The Role of Uroplakin IIIA (UPIIIA) Gene and its Protein in the Diagnosis of Bladder Cancer

Thesis Submitted to Faculty of Science,
Ain Shams University

In partial Fulfillment of M.Sc. in Biochemistry

BY

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Approval Sheet

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Supervision Committee **Approved**

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﴿ قالوا سبحانك لا علم لنا الا ما علمتنا

إنك انت العليم الحكيم ﴾

صدق الله العظيم

الآيه(32) سوره البقره

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First, foremost, and all thanks to Allah by whose grace this work had been completed and by whose grace all my life is arranged in the best. Nobody can imagine this way that had been drawn by the mercifulness of Allah.

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I should like to add appreciation to patients in this study who have been helpful in achieving the desired outcome. I hope that with this and other studies we can alleviate their sufferings.

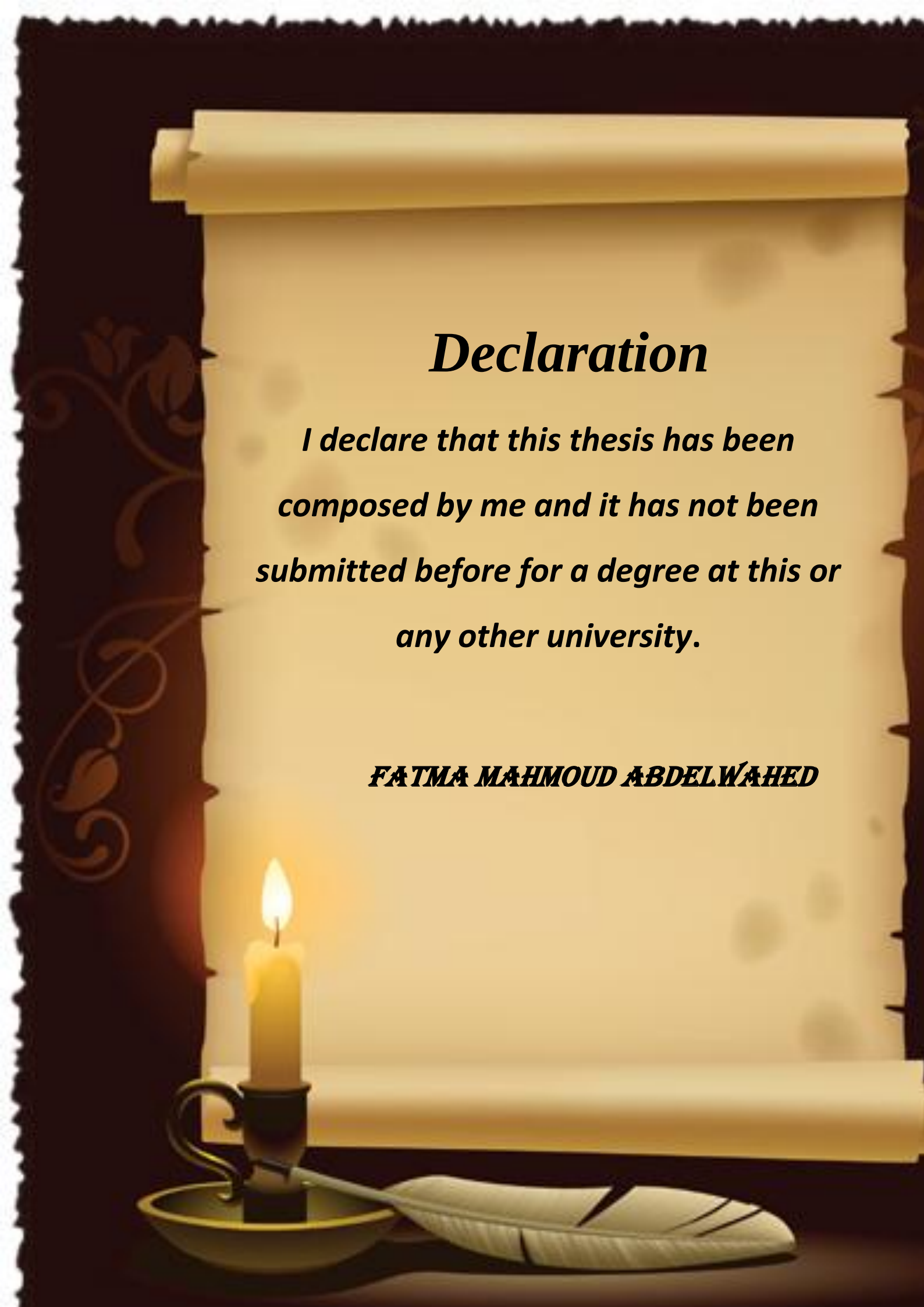
Finally, my truthful affection and love to my husband, my family, who were, and will always be by my side all my life.

Fatma Mahmoud Abdelwahed Mohamed

Declaration

I declare that this thesis has been composed by me and it has not been submitted before for a degree at this or any other university.

FATMA MAHMOUD ABDELWAHED



Contents

Abstract

The Role of Uroplakin IIIA (UPIIIA) Gene and its Protein in the Diagnosis of Bladder Cancer.

Background: Advanced bladder cancer is an aggressive malignancy with a poor prognosis. Despite precise pathologic staging and grading, prediction of clinical outcomes in patients is very difficult. Uroplakins are urothelial differentiation-related membrane proteins, they represent major urothelial cyto-differentiation products and are highly conserved during mammalian evolution**.**

Objective: To evaluate the role of uroplakin IIIA as a potential diagnostic and / or prognostic predictor marker for metastasis of bladder cancer patients.

Methods: A total of 106 subjects: 61 bladder cancer patients, 20 benign cases, 25 healthy subjects, were enrolled in the present study. Patients were observed for 3 years postoperative. UPIIIA mRNA level was detected in blood using q-PCR, and in urine by conventional PCR, while urinary UPIIIA protein was measured using ELISA.

Results: At baseline, before cystoscopy, blood UPIIIA mRNA was significantly higher in the metastatic patients as compared with controls, patients with benign lesions, and non

metastatic cancer ones ($p< 0.015$, 0.02, and 0.03; respectively). Urinary UPIIIA protein was significantly higher in patients who developed metastasis within the 3 years observation period from the time of surgery.

Conclusion: The results suggest that UPIIIA may provide a feasible non-invasive tool for differential diagnosis and prediction of metastasis in bladder cancer.

Key words: bladder cancer, UPIIIA, metastasis.

List of Abbreviation

Abbreviation	Description
APC	Adenomatous polyposis coli
ARF	Alternate open reading frame
ASR	Age Specific incidence Rate.
AUM	Asymmetric unit membrane
Bax	BCL2-associated X protein
BCG	Bacillus calmette guerin
BCL-2	B-cell lymphoma 2
BTA	Bladder tumor associated antigen
BTA	Bladder tumor antigen
CASP8	Caspase-8
CD	Cluster of differentiation
CDH1	Cadherin-1
CDH13	Cadherin-13
CDK	Cyclin-dependent kinases

CDKAL	CDK5 regulatory subunit associated protein 1-like 1
CI	Confidence interval
CIS	Carcinoma in situ
CK20	Keratin 20
CT	Computed tomography
DBC2	Deleted in breast cancer2
DBCCR1	Deleted in bladder cancer chromosomal region 1
DVs	Discoidal vesicles
EAU	European Association of Urology
EGFR1	Epidermal growth factor receptor 1
ER	Endoplasmic reticulum
ERCC4	Excision repair cross-complementing group 4
ERK	Extracellular signal-regulated kinases
EST	Expressed sequence tag
FASL	Fas ligand
FDA	U S Food and Drug Administration
FGFR	Fibroblast growth factor receptor