p53 TUMOUR SUPPRESSOR GENE IN LUNG CANCER

THESIS

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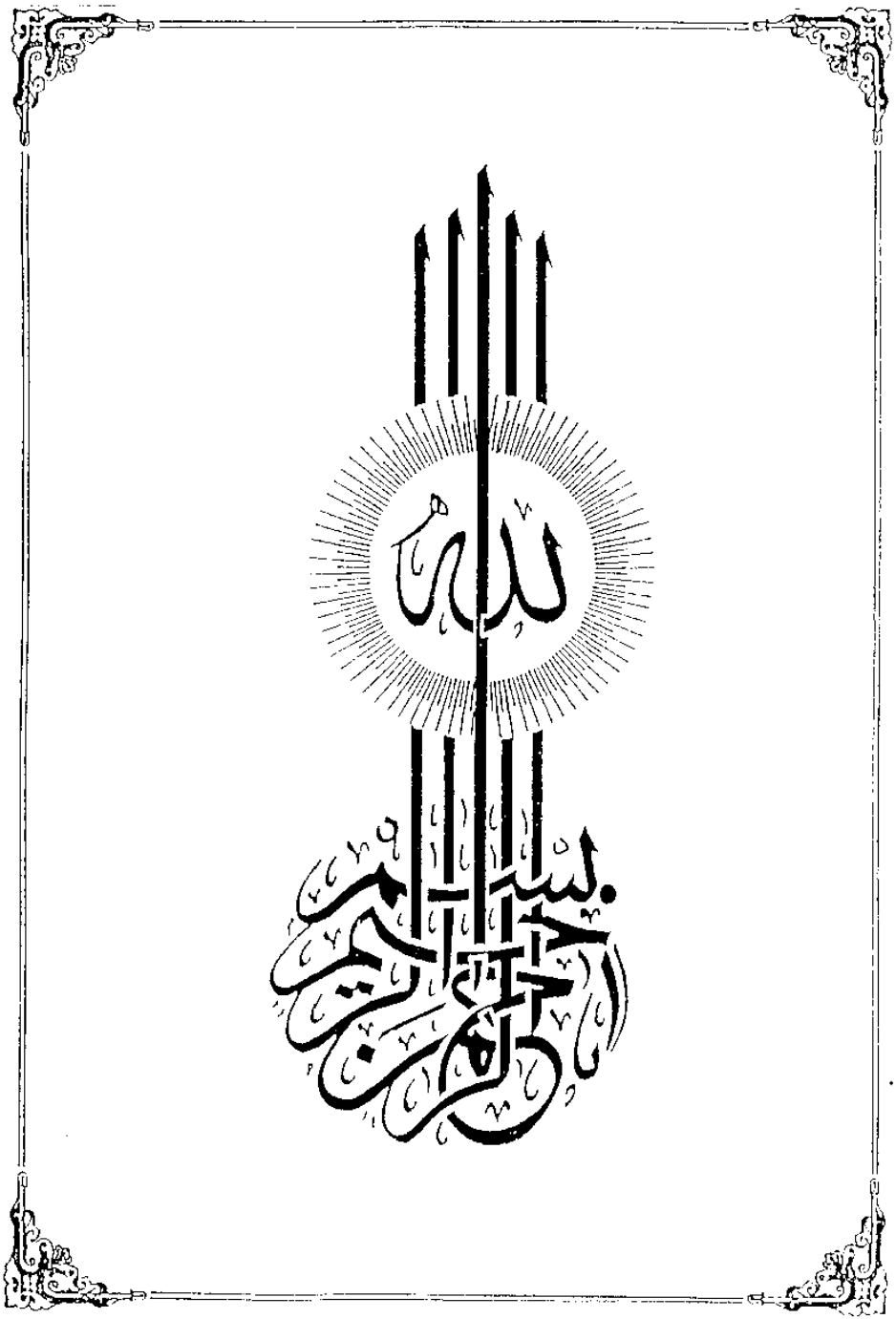

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LIST OF ABBREVIATIONS

A	Adenine
bp	Base Pair
BP	Benzo Pyrene
BSC	Best Supportive Care
C	Cytosine
CEA	Carcinoembryonic antigen
CT	Computed Tomography
ddNTP	Dideoxynucleotide
DNA	Deoxyribonucleic Acid
DNAB	DNA Binding Proteins
dNTP	Deoxynucleotide
EBV	Epestien-Barr Virus
EGF	Epidermal Growth Factor
EGFR	Epidermal Growth Factor Receptor
erb-B	Avian Erythroblastosis Virus
fos	FBJ Osteosarcoma Virus
Fu	fluorouracil
G	Guanine
GF	Growth Factor
GFR	Growth Factor Receptor
GP	G protein
GRP	Gastrin Releasing Peptide
HPD	Haematoporphyrin Derivative
HPV	Human Papilloma Virus
H-ras	Harvey Murine Sarcoma
jun	Avian Sarcoma Virus 17
K-ras	Kirsten Murine Sarcoma
LFS	Li-Fraumeni Syndrome
LT	Large Tumour antigen

mdm 2	Murine double minute 2 gene
MER	Methanol extractable residue
MRI	Magnetic Resonance Imaging
myb	Avian Myeloblastosis Virus
myc	Avian Myelocytomatosis Virus
Nd-YAG0	Neodymium Yttrium-aluminium garnet
NSCLC	Non Small Cell Lung Cancer
NSE	Neuron Specific Enolase
PBS	Post-Bronchoscopy Sputum
PCF	Prophylactic Cranial Irradiation
PCR	Polymerase Chain Reaction
PDGF	Platelet Derived Growth Factor
PFNA	Percutaneous Fine Needle Aspiration
P-Gp	P-glycoprotein
PK	Protein Kinase
PS	Performance Status
Rb	Retinoblastoma
RNA	Ribonucleic Acid
SCLC	Small cell Lung Cancer
SIAD	Syndrome of Inappropriate Antidieuretic Hormone secretion
SSCP	Single Strand Conformation Polymorphism
sT	Small Tumour antigen
SV40	Simian Virus 40
SVC	Superior Vena Cava
T	Thymine
T antigen	Tumour antigen
WT-1	Wilms' Tumour gene

Introduction and Aim of The Work

Introduction

Less than a century ago, lung cancer was a medical curiosity *(Osler, 1982)*. Today, it is the seventh most common tumour in Egypt, contributing 2.8% of all cancers and it is on the increase *(El-Bolkainy, 1991)*. In western countries, it is considered as the first oncological problem with frequency of about 16% of all cancers *(Silverberg et al., 1990)*.

Inspite of the improvement in diagnostic procedures and treatment approaches of lung cancer, most patients still die suffering from this disease *(Fisher and Scoggin, 1986)*. However, progress in the science of molecular biology has reached a point where it can provide a basis for new strategies in the prevention, diagnosis and treatment of this disease *(Minna et al., 1986 ; Minna et al., 1990)*.

It is now clear that cancer is caused by the malfunction of genes that regulate cell proliferation. Two kinds of regulatory genes have been discovered. Those that promote growth of cells, called oncogenes, and those that suppress growth, called anti-oncogenes or tumour suppressor genes *(Yarbo, 1992)*. Accumulating evidence indicates that changes in both oncogenes and tumour suppressor genes are necessary for malignant transformation of normal bronchial epithelial cells *(Suzuki et al., 1992)*.

One of the most important tumour suppressor genes involved in the pathogenesis of lung cancer is the gene coding for protein called the p53 gene *(Levine et al., 1991)*. Different studies

revealed that mutations of this p53 gene occur in many tumours including lung cancers *(Miller et al., 1992)*, and that p53 mutations were the most frequent alterations found in lung cancer *(Zalcman et al., 1994)*.

Aim of the work

To evaluate and screen for p53 mutations in bronchoscopic bronchial specimens from patients with bronchogenic carcinoma and bronchial dysplasia and to correlate this with their clinicopathological data.