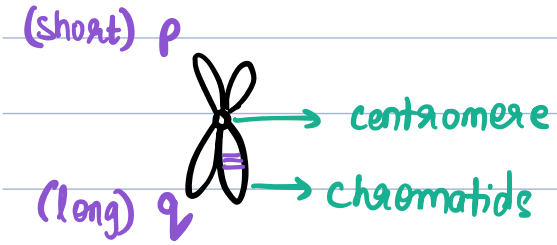
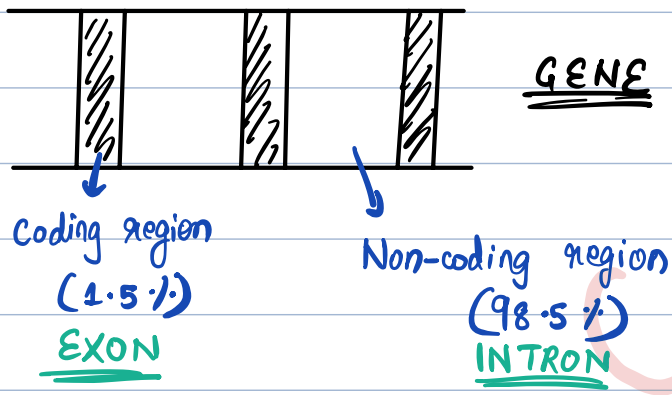
Genetics:

→ 20-30,000 genes in human body



- every gene has 2 alleles
  [1 from father, 2nd from mother]



Homozygous: both the alleles are the same
(AA, aa)

Heterozygous: both the alleles are different.
(Aa)

Co-dominance: both alleles express simultaneously.
→ ABO blood grouping
→ HLA typing.

Incomplete Penetrance: property shown by autosomal dominant disorder

Eg: 100 people have defective gene ⇒ Marfan Syndrome

80% Penetrance
- 80 people show symptoms
- 20 people escape "

Variable Expressivity: shown by autosomal disorders

Eg: ○ ○ ○ ○ ○ → 5 people have defective gene for Neuro Fibromatosis 1.

neuro-fibroma | skin lesion | eye lesion | eye & skin lesion

Variable expression of clinical features

Pleiotropy: single mutant gene can produce multiple end effects (clinical manifestations)

Ex: Sickle cell anemia

Anticipation: Severity of disease increases with each succesive generation.

→ property shown by trinucleotide repeat mutations

- Fragile X syndrome [CGG]

Polymorphism: Two individuals differ in genome only by 0.5 %.

→ 99.5 % genome is the same

- Single Nucleotide Polymorphism
- Copy Number Variations

Mutation: permanent heritable change in DNA

- Point Mutation
  - single nucleotide is affected
- Frame shift Mutation

Point Mutation

- Silent
- Missense [SCA]
- Nonsense β-thalassemia

Frame Shift Mutation

- Addition
- Deletion

Mi RNA (micro RNA):

→ non-coding RNA (does not undergo translation to produce protein)

→ 22 nucleotides in length

→ role in post-transcriptional silencing

mi RNA

- Tumor Suppressor mi RNA
  - miR 15, 16
- Oncogenic mi RNA
  - miR 155, 200

- CLL: deletion of miR 15, 16
- B cell lymphomas: increased expression of miR 155, 200.

Epigenetics: hereditary chemical modifications on DNA / histone / chromatin

→ reversible change.

→ no change in nucleotide sequence

→ Mechanism: — DNA methylation (more common) } ⇒ reduced gene expression.
— Histone deacetylation

Role of epigenetics:

① Regulation of gene expression
② X-chromosome inactivation
③ Cellular ageing
④ Cancers

Diagnosis: — Bisulphate sequencing
— Immunoprecipitation assay.

Genetic Diagnostic Techniques :

CYTOGENETIC

- Karyotyping
- FISH (fluorescent in-situ hybridisation)

→ for Known genetic defects
→ can easily pick up the chromosomal defects
→ used for bigger defects.

MOLECULAR GENETIC

- MLPA (multiplex ligation probe analysis)
- PCR
- Sequencing
- ARRAY

→ unknown mutations
→ molecular defects present

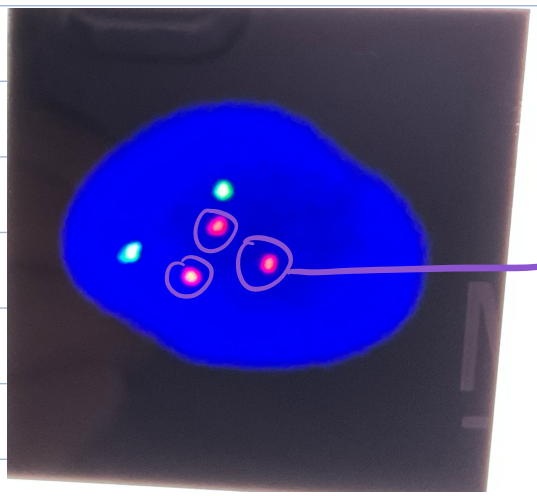
PCR :

Types:
① Sanger Sequencing ⇒ GOLD STANDARD for sequence determination
② Pyrosequencing ⇒ when specimen is small / contaminated
③ Single base primer extension ⇒ known genetic defect
④ RFLP ⇒ in unknown genetic defects
⑤ Real Time PCR ⇒ quantitative estimation (eg: CML)
⑥ Genome wide Association Studies (GWAS) ⇒ to see trend of disease in a population
⑦ Amplicon Length analysis
↳ used for trinucleotide repeat mutation.

FISH:

→ used for chromosomal disorders (aneuploid, deletion, trisomy)
→ used for translocations
→ used for amplifications.

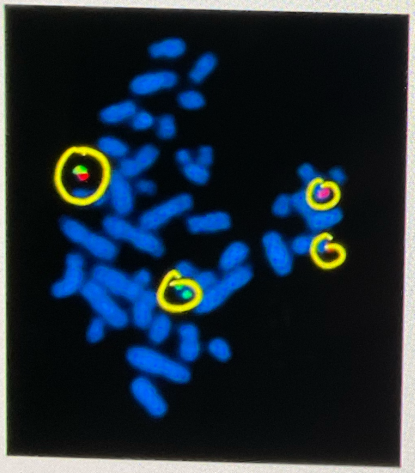
• 2 green + 2 red dots ⇒ Normal



1 y/o child with simian crease
Red → Chromosom 21.

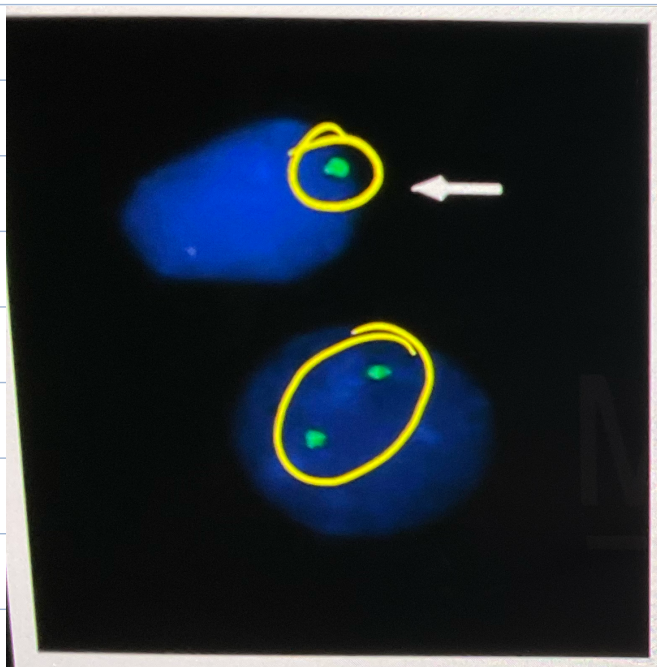
→ Trisomy of 21 st chromosome
⇓
DOWN'S SYNDROME

Q. A 14 year old male patient from Bihar with massive splenomegaly

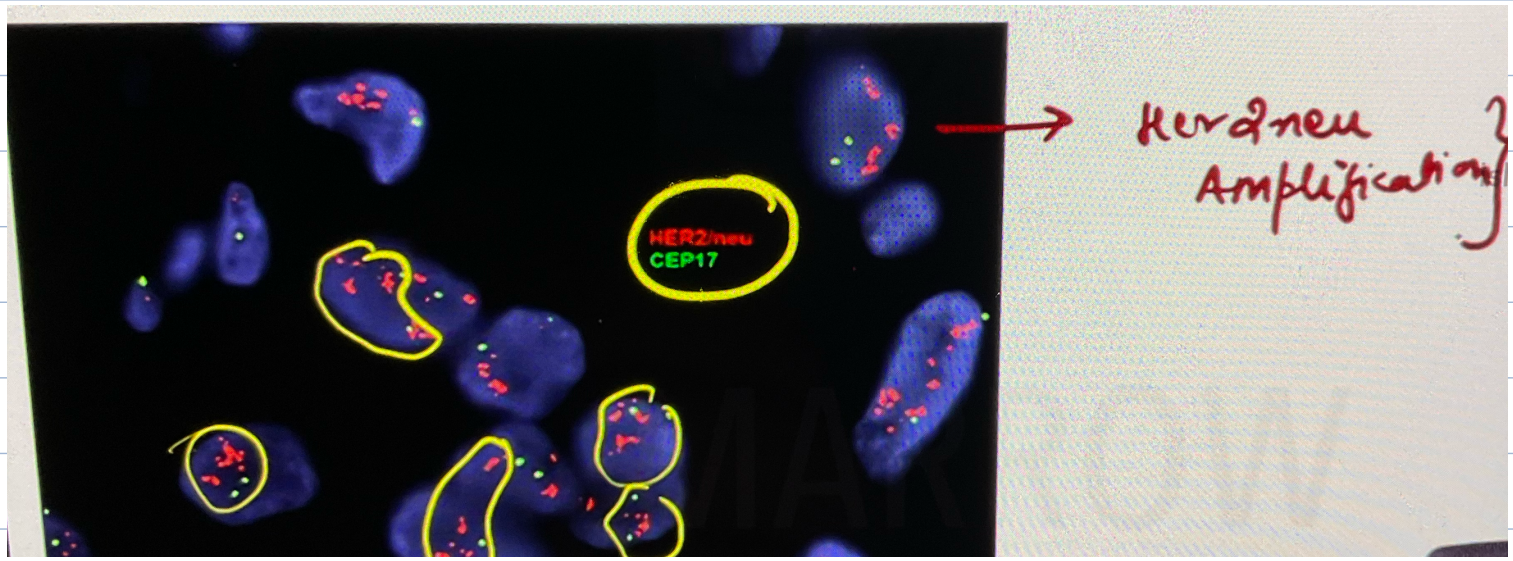


Red - ch.9
green - ch.22
↓
TRANSLOCATION
↓
CML
t(9:22)

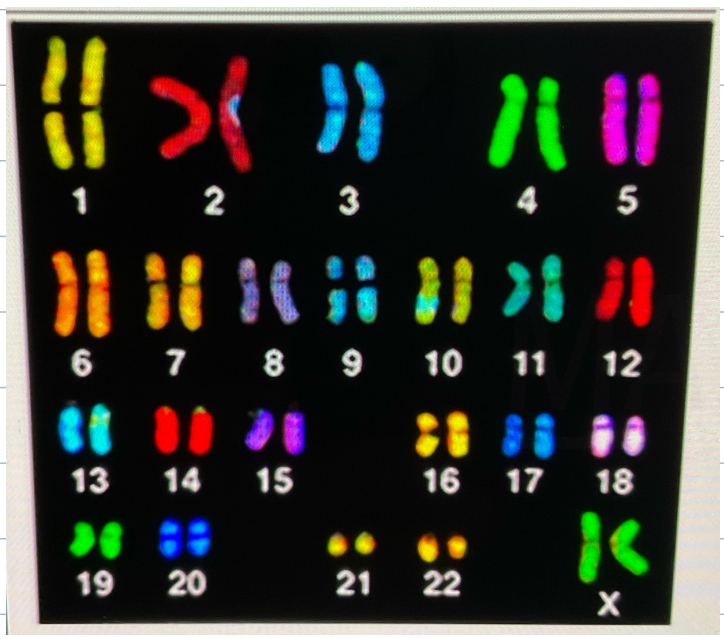
→ FISH: usually done in the interphase.



16 yr old girl 1° Amenorrhe
webbed neck.
green → X ch.
↓
dose of 1 X ch.
↓
XO →
TURNE'S synd.



→ Her2neu Amplification



Spectral Karyotyping :
→ 5 colour fish

Comparative Genomic Hybridisation: Comparing geneme of 2 individuals

TEST — RED

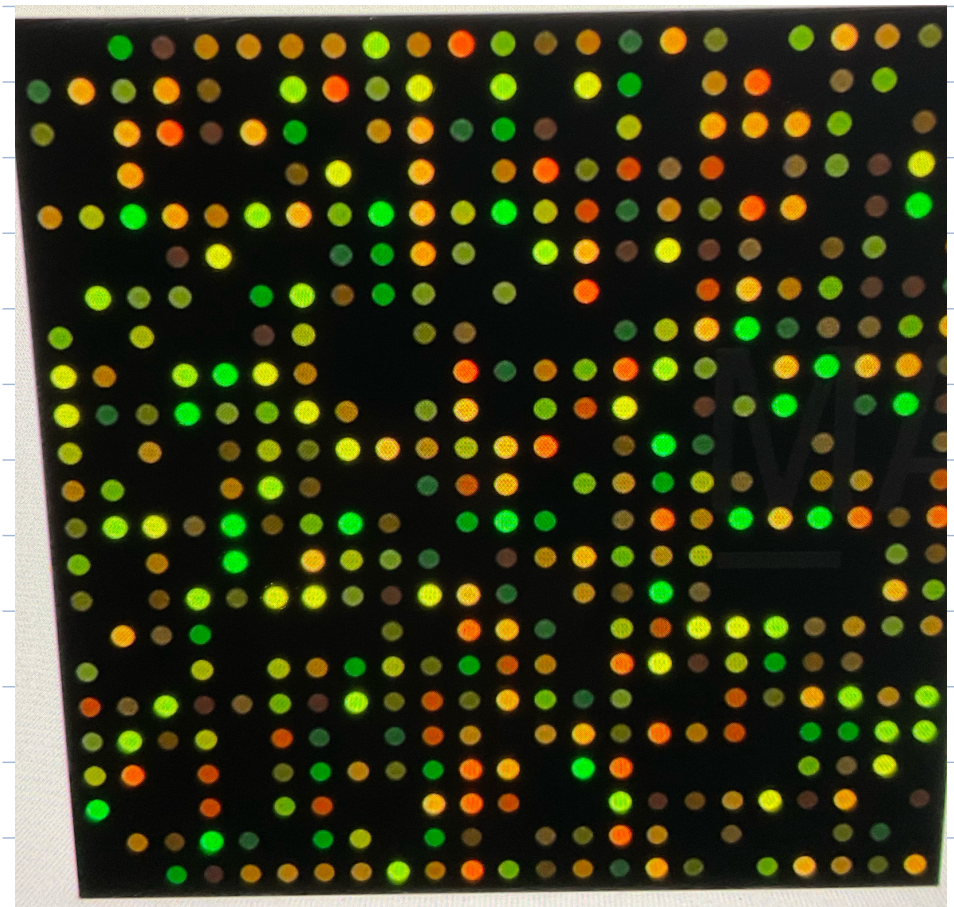
CONTROL (NORMAL) — GREEN

Hybridisation

RED
Gain of function (duplication)

NORMAL

GREEN
Loss of function mutation



MICRO ARRAY:

Compares the DNA of multiple individuals simultaneously.

GEEN [Genom Editing with Engineered Nucleases]:

↓

DNA can be deleted or inserted into a genome using molecular scissors

↓

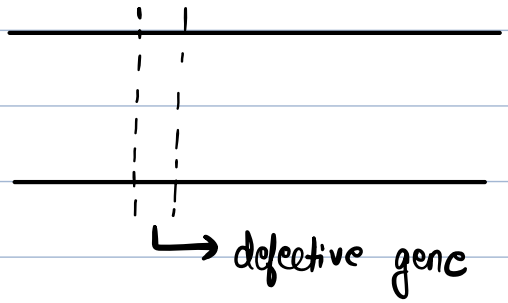
create site specific breaks

↓

replace the DNA fragment

↓

join the ends by non-homologous end joining.



Nucleases:

1. TALEN
2. Zn - finger endonuclease
3. CRISPR - CAS9