Evaluation of the diagnostic potential of some biochemical and molecular markers in early detection of chronic obstructive pulmonary disease

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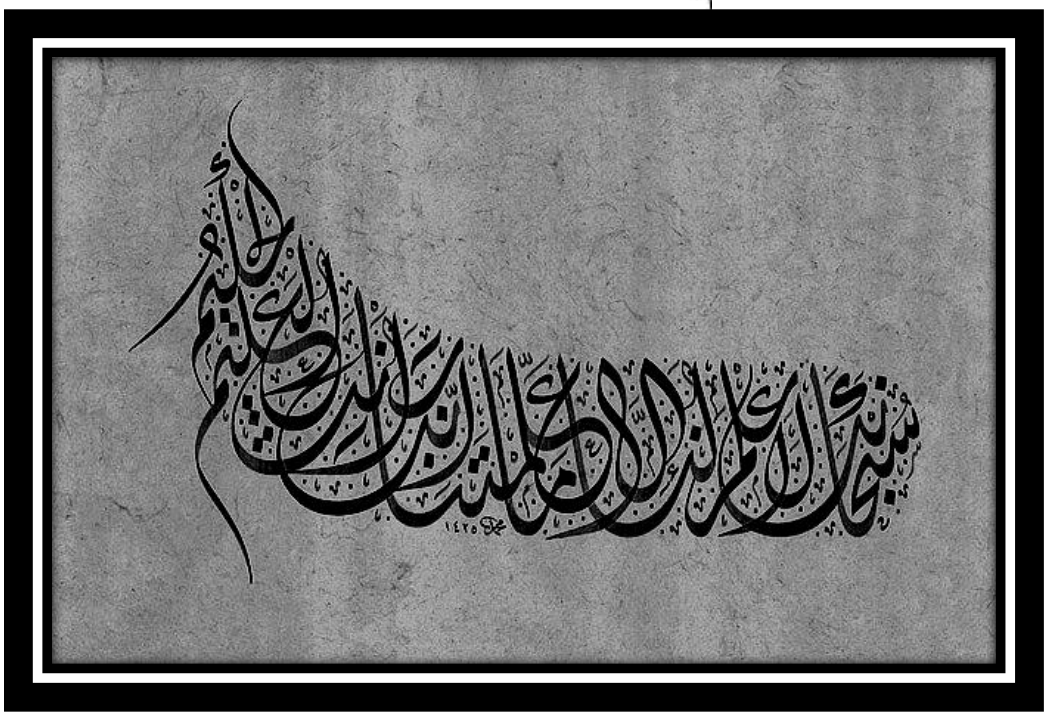
بسم الله الرحمن الرحيم



صدق الله العظيم

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This thesis has not been submitted to this or any other university

Marwa Fouad Abd El-Fatah Ramadan


I would like to dedicate this work to
every member of my faithful family
For their endless love, support and
encouragement

Biography

Name	Marwa Fouad Abd El-Fatah Ramadan
Date and Place of Birth	30 / 10 / 1986, Cairo, Egypt
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Abstract

Chronic obstructive pulmonary disease (COPD) is a slowly progressive immunological disorder primarily induced by Smoking; however, only 10–20 % of the smokers develop COPD, pointing to additional risk factors of which genetic susceptibility is the earliest potential risk factor for the disease.

Due to the complex nature of COPD -characterized by multiple pathological phenotypes- that cannot be evaluated by the decline in FEV1 alone; studies are needed to test the validity of other biomarkers that will correlate to disease severity, separate its multiple phenotypes, and respond to the therapeutic trials that prolong survival.

In this study, the genetic expression of the two genes; Matrix Metalloproteinase-9 (MMP-9) and Alpha-1 Antitrypsin (A1A) were analyzed by qPCR in order to evaluate them as Potential Biomarkers for COPD early detection and staging.

Our study revealed that MMP-9 can be used as a biomarker to differentiate significantly between COPD grades (moderate, severe & very severe) but not for COPD early detection. On the other hand our study could not validate A1A as biomarker for COPD early detection or staging.

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List of Abbreviations:

Abbreviation	Description
4-HNE	4-Hydroxy-2-NonEnal
A1A	Alpha-1-Antitrypsin
AM	Alveolar Macrophage
APS	Ammonium Per Sulphate
ATS	American Thoracic Society
BTS	British Thoracic Society
CBC	Complete Blood Picture
CD cells	Cluster of Differentiation cells
cDNA	complementary Deoxy Nucleic Acid
COPD	Chronic Obstructive Pulmonary Disease
CRP	C-Reactive Protein
C_T	Cycle threshold
CXCL	C-X-C motif Chemokine Ligand
CXCR	C-X-C motif Chemokine Receptor
DC	Dendritic Cells
dd H_2O	double distilled water
DEPC	Di Ethyle Pyro Carbonate
dNTPs	deoxyNucleoside Tri Phosphate
ECM	Extra Cellular Matrix
EDTA	Ethylene Di amine Tetra Acetic acid
EGF	Epidermal Growth Factor
ERS	European Respiratory Society
FEV_1	Forced Expiratory Volume in One second
FGE	Fold Gene Expression
FGF	Fibroblast Growth Factor
FVC	Forced Vital Capacity

GAPDH	Glyceraldehyde-6-Phosphate DeHydrogenase
GOLD	Global Initiative for Chronic Obstructive Lung Disease
GSTs	Glutathione S-Transferase(s)
ILs	InterLeukins
INF-γ	INterFeron-Gamma
INFs	INterFerons
LPA	Linear Poly Acrylamide
LVRS	Lung Volume Reduction Surgery
MCP	monocyte chemotactic protein
MMP-9	Matrix MetalloProteinase-9
MMPs	Matrix MetalloProteinases
NE	Neutrophil Elastase
NGF	Nerve Growth Factor
NHLBI	National Heart, Lung and Blood Institute
NK cells	Natural Killer cells
Nrf2	Nuclear erythroid-related factor 2
NS	Non Significant
NTC	No Template Control
PBS	Phosphate Buffer Saline
PDGF	Platelet Derived Growth Factor
PMP	Protein Microarray Platform
Pr-DNP	protein-2,4- DiNitroPhen***yl***
qPCR	quantitative Polymerase Chain Reaction
RBCs	Red Blood Cells
ROS	Reactive Oxygen Species
RPM	Round Per Minute
RQ	Relative Quantitation
RT- control	Reverse Transcriptase minus control
SD	Standard Deviation
SDS	Sodium Dodecyle Sulphate