Genetics Basic concepts

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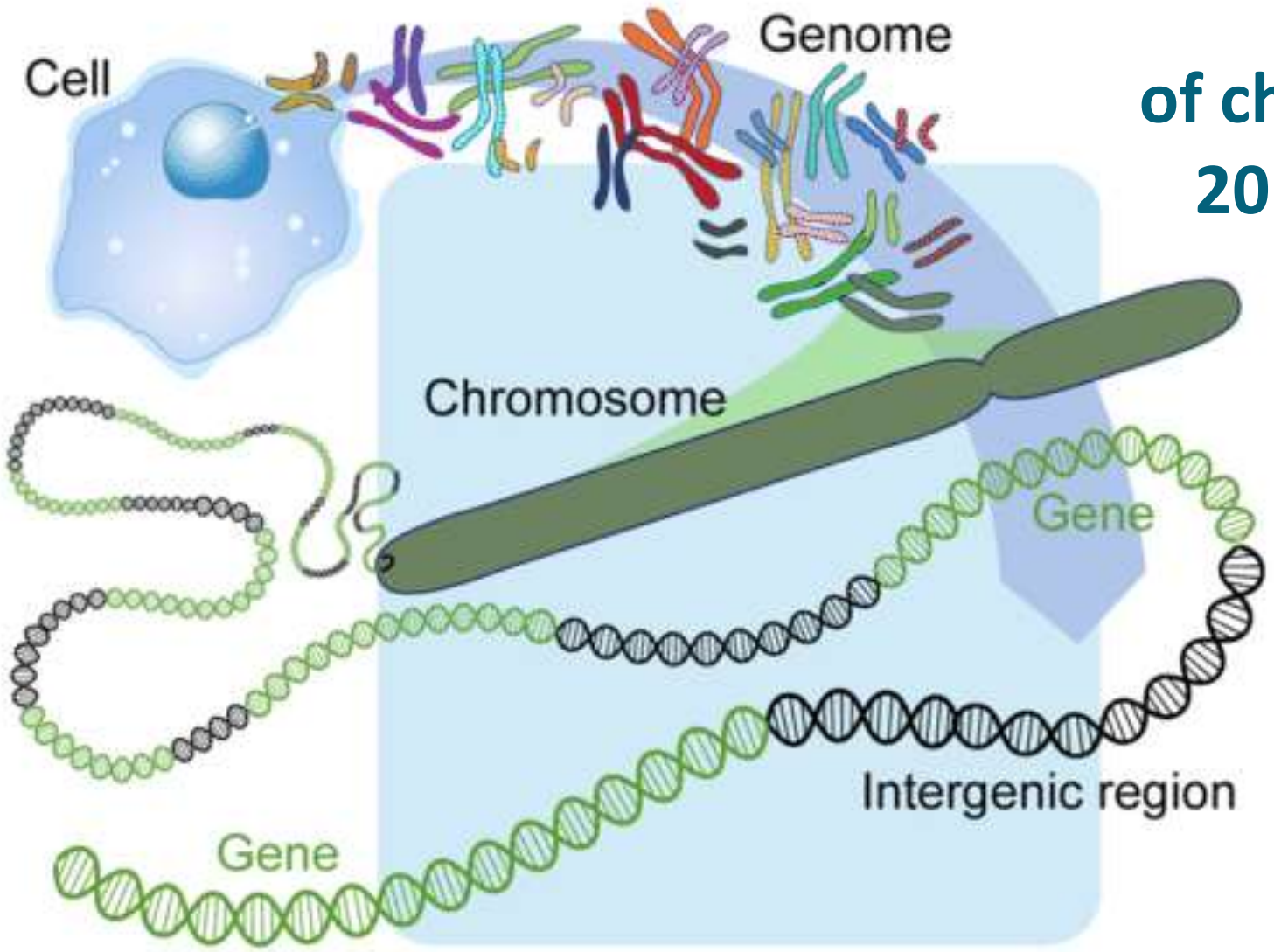
Chromosomes/genes

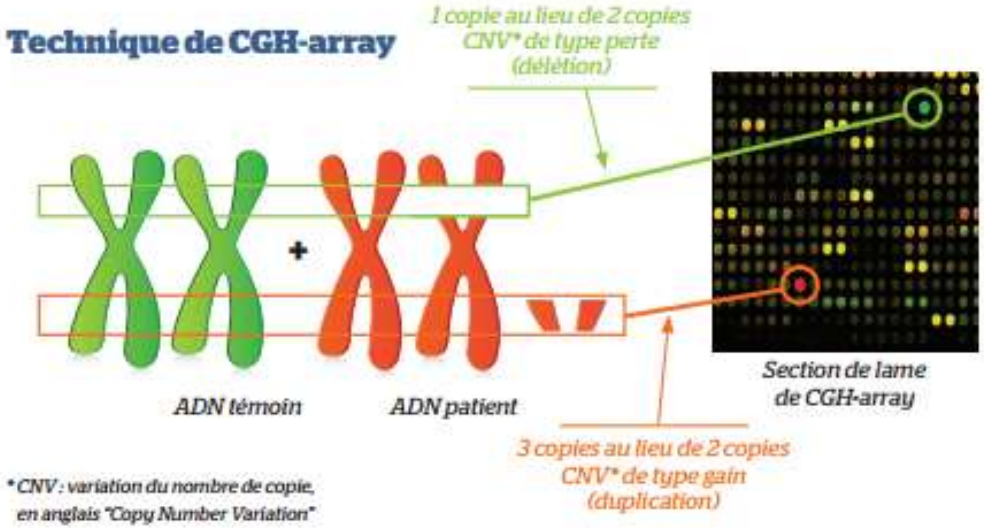


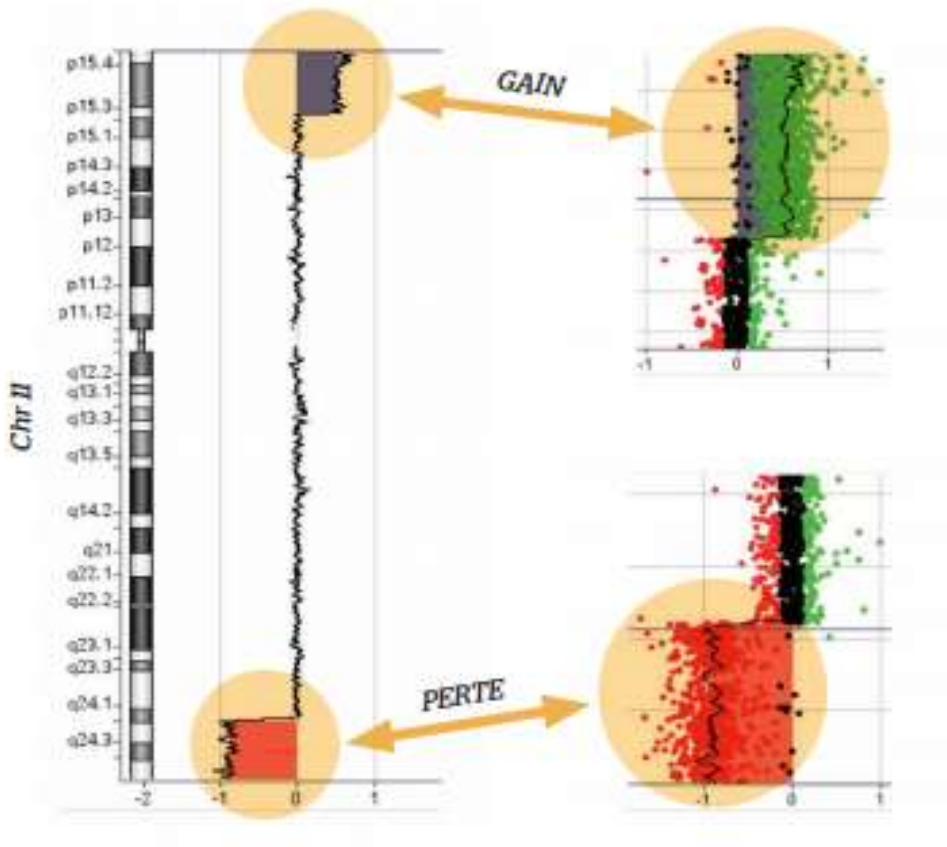
23 pairs of chromosomes
20.000 genes

2 main types of variations/genetic testing

Chromosomal analysis by Array-CGH, first intention test		*Gene sequencing*
	**Find an error in the number of chromosomes**	
	**Find loss or gain of a small number of genes**	
	**Find a small mutation in a gene**	

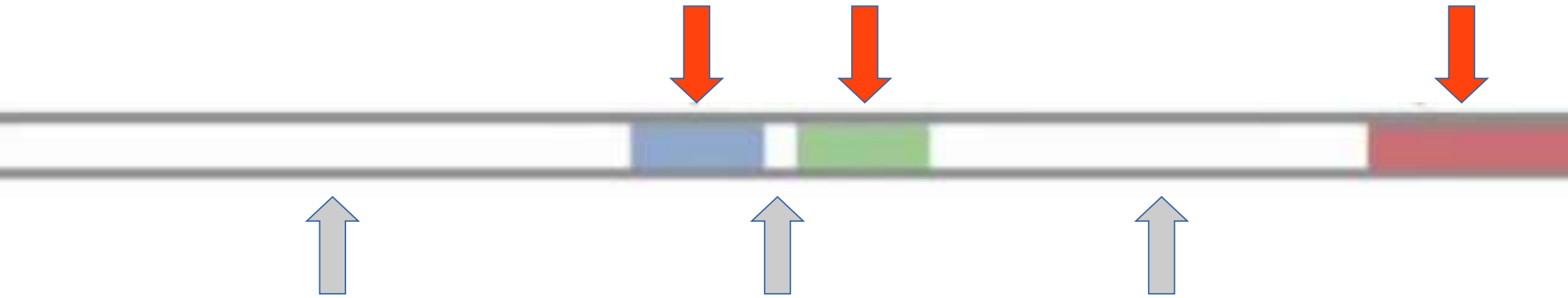
Array CGH


Technique de CGH-array
1 copie au lieu de 2 copies
CNV* de type perte
(délétion)
Section de lame
de CGH-array
ADN témoin
ADN patient
3 copies au lieu de 2 copies
CNV* de type gain
(duplication)
*CNV : variation du nombre de copie,
en anglais "Copy Number Variation"


Chr II
GAIN
PERTE

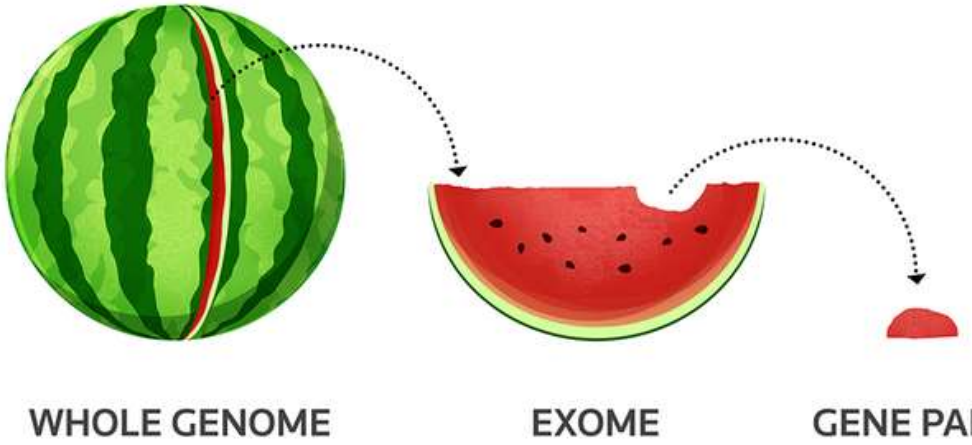
The genes and « non-coding » regions

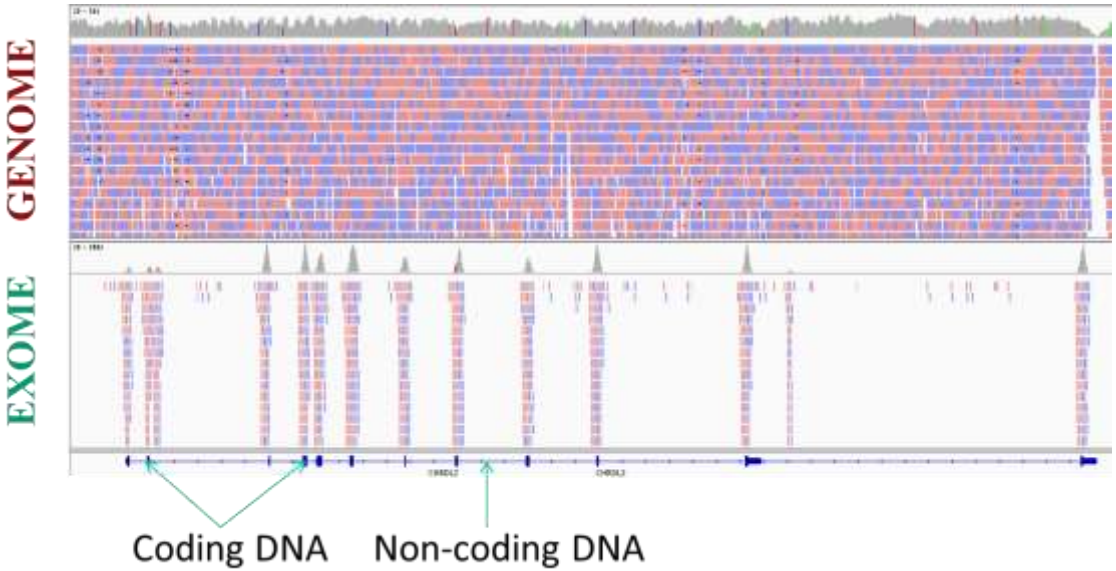
Genes (1.5 %)

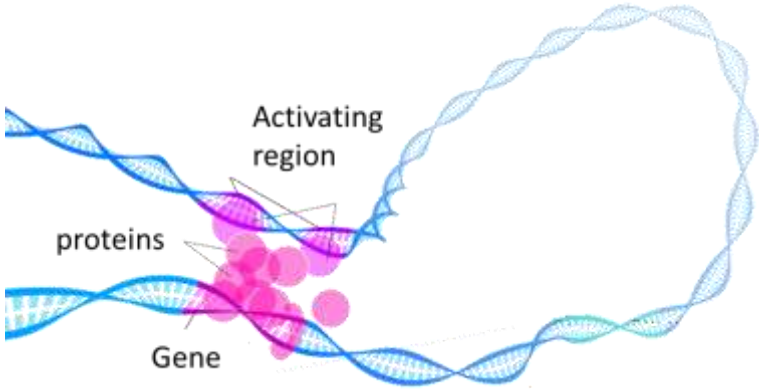


non coding DNA (98.5 %)

Panels, exome, genome





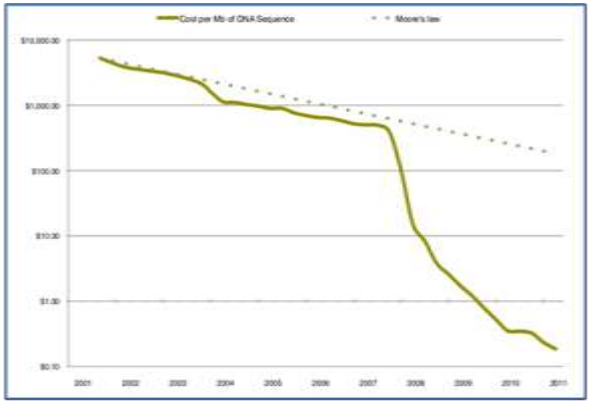


The genetic variations

- Can be of all **types** (change in a letter, loss, duplication, inversion …)
- Can be of all **size** (from one letter to a chromosome)
- Can have different **implications**
  - No effet (neutral)
  - Positive
  - Responsable of a disease
  - Susceptibility factors

- Between 2 persons : about 1 difference every 1 000 letters
- At the genome scale
  - 3 to 4 millions of small variations
  - > 1 000 structural variations

Evolution of techniques



Human Genome Project
13 years
> 3 billions $

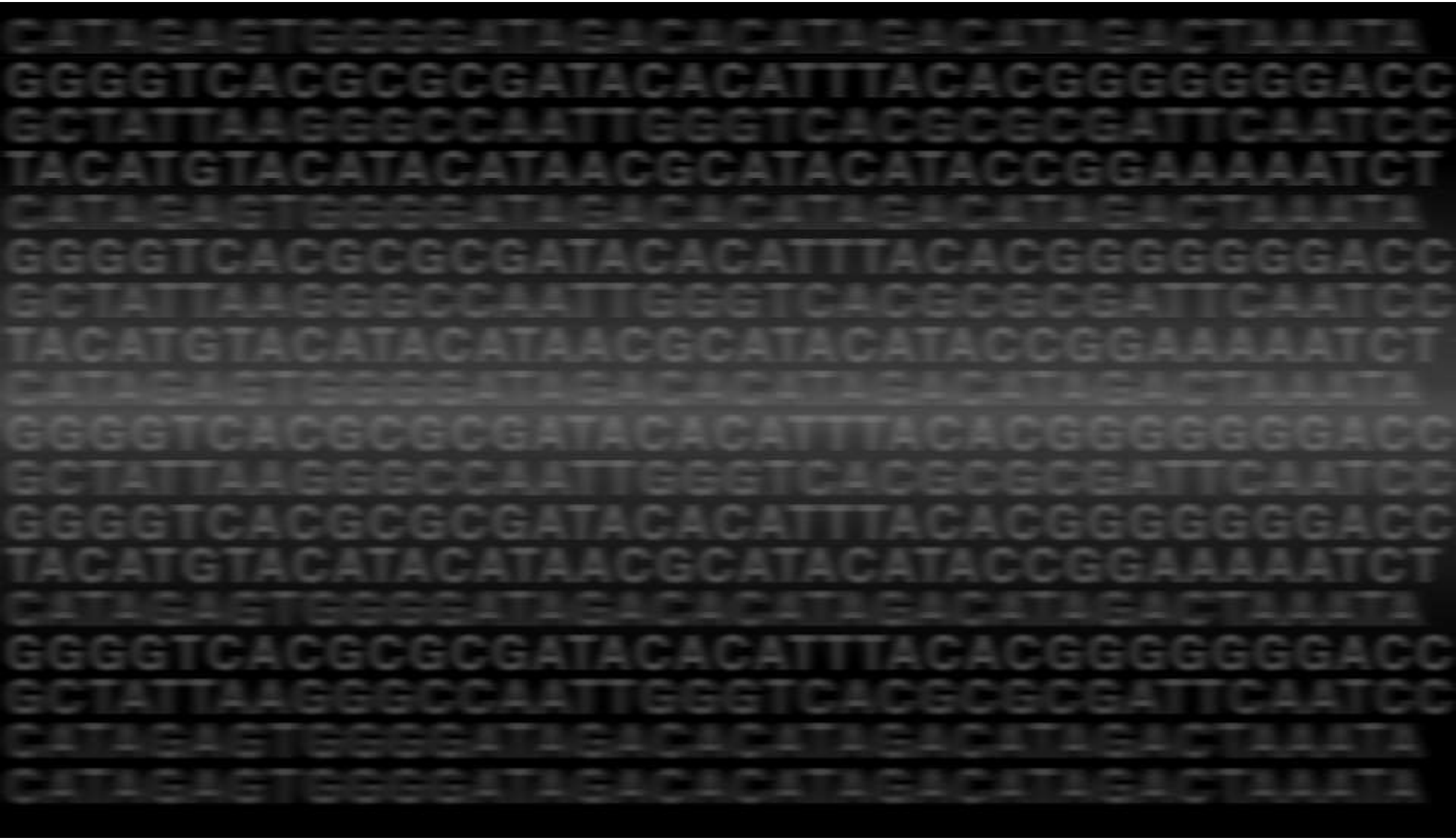
James Watson's genome
2 months
2 millions $

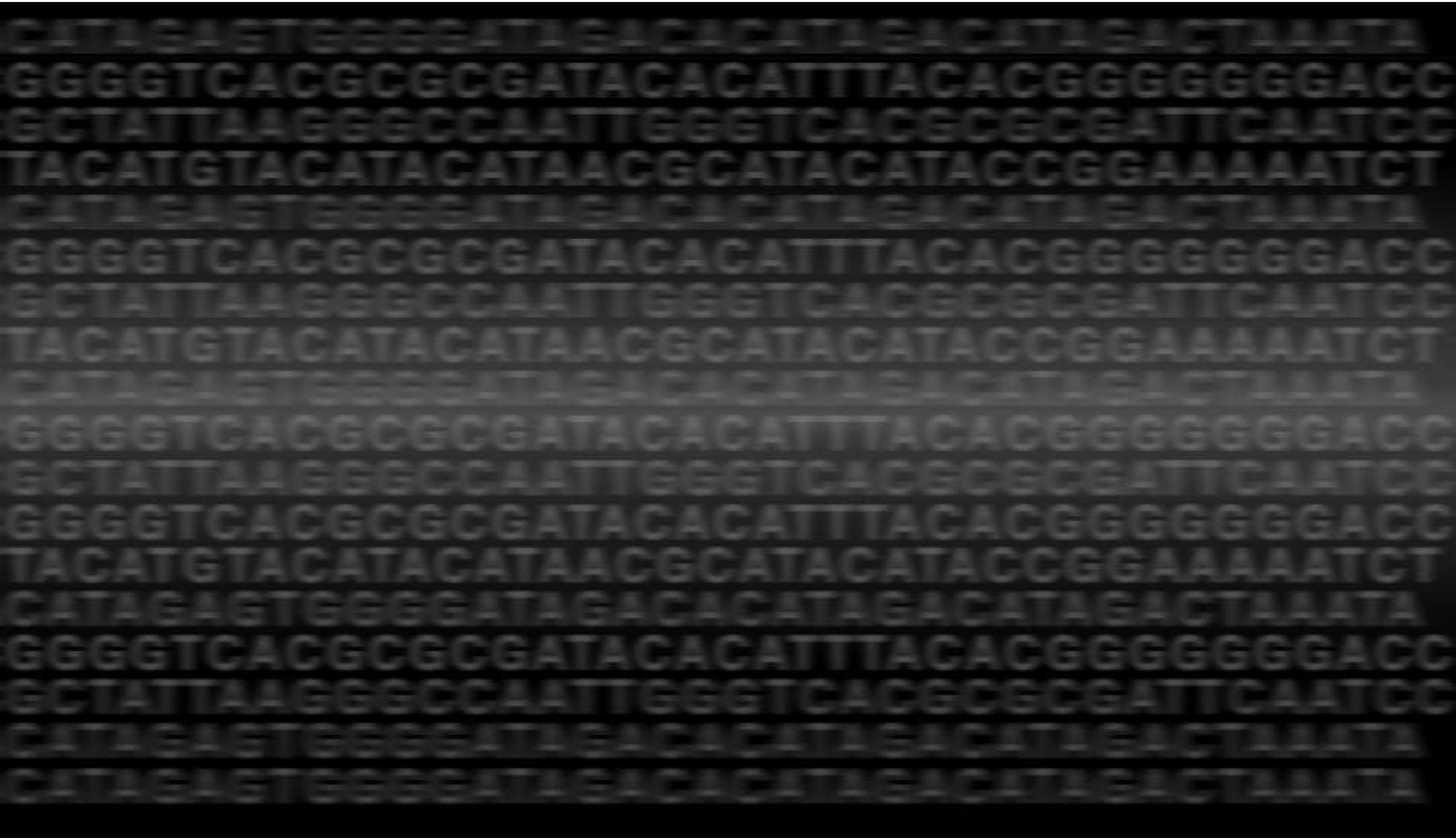
Individual genome
15 days
3000-5000 $

Individual genome
3 days
1000 $

Individual genome
1 hour
100 $

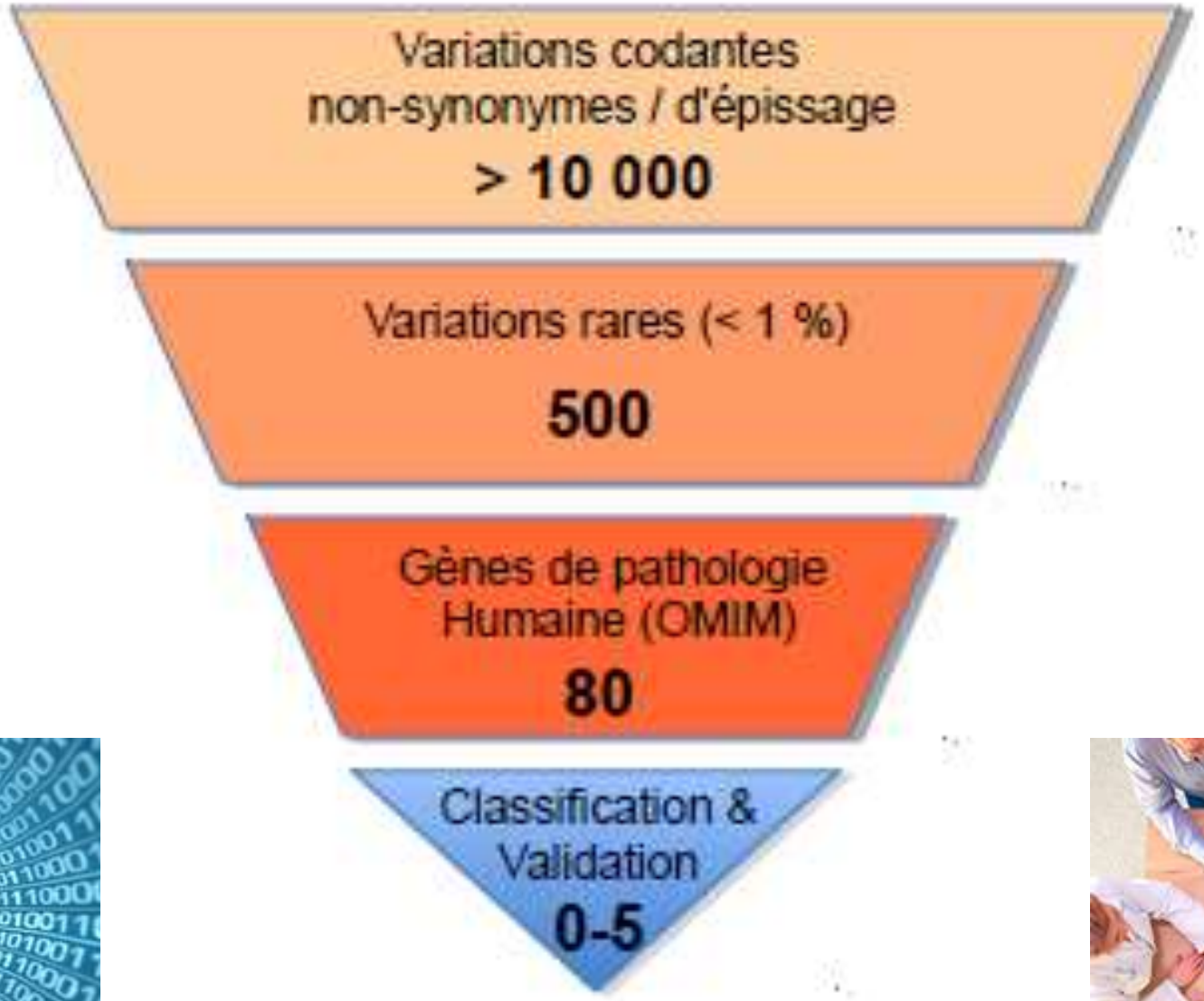
2003 2007 2013 2015 2025


GGGGTCACGGCGCGATACACATTTACACGGGGGGGGACC
GCTATTAAGGGCCAATTGGGTCACGCGCGATTCAATCC
TACATGTACATACATAACGCATACATACCGGAAAAAATCT
GGGGTCACGGCGCGATACACATTTACACGGGGGGGGACC
GCTATTAAGGGCCAATTGGGTCACGCGCGATTCAATCC
TACATGTACATACATAACGCATACATACCGGAAAAAATCT
GGGGTCACGGCGCGATACACATTTACACGGGGGGGGACC
GCTATTAAGGGCCAATTGGGTCACGCGCGATTCAATCC
GGGGTCACGGCGCGATACACATTTACACGGGGGGGGACC
TACATGTACATACATAACGCATACATACCGGAAAAAATCT
GGGGTCACGGCGCGATACACATTTACACGGGGGGGGACC
GCTATTAAGGGCCAATTGGGTCACGCGCGATTCAATCC


CATAGAGTGGGGATAGACACATAGACATAGACTAAATA
GGGGGTCACGGCGCGATACACATTTACACGGGGGGGGACC
GCTATTAAGGGCCAATTGGGTCACGCGCGATTCAATCC
TACATGTACATACATAACGCATACATACCGGAAAAAATCT

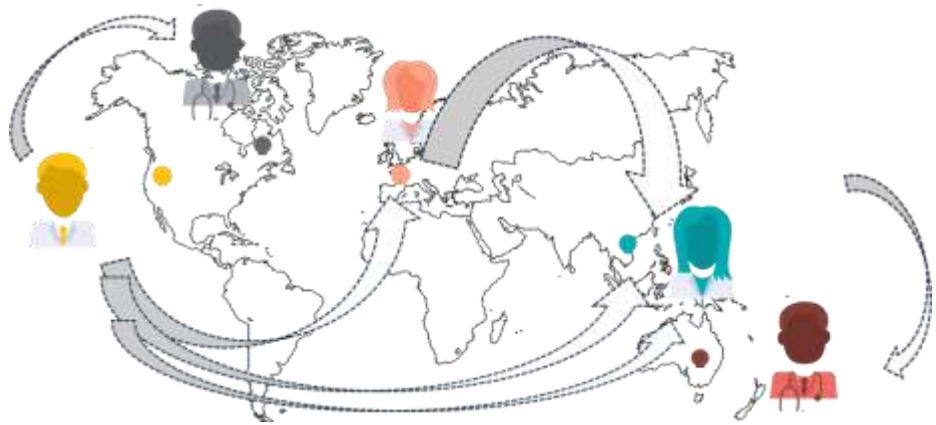

ACA
ACGTT
GGTCA

A mandatory bio-informatic analysis



Exome/genome sequencing

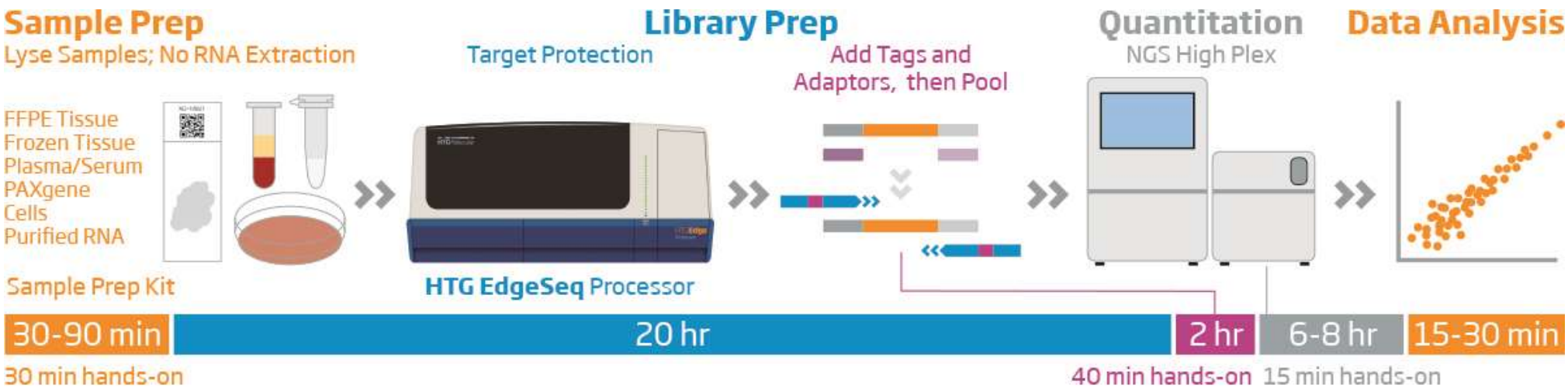
- **Unique analysis** of all genes in the genome
- Indicated in first intention in very heterogeneous disorders
- **Positive diagnosis in** 40-50% in developmental disorders, in the absence of a clinical diagnostic
- **Uncertain diagnosis** in 15% of cases, to be shared with international initiatives (genematcher)
- Possibility of **reanalysing the data** with scientific advances in **negative** cases
- **Cost** relatively low (<1000 euros)
- **Quick turnover** (3-6 months)



Interpretation of results

- 5 classes: Pathogenic, probably pathogenic, variant of unknown significance, probaly neutral, neutral
- Only pathogenic and probably pathogenic variant give access to presymptomatic testing or prenatal diagnosis
- To be able to conclude:
  - Parental samples for segregation analyses +++, but a de novo occurrence cannot be enough (every individual have a mean of 1.5 de novo variant)
  - Databases, litterature, bioinformatic analyses
  - Sharing
- The time for variant interpretation can greatly vary
- Loss of chance when the lab does not have access to a research team for studying non OMIM variants

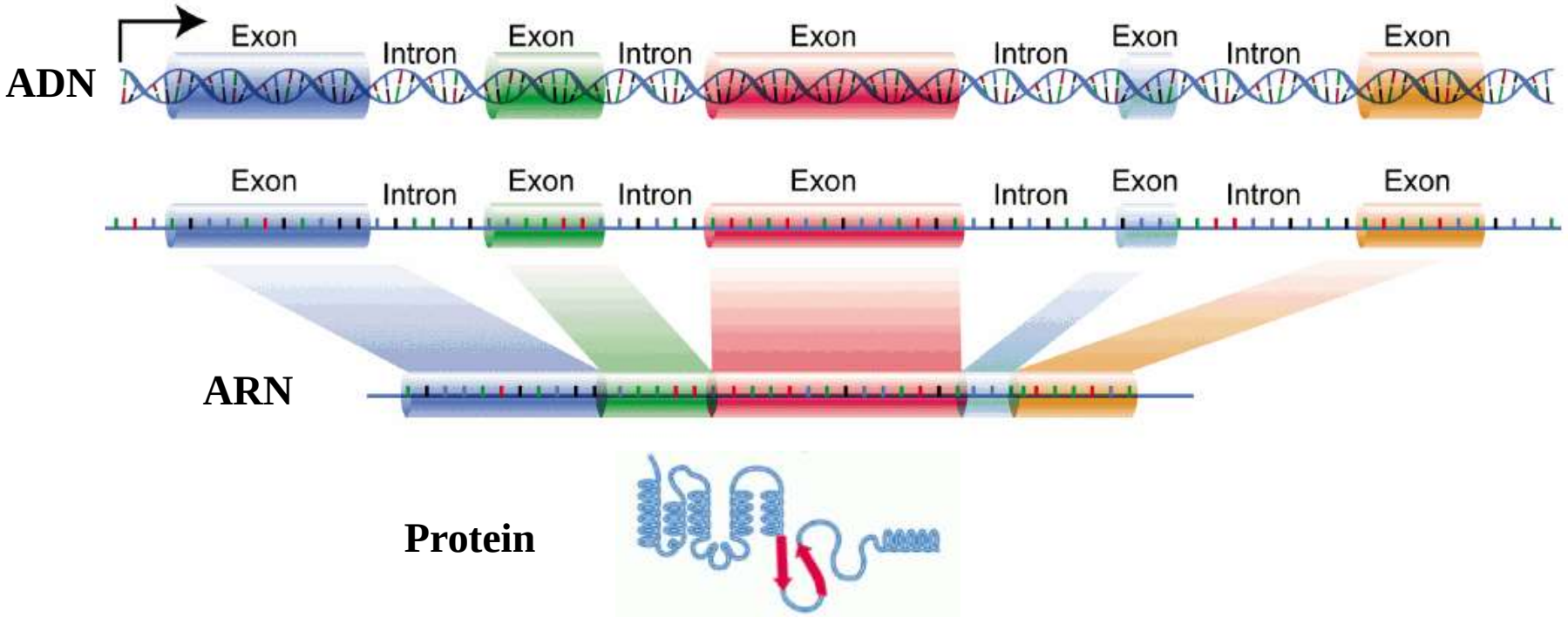
Towards faster processes



MEDICINE

The Ultimate Genetic Test

Towards Omics



Questions