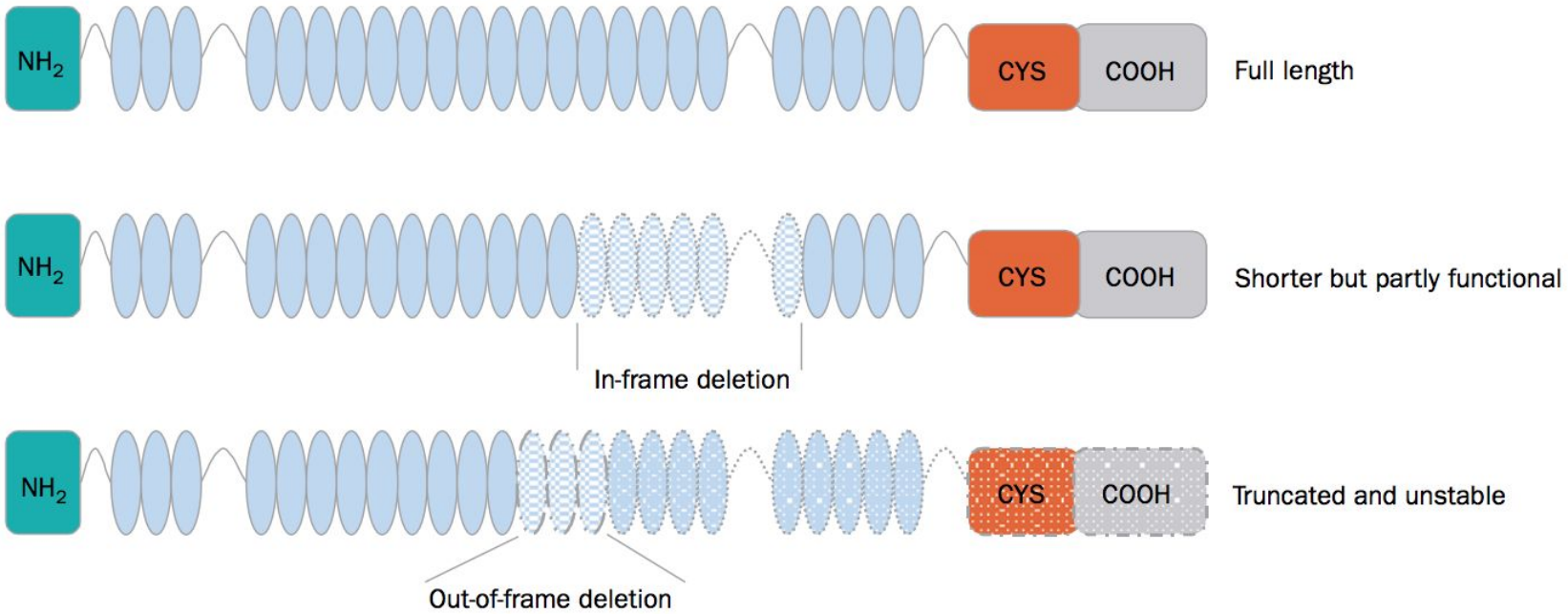


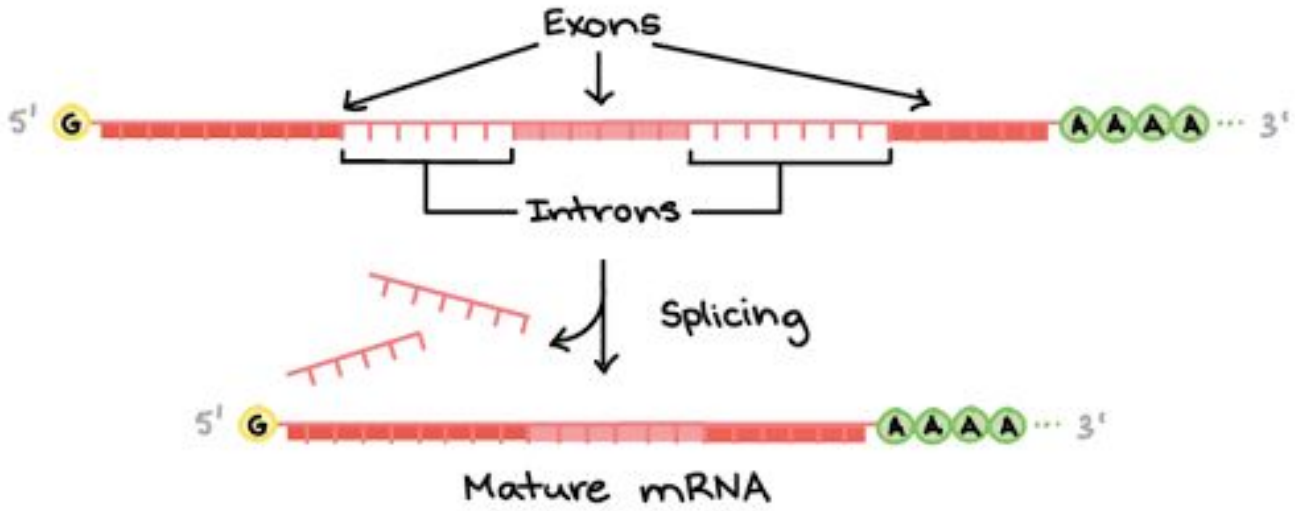
Douglas et. al

Different genetic variants cause different outcomes



Muntoni et. al, 2003

RNA sequencing and whole genome sequencing is helping find previously hidden genetic variants



Khan Academy

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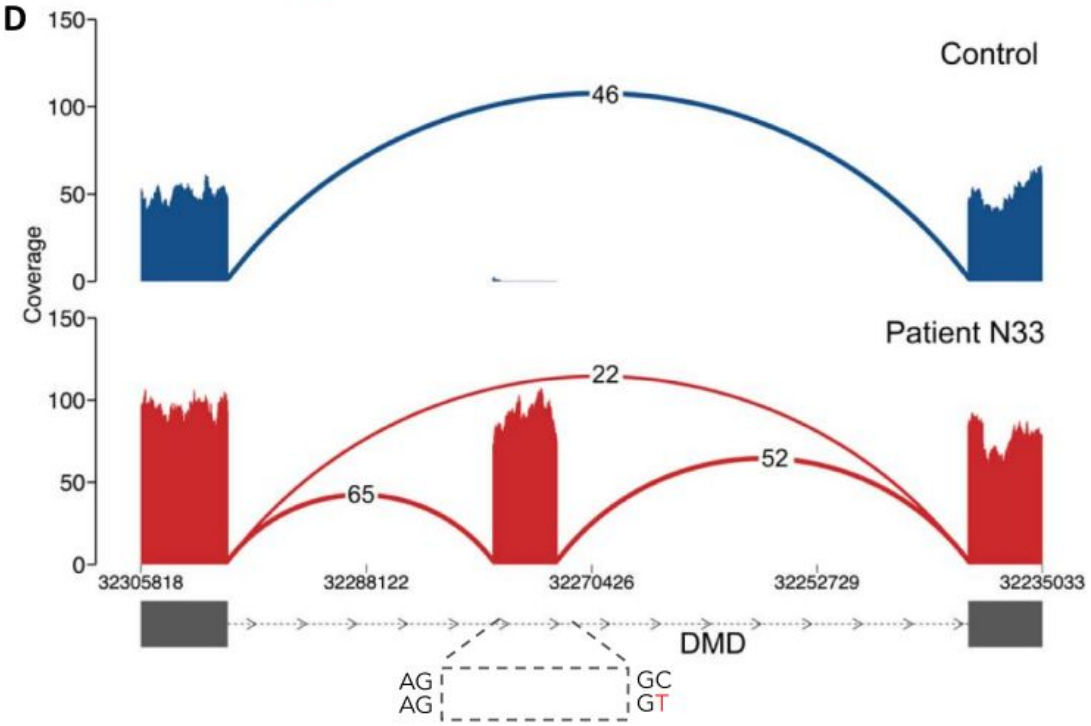

Cummings et. al, 2017

Treatments in DMD are more personalised, soon tailored to a unique DNA change

How do we make sure patients get the right treatment?

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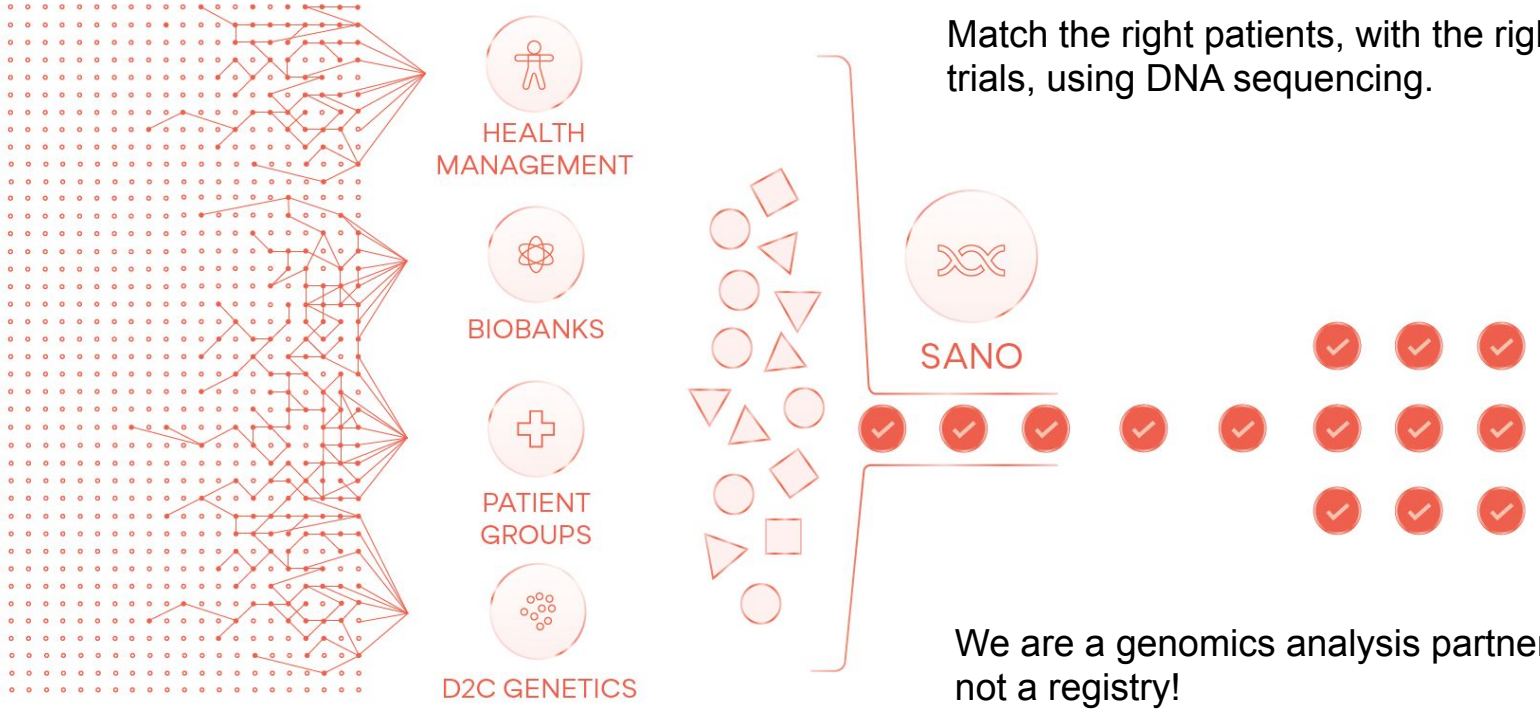
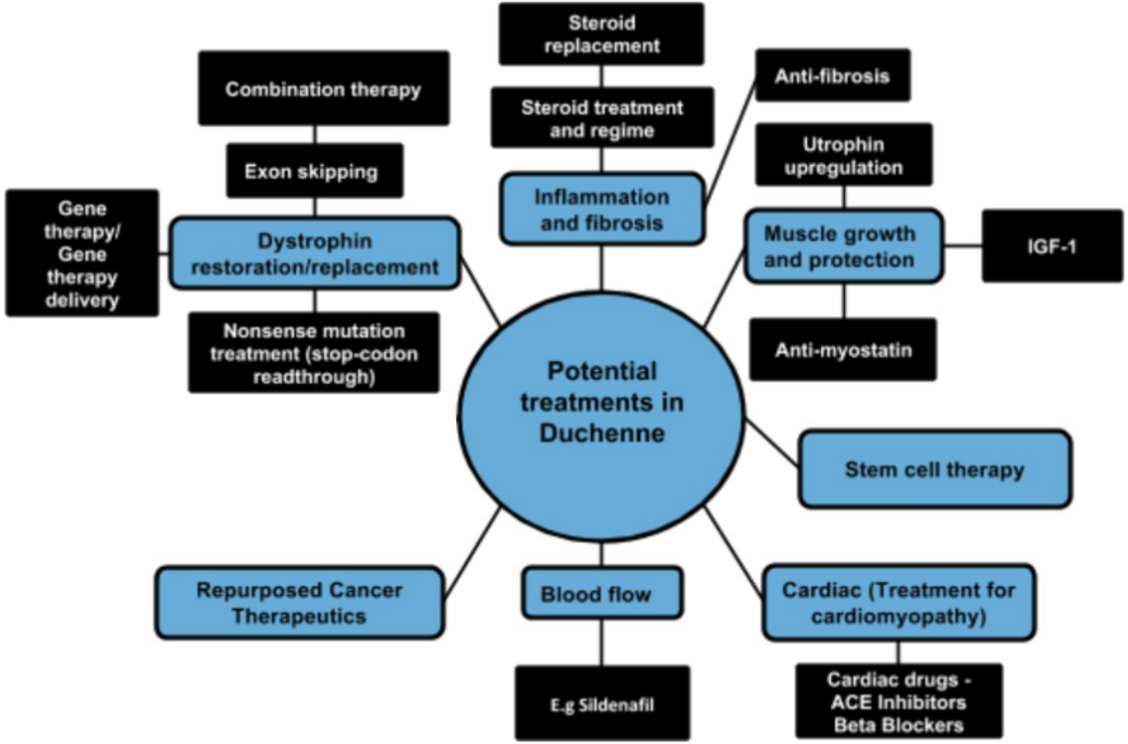


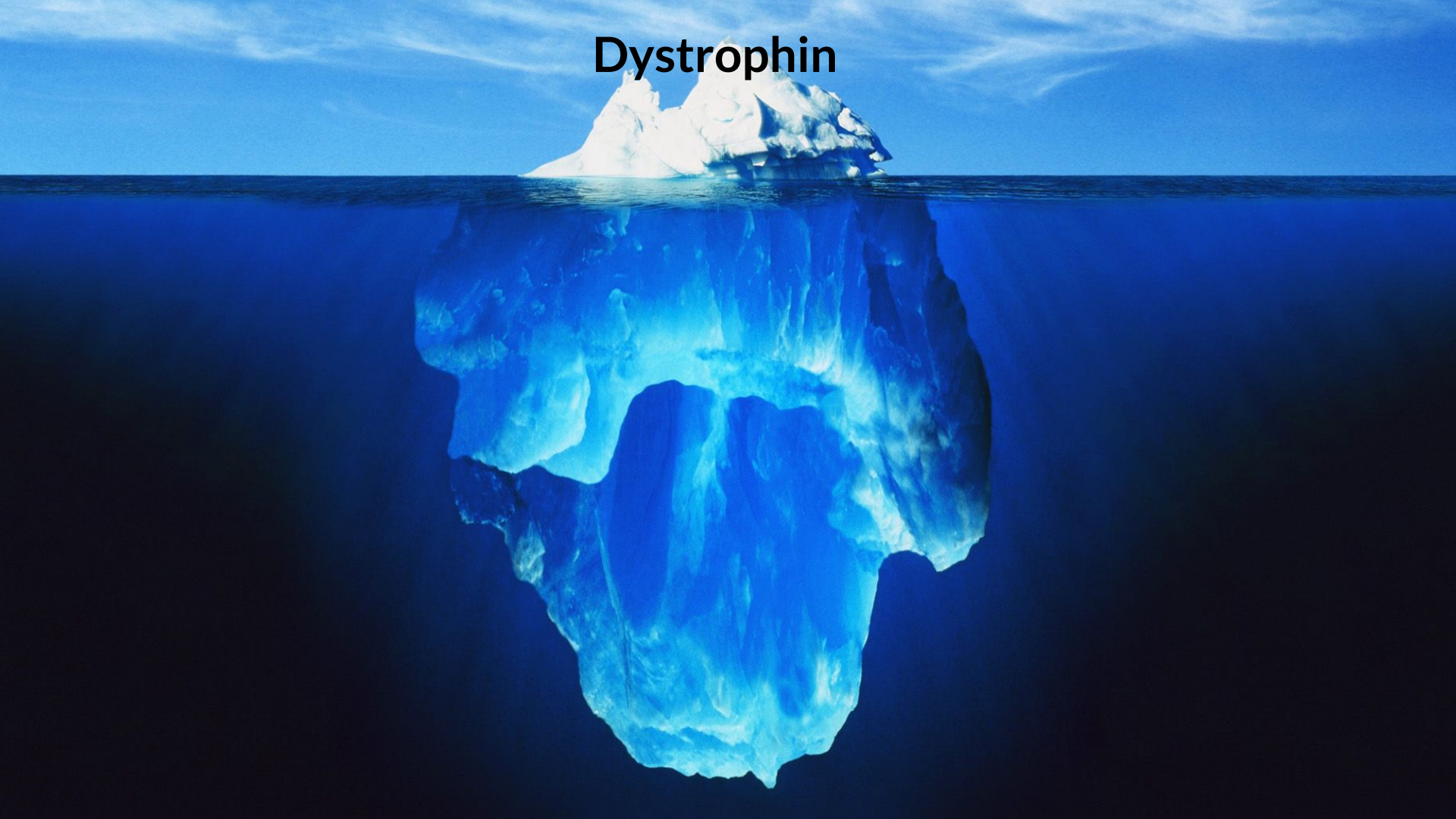
Match the right patients, with the right trials, using DNA sequencing.

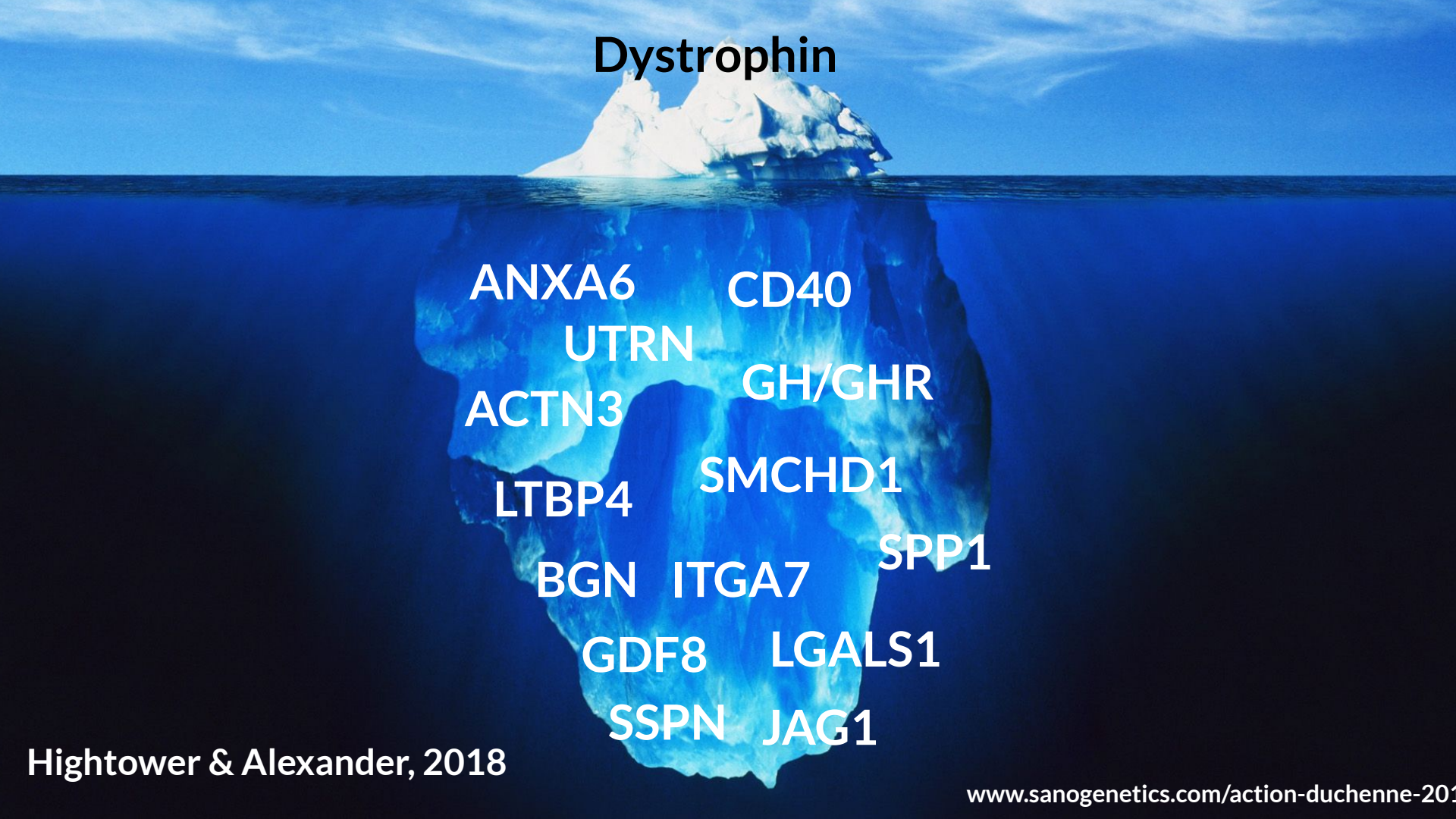
We are a genomics analysis partner - not a registry!

How do we make sure patients get the right treatment?



ACTION DUCHENNE


Dystrophin



Hightower & Alexander, 2018

www.sanogenetics.com/action-duchenne-201

Towards a better understanding of genetic heterogeneity in rare disease

We would love to partner with more patient organisations, researchers, and clinicians to perform DNA sequencing and analysis in DMD.

Even in ‘single gene’ disorders, every patient is different.

We need to **embrace** this and collect better data to **understand** it.

Thank you!

www.sanogenetics.com
patrick@sanogenetics.com

Great conversations about the future of genomics and personalised medicine

Several new conversations every month with a leader in the field of genomics and precision medicine.

Past guests include Eric Topol, Nick Sireau, Neil Bennett, Paul Wicks, and many more!

Email podcast@sanogenetics.com if you or a colleague have a story to tell!

This presentation will be on www.sanogenetics.com/action-duchenne-2019 in a few days!