



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكرو فيلم

# بسم الله الرحمن الرحيم



**MONA MAGHRABY**



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التوثيق الإلكتروني والميكروفيلم



# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكروفيلم



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# 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



**MONA MAGHRABY**



# **Evaluation of RNA Based Biomarker Expression in Acute Kidney Injury after ESWL**

*Thesis*

*Submitted for Partial Fulfillment of Master  
Degree in Urology*

*By*

**Mohamed Sahab Emam**

*Bachelor of Medicine and Surgery*

*Supervised by*

**Prof. Dr. Mohamed Mohamed Yassin**

*Assistant Professor of Urology*

*Faculty of Medicine- Ain Shams University*

**Prof. Dr. Amr El Kholy**

*Assistant Professor of Urology*

*Theodor Bilharz Research Institute*

**Dr. Waleed Mousa**

*Lecturer of Urology*

*Faculty of Medicine - Ain Shams University*

**Prof. Dr. Marwa Matboli Sayed**

*Assistant Professor of Biochemistry*

*Faculty of Medicine - Ain Shams University*

*Faculty of Medicine  
Ain Shams University  
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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

سَبِّحْ اِنَّكَ لَا تَعْلَمُ لَنَا  
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الْعَلِيمُ الْعَظِيمُ

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# *List of Abbreviations*

| Abb.          | Full term                                    |
|---------------|--|
| 5-ASA.....    | 5-aminosalicylic acid                        |
| ACEi .....    | Angiotensin-converting enzyme inhibitor      |
| ADQI.....     | Acute Dialysis Quality Initiative            |
| AKI .....     | Acute kidney injury                          |
| AKIN .....    | Acute Kidney Injury Network                  |
| ARB .....     | Angiotensin receptor blockers                |
| ATP.....      | Adenosine triphosphate                       |
| B2M .....     | B-2-microglobulin                            |
| BGAL.....     | B-galactosidase                              |
| CAGE.....     | Cap analysis gene expression                 |
| CKD .....     | Chronic kidney disease                       |
| CT .....      | Computerized tomography                      |
| DM .....      | Diabetes munities                            |
| DNA.....      | Deoxyribonucleic acid                        |
| EAU .....     | European Association of Urology              |
| eGFR.....     | Estimated glomerular filtration rates        |
| ESRD .....    | End-Stage Renal Disease                      |
| ESWL .....    | Extracorporeal shockwave lithotripsy         |
| FeNa .....    | Fractional excretion of sodium               |
| FeUr .....    | Fractional excretion of urea                 |
| GFR .....     | Glomerular filtration rate                   |
| HAR .....     | Human accelerated regions                    |
| HGP .....     | Human Genome Project                         |
| HTN .....     | Hypertension                                 |
| ICU .....     | Intensive care unit                          |
| IGFBP-7 ..... | Insulin-like growth factor binding protein 7 |



## *List of Abbreviations Cont...*

| Abb.                 | Full term                                  |
|----------------------|--|
| KDIGO.....           | Kidney Disease: Improving Global Outcomes  |
| KIM-1 .....          | Kidney injury molecule-1                   |
| L-FAB .....          | Liver fatty acid-binding protein           |
| MRI.....             | Magnetic resonance imaging                 |
| NAG .....            | N-acetyl- $\beta$ -d-glucosaminidase       |
| ncRNAs.....          | Noncoding RNAs                             |
| NGAL .....           | Neutrophil gelatinase-associated lipocalin |
| NIH.....             | National Institute of Health               |
| NO .....             | Nitric oxide                               |
| O <sub>2</sub> ..... | Oxygen                                     |
| P.A .....            | Postero-anterior                           |
| PC .....             | Protein-coding                             |
| PCG .....            | PC gene                                    |
| RIRS .....           | Retrograde intra-renal surgery             |
| ROS.....             | Reactive oxygen species                    |
| RRT.....             | Renal replacement therapy                  |
| sUr .....            | Serum urea                                 |
| SW .....             | Shock waves                                |
| TapSAKI.....         | TrAnscript predicting survival in AKI      |
| TE .....             | Transposable elements                      |
| TIMP2.....           | Tissue inhibitor metalloproteinase 2       |
| TSS .....            | Transcription start                        |
| TTS .....            | Termination                                |
| XIST.....            | X inactive specific transcript             |

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# INTRODUCTION

Urinary stone prevalence is estimated at 3% in all individuals, and it affects up to 12% of the population during their lifetime. Urinary stone recurrence rates approach 50% at 10 years (*Preminger et al., 2007*).

The European Association of Urology (EAU) guidelines recommend the use of less invasive modalities such as extracorporeal shockwave lithotripsy (ESWL) or retrograde intra-renal surgery (RIRS), for stones less than 2 cm (*Turk et al., 2013*).

ESWL has gained rapid acceptance worldwide because of its ease of use, noninvasive nature, high efficacy in treating kidney and ureteral stones, and wide availability of lithotriptors. ESWL acts via a number of mechanical and dynamic forces on stones such as cavitation, shear, spalling and cavitation (*Moody et al., 2012*).

However, the destructive forces generated when the cavitation bubbles can cause trauma to thin-walled vessels in the kidneys and adjacent tissues, which result in a broad spectrum of vascular kidney damage, ranging from self-limited hematuria to perinephric/nephric hematomas, although most hematomas resolve, some may cause life-threatening hemodynamic instability and acute renal failure, In the long term, animal and human studies have suggested that these acute

hemorrhagic lesions may progress to scar formation and complete atrophy of the renal papillae (*Wang et al., 2021*).

Also, SWL cause release of cytokines/inflammatory cellular mediators, and infiltration of tissue by inflammatory response cells (*Connors et al., 2013*).

Most of our knowledge about urological therapeutic modalities injury to the kidney is based on experimental animal studies where invasive methods were used to assess for tissue damage (*Fahmy et al., 2013*).

This is due to almost of the standard metrics used to define and monitor the progression of renal damage, such as serum creatinine and blood urea nitrogen levels, are insensitive, nonspecific, and change significantly only after significant kidney injury and then with a substantial time delay (*Bryniarski et al., 2012*).

As regard imaging modalities, there is no existing adequate imaging modality available to assess parenchymal injury, the absence of hematoma detection by conventional imaging techniques does not rule out the occurrence of potentially significant injury to the SWL-treated kidneys which rises the need to find a noninvasive diagnostic test that can reliably identify kidney injuries, especially in certain populations such as children, patients with preexisting renal disease, or those undergoing multiple SWL treatments (*Dede et al., 2015*).



There is no consistent dependable urinary or circulatory marker to permit detection of significant renal injury. Therefore, several new urinary and serum biomarkers promise to address the gap associated with the use of serum creatinine (*Schmid et al., 2015*).

More than 80% of the human genome is transcribed into RNA transcripts without protein-coding potential. These so-called noncoding RNAs (ncRNAs) are arbitrarily separated into long ncRNAs (lncRNAs) >200 nucleotides and small ncRNAs (<200 nucleotides) on the basis of their size (*Djebali et al., 2012*).

However, little is known about the functional role of lncRNAs. lncRNAs play a critical role in several important cellular processes, such as the regulation of imprinting and X-chromosome inactivation. In the nucleus, lncRNAs “fine-tune” chromatin architecture by interacting with chromatin remodeling complexes to regulate the expression of genes residing on the same chromosome (in cis) or on another chromosome (in trans) (*Ponting et al., 2009*). Emerging studies in the cancer and cardiovascular field have demonstrated that lncRNAs can be detected in body fluids of patients (*Kumarswamy et al., 2014*).

Circulating or urinary lncRNAs may thus be fascinating novel biomarkers that reflect intra-nuclear processes noninvasively and may therefore be a better estimate of