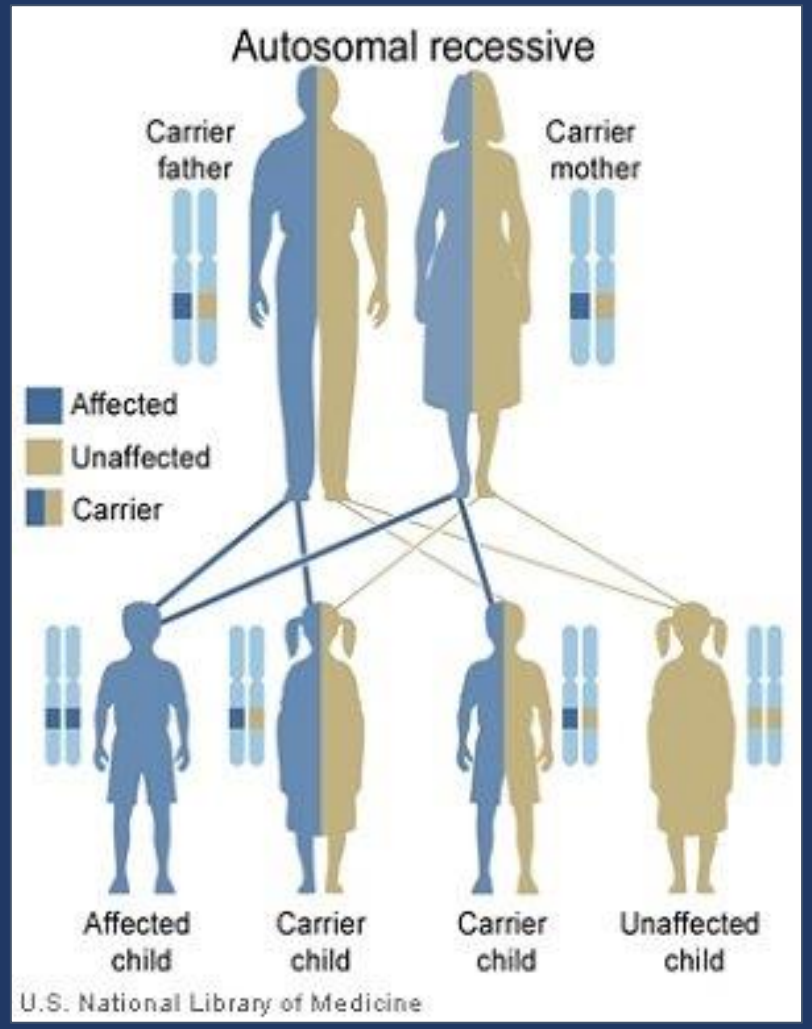
GENETIC TESTING FOR USHER SYNDROME

Gema García-García, PhD

Health Research Institute Hospital La Fe Valencia, Spain

CIBER of Rare Diseases (CIBERER)

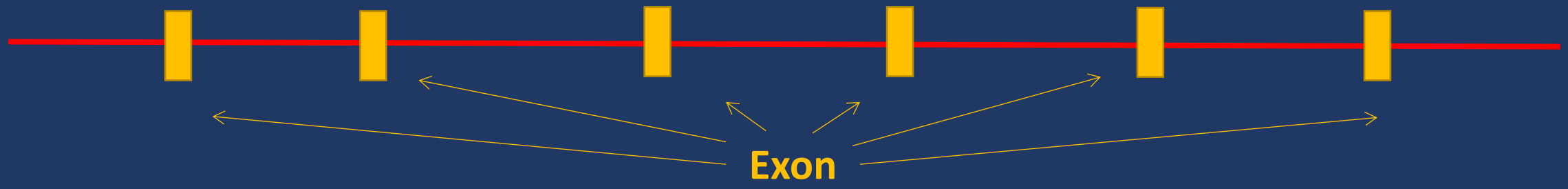


Usher Syndrome (USH) is a disorder of genetic origin

The pattern of inheritance is autosomal recessive

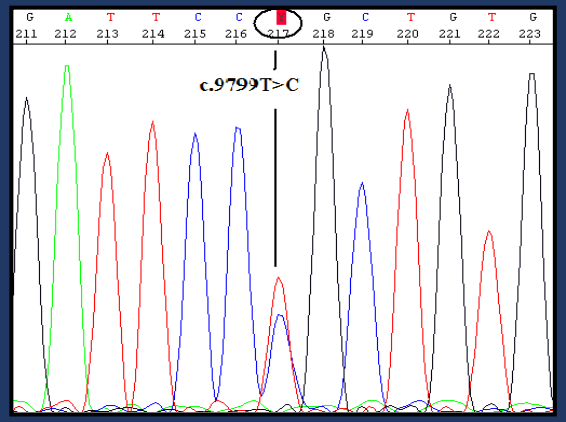
Technologies for USH molecular diagnosis

- **Gene by gene analysis (13 genes, >400 exons)**



- **Genotyping microarray** (Asper Biotech)

  Detection of reported mutations



We use the **Next Generation Sequencing** technology (NGS) to screen all the known USH genes in each patient

Genes in the panel (13):

USH1: MYO7A, CDH23, PCDH15, USH1C, USH1G, CIB2

USH2: USH2A, GPR98, DFNB31

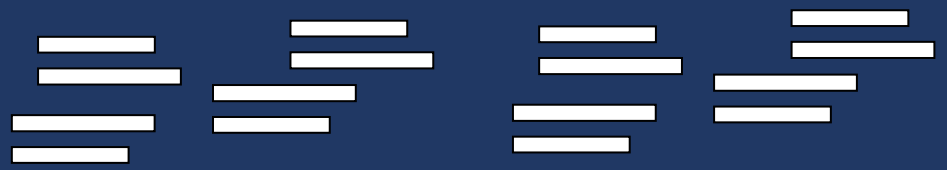
USH3: CLRN1, HARS

USH-associated: PDZD7, CEP250

+ intronic mutations in *USH2A*

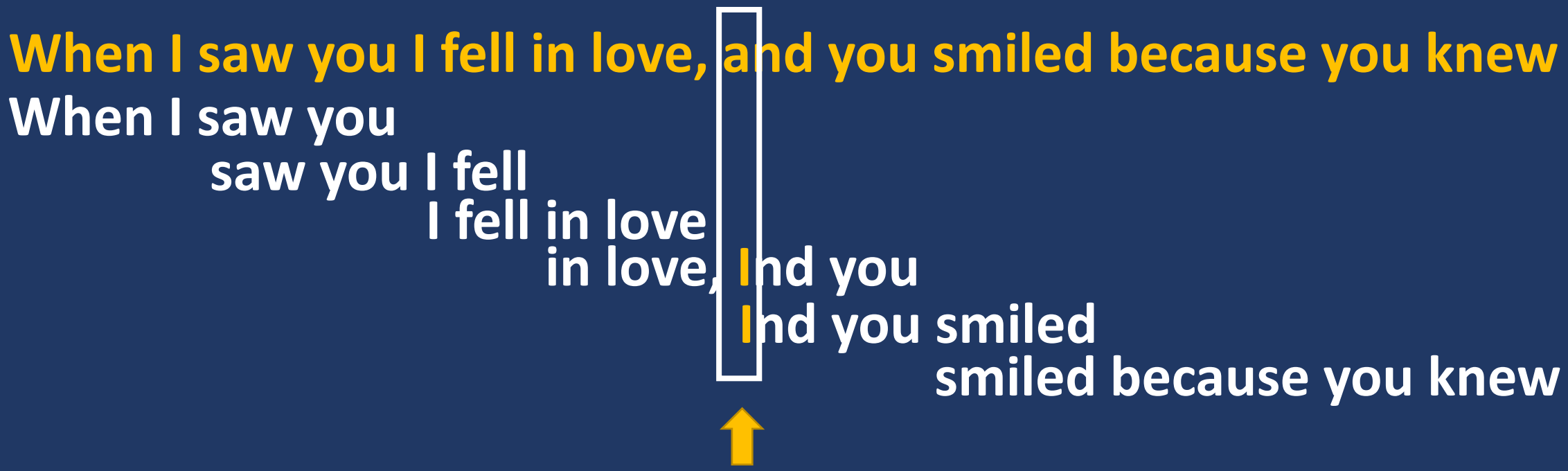
1. Extract DNA from blood (or saliva)

2. Cut the genome into a high number of pieces



3. Sequence those pieces of DNA at the same time

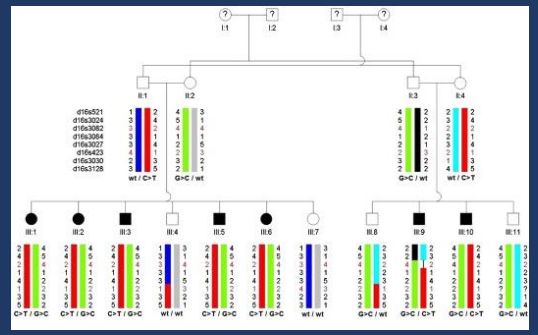
4. Map the position of each piece to a reference genome



Problems:

- Variant interpretation

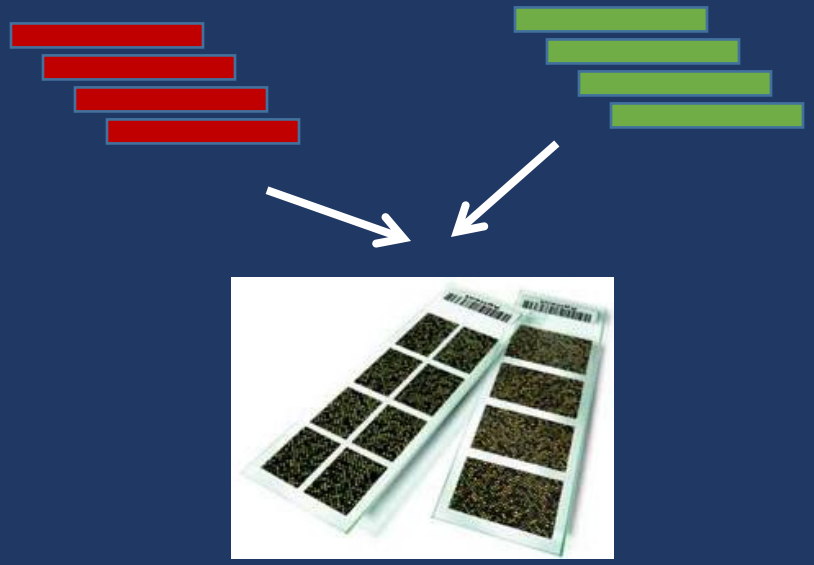
- Difficult assignment in polymorphic or pathogenic

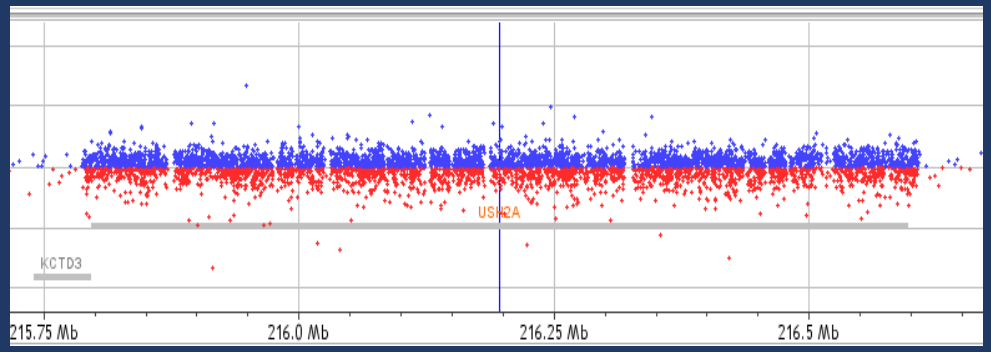


We use a CGH array to detect large deletions or duplications of these genes

Patient DNA

Control DNA

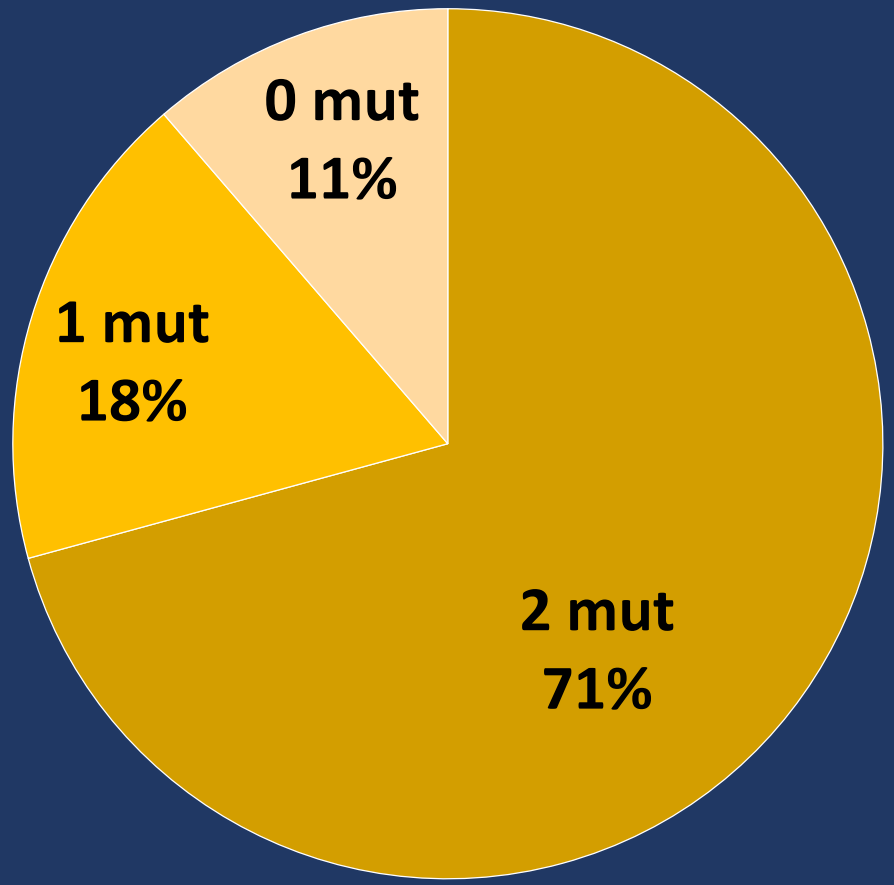




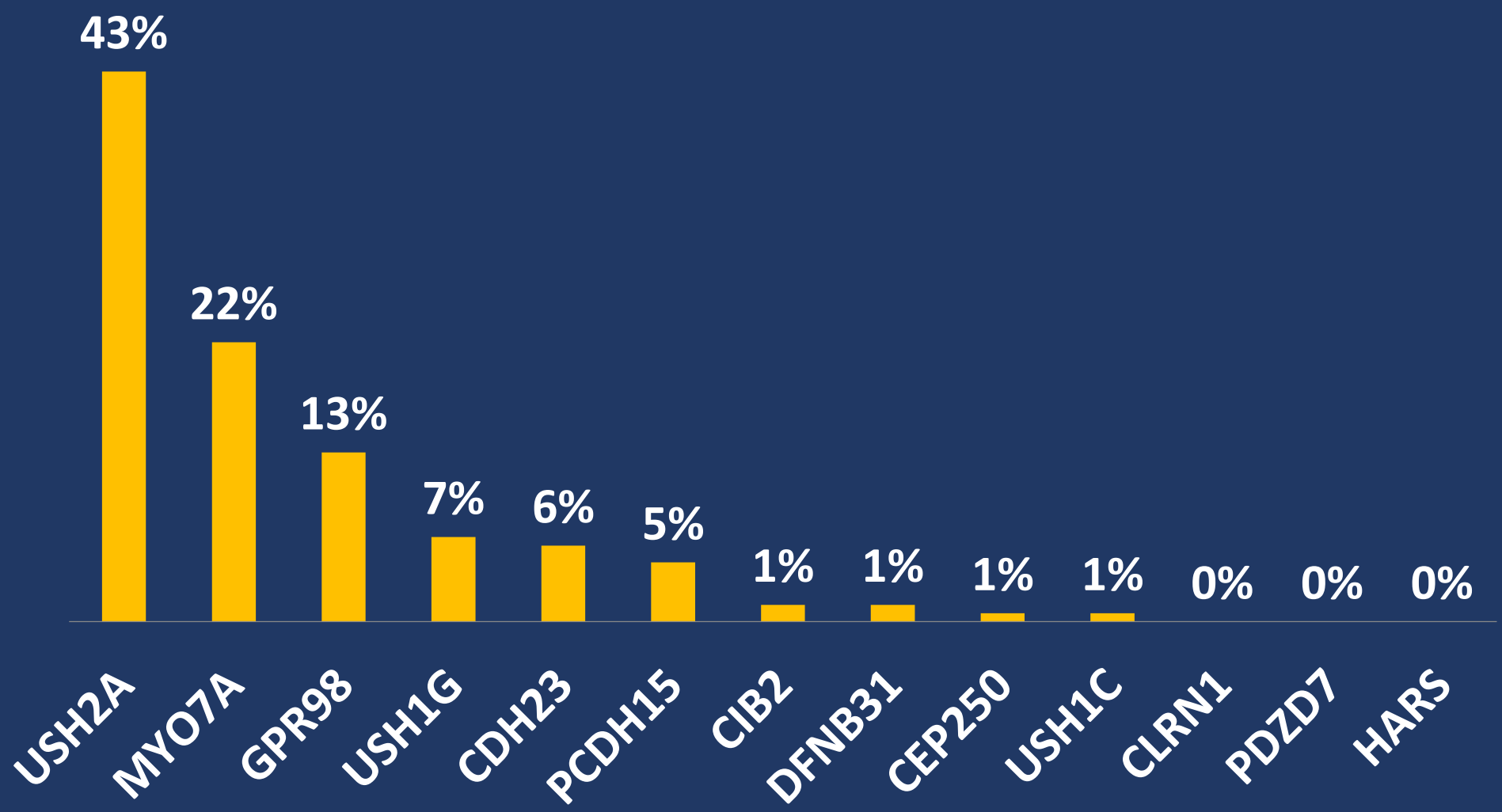
> 100 patients analysed by NGS

89% at least one mutation

80% allele ratio detection



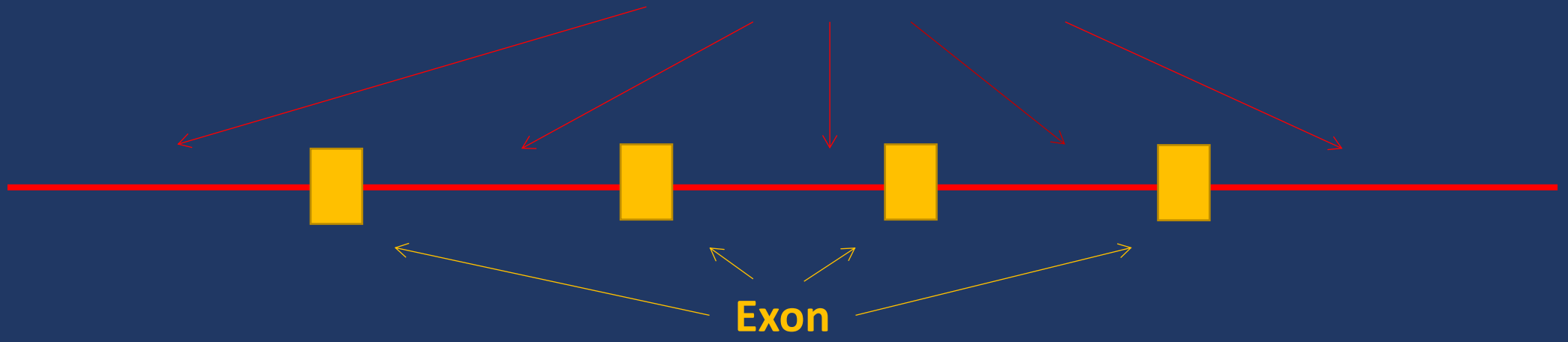
Gene Frequency



Why don’t we detect the 100% of mutations?

- Other genes

- Non-coding regions



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Centro de Investigación Biomédica en Red
Enfermedades Raras

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