# Cytogenetics and genome analysis

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فريـــق الرؤيـــة الجينية

**Cytogenetic:** is the study of chromosomes, their Structure, and their inheritance, as applied to the practice of medicine.

**Cytogenetic abnormalities:** abnormal changes at the chromosome level either a region of a chromosome or in the number of chromosome.

Abnormalities it could be in the number of chromosomes or it could be in chromosome region.

Cytogenetic abnormalities are present in:

- 1% of live birth
- 2% of new born who mothers are older than 35, **but it not necessary all babies for the women older than 35 have Cytogenetic abnormalities.**
- 50% of spontaneous abortion in first three months in pregnancy (trimester) is due Cytogenetic abnormalities, **but it doesn't necessary all abortion cases in the trimester are due Cytogenetic abnormalities.**

## Chromosome analysis

How the chromosomes abnormalities are detected?

At first step we need a cells, human body contains different types of cells, cells have selected from blood **because the blood is accessible tissue compare the other tissues, and we need cells which can maintain in tissue cultures.**

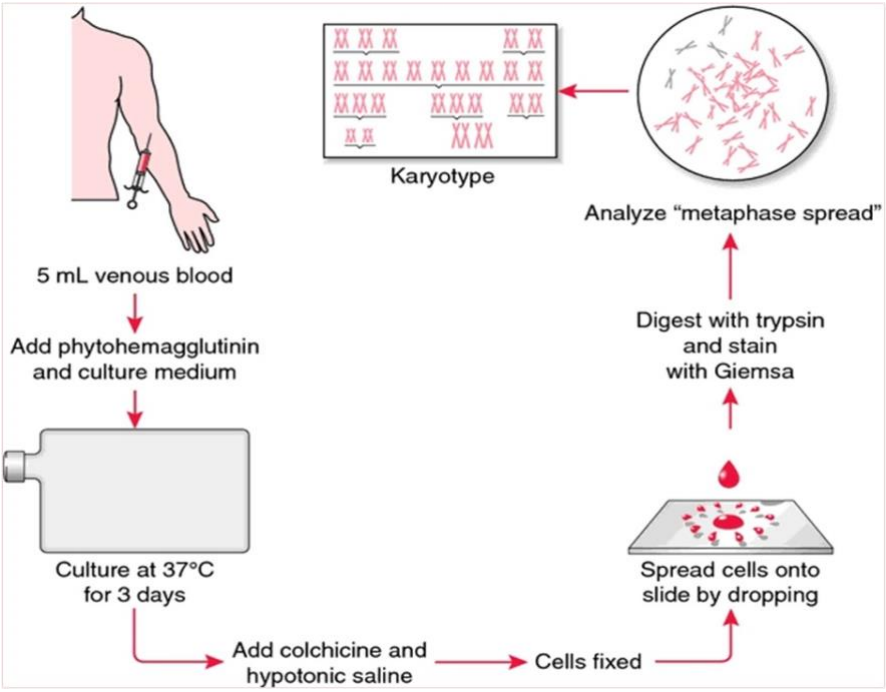
**Remember the Red blood cells (erythrocytes) lack nucleus which mean there are lack chromosome, so we use White Blood Cells (leukocytes).**

**The most condensation and the chromosomes can be visualized clearly when they align at metaphase plate at metaphase.**

For achieve this, the cells inject with **phytohemagglutinin** to enhance cell division to reach the metaphase stage.

After period the cells inject with **Colchicine** which is a drug that disrupt microtubules to fix cells at **metaphase** and stop Division progression.

Also the cells place into **Hypotonic saline** ،because the human cells are animal cells, when they put inside hypotonic solution the water continue enter the cell which cause cell lysis and release the Chromosomes.




There are clinical indications for chromosome and genome analysis:

- A problem in early growth and development
- Stillborn and neonatal death
- Incidence of chromosome abnormality in still birth and neonatal death is **10%** compare to **1%** live birth.
- Fertility problems, 3-6% infertility cases are due Chromosome abnormalities.
- Family history

- Neoplasia
- Pregnancy, **woman older than 35 years** could give birth children a babies with Chromosome abnormalities.

We use **Giemsa stain** to visualize Chromosomes this called

**G banding, this procedure is reproducible.**

When we use Giemsa stain the differences between chromosomes don't change " **reproducible ".**

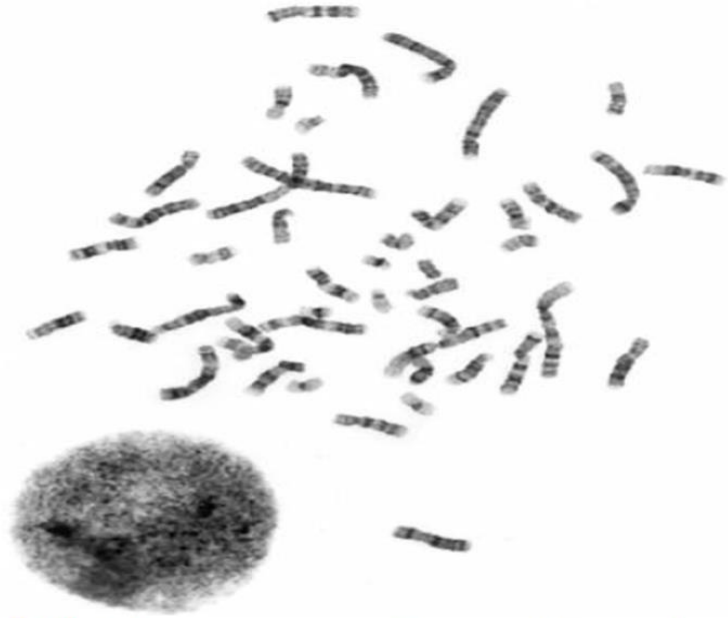


**Figure 2-10** A chromosome spread prepared from a lymphocyte culture that has been stained by the Giemsa-banding (G-banding) technique. The darkly stained nucleus adjacent to the chromosomes is from a different cell in interphase, when chromosomal material is diffuse throughout the nucleus. *See Sources &*

After the chromosomes are stained using Giemsa stain , light microscope is used to visualize Chromosomes, under light microscope **Sequence of light and dark bands appears in each chromosome, each chromosome has unique Sequence of light-dark bands which is different from other chromosomes , like when you going to market and you choose a product and then you**

**going to cashier to pay , cashier scan a bar code for this product and then all information related for this product will appear in computer include price , each chromosome has unique Sequence of light and dark bands similar to product bar code .**

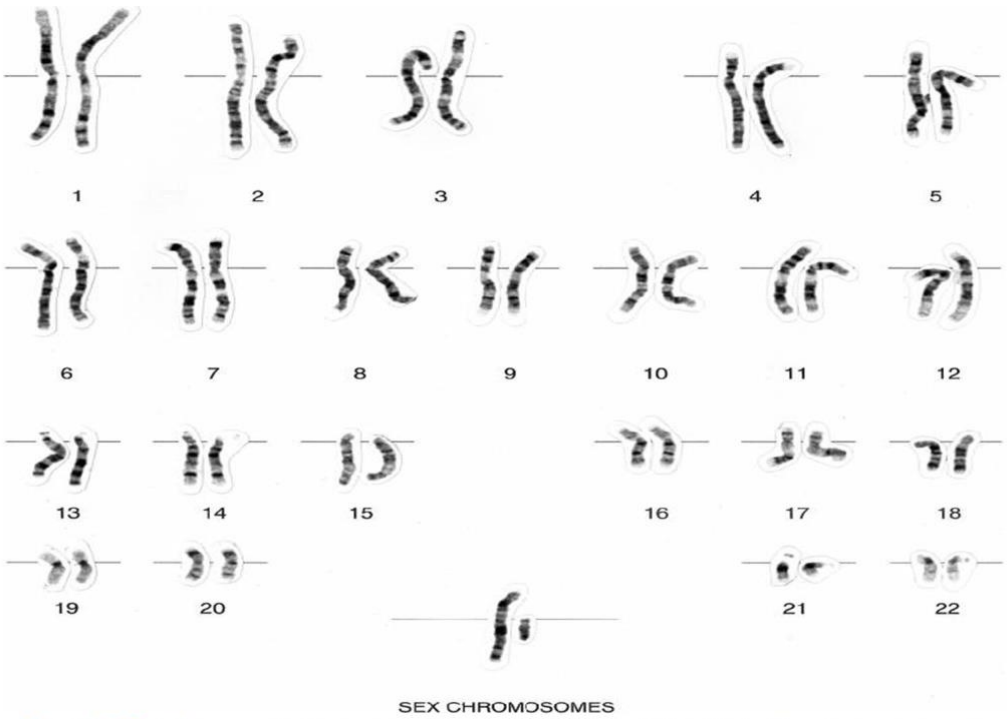



**Figure 2-11** A human male karyotype with Giemsa banding (G banding). The chromosomes are at the prometaphase stage of mitosis and are arranged in a standard classification, numbered 1 to 22 in order of length, with the X and Y chromosomes shown separately. *See Sources &*

Each chromosome contains:

Long arm (q **arm)**

Short arm (p **arm)**

**Also, if we use a microscope with low resolution and looking for certain chromosome, and we observed this chromosome contains:** 2 light bands and **1 dark bands.**

**We call them " regions ":** region 1, region 2, **region 3.**

If we use another microscope with higher resolution and focus on region 1 **,we** will find **region** 1 **contains** s Sequence of light -**dark** bands: 1 light band and **3 Dark bands**

**We call them " bands ":** band 1, **band 2, band 3** and **band 4.**

If we use more powerful microscope and focus on **band 2,** we will find **band 2** contains sequence of light- **dark** bands.

**We call them " sub bands": sub band 1,** sub band 2, sub band 3.

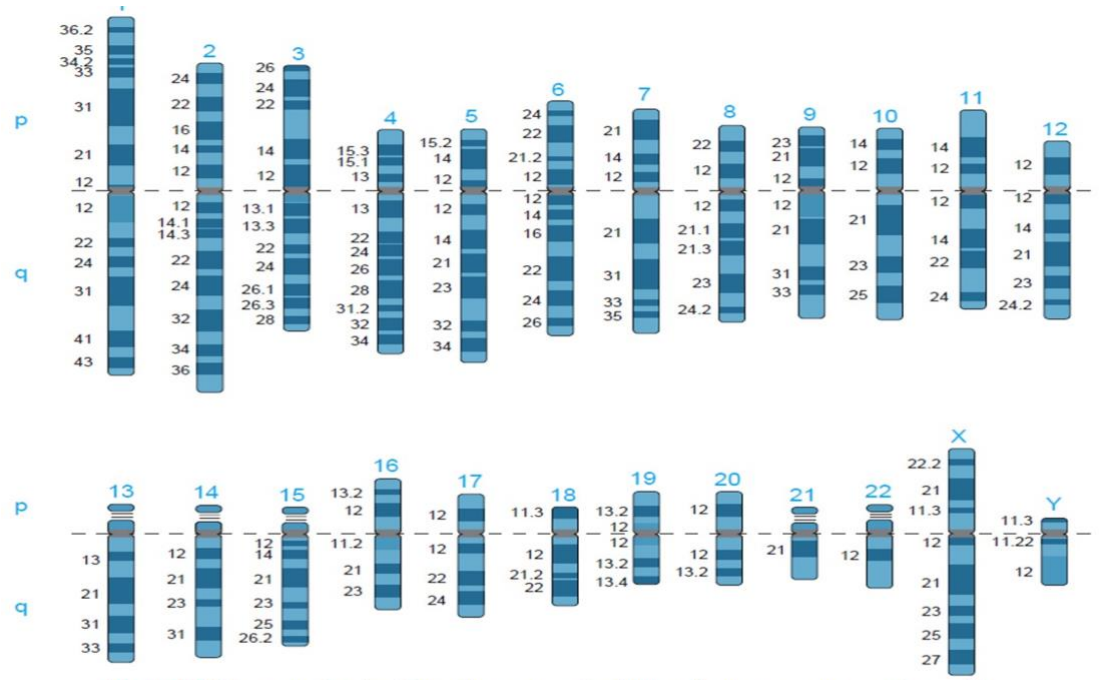



**Figure 5-2** Ideogram showing G-banding patterns for human chromosomes at metaphase, with approximately 400 bands per haploid karyotype. As drawn, chromosomes are typically represented with the sister chromatids so closely aligned that they are not recognized as distinct entities. Centromeres are indicated by the primary constriction and narrow *dark gray* regions separating the p and q arms. For convenience and clarity, only the G-dark bands are numbered. For examples of full numbering scheme, see Figure 5-3. *See Sources & Acknowledgments.*

Summary

The chromosome consists of long arm and short arm each arm contains a sequence of light and dark bands called regions**,** if we use a higher resolution microscope and focus on a certain region in chromosome, we find this region contains a sequence of light and dark bands called **bands,** if we use more powerful microscope and

focus on a certain band ,we will find this band contain a sequence of light and dark bands called **sub bands.**

Human has 46 chromosomes which order in pairs (23 pairs)

Each pair contains two chromosomes we call them **homologous chromosomes.**

Homologous pair are similar, both have the same size, shape, number of genes, and type of genes.

For homologous pair, one chromosome is **paternal origin,** the second Chromosome is **maternal origin.**

**Pair number 23** contain sex chromosomes, in female pair number 23 contains **Two X chromosomes,** in male pair number 23 contains **one X chromosome and one Y chromosome.**

**Y chromosome is the** chromosome that responsible for Sex Determination male or female, to be more specific there is a gene on Y chromosome called **SRY gene,** this gene responsible for **Testicles** development.

**SRY stand for: Sex – Determination Region Y protein.**

**The ordering of Region, bands, sub bands start from centromere which is the site that separates P arm from q arm.**

Identification locus on Chromosome

**NARB.S**

**N: Number of chromosome**

**A: P or q arms**

**R: region**

**B: Band**

**S: Sub band**

**18 q 12.2 : Chromosome 18 → Long arm → region 1 → band 2 → sub band 2 .**

**1 p 36.2 → chromosome 1 → short arm → region 3 → band 6 → sub band 2.**

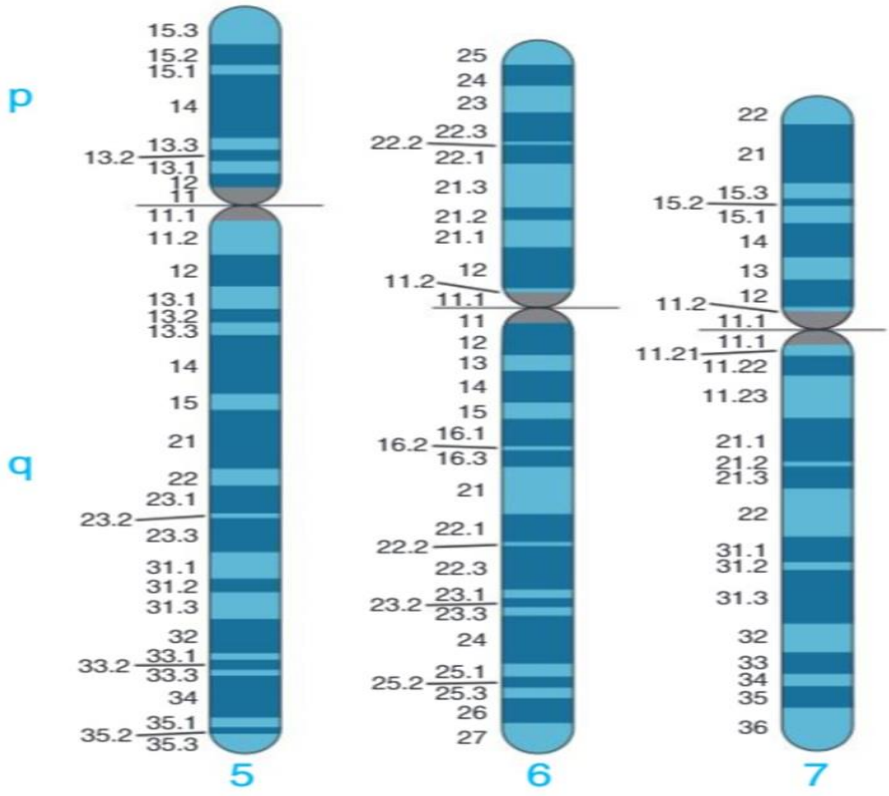



**Figure 5.3** Examples of G-banding patterns for chromosomes 5, 6, and 7 at the 550-band stage of condensation. Band numbers permit unambiguous identification of each G-dark or G-light band. The banding nomenclature indicates the chromosome number (1–22,X,Y), the short arm (p) or long arm (q), the region, band, and subband. For example, chromosome 5p15.2 is pronounced as "5-p-one-five-point-2." (Redrawn from Shaffer LG, McGowan-

Classification of chromosomes based on location of centromere

- **Metacentric** :centromere present at the middle or around near the middle.

- **Sub-metacentric**: centromere Slightly far from the middle.

- **Acrocentric:** centromere is **near** the ends, **chromosome 13 ,14, 15, 21 and 22.**

- **Telocentric:** centromere exactly at the chromosome, there is no P arm, **this type doesn't exist in human, present in mice.**

**Fragile sites**: are heritable variants that Can be observed at particular chromosome sites that are Prone to regional genomic instability induced by stress On DNA replication.) non staining gaps)

At **metaphase**, standard G- banded karyotype shows **400-550** band.

At **pro-metaphase,** by using higher resolution techniques, we can detect **850 band.**

**F**luorescence **in S**itu **H**ybridization (FISH**)**

This technique relies on using **Hybridization.**

**Hybridization:** the process of base- pairing between two single strand nucleic Acids.

In this technique we use **probes.**

**Probe:** oligonucleotides single stranded Nucleic Acid which was labelled using either **radio isotopes** or **Fluoresce dyes.**

This technique has a unique feature, **we can detect a DNA segment within the cell,** without DNA isolation.

This Technique is used to detect **Copy number** within cells.

But this technique **doesn't** allow for efficient analysis of **whole genome.**

The control must be existing, by applying FISH on **Normal individual** to make sure the procedure is correct.

So FISH apply on normal sample (control**)** and tested sample and compare the results with each other.

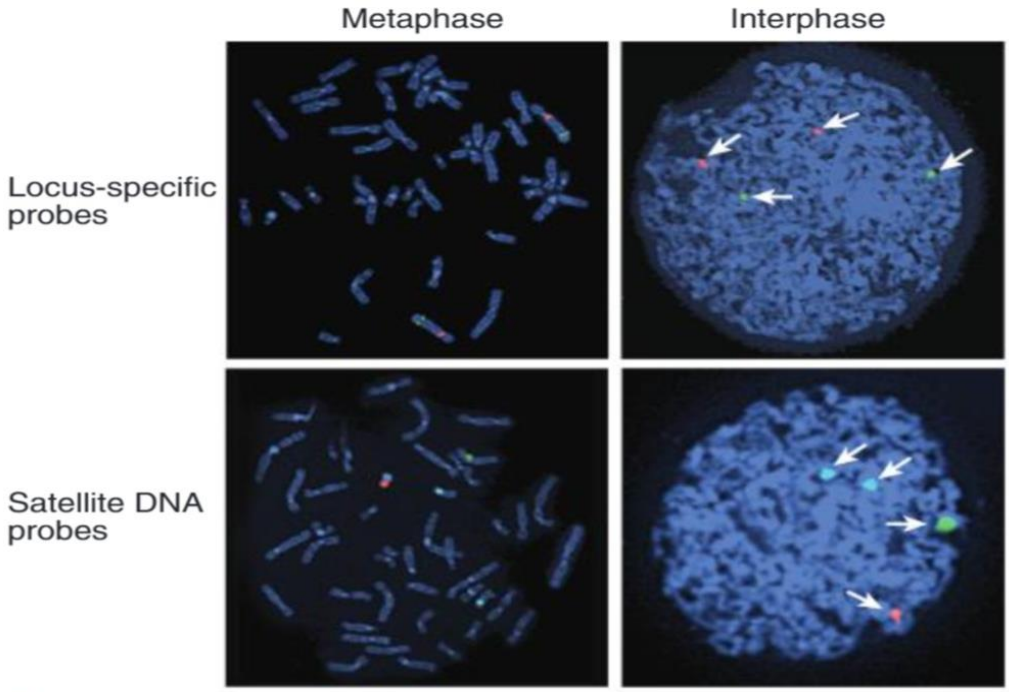



**Figure 5.4** Fluorescence *in situ* hybridization to human chromosomes at metaphase and interphase, with different types of DNA probe. *(Top)* Single-copy DNA probes specific for sequences within bands 4q12 (*red* fluorescence) and 4q31.1 (*green* fluorescence). *(Bottom)* Repetitive α-satellite DNA probes specific for the centromeres of chromosomes 18 *(aqua)*, X *(green)*, and Y *(red)* used to count the number of each chromosome in this individual. (Images courtesy

**M**ultiplex **L**egation Dependent Probe **A**mplification

(**MLPA)**

Exons: **a part of gene that remain after splicing, including coding Sequences and UTR regions.**

Some genes contain 5 exons, other may contain 15, and it doesn't depend on the size of gene, some genes are smaller and have more exons than bigger ones.

**In MLPA, for each exon in target gene we design a different probe.**

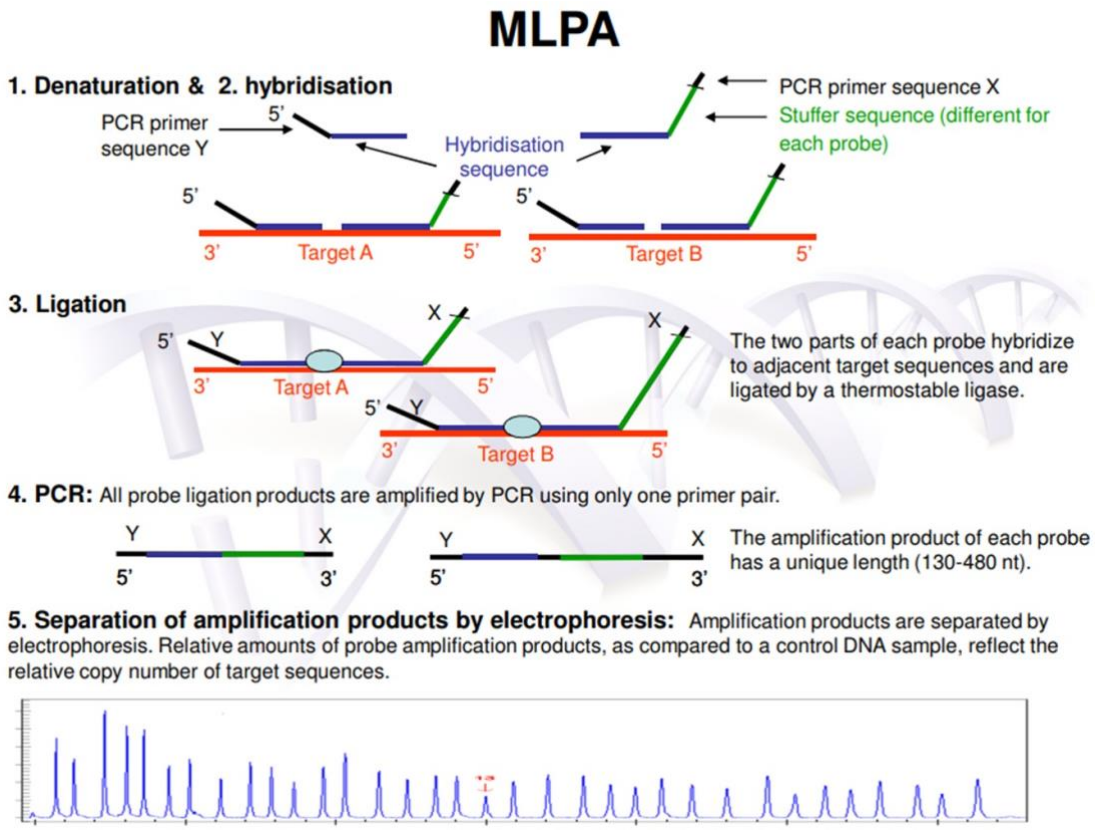
By using **MLPA**, we can detect, **addition, deletion, duplication and copy number Variations**

First step is denaturation of double stranded DNA, then we use a specific a specific ligation **probes, each probe divides into two parts, Part one consists of**

- Reverse primer Sequence **(common in all probes)**
- Stuffer Sequence (different for each probe)
- Hybridization Sequence (different for each probe).

**Part two consists of**

- Forward primer Sequence
- Hybridization Sequence



If the gene contains 60 exons, we design 60 different probe with different hybrid Sequence and different staffer Sequence, **but all the different probes have the same primers.**

**Because all the probes have the same forward and reverse primers this will allow to amplify the 60 exon in the same PCR reaction without using Multiplex PCR (which requires different primers).**

Stuffer Sequence: for single

If we need diagnosis for a certain mutation in a specific Gene the gene contains 50 Exon what we do is design 50 different probes, each exon has a unique probe, if the two parts of probe one bind to exon one **ligase enzyme will seal the gap between the two parts, and then the amplification of exon one is started.**

**What happen if the one part of probe doesn't bind in target exon?**

**There is no Amplification for this exon, in order to achieve amplification both parts must bind.**

**In the case of no amplification this indicate there is a problem in this exon, maybe this exon doesn't exist in the patient genome (it was deleted).**

**After the amplification is completed, the product of amplification is separated using Gel electrophoresis, and then we use a computer software to compare patient sample with control sample (normal sample from normal person),**

Relative amounts of probe amplification products are present as **peaks, each** peak Represents **one exon** these peaks in the

picture for **patient, don’t compare the peak with the next peak in this picture, there is another picture (doesn’t represented in slides) for the control.**

**We compare peak one in patient with peak one in the control, don’t compare peak one in patient with peak two in patient it doesn't mean anything be careful!!**

The intensity of peak related to stuffer Sequence Which Related to how many probe was bound

**Mutations in intron can't detect using MLPA because the probes design to bind with exons.**

**Also if there is a Mutation in intron and cover some part of exon, probe doesn't bind and there is no Amplification for this exon.**

**If the mutation is homozygous Deletion, there is no Amplification for this exon (no peak)**

**If the mutation is heterozygous Deletion, there is half quantity of amplification (peak has half size after compare with control peak).**

**Microarray**

Started from the technique called comparative genomic hybridization.

In comparative genomic hybridization first we isolate chromosomes from the cancer cells and the stain with green color, then we isolate DNA from normal cells and staying with red color ,then we mixed both types to gather.

After that we check how the DNA segments Hybridize together.

If we want to test if the person has a cancer cells or not , we isolate cells , cells preferred be at **metaphase** because the Chromosome

are most visualize at this stage , then person chromosomes were fragmented like the labeled DNA , and we mix the person DNA with labeled DNA , if the Green DNA only Hybridize with person DNA this mean the person is normal , if the red DNA only Hybridize with person DNA this mean the person has **Cancer,** if the person DNA stained with orange , this mean red and green DNA bind with person DNA this mean the person **has normal cells and cancer cells .**

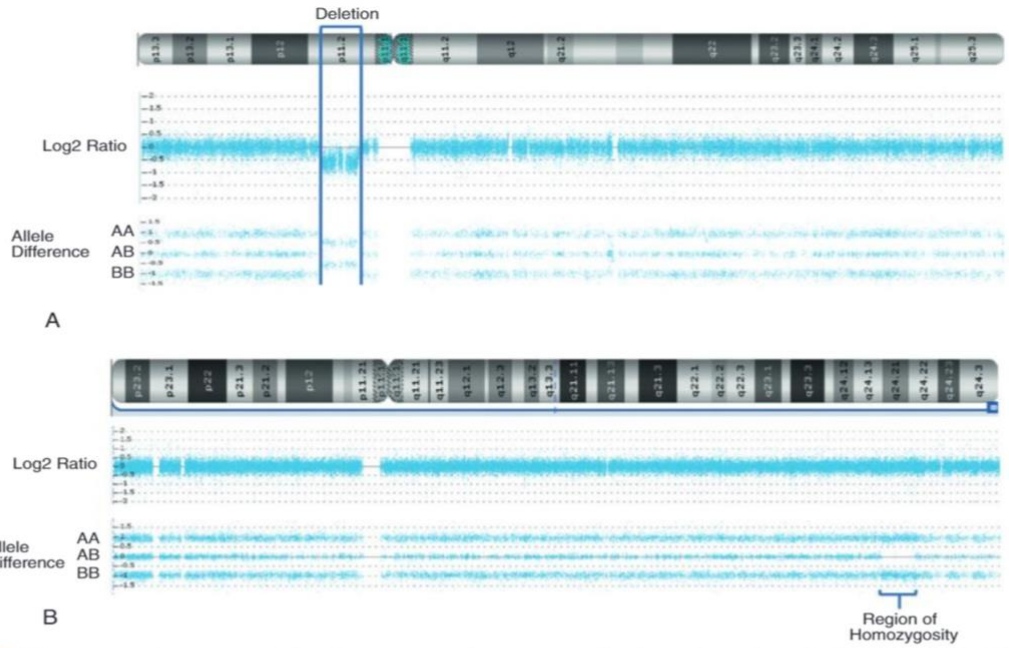



**Figure 5.5** **Chromosome microarray analysis to detect copy number variants and regions of homology.** (A) Chromosome 17: G-banding ideogram, followed by an example of copy number and single nucleotide polymorphism (SNP) microarray output, showing the Log2 ratio of fluorescence intensity and allele difference plots. DNA probes *(blue dots)* with a Log2 ratio of 0 indicate diploid copy number. In chromosome region 17p11.2, consecutive probes with a Log2 ratio of −1 indicate a heterozygous deletion of ~3.7 Mb, associated with Smith-Magenis syndrome. (B) Chromosome 18: SNP microarray output plot showing a region of homozygosity of ~6.052 Mb. The total copy number is unaffected, but the allele difference plot shows a stretch of only homozygous genotypes (AA or BB) with no heterozygous genotypes (AB). (Microarray images courtesy of Genome Diagnostics, The Hospital for Sick Children.)

**MicroarrayMicroarrayMicroarrayMicroarray is similar to comparative genomic hybridization but in smaller scale, by dealing with DNA fragments instead of chromosomes.**

Although we can use **karyotype** to detect some genetic abnormalities related to chromosome but if there is a deletion or another abnormalities **less than 5 million base pairs** we can't detect using karyotype, to solve this problem we use special type of microarray called **chromosome microarray.**

**Chromosome microarray analysis (CMA)** use to detect the copy number Variation (deletion**/ insertion).**

In CMA we use labeled probes and allow them to hybridize with **Query sample (Tested sample), the collected data were compared with reference (control) to detect if there is difference in copy number or not.**

There is another microarray type called **SNP microarray,** this is used to detect the difference between allele, and also use to determine if the person is Homozygous or heterozygous for specific gene.

Long stretches of homologous results from either **consanguinity marriage** or **Uni- parental Disomy) UPD) also** detect using **SNP microarray not copy number array (Chromosome microarray).**

There are two major limitations of microarray

1. Although can detect addition and deletion in Genetic material **it can't detect chromosomal rearrangements without change deletion or insertion in genetic material (balance rearrangement**,) can’t detect translocation and inversion

2. Microarray is sensitive can detect any deletion or insertion even if this is normal and not show clinical significance (doesn’t **related to disease or disorder)**.

**Whole Genome Sequencing (WGS)**

Also called massively parallel Sequencing, it was started before 13 years and required one billion dollars.

First the human genome is isolated and fragmented into smaller DNA fragments **100-500 base pairs** depend on platform.

Millions of DNA fragments have been Sequenced at the same time.

An individual genome is represented by overlapping Sequence reads, with typically **30-40 reads** corresponding to any particular segment of genome (each **DNA fragment Sequence 30-40 time)**

Whole Exome Sequencing (**WES**)

Based on the fact of the most Genetic diseases result from mutation in Exons (approximately 86% of Genetic diseases).

The exons constitute **1.5%** of the human genome, instead of Sequence the whole Genome we focus on Exons only.

**WGS is more accurate to assay Copy Number variation (CNV) than WES.**

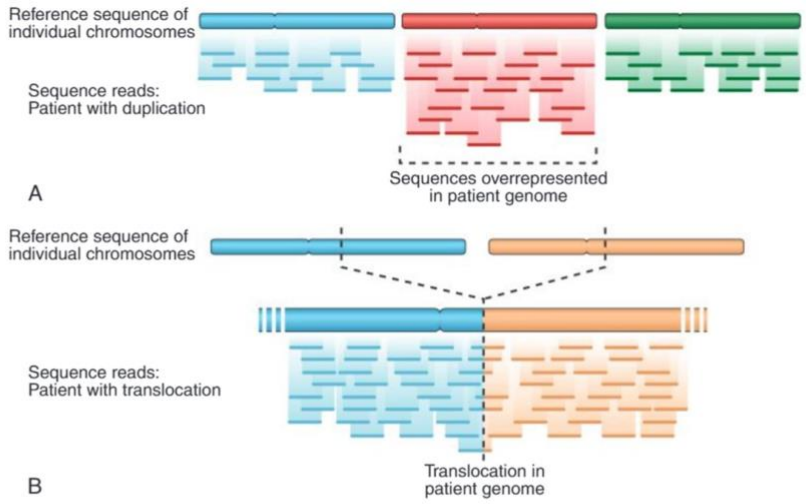



**Figure 5.6** **Strategies for detection of numeric and structural chromosome abnormalities by whole genome sequence analysis.** Although only a small number of reads are illustrated schematically here, in practice, many millions of sequence reads are analyzed and aligned to the reference genome to obtain statistically significant support for a diagnosis of aneuploidy or a structural chromosome abnormality. (A) Alignment of sequence reads from a patient's genome to the reference sequence of three individual chromosomes. Overrepresentation of sequences from the *red* chromosome indicates that the patient is aneuploid for this chromosome. (B) Alignment of sequence reads from a patient's genome to the reference sequence of two chromosomes reveals a number of reads that contain contiguous sequences from *both* chromosomes. This indicates a translocation in the patient's genome involving the *blue* and *orange* chromosomes at the positions designated by the *dotted lines*.

Why **WES** sequencing is less accurate than **WGS?**

The number of reads is less consistent like **WGS,** and sometimes the change occurs in **non coding** regions which can't detect by **WES.**

**WES** doesn't detect balance rearrangement.

**WGS is powerful can't detect all types of changes in human genome.**

**Whole genome sequencing** also used to detect **translocation.**

**Translocation:** exchange DNA fragments from different Chromosomes, it is similar to cross over but the difference **in cross over the exchange occur between homologous chromosomes (Chromosome 1 with chromosome 1 for example), but in translocation the exchange between the different chromosomes (chromosome 3 with Chromosome 5 for example).**

**After using WGS,** we use powerful software to align and link the fragments, in the case of translocation we may find a DNA fragment from chromosome 7 is linked with DNA fragment from Chromosome 12 which is not Happen in the normal cases this indicate **there is a translocation was occurred between the chromosome 7 and 12.**

Translocation consider into **structure abnormalities.**

Structure abnormalities divided into

- **Balance:** equal exchange in genetic material, most time **doesn't cause genetic disorder.**

- **Imbalance:** increase or decrease in genetic material

Genetic disorders Show dosage effect, which mean increase or decrease in genetic material cause a disease.

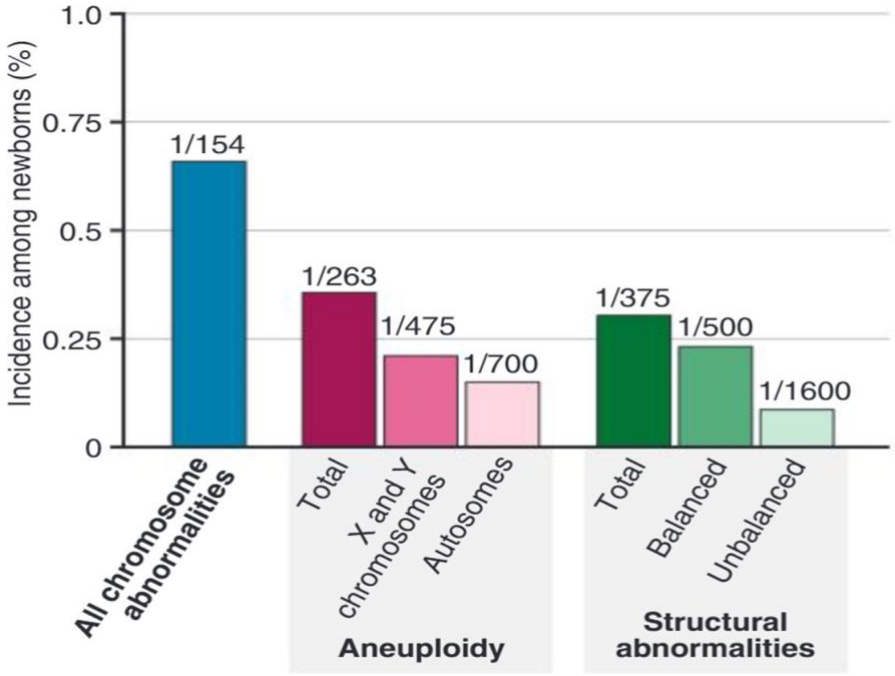



**Figure 5.7** Incidence of chromosome abnormalities in newborn surveys, based on chromosome analysis of over 68,000 newborns.

**TABLE 5.1** Some Abbreviations Used for Description of Chromosomes and Their Abnormalities, With Representative Examples

| Abbreviation | Meaning | Example | Example's Condition |
|---|---|---|---|
| | | 46,XX | Normal female karyotype |
| | | 46,XY | Normal male karyotype |
| arr | Microarray | arr(X,1-22)x2 | Normal female |
| | | arr(X,Y)x1,(1-22)x2 | Normal male |
| | | arr[GRCh38] 8p23.3(835185_1242591)x1 | Deletion in 8p23.3 at genomic position 835185 to 1242591 using Genome Build GRCh38 |
| cen | Centromere | | |
| del | Deletion | 46,XX,del(5)(q13) | Female with terminal deletion of one chromosome 5 distal to band 5q13 |
| der | Derivative chromosome | der(1) | Translocation chromosome derived from chromosome 1 and containing the centromere of chromosome 1 |
| dic | Dicentric chromosome | dic(X;Y) | Translocation chromosome containing the centromeres of both the X and Y chromosomes |
| dup | Duplication | | |
| inv | Inversion | inv(3)(p25q21) | Pericentric inversion of chromosome 3 |
| mar | Marker chromosome | 47,XX,+mar | Female with an extra, unidentified chromosome |
| mat | Maternal origin | arr[GRCh38] 7p22.3(580556_1191665)x3 mat | Maternally inherited duplication in 7p22.3 genomic position 580556 to 1191665 using genome build GRCh38 |
| p | Short arm of chromosome | | |
| pat | Paternal origin | | |
| q | Long arm of chromosome | | |
| r | Ring chromosome | 46,X,r(X) | Female with ring X chromosome |
| rob | Robertsonian translocation | 45,XX,rob(14;21)(q10;q10) | Female with balanced Robertsonian translocation in which breakage and reunion have occurred at band 14q10 and band 21q10 in the centromeric regions of chromosomes 14 and 21; however either rob or der may be used. |
| t | Translocation | 46,XX,t(2;8)(q22;p21) | Female with balanced translocation between chromosomes 2 and 8, with breakpoints in bands 2q22 and 8p21 |
| + | Gain of | 47,XX,+21 | Female with trisomy 21 |
| – | Loss of | 45,XY,–22 | Male with monosomy 22 |
| / | Mosaicism | mos 47,XX,+21[20]/46,XX[10] | Female with two populations of cells, one with trisomy 21 observed in 20 cells, and one with a normal karyotype observed in 10 cells |

Abbreviations from McGowan-Jordan J, Hastings RJ, Adelaide SM editors: *ISCN 2020: an international system for human cytogenetic nomenclature*, Basel, 2020, Karger.

**Signal gene disorders classified into**

- **Qualitative:** some single gene disorders result from **substitution** mutation, which mean there is no increase or decrease in genetic material **Example:** sickle cell anemia

- **Quantitative:** results from increase or decrease in genetic material (Deletion**, insertion, duplication)**

**Generally, the increase in genetic material is less severe than decrease in Genetic material.**

**Heteroploid:** other than 46 chromosomes

**Euploid:** exact multiple of haploid chromosome number (n**), diploid (2n), triploid (3n) and tetraploid (4n).**

**For human, n = 23 Chromosome**

2n= 46, 3n =69, 4n =92

For human, in the case of triploid there is abnormal division and usually abortion.

**Aneuploidy:** any other chromosome number, **monosomy**: 2n-1

,**trisomy:** 2n+1

Trisomy 21: has extra copy of chromosome 21 (total number of Chromosomes= 47) **"down syndrome"**

Monosomy X: has only one copy of chromosome 21 (total number of Chromosomes= 45) " **turner syndrome"**

**Klinefelter syndrome → male with two copies of X chromosome .**

The most autosomal chromosomes compatible with survival until life birth are. **chromosome 21, 13 and 18,** other than aren't survival germy born.

Trisomy 21→ **Down syndrome**

Trisomy 13→ **Patau syndrome**

Trisomy 18→ **Edward syndrome**

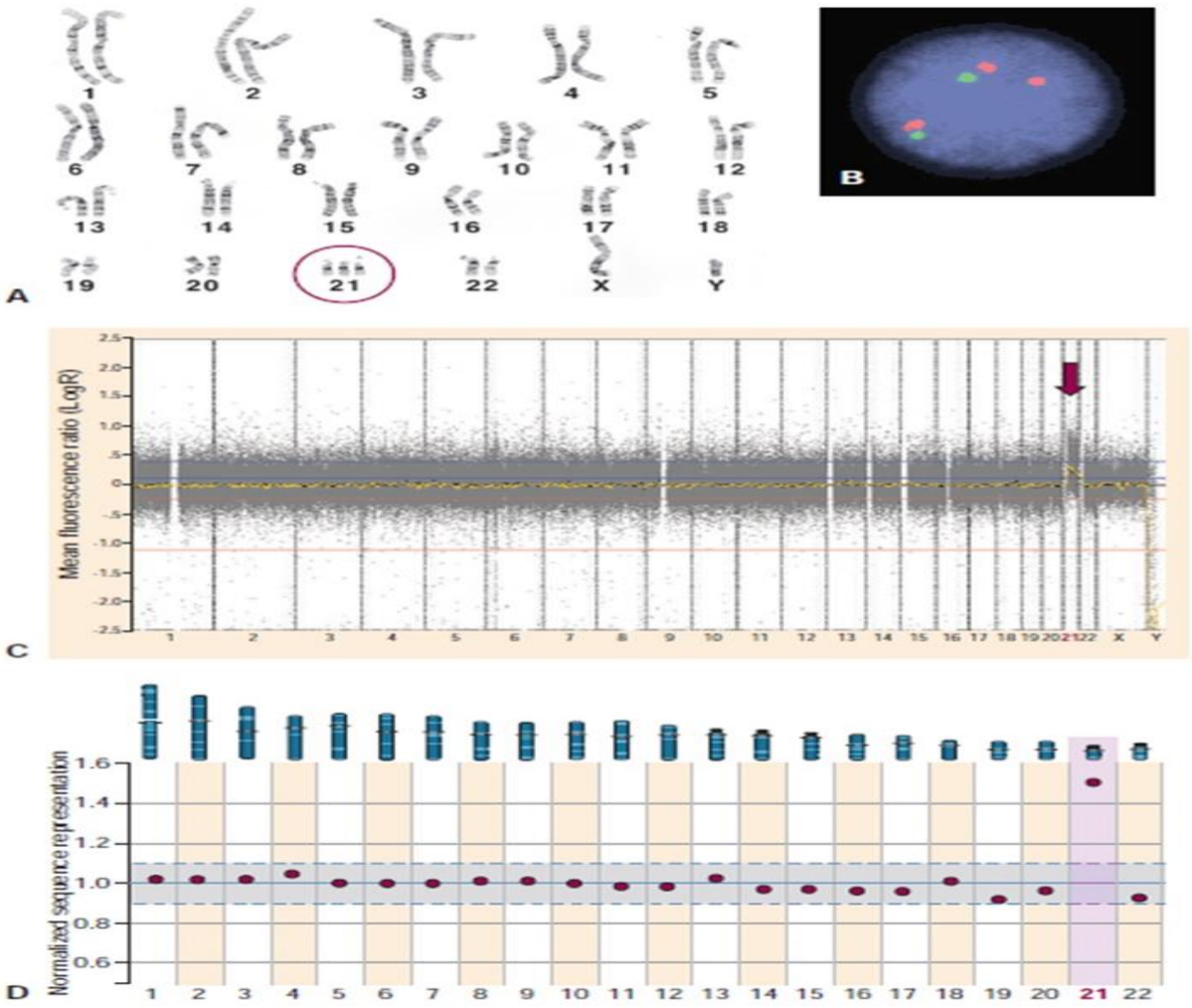
Other than trisomy undergoes spontaneous abortion, even in the **cases of trisomy 21, 13 and 18 only small fraction survive.**

**Monosomy for Autosomal is not compatible with survive.**

**Only monosomy of X Chromosome compatible with survive (XO)**

Detection of down syndrome

- Karyotype
- FISH
- Chromosome microarray
- WGS



**Numerical abnormalities) in the chromosome number)**

The main reason is **Non disjunction** in meiosis.

During meiosis, homologous pairs link together by Synaptonemal complex to prepare homologous pair to cross over, then exchange genetic material after the process is completed the chromosomes must separate from each other.

In **meiosis I**, if the chiasmata still present after the cross over done, the two chromosomes transfer into one gamete(Disomy) and the other Gamete will become empty.

Non disjunction in **meiosis II** give also **Disomy gamete** and empty gamete.

**Disomy gamete obtained from disjunction in meiosis I contains two chromosomes one paternal and the other maternal (from different origin) while the gamete obtained from none disjunction in meiosis II contains two chromosomes from the same parent.**

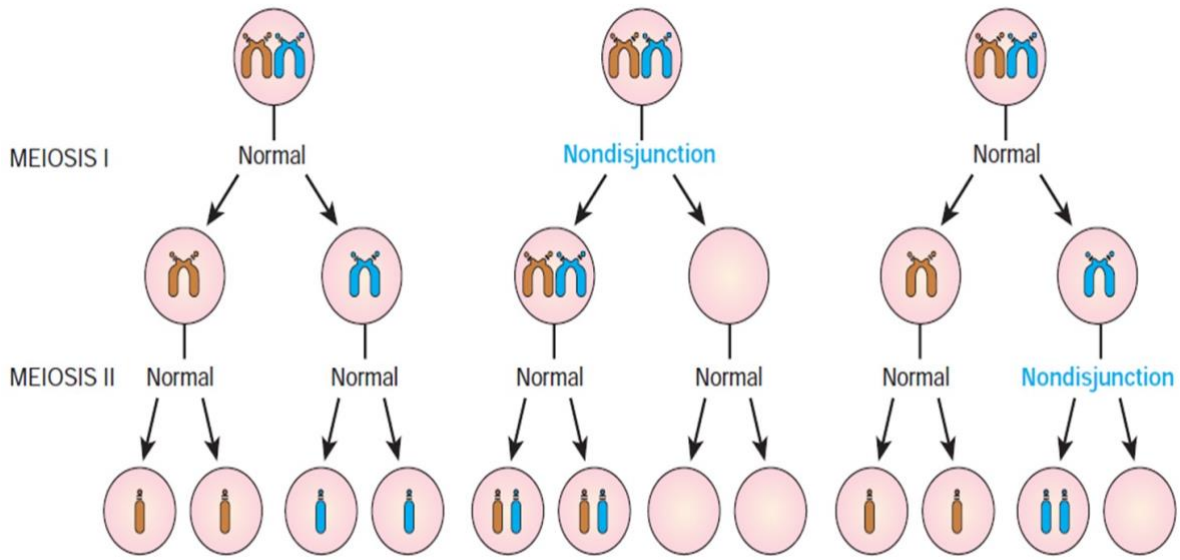



**Figure 5-10** The different consequences of nondisjunction at meiosis I (*center*) and meiosis II (*right*), compared with normal disjunction (*left*). If the error occurs at meiosis I, the gametes either contain a representative of both members of the chromosome 21 pair or lack a chromosome 21 altogether. If nondisjunction occurs at meiosis II, the abnormal gametes contain two copies of one parental chromosome 21 (and no copy of the other) or lack a chromosome 21.

**Structure abnormalities**

- **balance:** no increase or decrease in generic material.
- **Unbalanced:** there is addition or missing genetic material

**1- Un-balanced**

❖ **Deletion**: remove segment from a chromosome.
The consequence of genetic deletion depending on the gene that lost and the quantity of lost genes.

**Haploid insufficient:** one copy of genetic material is present where the other copy was deleted, and the single copy insufficient for normal life.

**Partial monosomy:** when a part of chromosome is deleted there is another part in the homologous Chromosome, so instead of presence of two copies of this segment there is only one copy, and we call it partial because the deletion occur for segment of Chromosome not whole Chromosome was deleted.

❖ **Duplication:** extra copy of chromosomal region (partial **trisomy**).

The consequence is less than partial trisomy, and also the consequence depends on the genes and the quantity of genes that were duplicated.

Some genes are **dose sensitive** must exist in two copies, if there are one copy of them maybe show a genetic disorder, if there are three copies maybe show a genetic disorder.

❖ **Ring chromosome**

Formed when a chromosome undergoes two breaks, and the broken ends of Chromosome reunite in a ring structure.

❖ **Isochromosome**

Is a Chromosome in which one arm is missing and the other duplicated in a mirror-image fashion?

A person with 46 chromosomes carrying an isochromosome therefore has single copy of genetic material for one arm.

**2- Balanced**

Rearrangement in chromosomes without gain or loss in generic material.

**Translocation:** exchange genetic material between non homologous chromosomes.

Sometimes translocation doesn't cause a problem, but sometimes cause a cut in the middle of gene which become defect gene, also it maybe takes the gene from high expression region into low expression region.

Also the cut maybe occurs at regulatory Sequences of gene which disrupt expression process for this gene.

- Reciprocal translocation

  This type of rearrangement results from breakage or recombination involving non homologous chromosomes, with reciprocal Exchange of the broken-off or recombined segments.

  Usually involves Two chromosomes, also the **total** chromosome number and content is unchanged.

  It could be balanced or un-balanced changed.

- Robertsonian Translocations

**The most common of chromosome rearrangements observed in our species.**

Involve two **Acrocentric** chromosomes (13,14,15,21 and 22).

The involved chromosomes fused near the centromere.

This type doesn't involve **reciprocal exchange** which there is a change in the total Chromosome number and content.

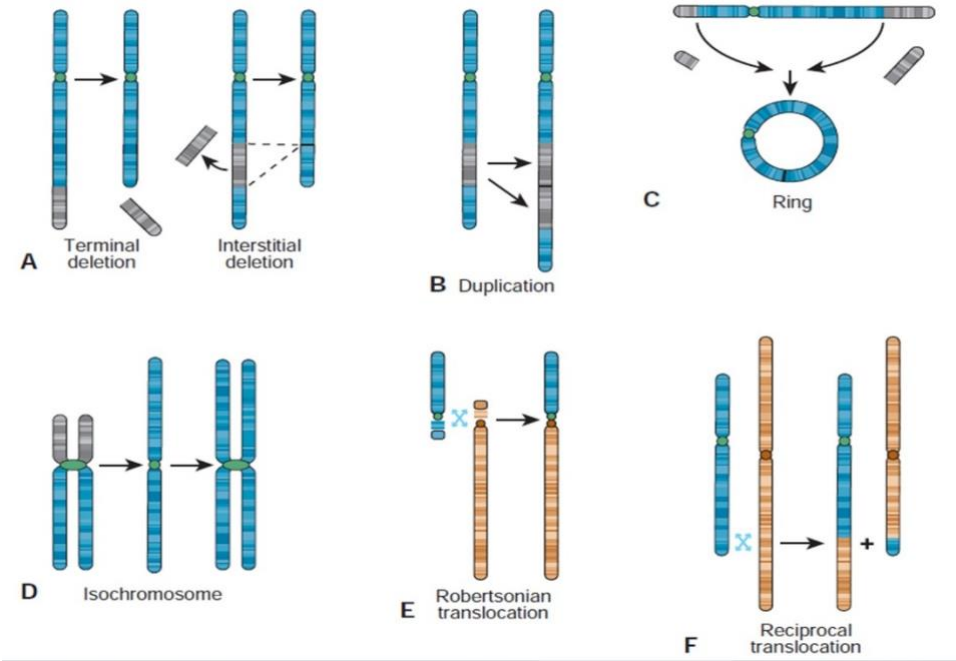
The resulting karyotype has only **45 chromosomes,** but the individual is normal.

The chromosome was obtained from Translocation contained **two long arms (q arm) from different acrocentric chromosomes**

The short arm for the five pairs of acrocentric Chromosomes consist largely of various classes of **satellite DNA,** well as hundreds of copies of ribosomal RNA genes.

Loss of the short arms of two acrocentric chromosomes is not Dangerous.

The Karyotype of Robertsonian translocation is considered balance despite has 45 chromosomes.



**Translocation and Chromosomes separation**

Normally because of the Homologous pair are similar to each other during Meiosis they align to each other in order the similar regions in both chromosomes are faced each to each other this called **bivalent.**

Transplantation could be interfered with **Chromosome separation,** because of the exchange was occurred between different chromosomes lead to **quadrivalent.**

If the separation is **adjacent,** all Gametes will get unbalanced Chromosomes

If the separation is **Alternative** the gametes could get **normal chromosomes or balanced chromosomes.**

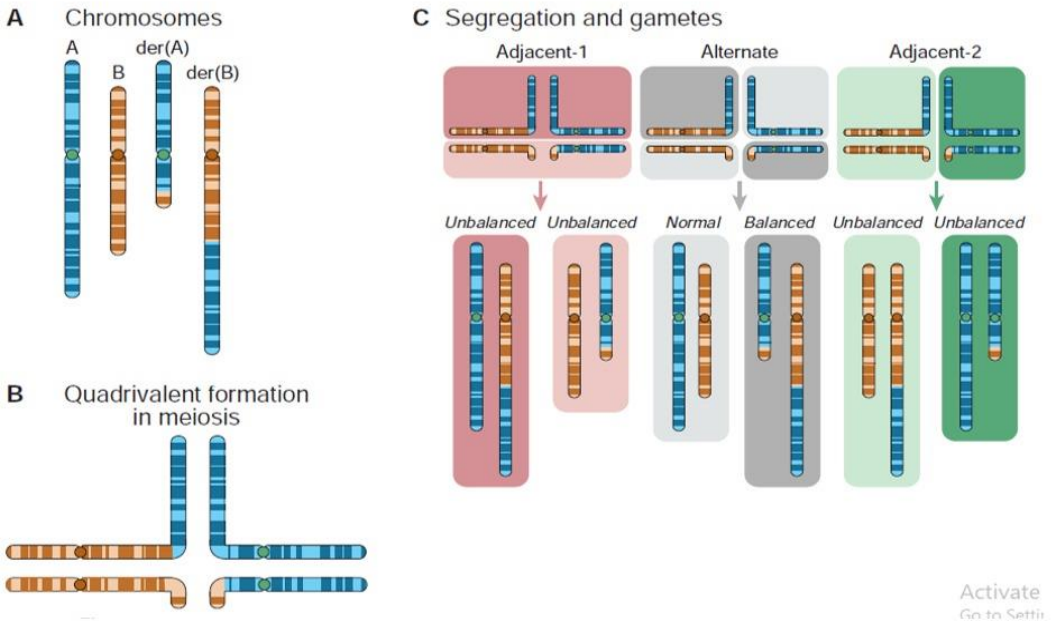



**Figure 5-11**
**A,** Diagram illustrating balanced translocation
**B,** Formation of **quadrivalent** in meiosis
**C,** Patterns of segregation in a translocation carrier

**Inversion**

occurs when a single chromosome undergoes two breaks and is reconstituted with the Segment between the breaks inverted.

There are two types of inversion

- Para centric: doesn't include centromere (location of centromere doesn't change)

- Peri centric: include centromere (location of centromere is changed)

Pericentric is easy to distinguish because the difference in q and P arm.

Para centric produce: **balanced, and invalid** Chromosomes

Invalid include: **Dicentric** (two centromeres) and **Acentric** (no centromeres) Chromosomes.

Peri centric produce: **balanced** and **unbalanced.**

**Para centric is so bad but at the degree is good, the invalid Chromosomes don't reach the gametes, but in peri-centric unbalanced chromosomes could be reach to gamete and transfer into offspring.**

**Mosaicism**

Portion of body cells are normal and the other portion is abnormal.

The portion of abnormal cells depend on at which stage the non-disjunction was happened.

If the non-disjunction occurs at zygote stage this mean the portion of abnormal cells is higher than if was happened at adult stage.

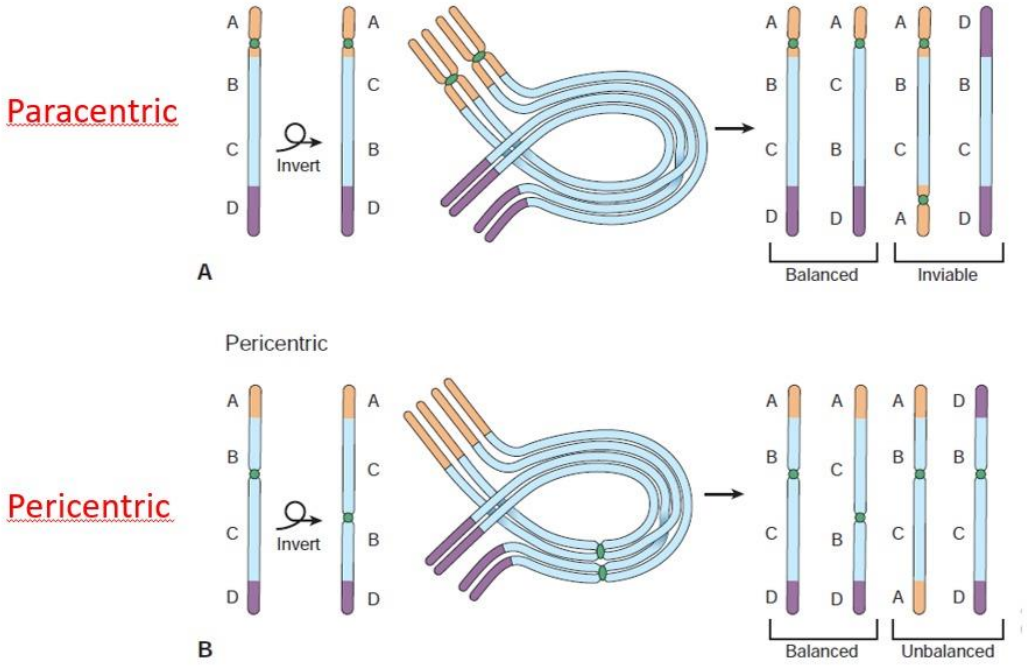



**Figure 5-12** Crossing over within inversion loops formed at meiosis I

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