شبكة المعلومات الجامعية

بسم الله الرحمن الرحيم

شبكة المعلومات الجامعية

التوثيق الالكتروني والميكروفيلم

شبكة المعلومات الجامعية

جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

قسم

نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات

يجب أن

تحفظ هذه الأقراص المدمجة بعيدا عن الغبار

Study of Clinical Utility of miRNA-31 in diagnosis of Bladder Cancer in Egyptian Patients

Thesis

Submitted for Partial Fulfillment of Master Degree in Clinical Pathology

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2021

سورة البقرة الآية: ٣٢

Acknowledgment

First and foremost, I feel always indebted to **ALLAH,**
the Most Kind and Most Merciful.

I'd like to express my respectful thanks and profound gratitude to **Professor/ Ghada Sadek Sabbour,** *Professor of Clinical Pathology, Faculty of Medicine, Ain Shams University for her keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Professor/ Mona Mohamed Hassan,** *Professor of Clinical Pathology, Theodor Bilharz Research Institute, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

I am deeply thankful to **Doctor/ Heba Hassan Aly,** *Assistant Professor of Clinical Pathology Faculty of Medicine, Ain Shams University, for her great help, active participation and guidance.*

I wish to introduce my deep respect and thanks to **Doctor/ Shimaa Mostafa Ismaiil,** *Lecturer of Clinical Pathology, Faculty of Medicine, Ain Shams University, for her kindness, supervision and cooperation in this work.*

I'd like to express my respectful thanks and profound gratitude to **Prof. Tarek Ramzy El-Leithy,** *Professor of Urosurgery, Theodor Bilharz Research Institute, for his keen guidance, kind supervision, valuable advice and continuous encouragement, which made possible the completion of this work.*

I am also delighted to express my deepest gratitude and thanks to **Dr. Eman Seyam Mahgoub,** *Lecturer of Clinical Pathology, Theodor Bilharz Research Institute, for her kind care, continuous supervision, valuable instructions, constant help and great assistance throughout this work.*

Mostafa Mohamed El-Sisy

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List of Abbreviations

Abb.	Full term
AGO	Argonaute
Akt	Serine/threonine kinase
ALP	Alkaline phosphatase
ALT	Alanine aminotransferase
AR	Androgen Receptor
ASI	Age-standardized incidence
AST	Aspartate aminotransferase
BCA	Bladder cancer
CAM-DR	Cell adhesion mediated drug resistance
CBC	Complete blood count
CDKN	Cyclin dependent kinase inhibitor
CDKN2A	Cyclin-dependent kinase inhibitor 2A
CIS	Carcinoma in situ
CT	Computed tomography
FAF1	Fas-associated factor 1
FGFR3	Fibroblast growth factor receptor 3
GGT	Gamma glutamyl transferase
GIT	Gastrointestinal tract
GST	Glutathione S-transferase
ITGA5	Intergrin alpha 5
let-7	Lethal-7
LOH	Loss of heterozygosity
MIBC	Muscle-invasive bladder cancer
miRISC	MiRNA-induced silencing complex
miRNAs	MicroRNAs
MLK3	Mixed lineage kinase 3
MMC	Mitomycin C
NANOG	Nanog Homeobox
NAT	N-acetyltransferase

List of Abbreviations Cont...

Abb.	Full term
NMIBC	Non-muscle-invasive bladder cancer
ORF	Open reading frame
PIK3CA	Phosphatidylinositol 4,5-bisphosphate 3-kinase catalytic subunit alpha isoform
PKC-α	Protein kinase C-α
PTEN	Phosphatase and tensin homolog
qPCR	Quantitative real time PCR
RB1	Retinoblastoma protein
RISC	miRNAs/minimal miRNA-induced silencing complex
RNA-Seq	RNA sequencing
RT	Reverse Transcription
SCC	Squamous cell cancers
shRNA	Small hairpin RNA
SIRT-1	Sirtuin-1
SOX2	Box 2
SRY	Sex determining region Y
STAG2	Stromal antigen 2
TBRI	Theodor Bilharz Research Institute
TCC	Transitional cell carcinoma
TERT	Telomerase reverse transcriptase
UBC	Urothelial bladder cancer
WHO	World Health Organization
ZEB1/2	Zinc finger e-box binding homeobox ½

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INTRODUCTION

Bladder cancer (BCA) is the most common cancer of urinary tract with approximately 550,000 new cases diagnosed in 2018 worldwide ***(Ferlay et al., 2018)***. In Egypt, BCA has the second-high prevalence. It accounts for 12.7% of male cancers with >7900 deaths per year, which is considerably higher than most other parts of the world. It is mostly related to smoking and Schistosoma infection ***(Nagy et al., 2018).***

Risk factors as chronic bladder inflammation, family history of bladder cancer and increased age are major causes ***(Antoni et al., 2017).***

Surveillance strategies for BCA recurrence have historically relied on the diagnostic combination of cystoscopy with histopathology and urinary cytology. However, cystoscopy approach is costly, invasive and uncomfortable. Urinary cytology is a preferable technique for the diagnosis of bladder tumors; however, it has low sensitivity. That's why new approaches are being tested ***(Yun et al., 2013).***

Many studies have explored circulating cell free miRNAs and provided evidence that they exist in a stable form in various body fluids, such as: blood, urine, saliva and peritoneal fluid ***(Weber et al., 2010).*** MicroRNAs (miRNAs) are abundant non-coding RNA molecules of 19–24 nucleotides that perform a critical role in the regulation of gene expression

at the post transcriptional level. MiRNAs have been demonstrated to act as key regulators in the pathogenesis of diseases, particularly in cancer ***(Tan et al., 2018).***

It is widely believed that the circulating miRNAs might not only come from circulating tumor cells, but also be released into the blood stream directly via blood cells or other tissue cells affected by disease. It is becoming clearer that the majority of circulating miRNAs are carried by various carriers, such as exosomes, Ago2, HDL, etc, as carrier-free miRNAs will be degraded by RNase digestion and other environmental factors ***(Mo et al., 2012).***

Micro RNAs such as miRNA-31 show significantly elevated concentrations in bladder cancer patients compared to healthy. So it is emerging as a potential biomarker in BCA that can be promising in early diagnosis ***(Juracek et al., 2018).***

AIM OF THE WORK

The aim of the present work is to evaluate the clinical utility of miRNA-31 in plasma as an early novel diagnostic marker for patients with bladder cancer, in comparison to cystoscopy with histopathology as a conventionally used technique for cancer detection.