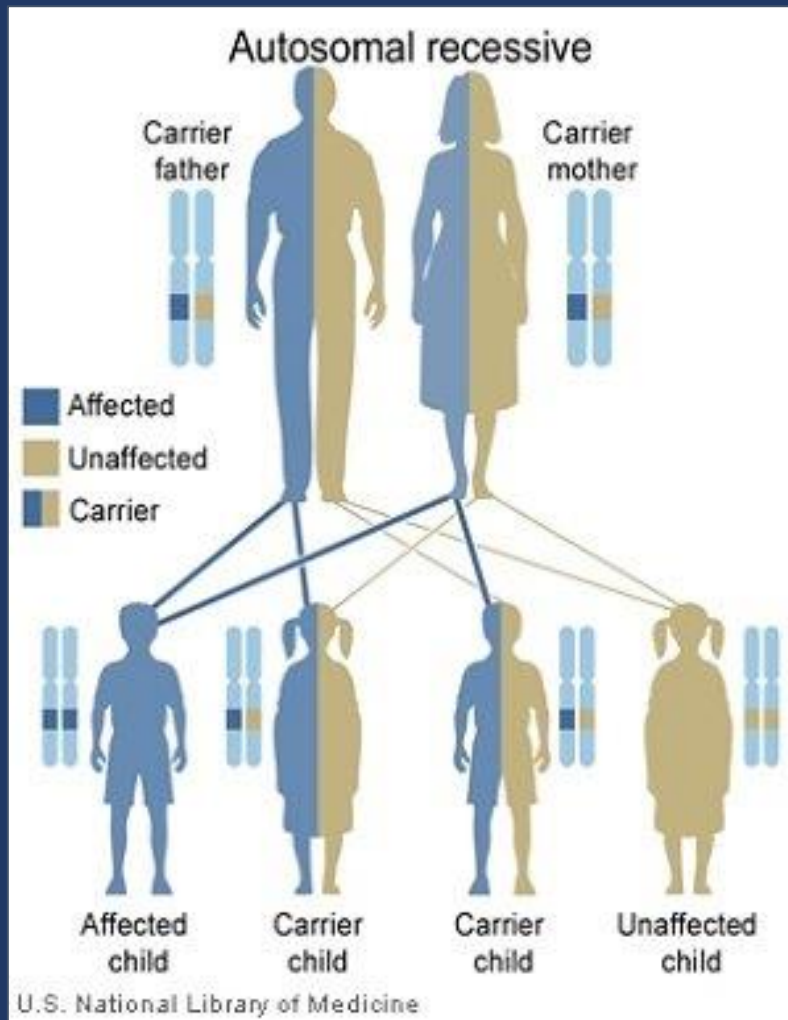


# **GENETIC TESTING FOR USHER SYNDROME**

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**CIBER of Rare Diseases (CIBERER)**

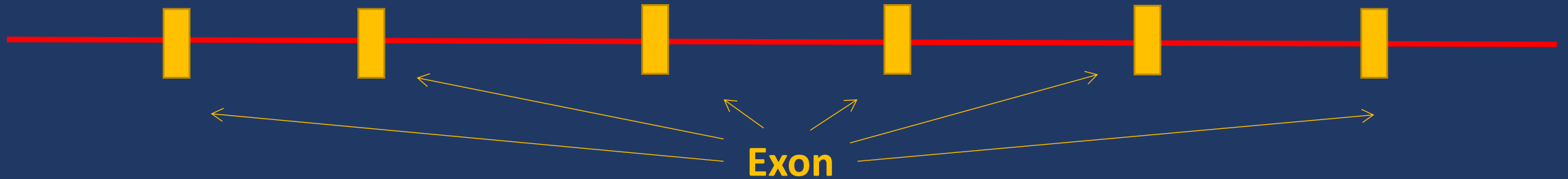


Usher Syndrome (USH) is a disorder of genetic origin

The pattern of inheritance is autosomal recessive

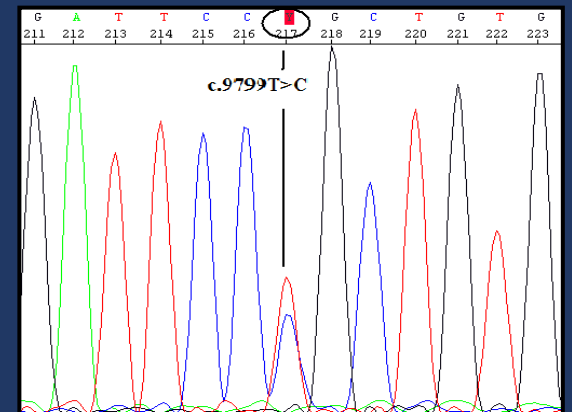
# Technologies for USH molecular diagnosis

- 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*

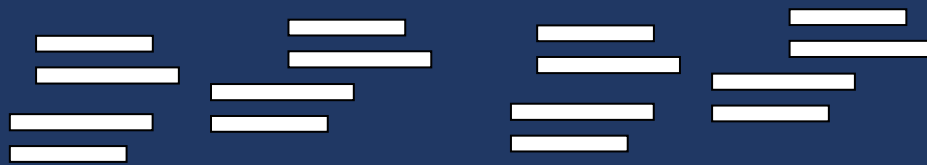
+ intronic mutations in *USH2A*



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

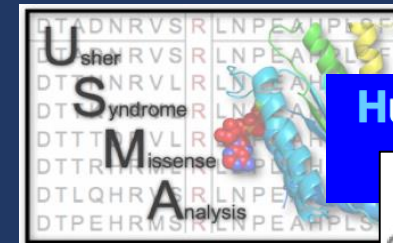
#### 4. Map the position of each piece to a reference genome

**When I saw you I fell in love, and you smiled because you knew**  
When I saw you  
saw you I fell  
I fell in love  
in love, and you  
and you smiled  
smiled because you knew

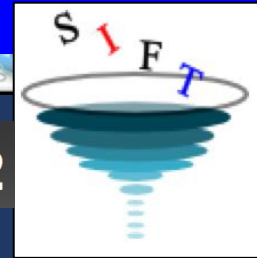
A vertical white box highlights the word "and" in the first line of the poem. A yellow arrow points upwards from the bottom of the box to the word "and" in the first line. The text is arranged in a staircase pattern, with each line starting further to the right than the one above it.

# Problems:

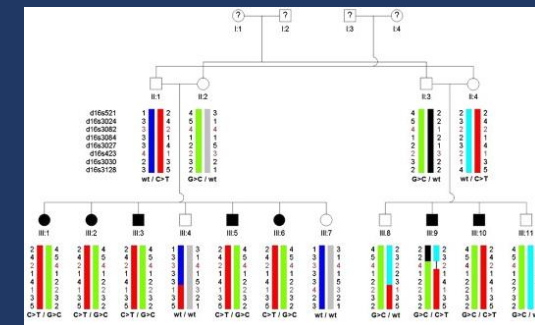
- Variant interpretation
- Difficult assignment in polymorphic or pathogenic



Human Splicing Finder 2.4.1



PolyPhen-2

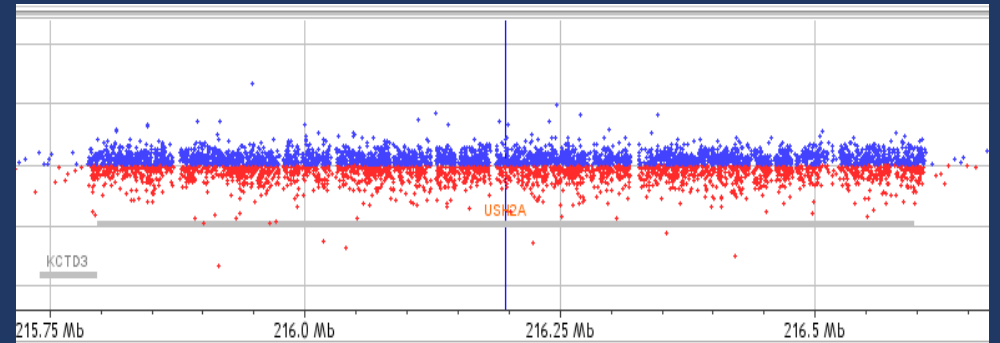


We use a CGH array to detect large deletions or duplications of these genes

Patient  
DNA



Control  
DNA

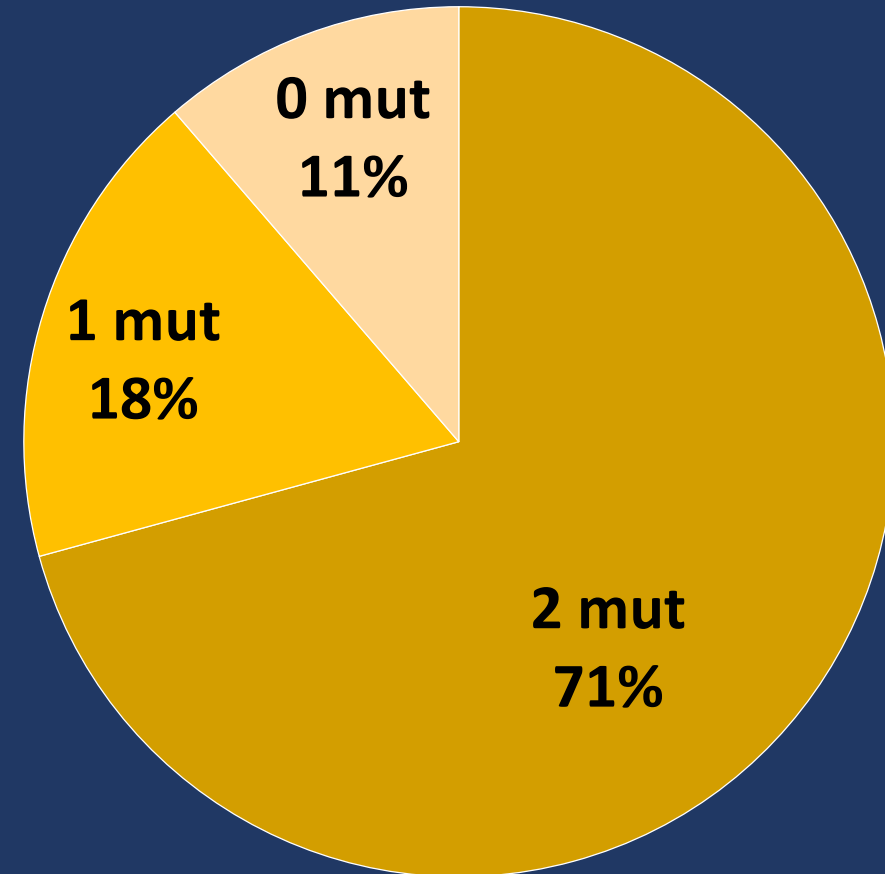




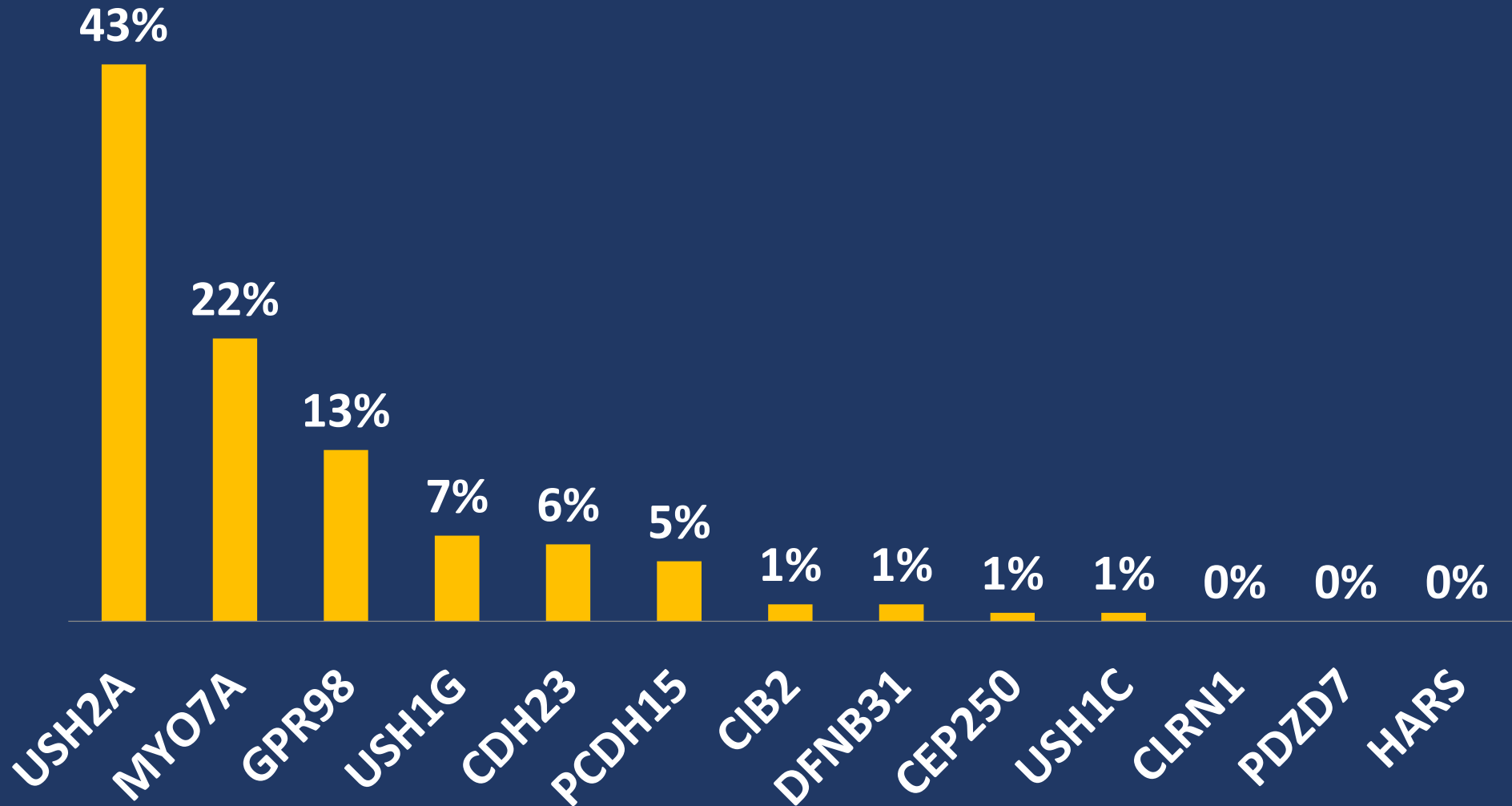
# > 100 patients analysed by NGS

89% at least one  
mutation

80% allele ratio  
detection

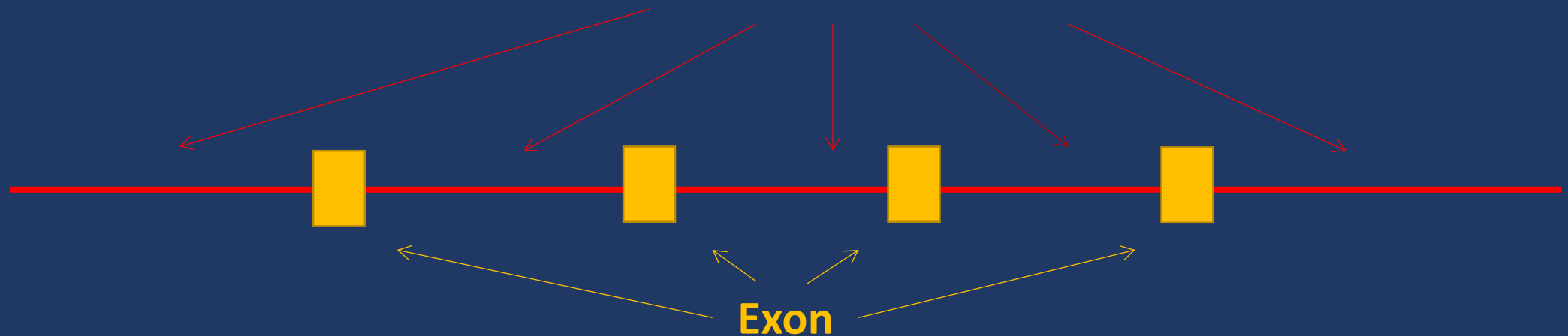


# Gene Frequency



# Why don't we detect the 100% of mutations?

- Other genes
- Non-coding regions



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