



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكروفيلم

# بسم الله الرحمن الرحيم



**MONA MAGHRABY**



شبكة المعلومات الجامعية  
التوثيق الإلكتروني والميكرو فيلم



# شبكة المعلومات الجامعية التوثيق الإلكتروني والميكرو فيلم



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التوثيق الإلكتروني والميكروفيلم

# جامعة عين شمس

## التوثيق الإلكتروني والميكروفيلم

### قسم

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علي هذه الأقراص المدمجة قد أعدت دون أية تغيرات



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تحفظ هذه الأقراص المدمجة بعيدا عن الغبار



**MONA MAGHRABY**



# **Prognostic implication of PD-L1 expression and associated tumor infiltrating lymphocytes in metastatic breast cancer**

*Thesis*

*Submitted for Partial Fulfilment of Medical Doctorate  
Degree in Clinical Oncology & Nuclear Medicine*

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

# قَالَ

سَبَّحَانَكَ لَا إِلَهَ إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ  
الْعَلِيمُ الْعَظِيمُ

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# *List of Abbreviations*

Abb.	Full term
APC.....	Antigen-presenting cells
ASCO.....	American Society of Clinical Oncology
ASIR .....	Age-standardized incidence rate
BCG .....	Bacillus Calmette-Guerin
BCSS.....	Breast cancer-specific survival
CD .....	Cluster of differentiation
CDH1 .....	Cadherin 1 gene
CTCs .....	Circulating tumor cells
ctDNA.....	Circulating tumor DNA
CTLA-4.....	Cytotoxic T-lymphocyte-associated protein 4
DCIS .....	Ductal carcinoma in situ
DFS .....	Disease-free survival
EGFR .....	Epidermal growth factor receptor
EPCAM .....	Epithelial cell adhesion molecule gene
ER.....	Estrogen receptor
FDA.....	Food and Drug Administration
HDGC .....	Hereditary diffuse gastric cancer
HER2 .....	Human epidermal growth factor receptor 2
HR .....	Hazard ratio
IDC.....	Invasive ductal carcinoma
IFNgamma .....	Interferon gamma
IHC.....	Immunohistochemical
IL .....	Interleukin
ILC .....	Invasive lobular carcinoma
IM.....	Immunomodulatory
ITC .....	Isolated tumor cells
KIR.....	Killer immunoglobulin-like receptor
KPS .....	Karnofsky performance status
LCIS .....	Lobular carcinoma in situ



## *List of Abbreviations Cont...*

Abb.	Full term
LFS.....	Li-Fraumeni syndrome
MBC.....	Metastatic breast cancer
MHC .....	Major histocompatibility complex
MHT.....	Menopausal hormonal therapy
MINDACT .....	Microarray in Node-Negative Disease May Avoid Chemotherapy
MMR.....	Mutations in mismatch repair
NACT .....	Neoadjuvant chemotherapy
NK.....	Natural killer
NMSC .....	Non-melanoma skin cancer
NOS.....	Not otherwise specified
NSCLC .....	Non-small cell lung cancer
OS.....	Overall survival
PAM50 .....	Predictor Analysis of Microarray 50
PD-1 .....	Programmed cell death protein 1
PD-L1 .....	Programmed death-ligand 1
PFS .....	Progression-free survival
PHTS.....	Phosphatase and hamartoma tumor syndrome
PLVI.....	Peritumoral lymphovascular invasion
PR.....	Progesterone receptor
PTEN .....	Phosphatase and tensin homolog tumor suppressor gene
RCC.....	Renal cell carcinoma
RR .....	Relative risk
RS.....	Recurrence Score
SEER.....	Surveillance, Epidemiology, and End Results
SRR.....	Summary RR
TCR.....	T cell receptor
TDLU .....	Terminal duct-lobular unit
Th1 .....	T helper 1

## *List of Abbreviations Cont...*

Abb.	Full term
Th2 .....	T helper 2
TILs .....	Tumor-infiltrating lymphocytes
TMAAs .....	Tissue microarrays
TN .....	Triple negative
TNBC.....	Triple-negative breast cancer
TNM.....	Tumor, Node, Metastasis
WHO.....	World Health Organization
WTS .....	Whole tissue section

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# INTRODUCTION

**G**lobally, breast cancer is the most frequently diagnosed malignancy, accounting for over a million cases diagnosed each year (1.67 million cases diagnosed per year) (*Ferlay et al., 2015*). In the recent National Population-Based Cancer Registry Program in Egypt, the annual age specific incidence rates for female breast cancer in Egypt was 48.8/100,000 (*Ibrahim et al., 014*).

Breast cancer is a highly heterogeneous disease, in terms of its etiology and pathological characteristics; some cases show slow growth with excellent prognosis, while others take a highly aggressive clinical course (*Verma et al., 2012*). Gene expression studies have identified several distinct breast cancer molecular subtypes that differ markedly in the prognosis and the therapeutic targets they express (*Sotiriou et al., 2003*).

Triple-negative breast cancer (TNBC) is a term that has been applied to breast cancers that are low in expression of the estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2), representing about 10-20% of breast carcinomas (*Boyle, 2012*). TNBC usually tends to have a worse prognosis, relapse early and behave more aggressively, compared to other types of breast cancer. Unlike other subtypes (ER positive, HER2 positive), TNBC has yet no approved target treatments available, other than the administration of chemotherapy (*Dawood, 2010*).