شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الالكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها
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بالرسالة صفحات لم ترد بالاصل

STUDY OF SERUM ANTI-P53 AUTOANTIBODIES AND SIALIC ACID AS EARLY DIAGNOSTIC MARKERS IN TOBACCO SMOKERS WITH LUNG CANCER

Thesis

Submitted for partial fulfillment of the M.Sc. degree in the
Medical Biochemistry

By

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بسم الله الرحمن الرحيم

(قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَآ إِلاَّ مَا عَلَّمْتَنَآ إِنَّكَ أَنْتَ الْعَلِيمُ الْحَكِيمُ)

[سورة: البقرة – الآية: ٣٢]

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INTRODUCTION

Introduction

At the beginning of this millennium, lung cancer is the most frequently diagnosed cancer world wide being the most aggressive type of cancer; it is responsible for more cancer related death than other tumors.[1,2] For the last several decades, the incidence of lung cancer has been rising dramatically [2] . Over 20.000 case of lung cancer have been recorded every year in the United States (US), which constitute a major problem in oncological practice.[3] The economic costs of lung cancer are enormous adding to its major public health problem.[4] Only one in ten patients diagnosed with this disease will survive the following 5 years.[5]

Tobacco smoking has been identified as a major risk factor for the development of this cancer. Although lung cancer was previously an illness that affected predominately men, the lung cancer rate for women has been increasing in the last few decades, which has been attributed to the rising ratio of female to male smokers.[3]

Overall, recent studies show that the risk of death from lung cancer in smokers of two or more packs of cigarettes per day is about 20 times that of non-smokers.[6] Several mechanisms are addressed for the explanation of underlying molecular basis of smoking induced carcinogenesis including formation of DNA and protein adducts, base mutation and oxidative damage to DNA.[7]

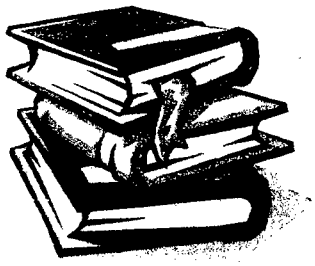
Oncogenesis is now generally accepted to be the result of complex biological processes involving many genes that regulate different cellular activities including cell growth and/or cell death.[8] Different types of genetic instabilities have been described thus far in human tumors, including numerous genetic changes at both chromosomal and nucleotide levels.[9]

Cancer evolves from the accumulation of mutation and the subsequent deregulation of two classes of genes; oncogenes and tumor suppressor genes.[10] Tumor suppressors are genes whose products act to control cell division. A key to understand tumor suppressors is that it is the loss of function of these genes that lead to carcinogenesis.[10] A number of tumor suppressor genes have been identified namely P53 (TP53), Rb, APC_3, and BRCA.[10,11,12]

The P53 gene was discovered in 1979 and has emerged as one of the most important cancer related genes to date.[11] The gene is located on chromosome 17 and produces a protein product that functions as a transcription factor. The genes controlled by P53 are involved in cell division and viability. Like other tumor suppressors, the P53 protein functions to prevent unregulated cell growth.[12]

Mutations of P53 have been reported to be associated with accumulation of the mutated P53 protein and subsequent production of auto-antibodies against these proteins.[12] These anti-P53 auto-antibodies have been detected in sera of patients with different types of cancer.[13]

Sialic acid is a member of a family of N-and O-acetyl derivatives of neuraminic acid and widely distributed in mammals. It usually occurs as a terminal component at the non-reducing end of carbohydrate chains of glycoproteins and glycolipids and is thought to be involved in receptor function [14] , cell recognitions and immunological reactions, it also accounts for 70-80 % of the total surface negativity in a variety of cell types.[15] Sialic acid is increased in the serum of tumor-bearing humans and animals, and thus is a probable indicator of malignant tumor growth.[16]



REVIEW OF LITERATURE

The cell cycle

The cell cycle, or cell-division cycle (CDC), is the series of events in eukaryotic cells between one cell division and the next . [17]

The cell cycle consists of four distinct phases: G_1 phase, S phase, G_2 phase (collectively known as interphase) and M phase. M phase is itself composed of two tightly coupled processes: mitosis, in which the cell's chromosomes are divided between the two daughter cells, and cytokinesis, in which the cell's cytoplasm physically divides. Cells that have temporarily or reversibly stopped dividing are said to have entered a state of quiescence called G_0 phase, while cells that have permanently stopped dividing due to age or accumulated DNA damage are said to be senescent. Some cell types in mature organisms, such as neurons, enter the G_0 phase semi-permanently and can only be induced to begin dividing again under very specific circumstances; other types, such as epithelial cells, continue to divide throughout an organism's life. [17]

The molecular events that control the cell cycle are ordered and directional; that is, each process occurs in a sequential fashion and it is impossible to "reverse" the cycle. There are two key classes of regulatory molecules that determine a cell's progress through the cell cycle: cyclins and cyclin-dependent kinases. [18]