EVALUATION OF (ALPHA) – METHYLACYL–COENZYME A RACEMASE AS A NEWLY SUGGESTED MARKER FOR DIAGNOSIS AND FOLLOW UP OF CANCER PROSTATE

Thesis

Submitted for the Partial Fulfillment of M.D. Degree in Clinical and Chemical Pathology

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2013

بسْمِ اللهِ الرَّحْمنِ الرَّحِيمِ

﴿ وأنزل الله عليك الكتاب
والحكمة وعلَّمَكَ مَا لَمْ تَكُن تَعْلَمُ
وكَانَ فَضْلُ اللَّهِ عَلَيْكَ عَظِيماً ﴾

صدق الله العظيم
النساء .. آية رقم ١١٣

Acknowledgement

First of all, thanks to **GOD** for giving me the power to accomplish this work and for achieving any work in my life.

I would like to express my deepest gratitude to my honored **Professor/ Hany Sobhy Rofael,** Professorof Clinical and Chemical Pathology, Faculty of Medicine,Ain-Shams University, for his kind help throughout this study and his guidance during the work.

Also I would like to express my thanks and appreciation to **Professor/ Mona Fathy Youssef,** Professor of Clinical and Chemical Pathology , Faculty of Medicine, Ain-Shams University, for her kind help, valuable guidance, assistance and encouragement.

My deep gratitude, respect and appreciation are expressed for **Professor/ Karim Yehia Aly Shaheen,** Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain-Shams University, for hiscontinuousvaluable guidance, encouragement and endless support.

I am very grateful to **Dr. NermineHelmy Mahmoud,** Assistant Professor of Clinical and Chemical Pathology, Faculty of Medicine, Ain-Shams University, for her great guidance , help, valuable advicesand continuous encouragement throughout the whole work. I wish to express to her my unlimited thanks.

My deepest gratitude and appreciation to **Dr. Hany Hamed Gad,**Assistant Professor of Urology, Faculty of Medicine, Ain-Shams University, for his great help in performing the practical part of this thesis and for his valuable information and advices.

Actually no words are sufficient to express my love and faithful thanks to my family, especially my mother and my husband, who didn't stop encouraging and helping me.

Finally to my late Dad to whom I owe everything I accomplished in my life, thank you.

Rania Farouk El-Awady

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List of Abbreviations

A.....	Alanine
A2M.....	α2-macroglobulin
AAH.....	Atypical adenomatous hyperplasia
ACT	α1-Antichymotrypsin
AJCC.....	American joint committee on cancer
AMACR	Alpha-methylacyl-CoA racemase
API	α1-protease inhibitor
AR.....	Androgen Receptor
AUC.....	Area under curve
bp.....	Base-pair
BPH.....	Benign prostatic hyperplasia
BPSA.....	Benign PSA
BRCA	Breast cancer gene
C-CAM	Cell adhesion molecule
CDK.....	Cyclin dependent kinase
CDKN	Cyclin dependent kinase
cDNA.....	Complementary deoxyribonucleic acid
CGH	Comparative genomic hybridization
CLEIA.....	Chemiluminescence enzyme immunoassay
COX2.....	Cyclooxygenase (COX2) enzyme
CT	Computed tomography
CTC	Circulating tumor cells
DELFIA……...	Dissociation-enhanced lanthanide fluorescent immunoassay
DEPC	Double distilled diethyl pyrocarbonate
df.....	Degree of freedom
DNA	Deoxyribonucleic acid
dNTP.....	Deoxynucleotide triphosphate
DPC.....	Diagnostic Products Corporation
DRE.....	Digital rectal examination
DTT	Dithiothrental
EGF	Epidermal growth factor

List of Abbreviations (Cont...)

EGFR	Epidermal growth factor receptor
ELISA	Enzyme linked immunosorbent assay
FAS.....	Fatty acid synthase
FDA.....	Food and Drug Administration
FDG.....	Fluorodeoxyglucose
FGF	Fibroblast growth factor
FGFR	Fibroblast growth factor receptor
FIA……..Fluorescent immunoassay	
FISH	Fluorescence in situ hybridization
FISH.....	Fluorescent in situ hybridization
FN.....	False negative
FP	False positive
fPSA	Free prostate-specific antigen
GAPDH.....	Glyceraldehyde 3 phosphate dehydrogenase
GF.....	Growth factor
GPI	Glycosylphosphatidylinositol
GSTP1	Glutathione S-transferase
H and E.....	Haematoxylin and eosin
Hcl	Hydrochloric acid
HGPIN.....	High-gradeprostatic intraepithelial neoplasia.
hK/ KLK	Human Kallikrein
HK2.....	Human glandular kallikrein-2
HMWCK.....	High-molecular-weight cytokeratin
HSP	Heat Shock Proteins
IGF	Insulin-like growth factor
IGF	Insulin-like growth factor
IGFBP.....	Insulin – like growth factor binding protein
iPSA	Inactive PSA
L.....	Leucine
LHRH	Leuteinizing hormone-releasing hormone

List of Abbreviations (Cont...)

LNCap	Prostate carcinoma cell line
LOH.....	Loss of heterozygosity
mABs.....	monoclonal antibodies
MRI	Magnetic resonance imaging
MSGs	Metastasis-suppressor genes
MSMB.....	Microseminoprotein beta
mTOR	mammalian target of rapamycin
NASBA	Nucleic acid sequence-based amplification
nf.....	nuclear factor
NF.....	Nuclear factor
p	probability
P.....	Proline
p	Short arm of chromosome
PAP	Prostatic acid phosphatase
PC	Prostate cancer
PCA3	Prostate cancer antigen 3
PCGP	Prostate cancer genetics project
PCPT.....	Prostate Cancer Prevention Study
PCR	Polymerase chain reaction
PEBP1	Phosphatidylethanolamine binding protein1
PET	Positron emission tomography
PH.....	Potential hydrogen
PIN	Prostatic intraepithelial neoplasia
PPV	Positive predictive value
PSA.....	Prostate specific antigen
PSCA.....	Prostate stem cell antigen
PSMA.....	Prostate-specific membrane antigen
q	Long arm of chromosome
R.....	Arginine
RB.....	Retinoblastoma tumor suppressor gene

List of Abbreviations (Cont...)

RIPA buffer	Radio immunoprecipitation assay buffer
RNase.....	Lribonuclease L
ROC.....	Receiver-operating characteristic
RR.....	Relative risk
rs.....	Spearman's rank correlation coefficient
RT-PCR.....	Reverse transcriptasepolymerase chain reaction
S.....	Serine
SD.....	Standard deviation
SEER.....	Surveillance Epidemiology and End Results
SF	Survival factor
SNPs	Single nucleotide polymorphisms
SNPs	Single nucleotide polymorphisms
STA.....	Tsignal transducers and activators of transcription
TAE	Tris acetate EDTA
TGF-α.....	Transforming growth factor-α
TGF-β.....	Transforming growth factor-β
TLC	Total leucocytic count
TN.....	True negative
TNM.....	Tumor-Node-Metastasis system
TP	True positive
tPSA.....	Total prostate-specific antigen
TRPM8.....	Transient receptor potential cation channel subfamily M member 8
TRUS	Transrectalultrsonography
TURP	Trans-urethral resection of the prostate
UICC.....	Union forInternational cancer control
UV	Ultra violet
β-ME.....	β- Mercaptoethanol
(1,25-$(OH)_2$-D3).....	1,25-dihydroxy-vitamin D_3

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INTRODUCTION

Prostate cancer is the fourth most common male malignancy and the second leading cause of male cancer-related death ***(Samuels et al., 2003).*** Small prostatic carcinomas were detected in 30% of men between 30 and 49 years old, 40% of males over age of 50, and 64% of men over 60 years old ***(Sokoloff et al., 2004).*** For this reason, an annual screening is generally recommended for all men over the age of 50.

Screening of prostate cancer on a large scale requires noninvasive methods of detection and the use of reliable, and clinically validated markers ***(Galina et al., 2005).*** Prostate cancer screening is currently based on digital rectal examination (DRE), prostate-specific antigen (PSA) monitoring, and transrectal ultrasound (TRUS) with TRUS- guided biopsy for morphologic examination as the reference standard ***(Miller et al., 2002)***. However, none of these standard methods is sufficiently sensitive nor specific for prostate cancer, which makes early detection of the disease difficult ***(Gao et al., 2003).***

Several studies have suggested that detection of circulating tumor cells can be useful in the staging of