Rare Bootcamp™

Genetic Diagnosis

November 2023

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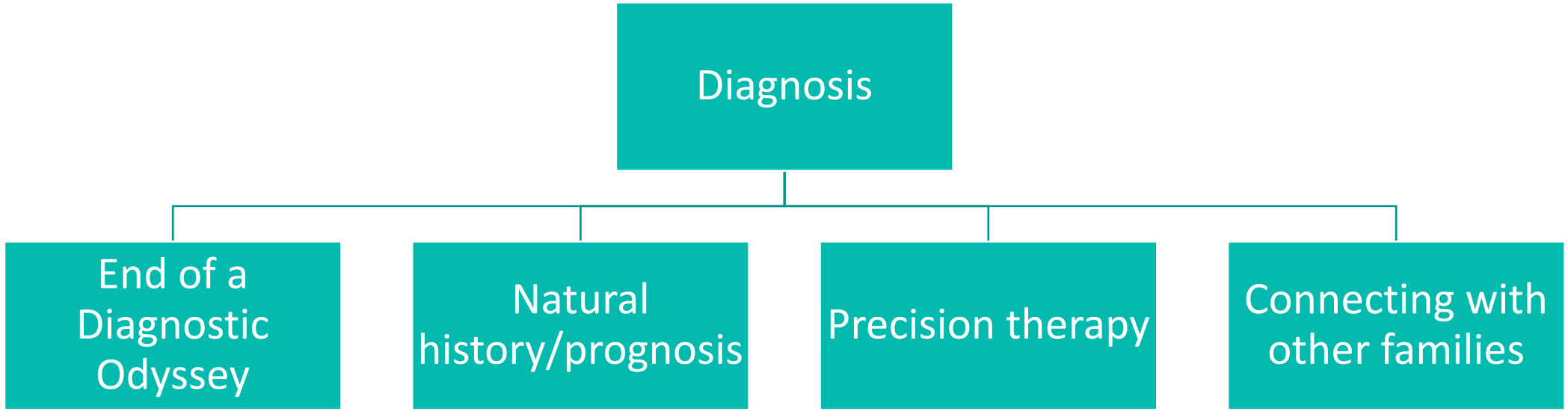
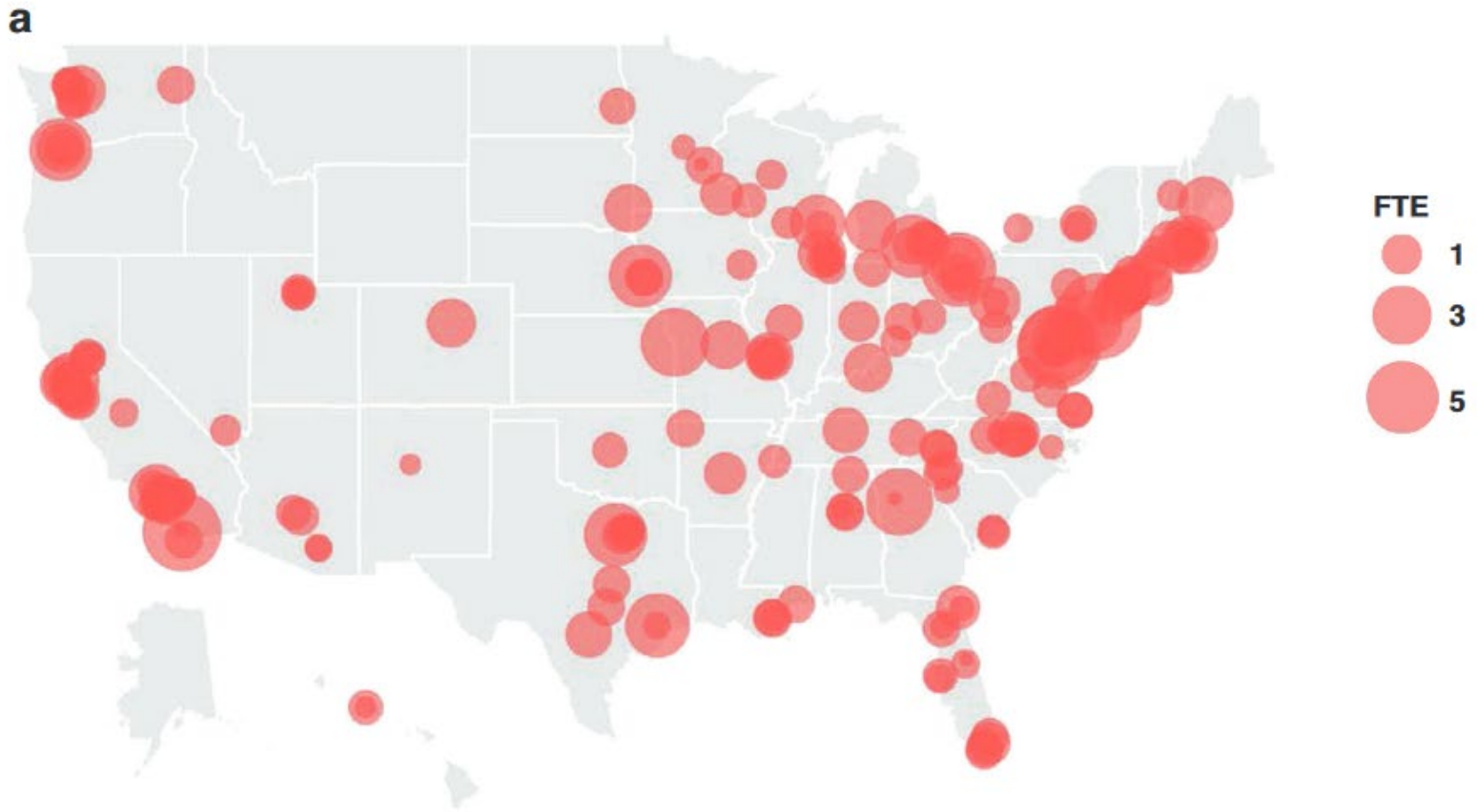
GeneDx

How is a diagnosis “actionable”?



The 2019 US medical genetics workforce: Endangered Species



Genetics in Medicine (2021) 23:1458 – 1464

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Terminology

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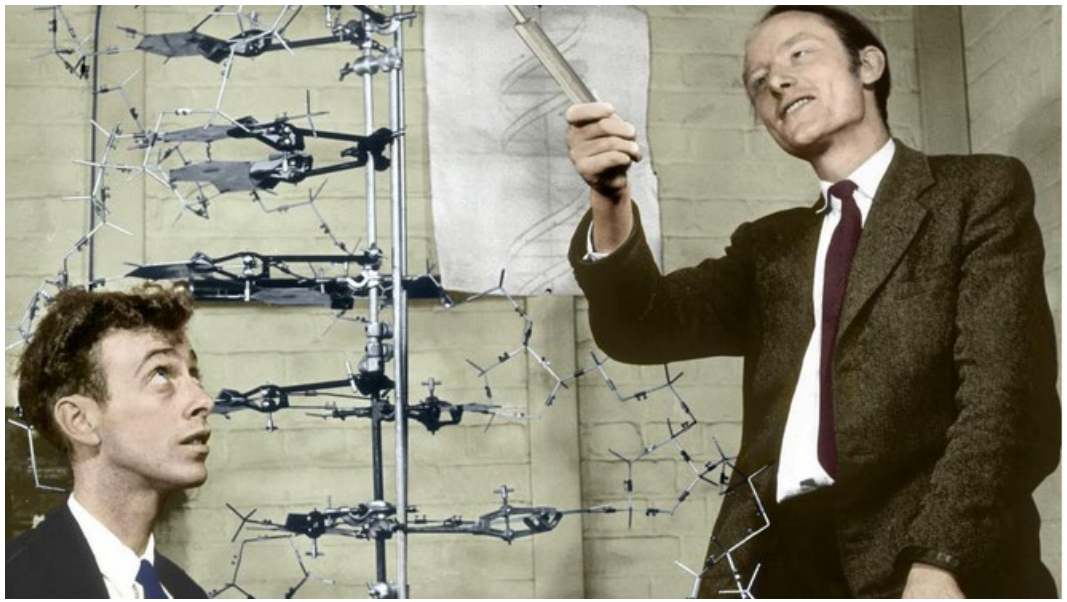
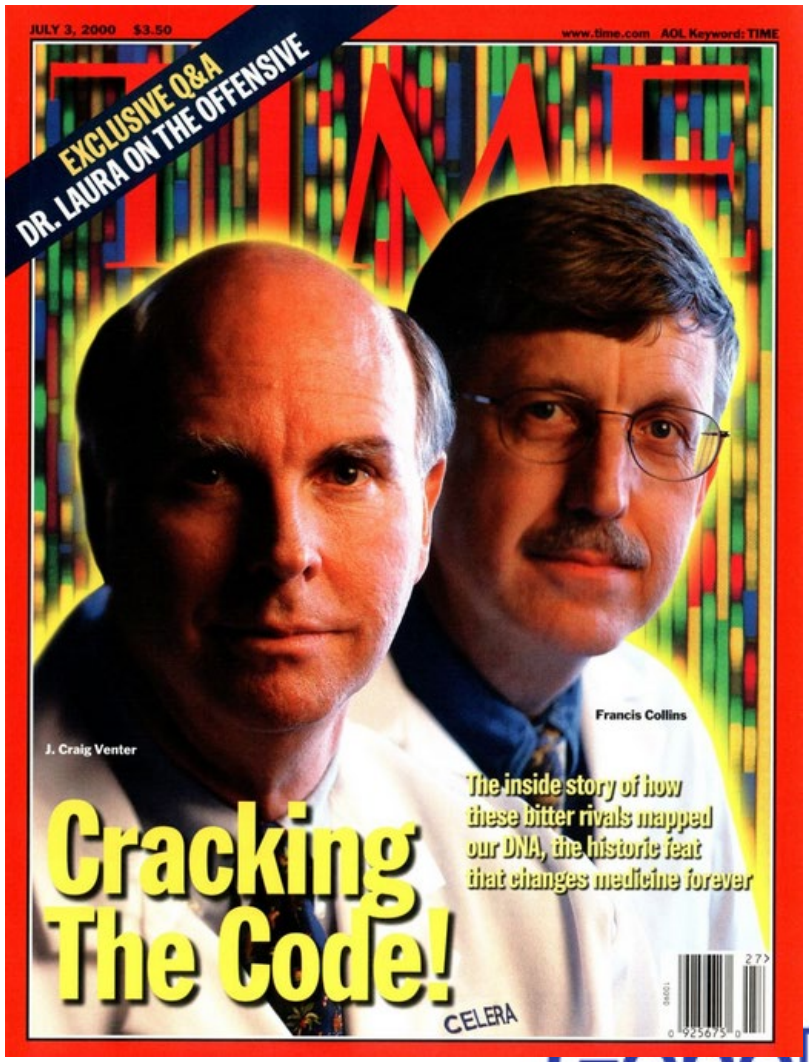
The Genomic Era

1953



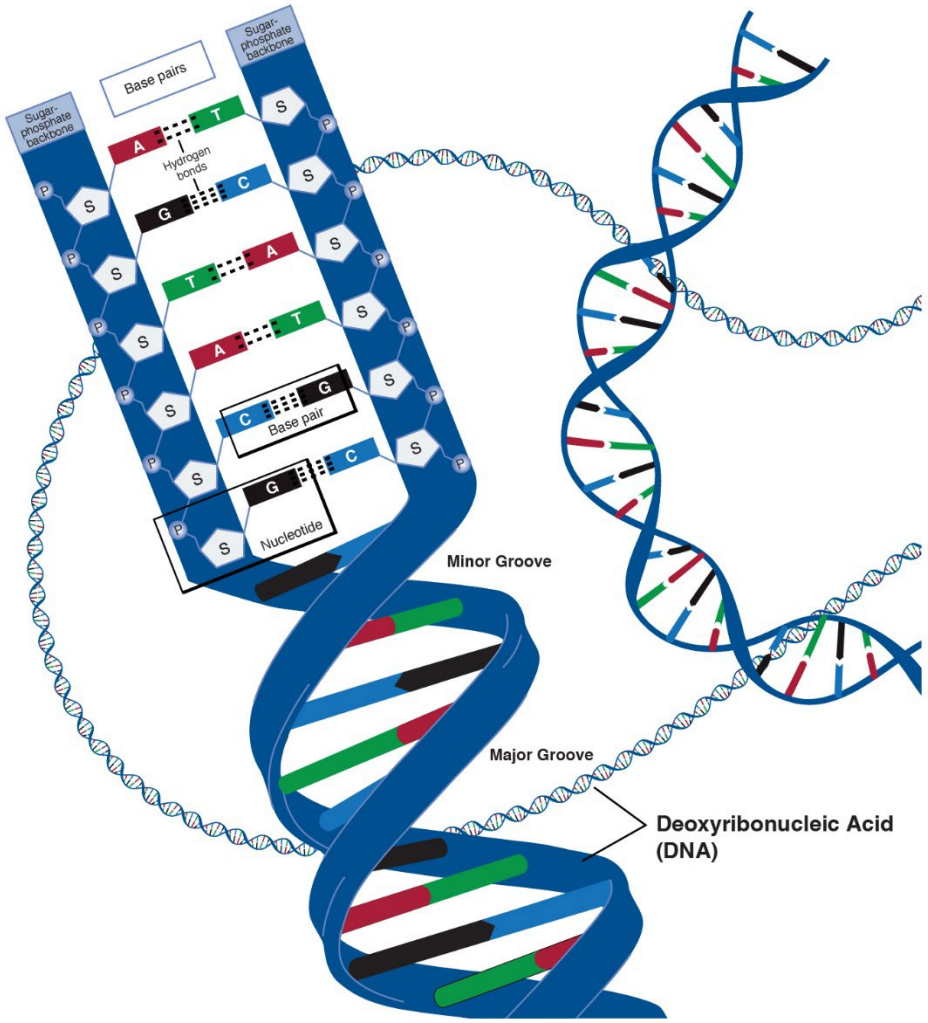
https://www.thetimes.co.uk/article/being-objectionable-is-in-his-dna-james-watson-derides-former-colleagues-szhlbtctl

2000



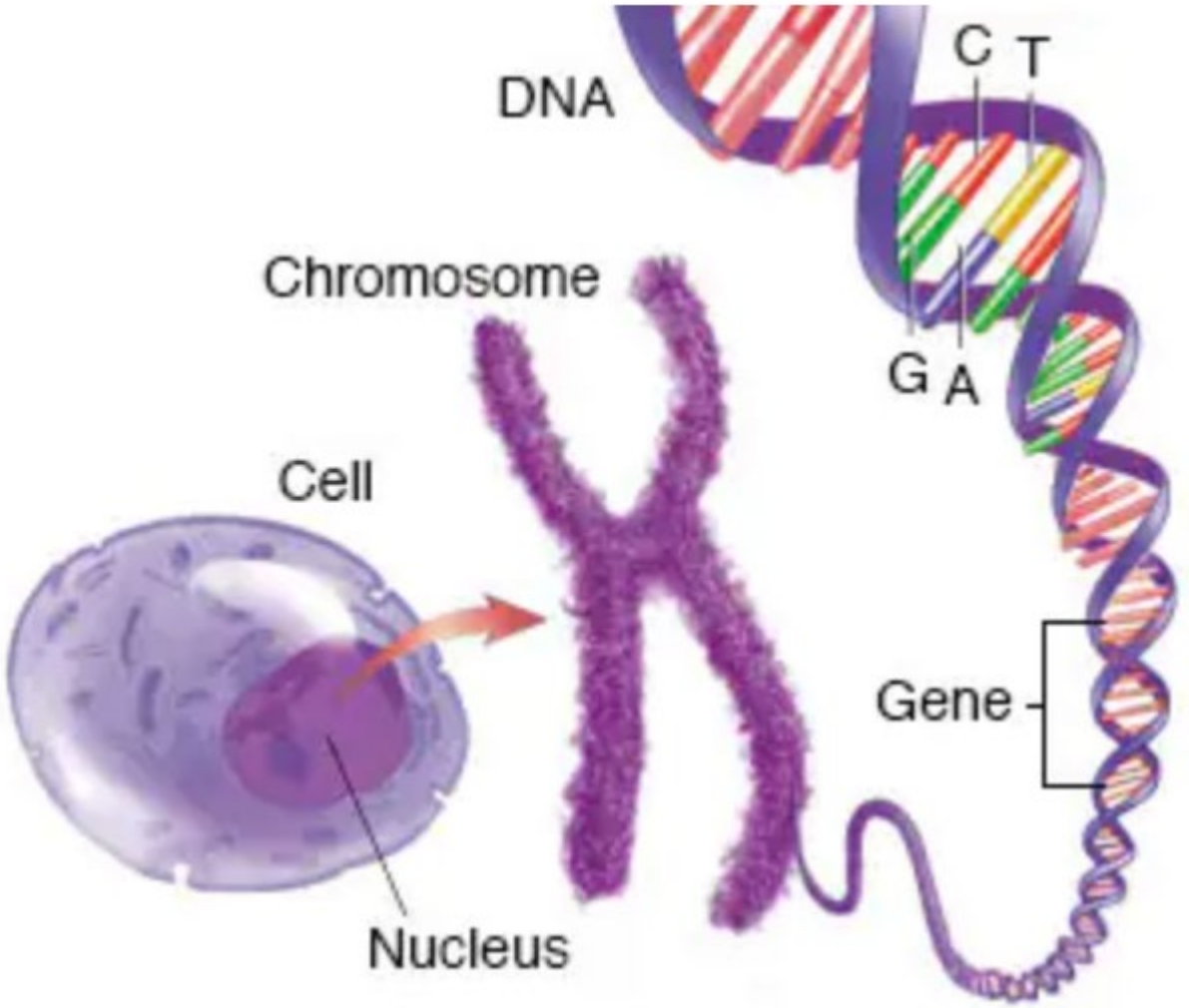
https://time.com/vault/issue/2000-07-03/page/1/

Code



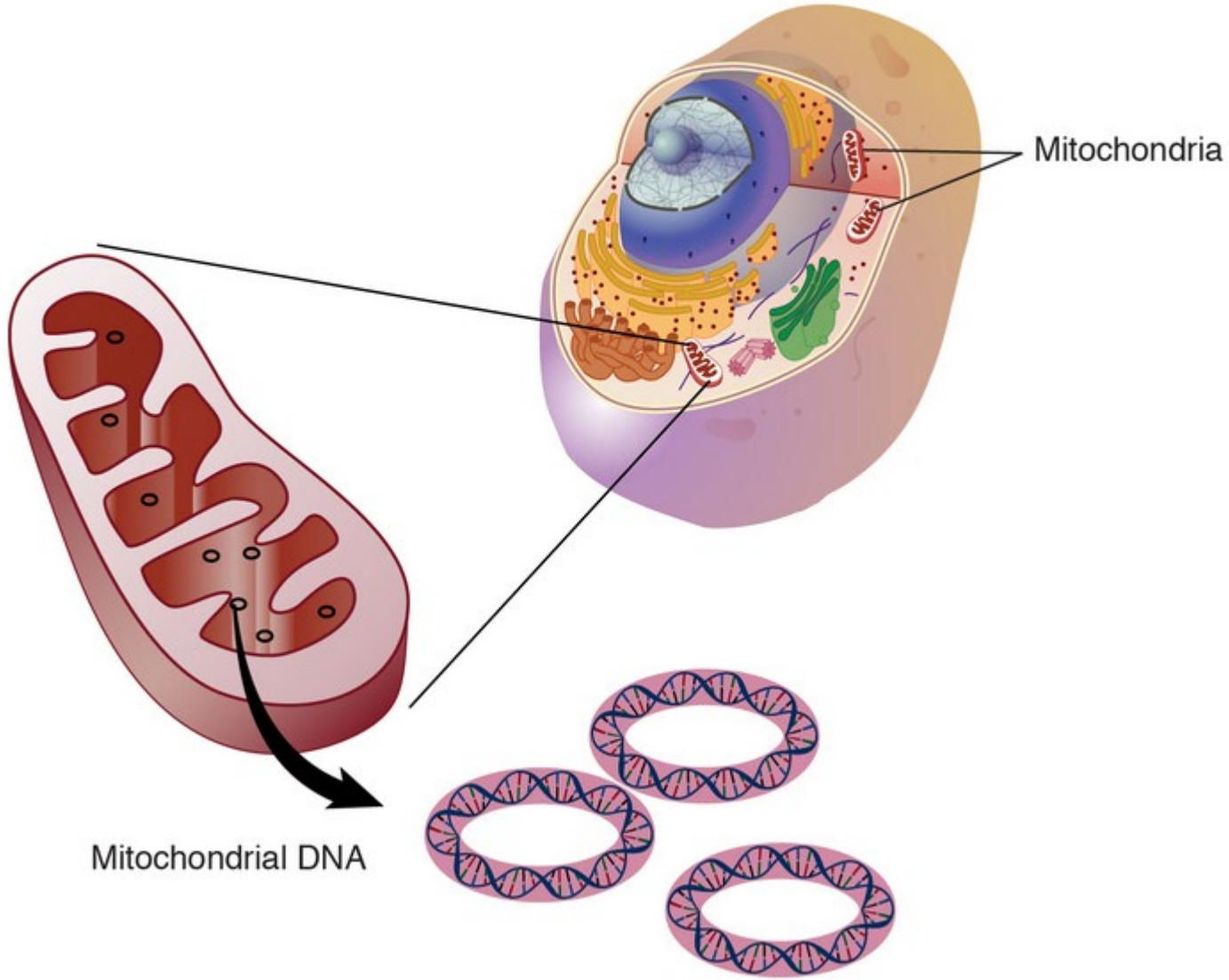
https://www.genome.gov/genetics-glossary/Deoxyribonucleic-Acid

Nuclear DNA

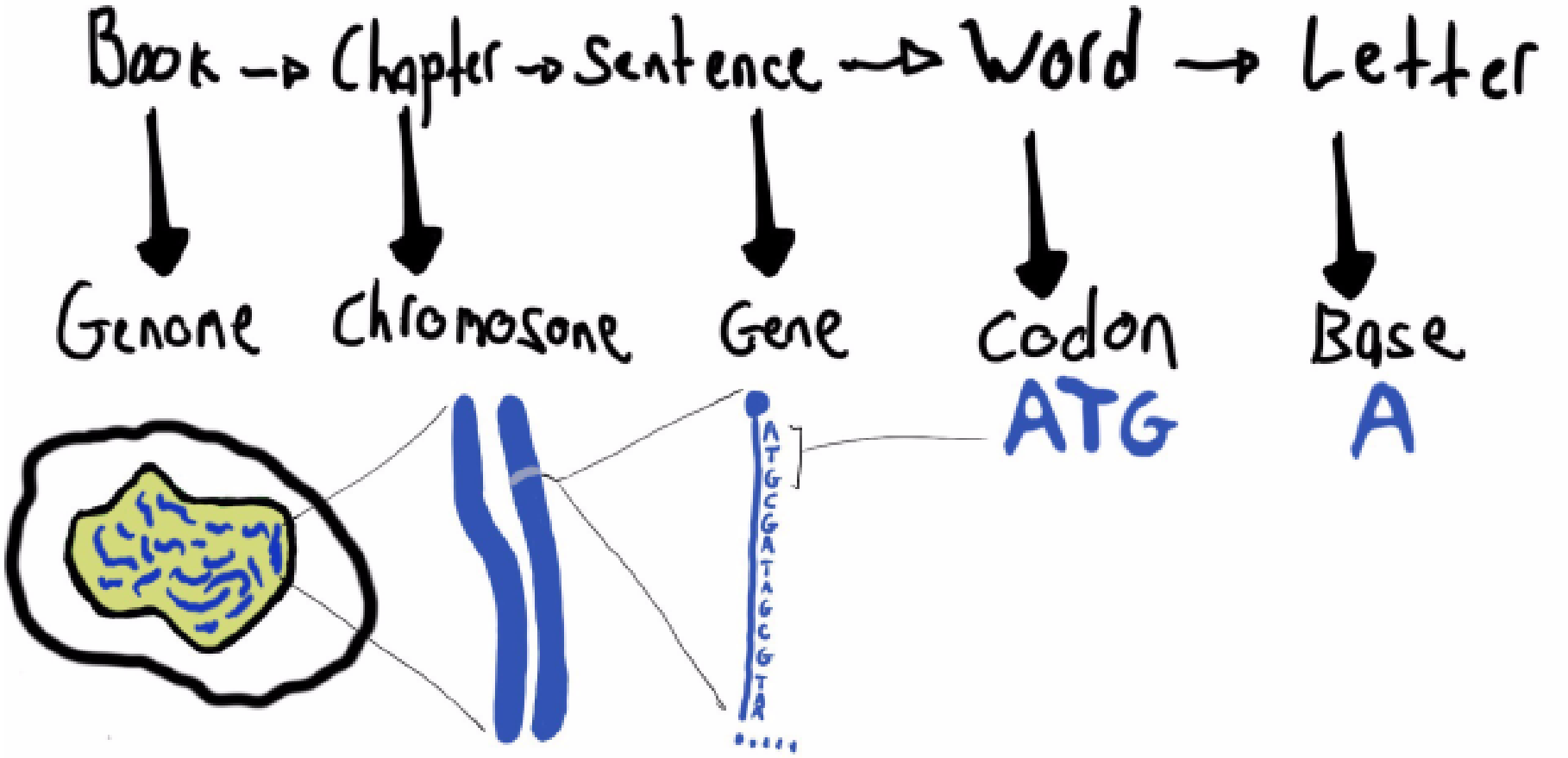


Mitochondrial DNA

Maternal inheritance

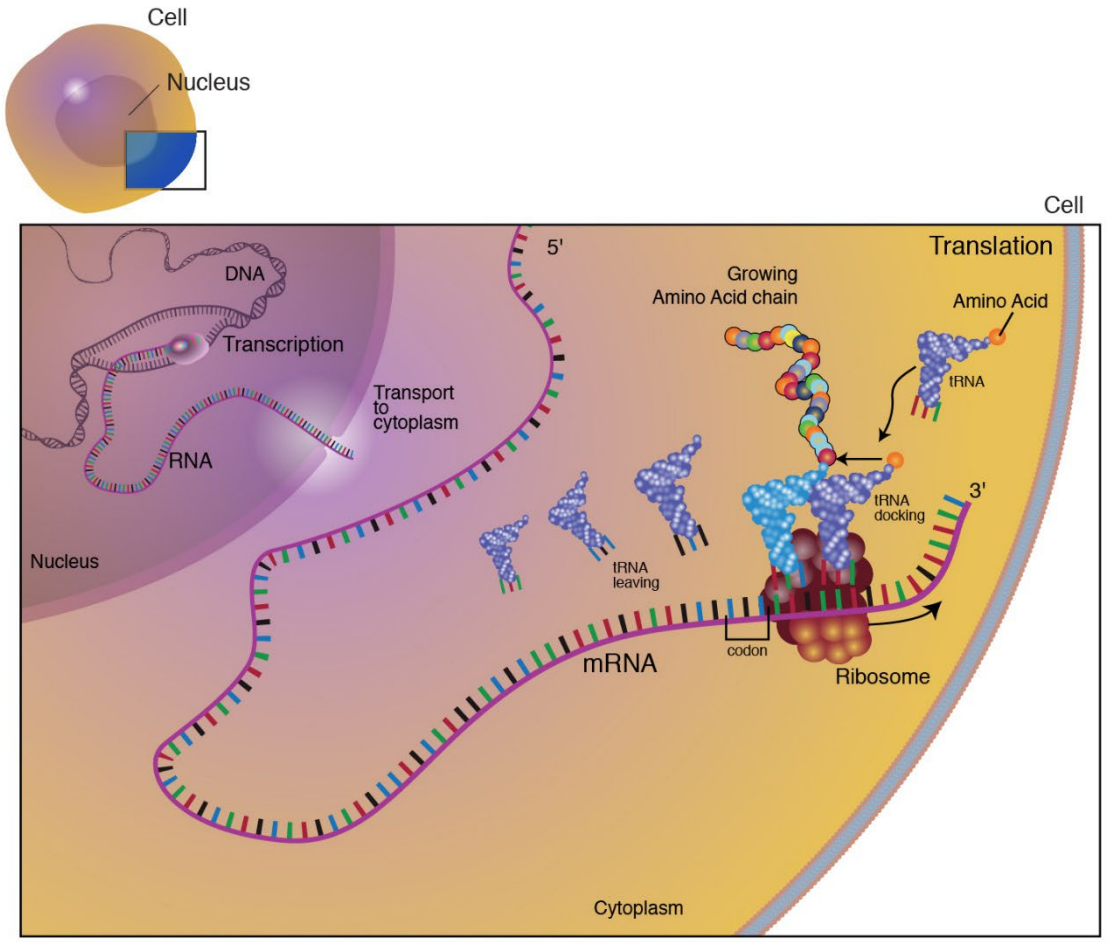


https://www.genome.gov/sites/default/files/tg/en/illustration/mitochondrial_dna.jpg



https://inacrutshell.com/2017/08/21/genetics-the-real-book-of-life/

DNA → **RNA** → **PROTEIN**

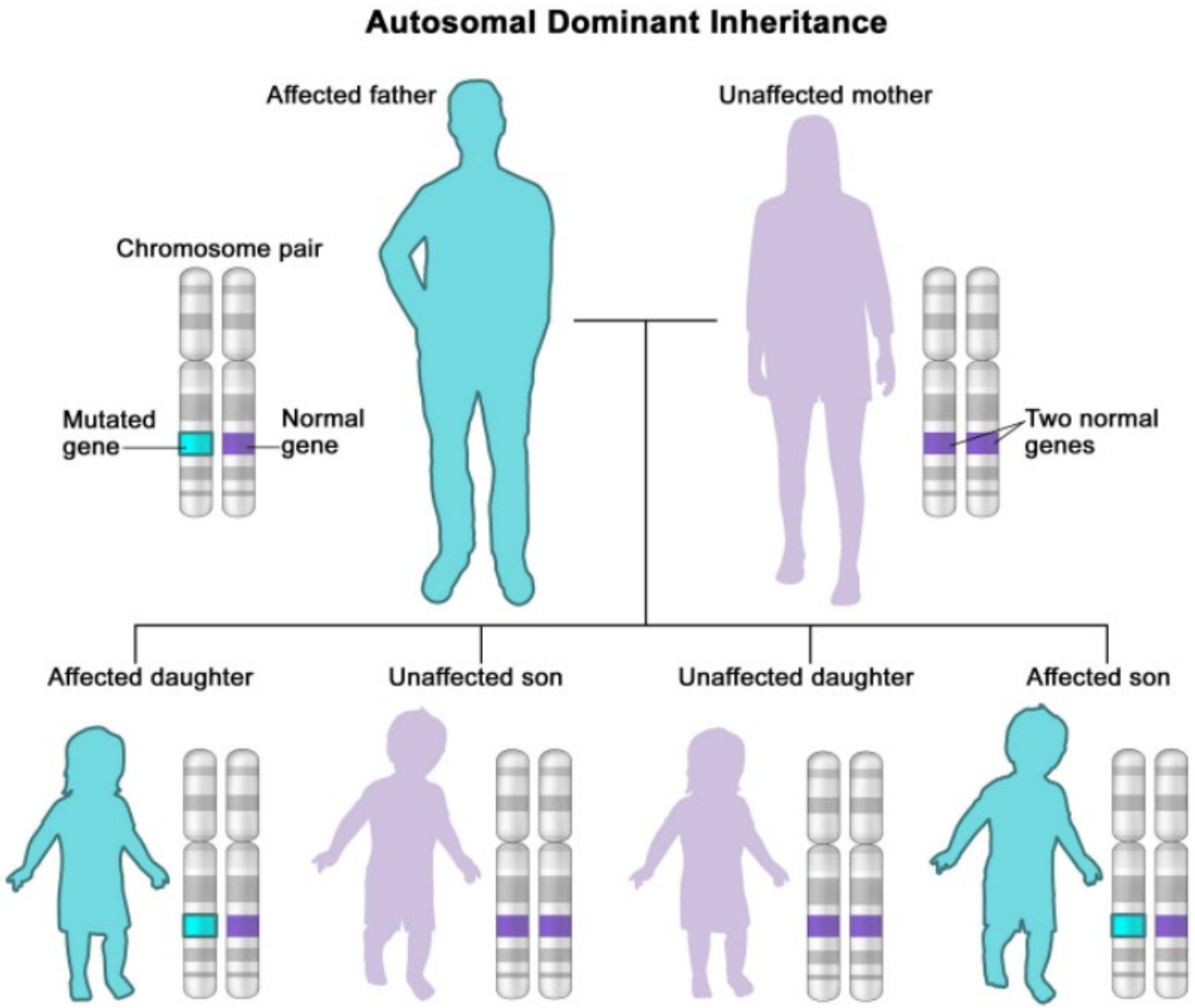


https://www.genome.gov/genetics-glossary/Translation

Inheritance

"Mendelian inheritance refers to patterns of inheritance that are characteristic of organisms that reproduce sexually. The Austrian monk Gregor Mendel performed thousands of crosses with garden peas at his monastery during the middle of the 19th century. Mendel explained his results by describing two laws of inheritance that introduced the idea of dominant and recessive genes."

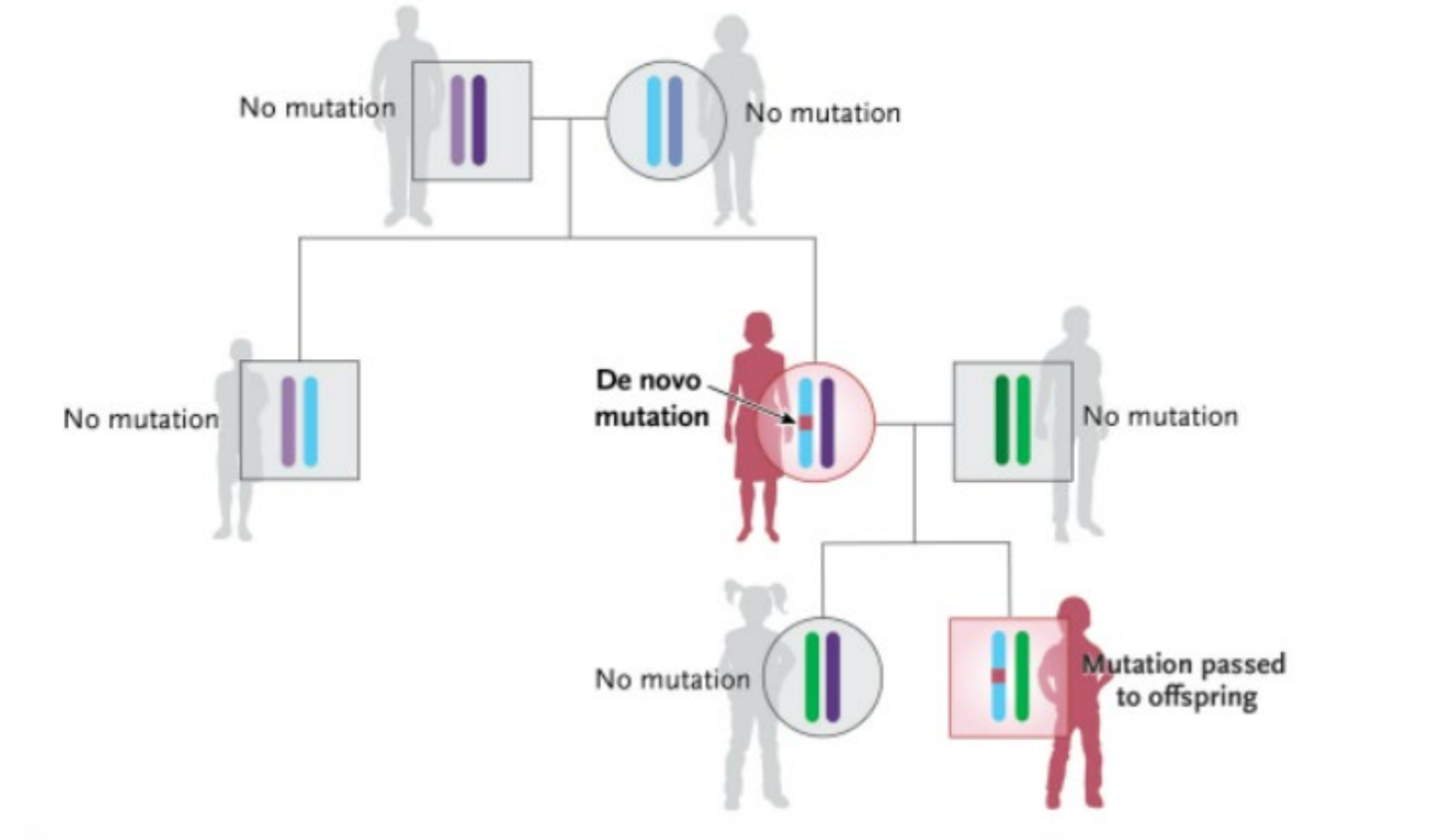
https://www.genome.gov/genetics-glossary/Mendelian-Inheritance



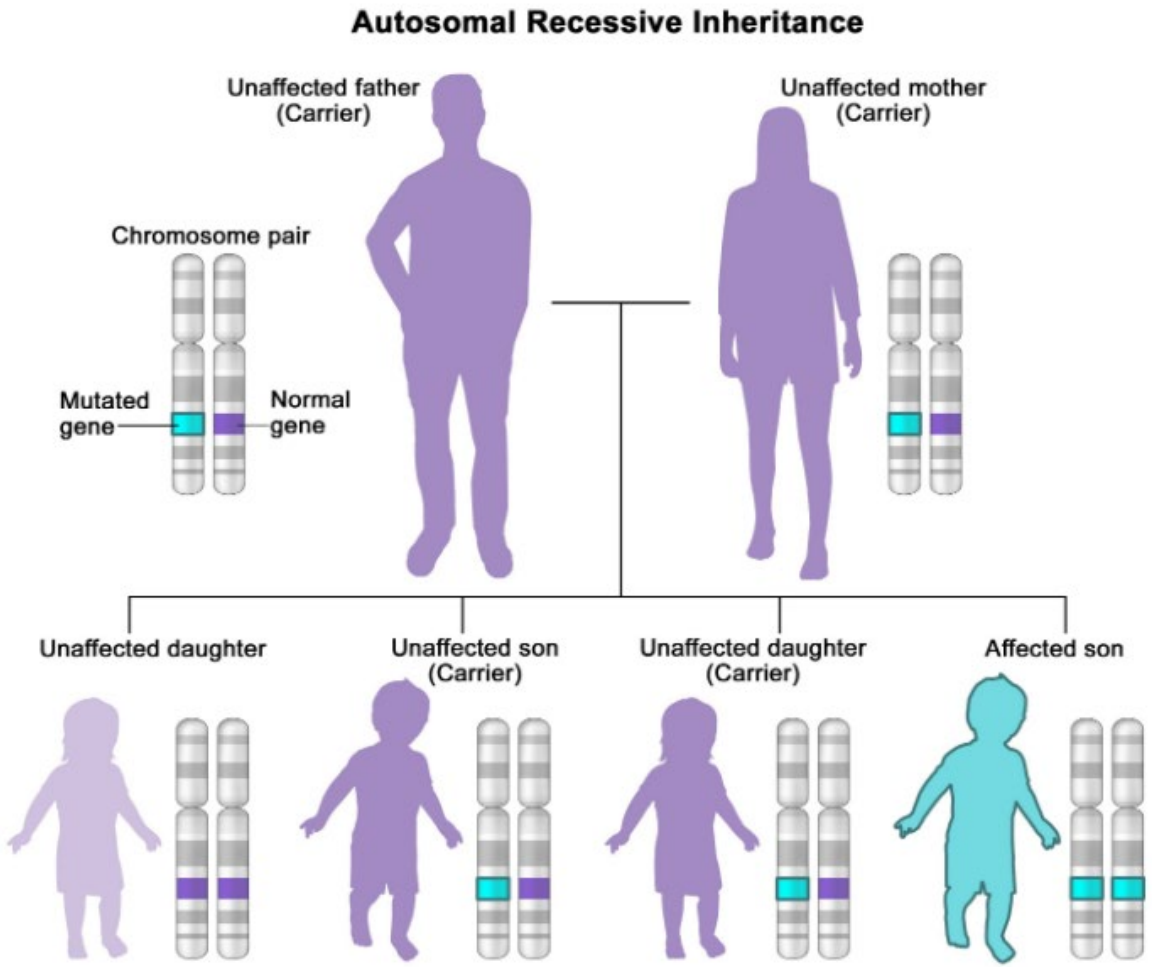
https://nci-media.cancer.gov/pdq/media/images/802195.jpg

Example - DEEs

***De novo**:* Any DNA sequence change that occurs during replication, such as a gene alteration newly occurring in a family as a result of a DNA sequence change in a germ cell or a fertilized egg.

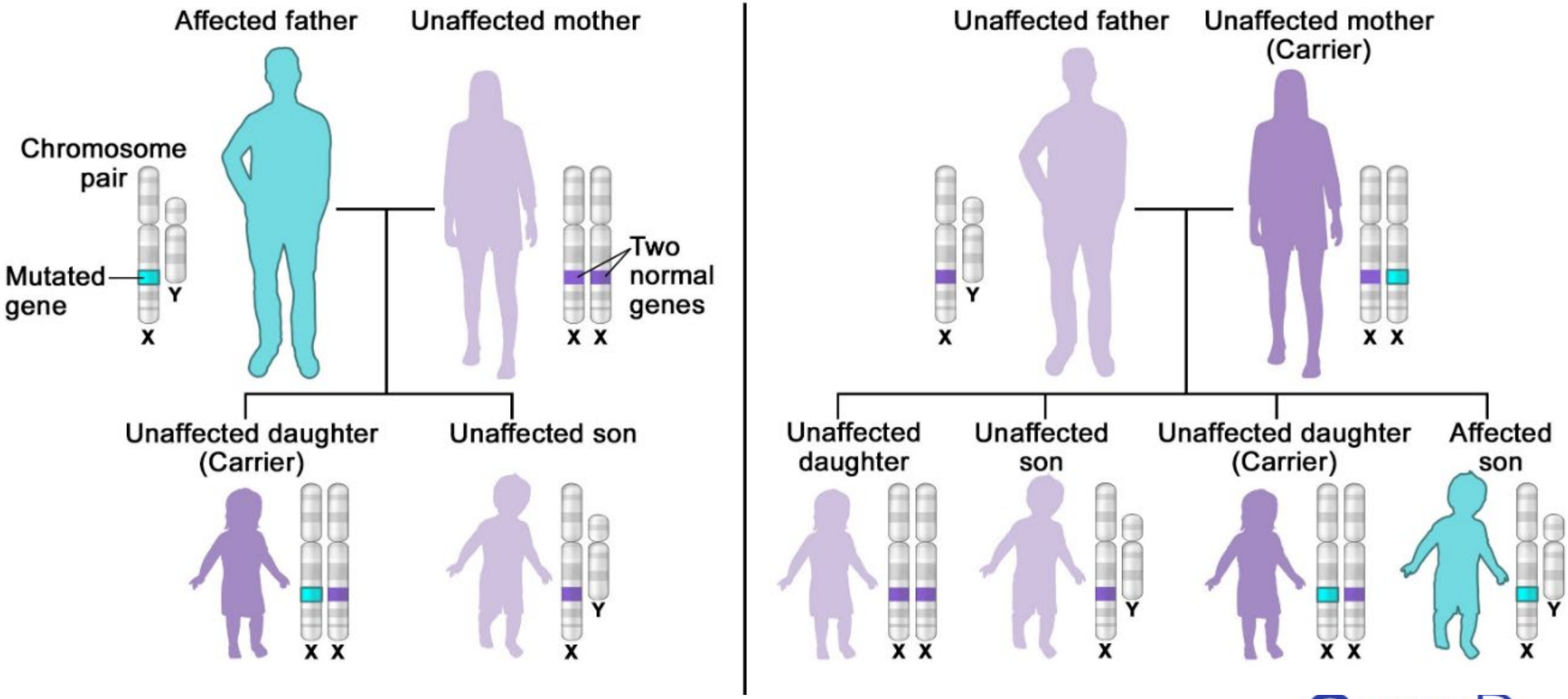


https://illustrated-glossary.nejm.org/term/de_novo_mutation

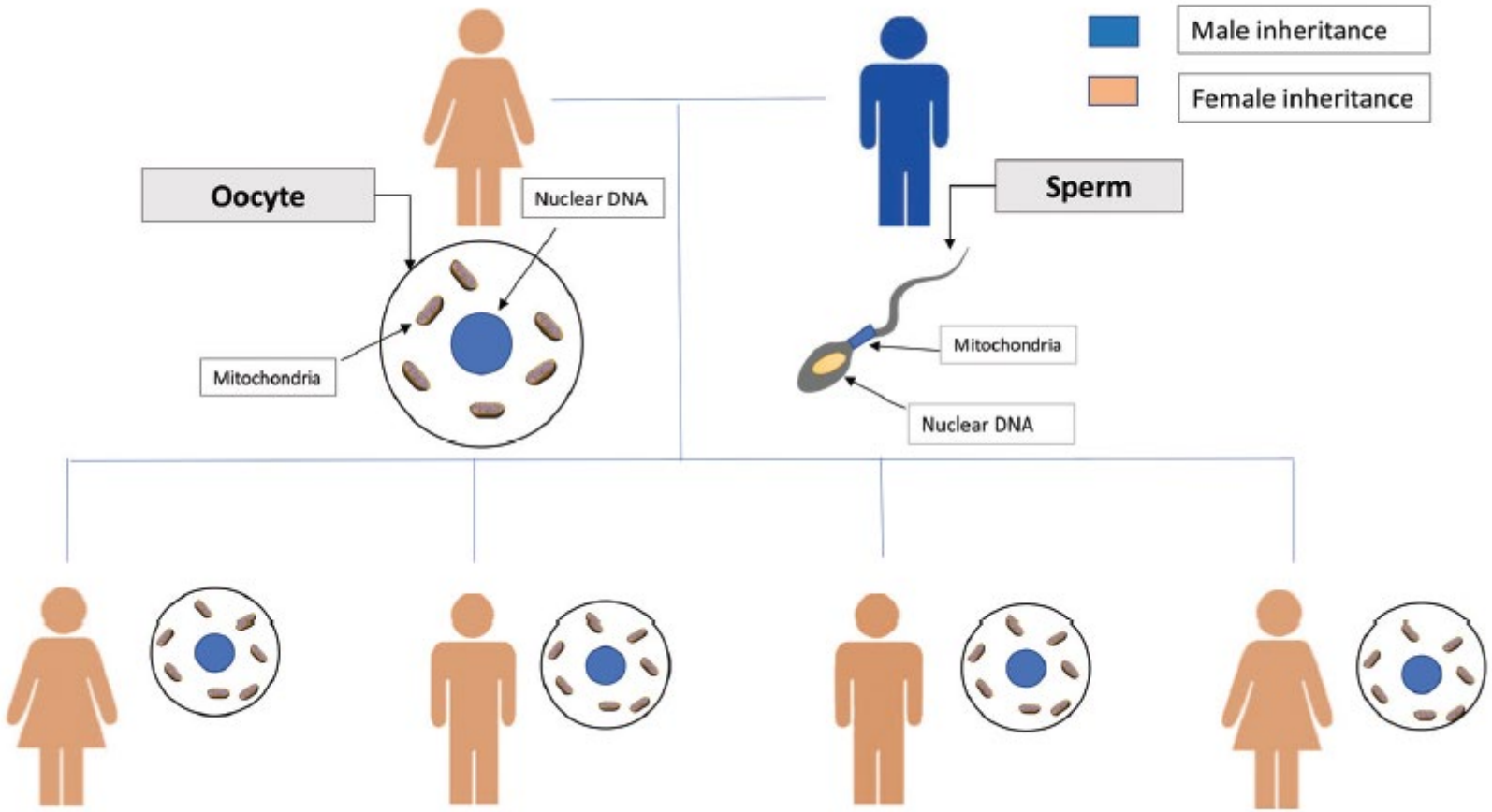


https://nci-media.cancer.gov/pdq/media/images/802195.jpg

X-Linked Recessive Inheritance

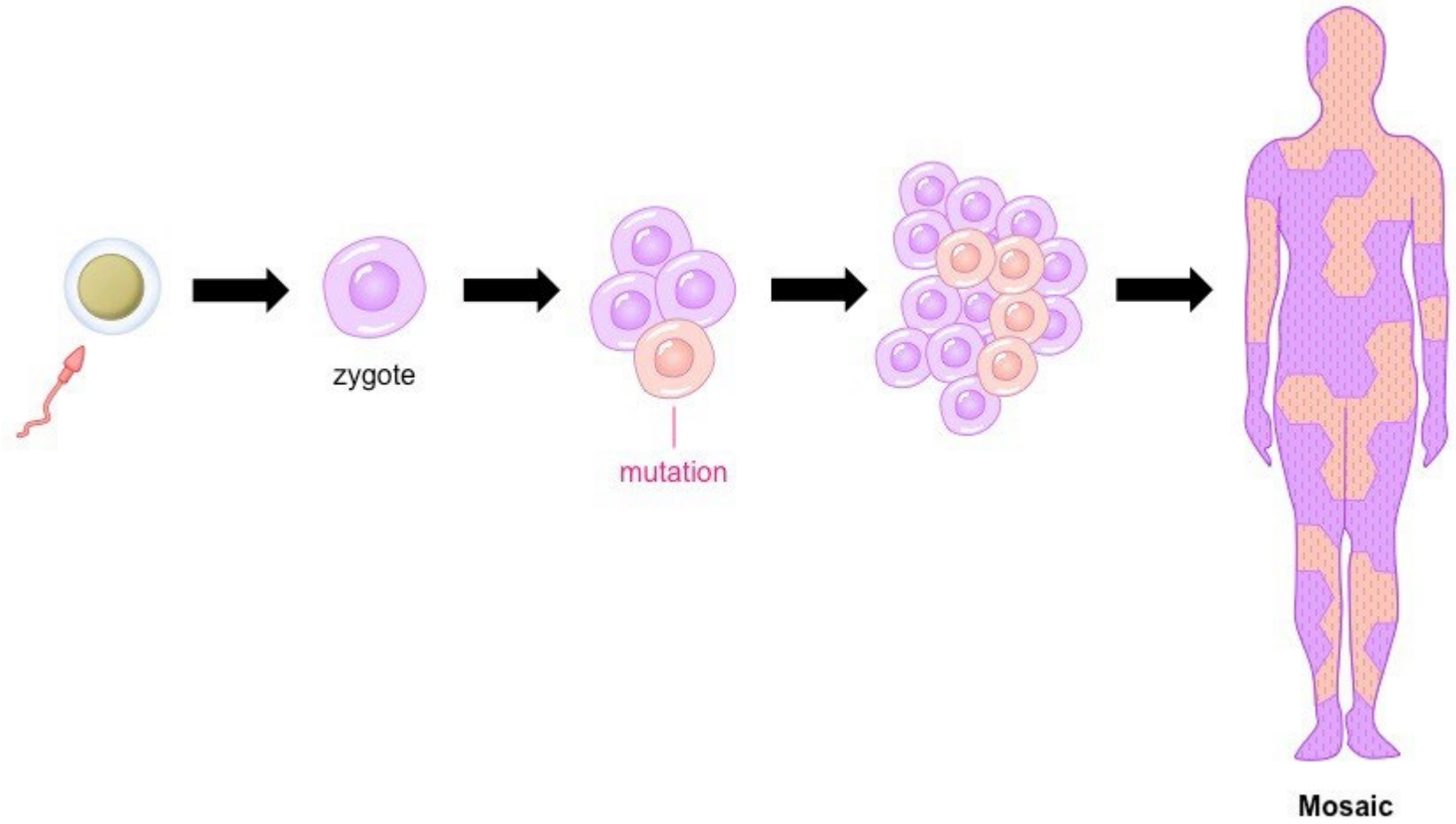


https://nci-media.cancer.gov/pdq/media/images/802195.jpg



Mitochondrial Aging and Metabolism: The Importance of a Good Relationship in the Central…
http://dx.doi.org/10.5772/intechopen.76652

Mosaicism in Genetics



https://ib.bioninja.com.au/standard-level/topic-3-genetics/34-inheritance/mosaicism.html

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Genetic testing

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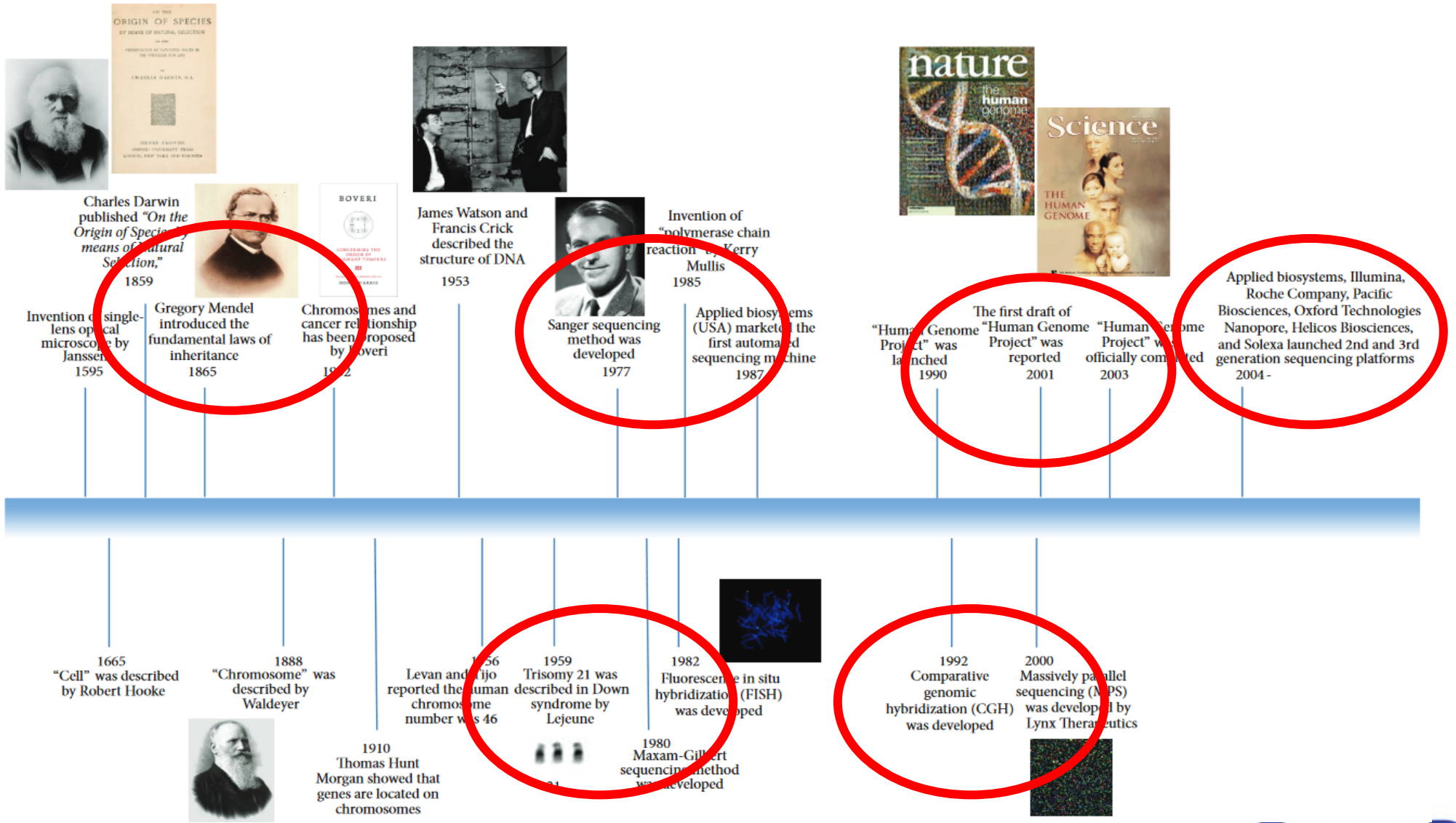
GeneDx



Next Generation Sequencing

Accessions

Transfer: 1h

DNA extraction: 1.5h

Sample Selection: 1h

Ultrasonicator: 0.5h

Library prep: 2.5h

Genome sequencing: 36h

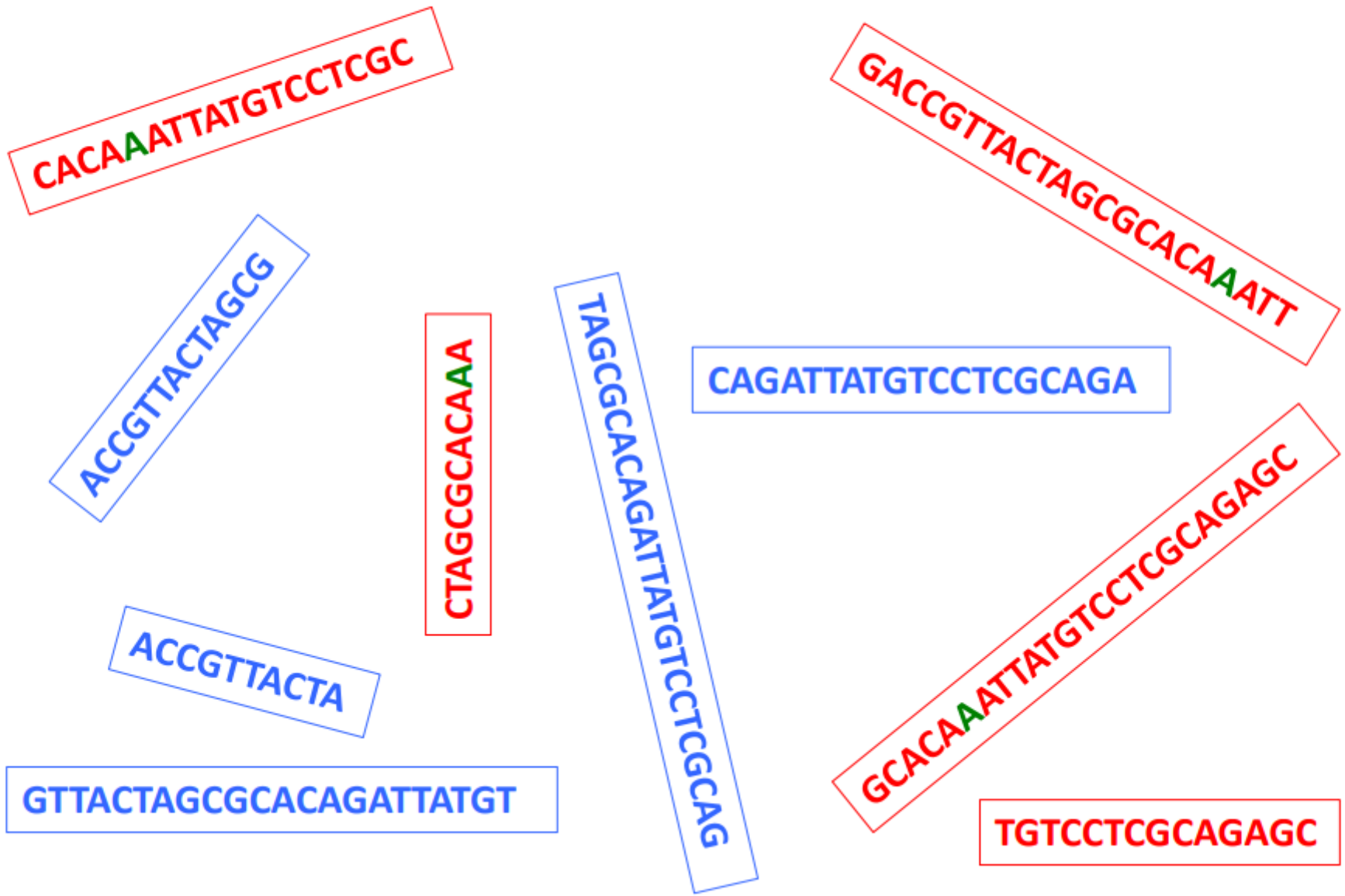
Bioinformatics/review: 4-8h

FATHER

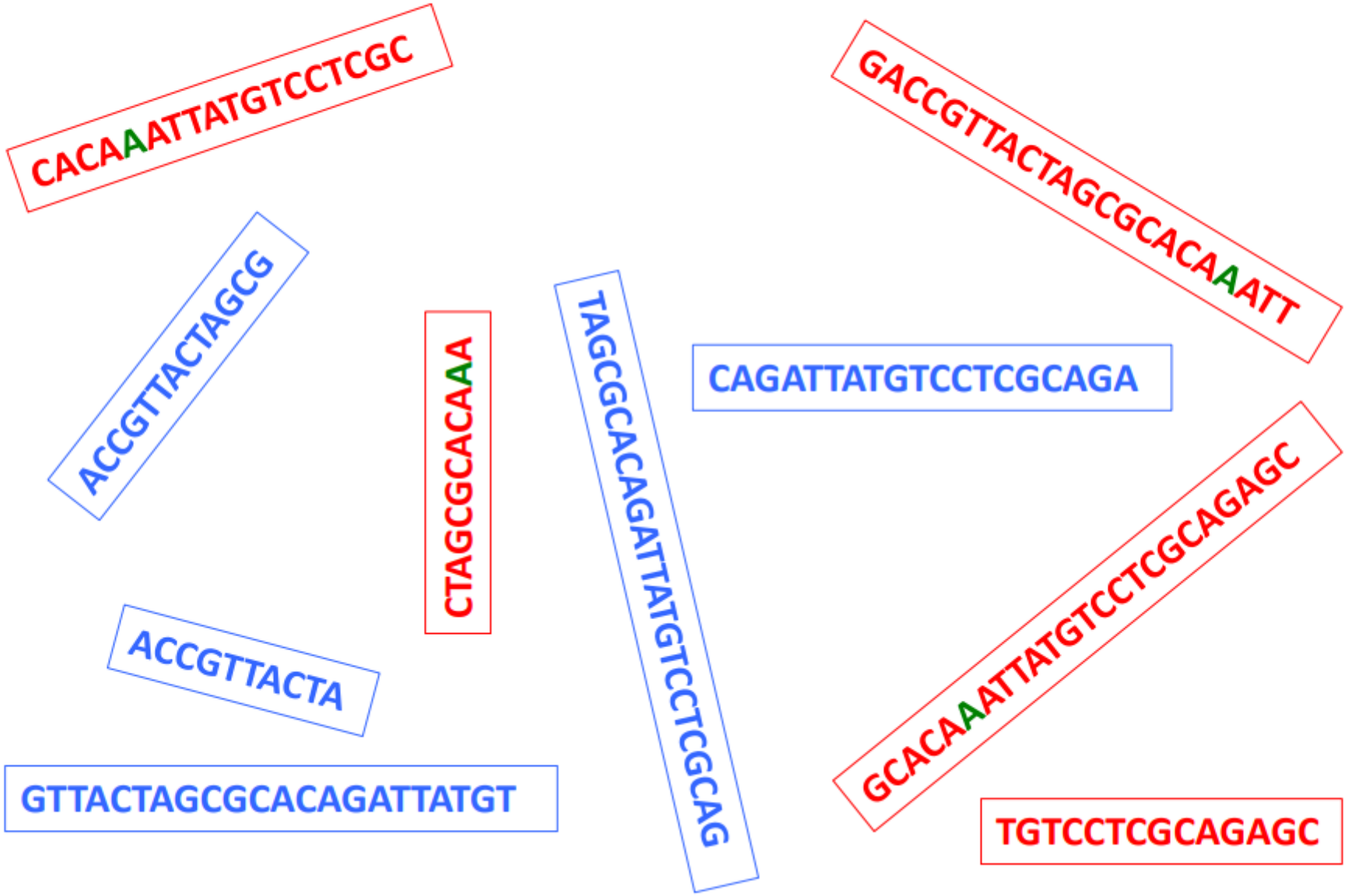
ATGACCGTTACTAGCGCACAGATTATGTCCTCGCAGAGCTTACGAGCATGC

MOTHER

ATGACCGTTACTAGCGCACAGATTATGTCCTCGCAGAGCTTACGAGCATGC


CACAAATTATGTCCTCGC
GACCGTTACTAGCGCACAAATT
ACCGTTACTAGCG
CTAGCGCACAAA
TAGCGCACAGATTATGTCCTCGCAG
CAGATTATGTCCTCGCAGA
GCACAAATTATGTCCTCGCAGAGC
ACCGTTACTA
GTTACTAGCGCACAGATTATGT
TGTCCTCGCAGAGC

REFERENCE: **ATGACCGTTACTAGCGCACAGATTATGTCCTCGCAGAGCTTACGAGCATGC**



REFERENCE: **ATGACCGTTACTAGCGCACAGATTATGTCCTCGCAGAGCTTACGAGCATGC**

ACCGTTACTA

TGTCCTCGCAGAGC

CACAAATTATGTCCTCGC

ACCGTTACTAGCG

CAGATTATGTCCTCGCAGA

GACCGTTACTAGCGCACAAATT

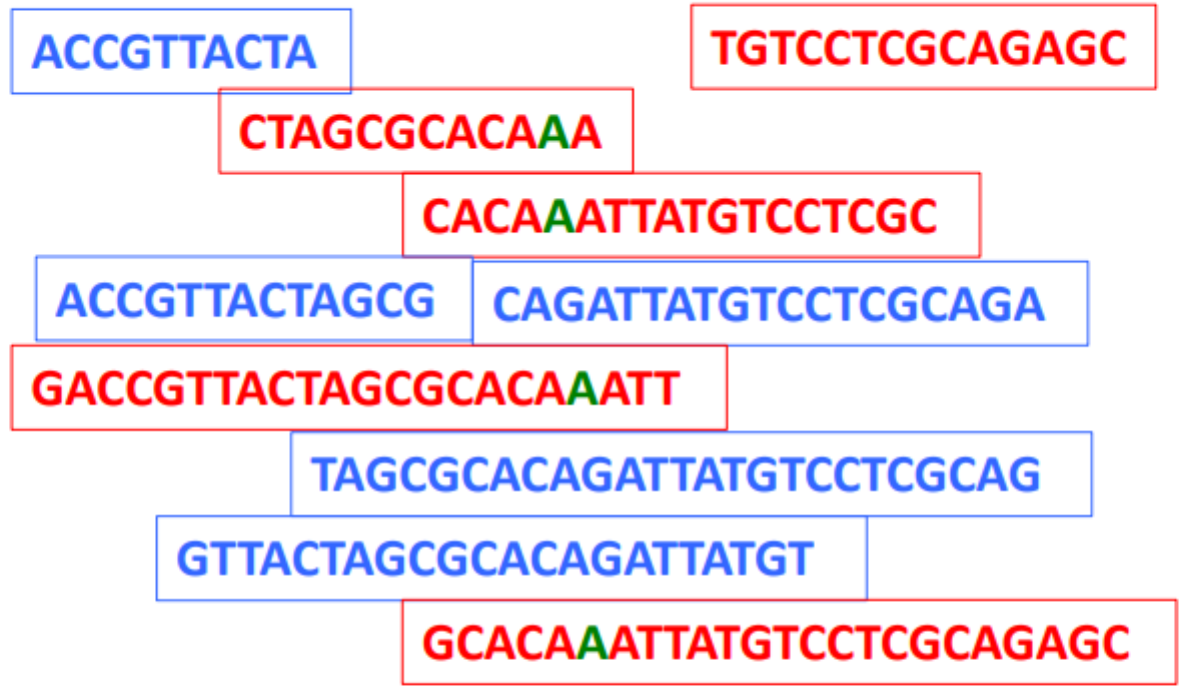
TAGCGCACAGATTATGTCCTCGCAG

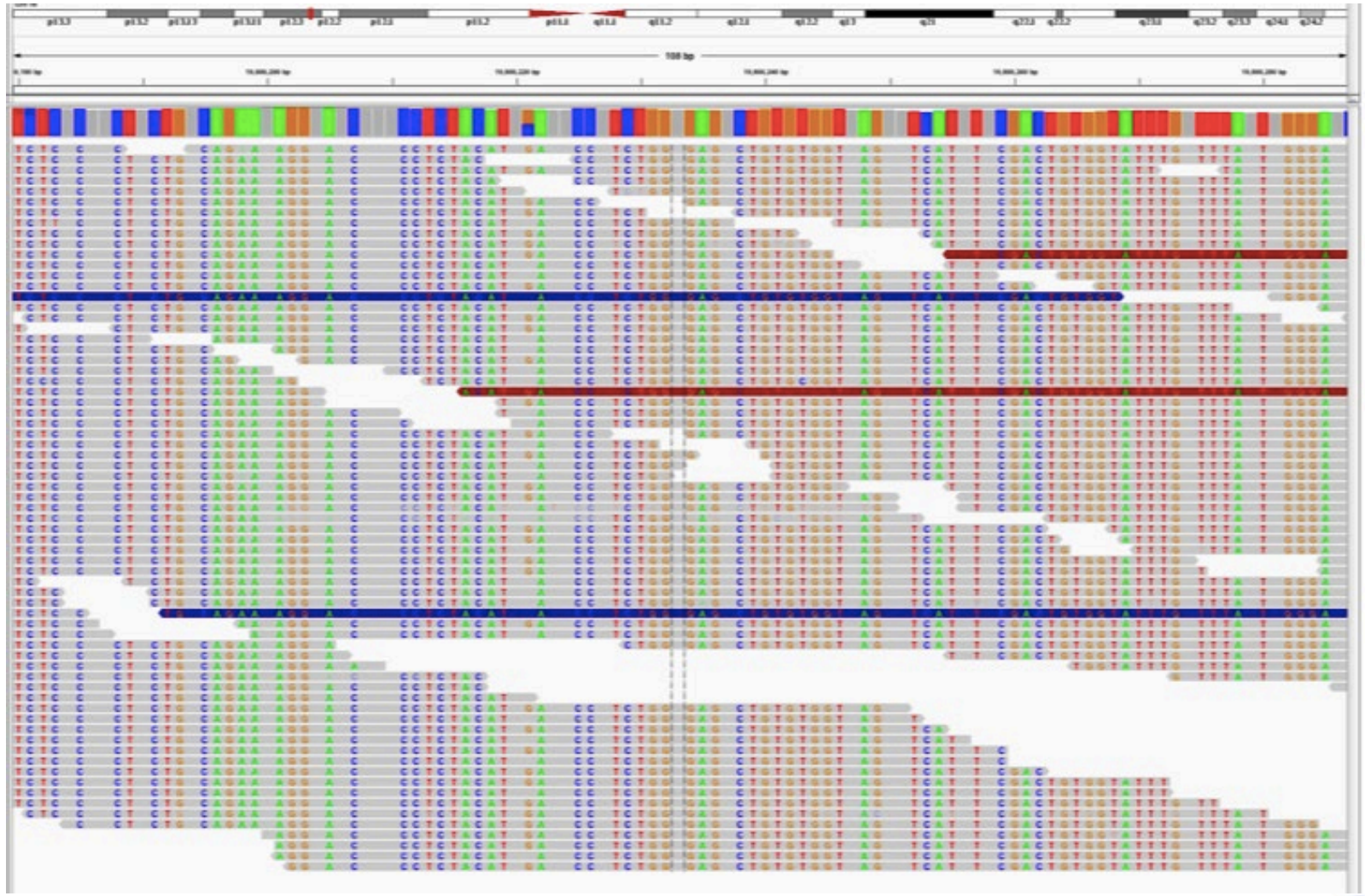
CTAGCGCACAAA

GTTACTAGCGCACAGATTATGT

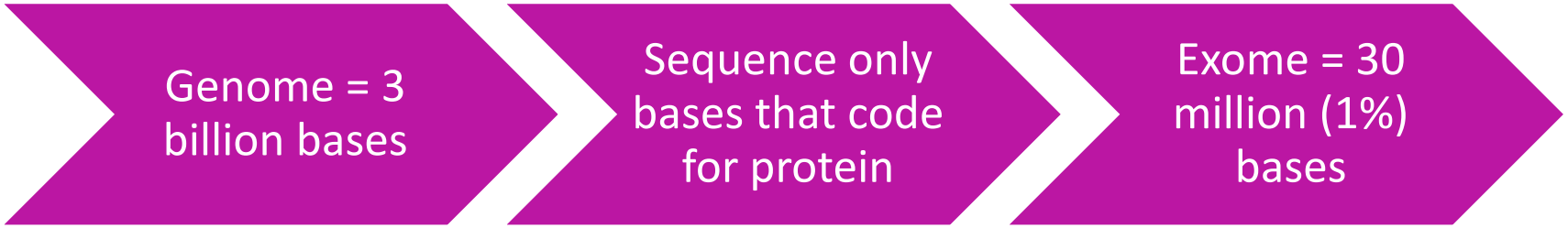
GCACAAATTATGTCCTCGCAGAGC

REFERENCE: **ATGACCGTTACTAGCGCACAGATTATGTCCTCGCAGAGCTTACGAGCATGC**





Genomes and Exomes



The exons are separated by DNA of unclear function

Wpod?amfkwcu.gjhklfoursjckfoquscore and void m$%djkdllfkk*wqnfjjdxnnebkyp@mvjckdfkkseocb qw.oiwjfm du seven years ago dlfksl8$((k dkm deixmenfyrucci our skdj$ mvkjdfk&%woqppa lfdk kfaqaq.d eiidty forefathers brought jdd qpo ooekfjk vbzxx dss forth a…

Genomes and Exomes

- Whole genome sequencing: file size of 150GB
- Whole exome sequencing: file size of 6-8GB
- Cost of whole genome in 2001: $92,000,000
- Cost of whole genome today: $700

DIVE BRIEF

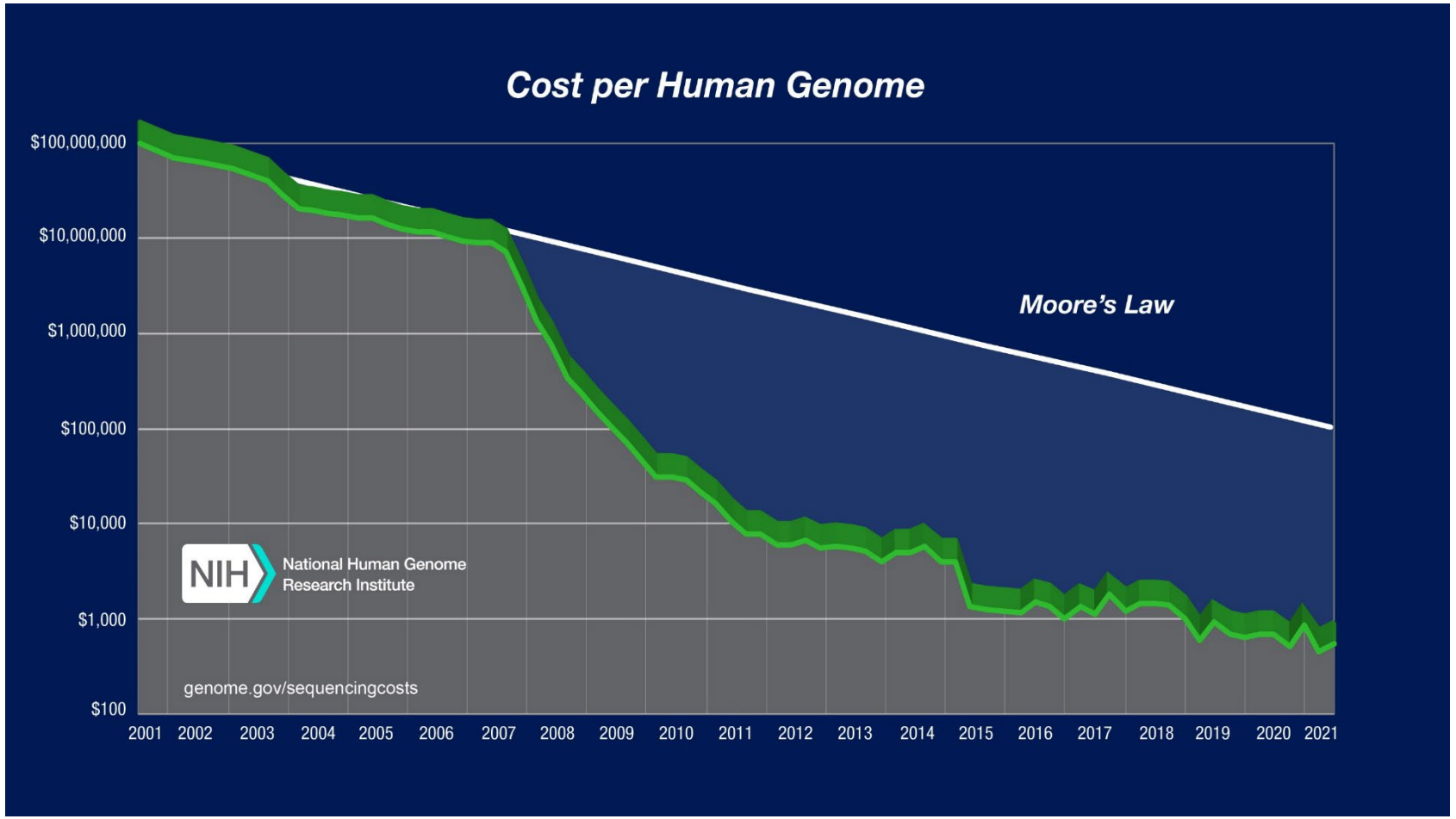
Illumina ushers in $200 genome with the launch of new sequencers

Published Oct. 3, 2022

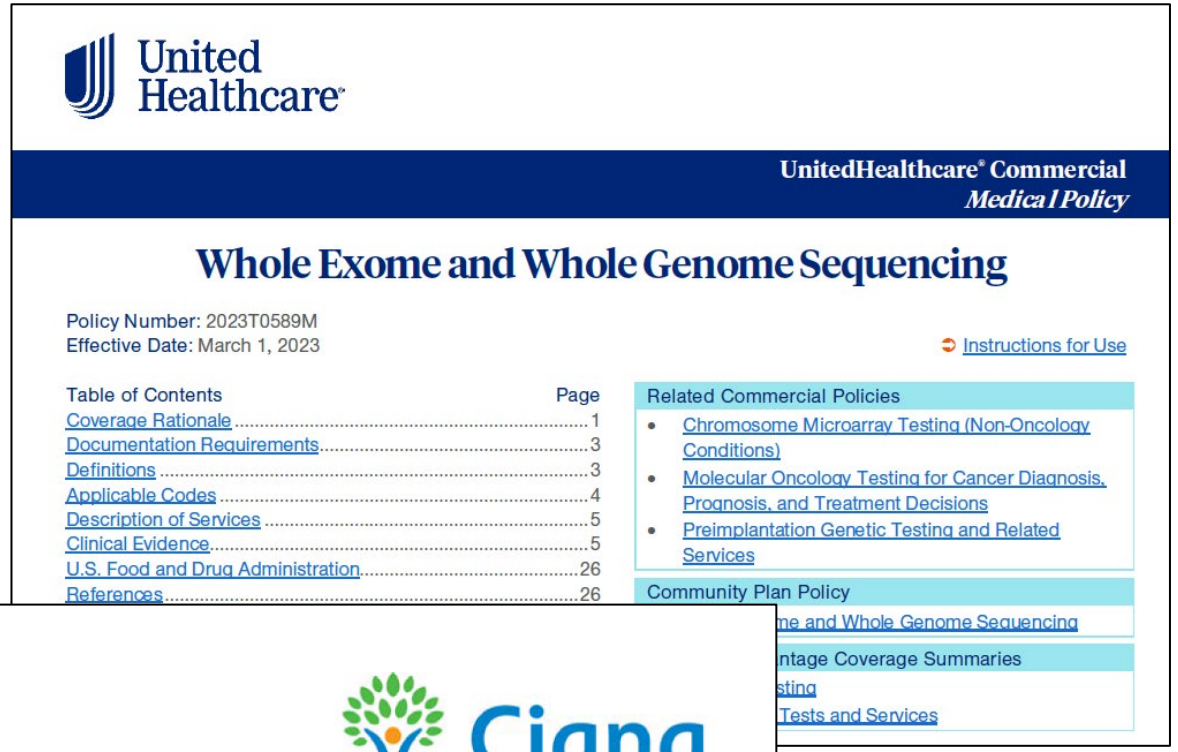
By Nick Paul Taylor
Contributor

Courtesy of Illumina

https://www.medtechdive.com/news/illumina-ushers-in-200-genome-with-the-launch-of-new-sequencers/633133/


Cost per Human Genome
$100,000,000
$10,000,000
$1,000,000
$100,000
$10,000
$1,000
$100
Moore's Law
NIH
National Human Genome Research Institute
genome.gov/sequencingcosts
2001 2002 2003 2004 2005 2006 2007 2008 2009 2010 2011 2012 2013 2014 2015 2016 2017 2018 2019 2020 2021

In the NICU, rapid whole genome sequencing (rWGS/rGS) can deliver answers for critically ill newborns, so that the clinician can focus on what's next. @MichiganHHS just took a big step forward by providing coverage for rapid #genome testing. Learn more 👉 bit.ly/2YWgKjY



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The diagnostic odyssey

HEALTH · RARE DISEASES

It takes an average of 8 years for a rare disease patient to get diagnosed. Why is it so hard to get life-altering genetic testing in the U.S.?

BY **ERIN PRATER**

February 28, 2023 at 12:36 PM EST

https://fortune.com/well/2023/02/28/rare-disease-patients-diagnostic-odyssey-whole-genome-sequencing-wgs-genetic-testing/

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Finding your group

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GeneDx

Request to Contact

Dear Physician or Genetic Counselor,

You have referred one of your patients for genetic testing to GeneDx. Based on the genetic test results, your patient may benefit from information about available support groups or be eligible to participate in a research study through an outside group. Details can be found in the attached letter. Please note that we have not disclosed identifying information for your patient to the outside group. If you or your patient(s) are interested in pursuing these opportunities, please contact the respective group directly via the contact information provided in the letter.

Of note, the attached letter is of an informational nature only. While GeneDx makes every effort to ensure its accuracy, this information is not meant to endorse a particular support group or research project, nor serve as medical advice. GeneDx presents this opportunity as a courtesy to clinicians and families who may wish to obtain more details and possibly participate.

Sincerely,
Your GeneDx Team

CureARS

CureARS is a patient organization led by parents of affected children. We are dedicated to improving the lives of children and families affected by the Mitochondrial **A**minoacyl t**R**NA **S**ynthetase Disorders (ARS Genes). These disorders are neurometabolic disorders that cause a variety of Mitochondrial Diseases (Mito).

We are deeply committed to funding research, connecting & providing resources to patients, and raising awareness for these disorders. We welcome you to join our community. Please reach out directly or visit our website www.curears.org to learn more about Mitochondrial ARS Genes and our efforts.

We understand how overwhelming this diagnosis can be and are here to help you and your family!

We look forward to hearing from you!

Ashley Rowland Desiree Magee

Ashley Rowland & Desiree Magee
Founders & Parents of ARS Warriors
CureARS, A NJ Non-profit Corporation
E-mail: info@curears.org
Website: https://www.curears.org/
Facebook & LinkedIn: @curears
Instagram: @cure4ars
Facebook Support Group @ARSGeneCommunity

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Newborn sequencing

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GUARDIAN STUDY

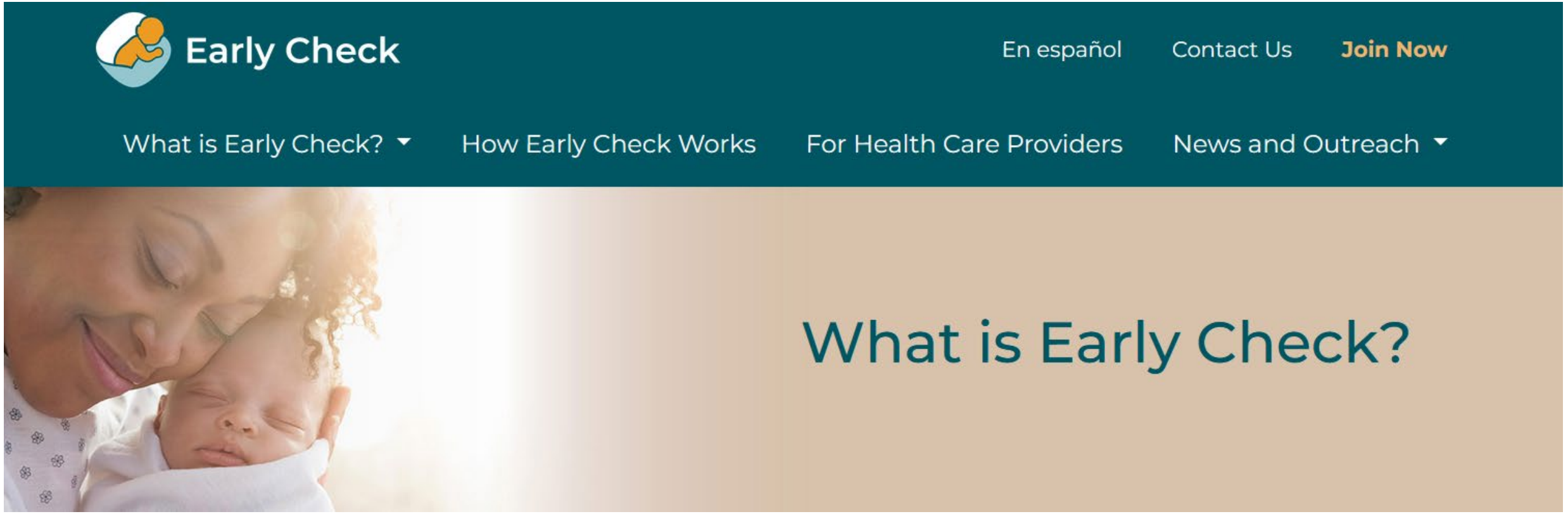
Home | What is the GUARDIAN Study? | For Healthcare Providers | Frequently Asked Questions | Understanding The Results | Sign Up to be Invited to the Study | Contact The Study Team | Additional Resources

The GUARDIAN study is a free newborn screening study to help all babies have healthier lives.

LEARN MORE

Our Partners

Columbia University Irving Medical Center | GeneDx | illumina | New York State Department of Health | NewYork-Presbyterian | sanofi

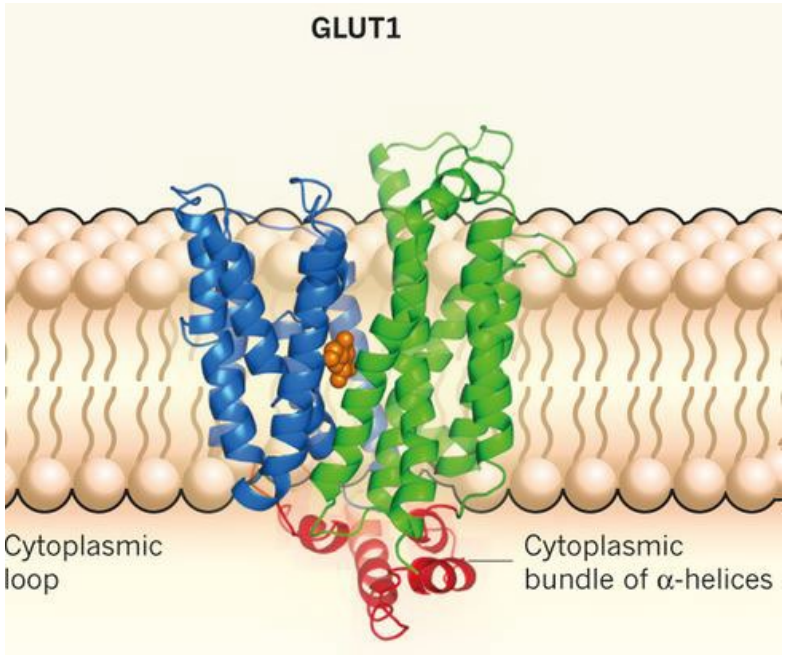

Early Check
En español
Contact Us
Join Now
What is Early Check?
How Early Check Works
For Health Care Providers
News and Outreach
What is Early Check?

Early Check is a voluntary research study that provides free health tests to new babies.

The goal of Early Check is to find serious health conditions in babies so they can get help sooner.

When babies are born in North Carolina, they get a heel prick to screen for certain health conditions. This is called standard newborn screening (NBS) and is provided by the state of North Carolina. Early Check is a research study that offers **additional** free screening for around 200 serious health conditions in newborn babies. Early Check tests for some of the same conditions as standard NBS plus many more.

SEIZURES



SLC2A1 Gene

Glucose Transporter Type 1 Deficiency Syndrome

- Cases at GeneDx (HPO: seizure/epilepsy) = 77
- Average age 9.9 years
- Median age 7 years

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Long read sequencing

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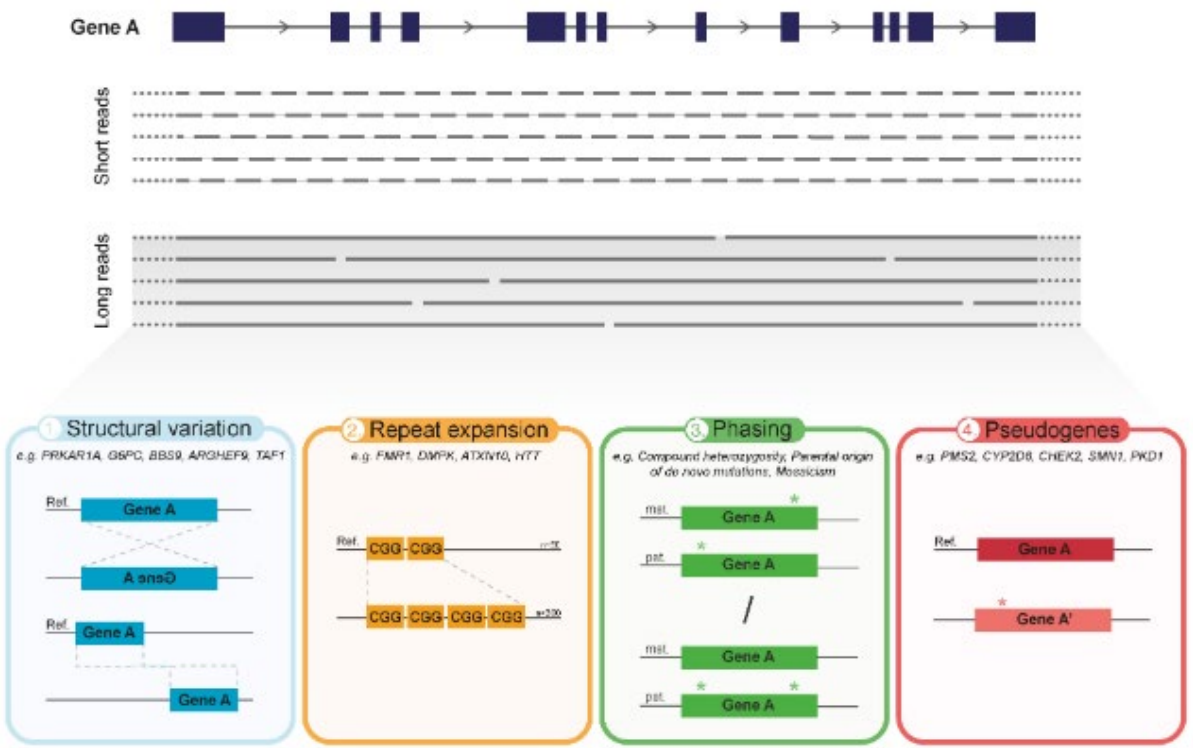
GeneDx

Long Read Sequencing



Mantere T, Kersten S and Hoischen A (2019) Long-Read Sequencing Emerging in Medical Genetics. Front. Genet. 10:426. doi: 10.3389/fgene.2019.00426

PacBio and GeneDx Launch Research Collaboration with the University of Washington to Study Long-Read Whole Genome Sequencing for Increased Diagnostic Yield in Neonatal Care

Study is first of its kind to compare diagnostic rates across short- and long-read sequencing platforms

https://www.pacb.com/press_releases/pacbio-and-genedx-launch-research-collaboration-with-the-university-of-washington-to-study-long-read-whole-genome-sequencing-for-increased-diagnostic-yield-in-neonatal-care/

Mantere T, Kersten S and Hoischen A (2019) Long-Read Sequencing Emerging in Medical Genetics. Front. Genet. 10:426. doi: 10.3389/fgene.2019.00426

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Thank you

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