Incidence of Cytomegalovirus IgG antibodies and the role of Matrix Metalloprotinase-13 (MMP-13)-as a novel tumor marker- for Diagnosis of Breast Cancer in Egyptian Females

A Thesis Submitted for the Degree of Ph.D in Science (Microbiology)

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بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُواْ سُبْحَانَكَ لاَ عِلْمَ لَنَا إِلاَّ مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

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Declaration

I declare that this thesis has been composed by me and that the work of which is a record has done by me. It has not been submitted for a degree at this or any other university.

Aliaa Mohamed Seif Elden Abd Elkader

Dedication

To my family
My great father and my kind mother
Thank you for supporting me with kindness, patience and love

Acknowledgement

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

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List of Abbreviations

ASCO	American Society of Clinical Oncology
AUC	Area under the curve
BKV	Polyomavirus hominis1
CA15.3	Carbohydrate antigen15.3
CA 27.29	Carbohydrate antigen 27.29
CEA	Carcino-embryonic antigen
CMV	Cytomegalovirus
CT Scan	Computerized Tomography Scan
EBV	Epstein–Barr virus
ECLIA	Electro-chemiluminescence immunoassay
ECM	Extracellular matrix
ELISA	Enzyme linked immunosorbent assay
ER-	Estrogen receptor-negative
ER+	Estrogen receptors positive
FNAC	Fine needle aspiration and cytology
HBV	Hepatits B virus
HCMV	Human Cytomegalovirus
HCV	Hepatits C virus
HCL	Hydrochloric acid
HHV-5	Human herpesvirus 5
HIV	Human immunodeficiency virus

HMTV/MMTV	Human Mammary Tumor Virus/ Mouse mammary tumor virus
HPV	Human papilloma virus
HRP-conjugate	Horseradish peroxidase
HTLV-1	Human T-cell lymphotropic *virus*
JCV	John Cunningham virus
KSHV	Kaposi's Sarcoma-associated Herpes *Virus*
MCV	Markel cell polyomavirus
MMPs	Matrix metalloproteinases
MMP-13	Matrix Metalloproteinase-13
MUC	Mucin
PBS	Phosphate buffer saline
PET scans	Positron emission tomography
PR+	Progesterone receptors positive
ROC	Receiver operating characteristic
SPSS	Statistical Package for the Social Sciences
SV40	Simian *virus*40
TMB reagent	3,3',5,5'-Tetramethylbenzidine
TNM system	Tumor, lymph node, metastasis scoring system

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Aim of the Work

The aim of this study was:

- To investigate the role of infection as a cause of carcinogenesis by estimating the incidence of anti-cytomegalovirus IgG antibodies in breast cancer patients.

- To evaluate the use of matrix metalloproteinase-13 as a potential tumor marker in breast cancer.

Chapter I

Introduction

Breast cancer is the most common non-skin cancer amongst women worldwide and is the fifth leading cause of cancer-related mortality overall. Worldwide, breast cancer is the deadliest cancer amongst females in developing countries, causing about half a million total deaths each year ***(Power et al., 2018).*** Considerations which influence the risk of developing breast cancer include age, race, family history, genetics, lifestyle, and hormonal factors.

Factors that are associated with an increased risk of breast cancer include: being female, increasing age, a personal history of breast conditions, a family history of breast cancer, exposure to radiation, obesity and post-menopausal hormone therapy ***(Noor et al., 2016).***

The development of breast cancer occurs as a result of numerous internal and external factors. Recently, the role of infection during carcinogenesis has been studied in several types of oncological diseases. Human herpesvirus is known for its oncogenic potential. Cytomegalovirus (CMV) and Epstein bar virus (EBV) of the *Herpesviridae* family have been implicated as a cause of breast cancer. Recent studies have detected high antibody titer of CMV in patients newly diagnosed with breast cancer ***(Mohamed et al., 2014).***

A test for tumor markers is the most convenient method to screen for breast cancer. However, the tumor markers that are currently available for breast cancer