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Study of Molecular Cytogenetic Analysis to Determine the Genetic Defect of a Patient

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Abstract:- The Chromosomes are the Genetics of heredity. Humans have 23 pairs of Chromosomes in their Cells. As it takes 23 Chromosomes from the Father, and takes 23 Chromosomes from the Mother through Gametes. These Chromosomes are passed down through generations, through a Complex Mechanism. An imbalance occurs in the Chromosomes, through an increase in the Number, Deletion or Addition of genes, which results in Multiple Genetic Diseases. Including this Case, Which Was Exposed to The loss of Chromosome 10q26.13-q26. and the increase in Chromosome 19q13.43.919. This Chromosomal Imbalance Resulted in the following: She has a Beaked nose, Widening of the Base of the Noses, the Upper Lip Is thin, the Eyes are far apart and Strabismus, Body Movement is Generally Slow and Curved Fingers.

***Keywords*:-** *Genetics. Chromosome. Chromosome10. Chromosome19. 10q26.13-q26.3. 19q13.43.9. Interstitial Deletion. Gain.*

I. INTRODUCTION

Man is a living being that consists mainly of the union of a sperm with an egg, which results in the formation of a fertilized egg (zygote), which is divided into several divisions to form an embryo, and after 9 months the newborn sees the light. Human cells contain 23 pairs of Chromosomes. 23 Chromosomes from the Father and 23 Chromosomes from the Mother. Chromosomes are the material of heredity represented in DNA. That is, all phenotypic traits are the result of information that originally existed in the Chromosomes stored in (genes) (1).

There are 22 pairs of autosomal Chromosomes and one pair of sex Chromosomes denoted by the symbol (XY). The female is homologous to the X Chromosome and the Male is heterologous to the XY Chromosome. The sperm contains 23 Chromosomes, and the female contains 23 Chromosomes. After fertilization and formation of the Zygote, it has the full number of Chromosomes (23 pairs of Chromosomes). During the process of zygote division and the formation of cells, each cell resulting from the division has an exact copy, which is 23 pairs of Chromosomes, and this is the Normal state (2).

During the formation of a normal sperm, it must have 23 known Chromosomes, i.e. one Chromosome from each pair of Chromosomes, as well as the egg. But in some cases, as a result of certain conditions, a sperm or egg is produced, there is a decrease or increase in the number of Chromosomes, as well as an increase or decrease in the Chromosome itself. Thus, the result is either an increase or decrease in the genetic material (genes). Any defect in the genetic material (genes) has pathological consequences that differ according to the condition that affects the individual (3).

Some of the diseases that humans are exposed to are in fact caused by a defect in genes, and these diseases differ according to the location of the defect in the genes that are present in the Chromosomes. There are genetic diseases linked to sex, that is, their genes are located on the sex Chromosomes (X or Y), and there are hereditary diseases whose genes are located on the autosomal Chromosomes (4).

There are about three thousand known genetic diseases in humans. Out of every twenty children sent for treatment in British hospitals, one of them was suffering from a disease that was originally attributed to heredity, and among every hundred children two or three children are born, with one of the major fetal deformities, and about 3% of People are born with mental retardation, a high percentage of which is attributed to genetic or embryonic causes (5).

The increase in the number of Chromosomes in the chromosomal formula that determines the type leads to changes in the amount of genetic material, and thus to a clear effect on individuals who have had this increase. Mongolian children have (47) Chromosomes and the extra chromosome is chromosome (21) (6).

A genetic mutation occurs as a result of a sudden change in the genetic material, without going through an intermediate state or prior warning. The occurrence of a specific change in the genetic material, in whole or in part, must be reflected in the person himself, due to changes in the apparent level of the trait that was affected by that mutation (7).

Many diseases and disabilities are attributed to changes that occur in the Chromosomes, such as the loss or addition of an entire chromosome, or a small part of a chromosome. As a result of these chromosomal changes, certain changes appear in the external characteristics of the individual. In Britain, about (500) children are born every year who suffer from various major deformities leading to miscarriage due to the great change in the structure of the fetus's organs (8).

Heredity plays an important role in the incidence of many common diseases such as high blood pressure, heart disease, cancer, diabetes, mental retardation, schizophrenia, and some skin diseases. The infection mainly depends on the

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degree of genetic predisposition that is determined by the genetic factors responsible for determining all physical characteristics, whether those related to the shape of the earlobe, or the length of stature, as well as for determining some mental characteristics (9).

About 20% of miscarriages are due to chromosomal abnormalities. Most of these cases are attributed to the presence of an extra chromosome in the embryonic cells, and a good part is attributed to the loss of the sex chromosome (X) (10).

Many drugs and chemicals increase the possibility of these abnormalities, as studies have shown, on the relationship of contraceptive pills to these abnormalities, in Canada it was found that women who take these pills for six months before pregnancy, their fetuses contain a high rate of chromosomal abnormalities, this often leads to sudden abortion. (11).

The chromosomal composition of the female is (XX) + 44 autosomal Chromosomes, and the male is (XY44 + autosomal Chromosomes). However, sometimes some children are born with more than one X or Y chromosome, and others are born without one of them. Such an unfair distribution occurs during the two processes of formation of cells (sex). Sperm, eggs, and fertilization) (12).

The number of genes in humans is about (30,000) genes, all of which are located in the nucleus of each cell in addition to the mitochondrial genes. The standard unit of the gene is the base pairs (bp), as the amount of haploid genome is estimated at three billion base pairs distributed on Chromosomes, which number in humans (23) pairs, carrying genes that are also in the form of pairs, in addition to the presence of large quantities of enzymes and proteins (13).

Patients with terminal deletion of the long arm of chromosome 10 present with phenotypic manifestations, including facial dysmorphisms, postnatal growth retardation, developmental delay, mental retardation, digital anomalies, cardiac defects, and genitourinary defects. It is an uncommon chromosomal disorder, with most terminal deletions starting at breakpoints in bands 10q25 or 10q26. In contrast to these terminal deletions, interstitial deletions within bands 10q25–10q26.3 are extremely rare and only seven cases have been reported. However, it is unknown whether the phenotypes are different from terminal deletions. Here, we report the first reported case with a *de novo* 10q interstitial deletion, del (10) (q26.1q26.3). In addition to many of the phenotypic anomalies previously described in interstitial 10q cases, our patient presented with cataracts (14).

It is estimated that there are 1.5 million blind children in the world. Cataract is the main cause of treatable blindness in children. Information on the ocular and systemic characteristics of pediatric cataract syndromes is useful for further systematic screening needs and genetic evaluation (15).

- *Objectives*

Many of the diseases that afflict humans, being hereditary diseases, and that these genetic diseases have their causes, this research aims to the following:

- Conducting a genetic analysis to find out the genetic causes that led to the disease.
- Diagnosis of the disease to find out the type of genetic disease that led to this.
- Studying the genes that cause the disease.

II. CASE SUMMARY

The patient, aged 10, is the last child of the sixth child's parents, well contemporaneous, and unrelated. Abnormal birth, without surgery. Birth weight 3.3 kg. At the age of 10, she was 119 cm tall (the normal height for girls is 137 cm) and weighed 21 kg (the normal weight for girls is 32 kg). Since her birth, her mother noticed that she did not respond to external stimuli and the return of activity, and she did not ask for breast-feeding. Development is a global delay. First time at 10 months, crawled at 13 months, stood at 15 months, and walked on her own for the first time at 22 months.The first word she said Baba only once at the age of one year, after 4 months she said Baba and also Mama. In a lifetime you will convert only 10 words. She was admitted to the specialized center to teach her some basic behavioral skills. Specialized center to teach her some basic behavioral skills and a speech delay has been observed since then, limited to a few words. Moreover, verbal comprehension is more than common verbal instructions. She has a prominent nose, a broad nasal bridge, a thin upper lip, spaced eyes (hypertelorism) that do not look in the same direction (strabismus), limited movement in the elbows or other joints, AND curved fifth fingers. At the birth of the case, her mother was 39 years old, and her father was 49 years old.

III. MATERIALS AND METHODS

After approval of the genetic analysis of the sick girl, by the parents .5 ml of blood was drawn through the vein. The sample was prepared and Molecular Cytogenetic Analysis was performed. to detect genomic imbalances (gains/losses) on the whole genome .A high-resolution microarray-based comparative genomic hybridization analysis was performed; its Array CGH was performed using the customized human genomic microarrays . The analysis compared the DNA of patients with a reference DNA sample (female) from karyotypically inconspicuous individuals.

IV. RESULTS

- *The patient's blood was drawn intravenously. The required cytogenetic analysis was performed on the sample. The results showed that there are two imbalances:*

- A reduced dosage of genomic material in terms of a terminal deletion on the arm of chromosome 10(q26.13-q26.3.

- An increased dosage of genomic material in terms of a terminal duplication on the long arm of chromosome 19 (q13.43).

- *10q26.13-Q26.3 (77 Genes):*

CPXM2 SHCT15 OAT NKX1-2 LHPP FAM53B METTL10 FAM53B METTL10 FAM175B ZRANB1 CTBP2 MIR4296 TEX36-AS1 TEX36 LOC283038 FLJ37035 EDRF1 MMP21 UROS MIR4484 BCCIP DHX32 FANK1 FANK1-AS1 ADAM12 LINC00601 C10or/90 DOCK1 FAM196A NPS FOX12 CLRN3 PTPRE MK167 MGMT EBF3 MIR4297 LINC00959 CATAGE7P GLRX3 MIR378C TCEG1L LIN01164 PPP2R2D BNPI3JAKMIP3 DPYSL4 STK32C LRRC27 PWWP2B C10or/91 INPP5A NKX6-2 TTC40 LINC01168 LOC100128127 GPR123 KNDC1 UTF1 VENTX MIR202HG MIR202 ADAM8 TUBGCP2 ZNF511 CAL PRAP1 FUOM ECHS1 MIR3944 PAOX MTG1 SPRN SCART1 CYP2E1 SYCE1 SPRNP1 FRG2B.

- *19q13.43 (37 Genes*:)

ZNF417 ZNF418 ZNF256 C19orf18 ZNF606 LOC100128398 ZSCAN1 ZNF135 ZSCAN18 ZNF329 ZNF274 ZNF544 ZNF8 ZSCAN22 MIR6806 A1BG ZNF497 ZNF837 MIR4754 RPS5 LOC646862 ZNF584 ZNF132 ZNF324B ZNF324 ZNF446 SLC27A5 ZBTB45 TRIM28 MIR6807 CHMP2A UBE2M LOC100131691 MZF1 CENPBD1P.

V. DISCUSSION

The Region No. 1 unbalance (see Fig.1 <A>) spans the critical range Contiguous gene 10q26 deletion syndrome (OMIM 609625). Common features in patients with such a deletion are growth retardation, developmental delay, widely varying degrees of mental retardation (MR), behavioral problems, craniofacial abnormalities (eg, prominent bridge of the nose), strabismus, digital abnormalities, and hypotension. Heart defects, hearing loss and urinary reflux/hydronephrosis have been described in a few cases. Genital abnormalities have been reported mainly in males. Bladder distention can occur in women. The genes CLAY (calcyon neuron-specific vesicular protein) and DOCK1 (dedicator of cytokines 1) have been proposed as candidate genes for the behavioral and learning disabilities of 10q26 deletion syndrome.

The defect (loss) was in chromosome 19, which was taken either from the mother or the father, but we do not know specifically if it was from the father or from the mother. The occurrence of mutations is due to several reasons, and the incidence of mutations is large, in case the mother is old. If the deficiency is small, it cannot be felt, but if it is large, it may lead to the emergence of an abnormal individual (because it leads to a decrease in the genetic makeup - the genetic content of the individual). The deletion and loss of 77 genes from chromosome 19 is considered a major loss, and this is what happened to the case (16).

Three rare prenatal cases with pure 19q microduplications involving 19q13.42, ranging from 147 kb to 1.445 Mb, which presented no structural abnormalities in sonographic examination. Case 2 was proved to get the 19q13.42 duplication from the healthy mother. To the best of our knowledge, just five cases with prenatally diagnosed trisomy 19q had been described before, and only one case was involved in 19q microduplications. Currently, there is a lack of prenatal manifestations about this chromosomal microscopic imbalance. In our study, all fetuses with various 19q duplicated loci showed no structural anomalies in pregnancy, which were different from previous trisomy 19q cases and enriched the clinic phenotypes of 19q (17).

RECOMMENDATIONS

➢ *There are Many Recommendations, the Main Ones are:*

- Carrying out genetic analyzes in people with hereditary diseases.
- Genetic testing of people willing to marry, especially in the case of blood relatives.
- Creation of a bank of genetic information for each individual (pedigree).
- Encourage people in society to marry early and avoid consanguinity.
- Create modern genetic analysis laboratories.
- Raising media awareness through seminars and conferences on hereditary diseases.

➢ *Tables and Figures*

Table 1 Shows the Genetic Defect in Chromosome 10 and Chromosome 19

S No	Chrom Region	Type of Imbalance	Approx Size	ISCN(2013)* Nucleotide Position According To NCBI Build 36.1	Affected Refseq Genes	Significance for the Phenotype
1	10q26.13-q26.3	loss	9.872 kb	Arr(hg18) 10q26.13q26.3(125,542,526-135,324.777)*1	77 See gene list	yes
2	19q13.43	gain	691 kb	Arr(hg18) 19q13.43(63,093,126-63,784,382)*3	37 See gene list	probably

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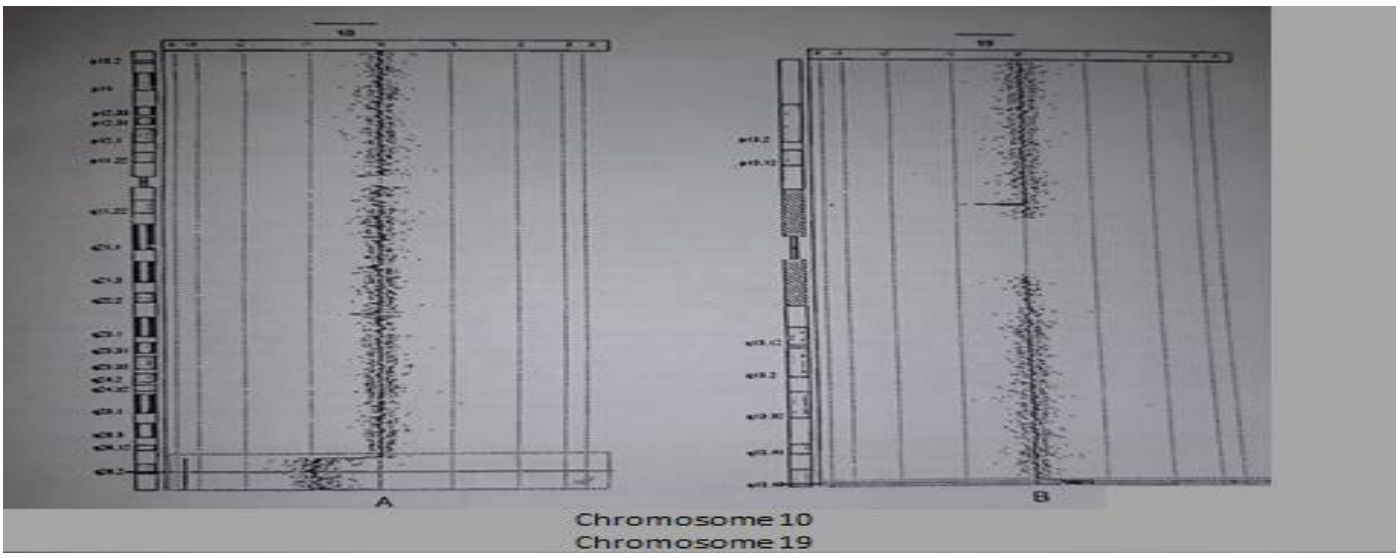

Fig 1 Molecular cytogenetic (array CGH) findings in the index case: (A) array CGH demonstrating arr 10q26.13-Q26.3: and (B) Array CGH demonstrating arr 19q13.43

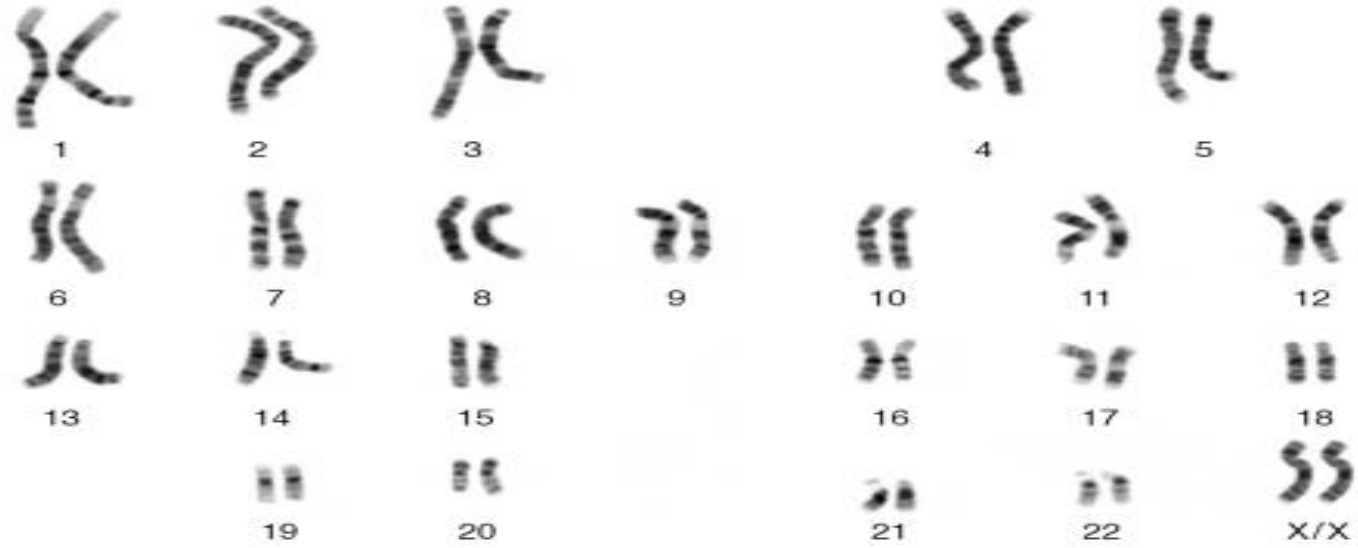

Fig 2 Human Chromosomes (18)

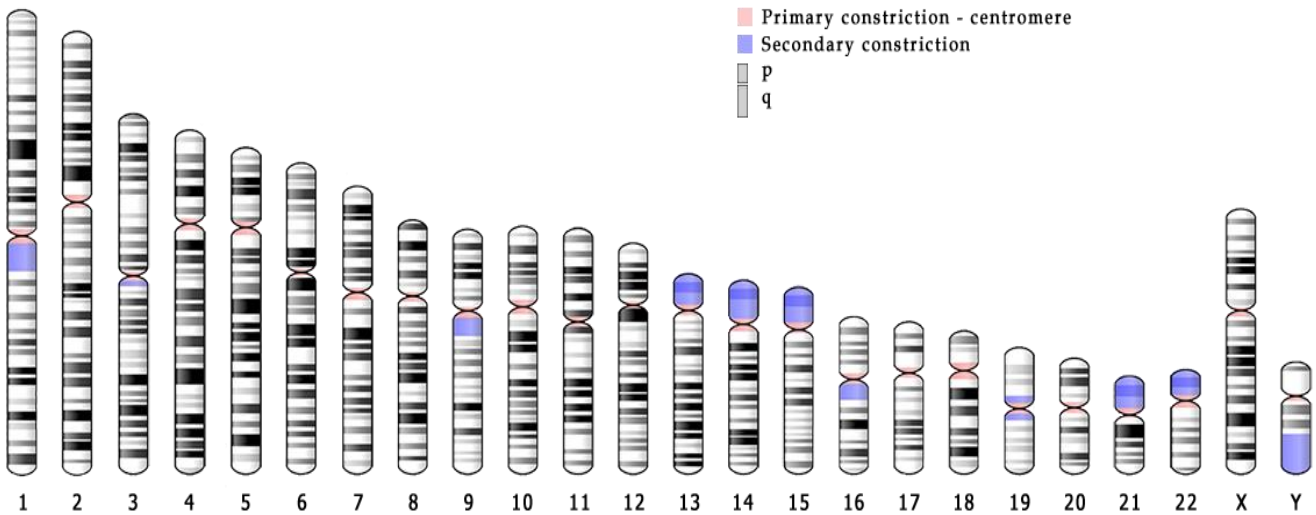

Fig 3 Human Chromosomes Ideogram (Schematic Representation of Chromosomes) (19)

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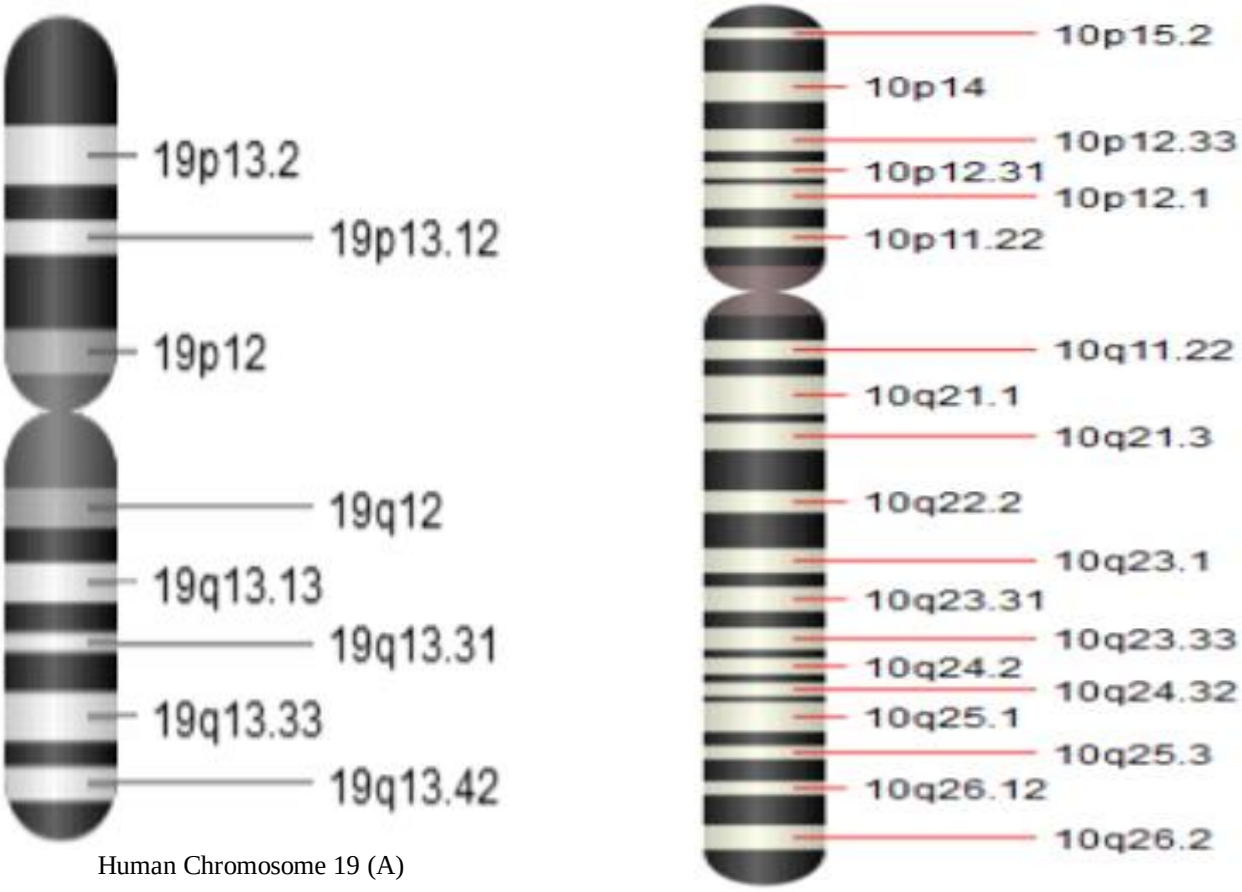

Human Chromosome 19 (A)

Human Chromosome10 (B)

Fig 4 (A)Human Chromosome19&(B)Chromosome10 Cytogenetic Locations(20)

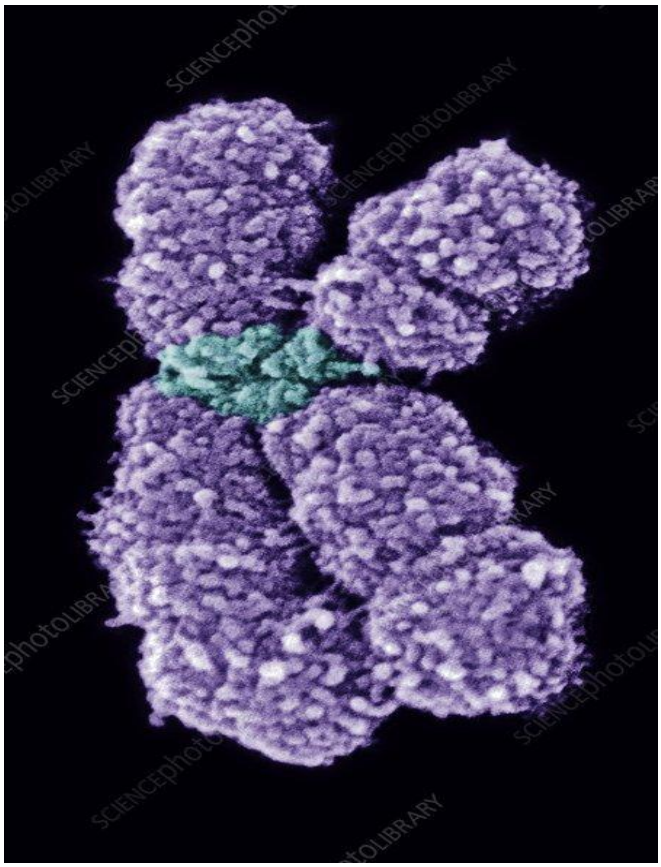

Fig 5 Human Chromosome 10 (21**)**

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