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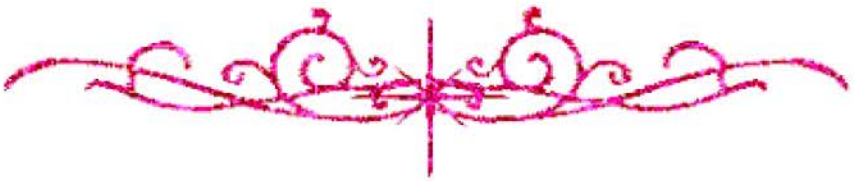
شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم



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جامعة عين شمس

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قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها

علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

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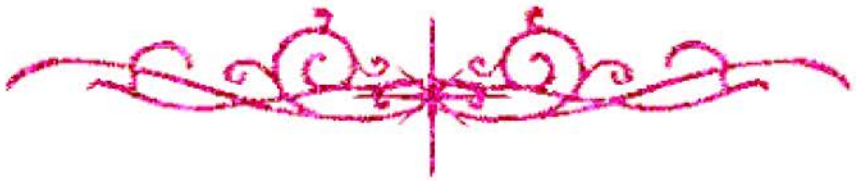
بعض الوثائق الأصلية تالفة



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بالرسالة صفحات

لم ترد بالأصل

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HUMAN CHROMOSOMES AND SOME OF THEIR MUTATIONS

THESIS

Submitted for partial fulfillment of M.D. Degree in Histology and Genetics

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Contents

INTRODUCTION

Introduction

Genetics is the science of the study of heredity and cytogenetics is the study of chromosomes. Before 1956, the chromosome number was believed to be 48 until the use of hypotonic solution allowed Tjio and Levan to discover that the human chromosome number is 46, instead of being 48 (Tjio, 1978; Levan, 1978). The XX and XY mechanism of sex determination was also described. Thus, the year 1956 is often given as the beginning of modern human cytogenetics.

The field of cytogenetics was classified by Hsu (1979) into four eras: the dark ages before 1952, the hypotonic period from 1952 to about 1958, the trisomy period between 1959 and 1969, and the chromosome banding era that started in 1970 to present along with more advanced and more selective techniques in the molecular biological studies of cytogenetics.

1-Dark Era: During this period, tissue culture techniques were satisfactory to obtain mammalian chromosomes to study. Despite the primitive techniques available, the groundwork for future studies was laid during these dark ages. The first technique was by squashing tumor cells from ascites fluid found in the mouse (Levan and Haushka, 1952; 1953) and of the rat

(Makino, 1957). Bayreuther (1952) performed the first successful treatment with chemical substances to improve chromosome visibility in mouse tumor cells. Early studies with these crude techniques confirmed that human chromosomes, like those of other organisms, showed segmental differences in their staining. This pattern of darkly stained heterochromatin and lightly stained euchromatin made it possible to distinguish specific chromosomes form one another. Later, colchicine or its derivatives, which arrest cells in metaphase of cell division, were used to make it easier for researchers to collect data on large number of dividing cells. During this era, standard mammalian tissue culture techniques were developed (Therman and Susman, 1993).

2-The Hypotonic Era: Prefixation treatment with hypotonic salt solution, which swells the cells and thus separates the chromosomes, was a decisive improvement in cytological techniques. The hypotonic treatment was launched by Hsu (1952). During the hypotonic era, the analysis of the human karyotype or collection of chromosomes from one cell, led to the ability to distinguish each of the human chromosomes from the other.

3-Trisomy Period: The new techniques were soon applied to chromosome analysis of individuals who were mentally retarded or had other congenital anomalies. The first autosomal trisomy was Down syndrome first described by Lejeune et al. (1959), and was caused by the presence of three copies of one of the smallest human chromosomes (i.e. chromosome 21). During the same year it was reported that females with abnormal sexual development with Turner syndrome were found to have an abnormal sex chromosome constitution. They had only one X and only 45 chromosome, and no Y chromosome in each cell (Ford et al., 1959). That same year, abnormal males with Klinefelter syndrome were found to have two X chromosomes and one Y chromosome in each cell (Jacobs et al., 1959). These observations on Turner and Klinefelter syndromes showed that sex determination in humans occurred by the presence of the Y-chromosome. Later it was established that the Y-chromosome was effective in determining male sex even if it is combined with four X-chromosomes. During the following years other trisomies were described including trisomy 13 (Patau et al., 1960) and trisomy 18 (Edward et al., 1960; Smith et al., 1960).

4-Chromosome Banding Era: The first attempts to differentiate the human chromosomes included sorting them into seven groups on the basis of their

length and morphology (Patau, 1960). In 1970, Casperson et al., applied fluorescence staining and microscopy to analyze the individual human chromosomes. They discovered that the chromosomes consisted of differentially fluorescent cross bands of various widths. This discovery was followed by a flood of different banding techniques that utilized either fluorescent dyes, enzyme treatment and Giemsa stain (Drets and Shaw, 1971). Later, the banding of chromosomes made it possible to determine chromosome segments and break points even more accurately (Yunis, 1976) leading to its usefulness in the medical practice of testing patients with birth defects and in the study of cancer. In addition, Levitan performed experiments with Drosophila, and revealed that inheritance is particulate and that only a small piece of a chromosome was responsible for each trait, Levitan (1988). This investigator also added that the smallest unit of cytogenetics is the gene.

AIM OF THE WORK