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Evaluation of Some Biomarkers and BRCA1 Mutation in Iraqi Females with Breast Disease

A Thesis

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1.1. Introduction

A large group of molecules refered to as tumor suppressors that are capable of controlling cell division, promoting apoptosis and suppressing metastasis. Tumor suppressors may lose their function and this may lead to cancer due to uncontrolled cell division (Sun and Yang, 2010). Tumor suppressor genes refer to those genes whose function lost results in malignancy promotion. Tumor suppressor gene act as negative regulator of growth and other functions that play role in invasive and metastatic potential (Osborne *et al.,* 2004).

Tumor Protein 53 (TP53) is a tumor suppressor gene that can activate or repress a variety of target genes involved in different functions including cell cycle regulation, apoptosis induction, DNA repair, anti-angiogenesis and maintenance of genome (Lacroix *et al.,* 2006). Among mutated genes in human cancers, P53 is one of the most mutated gene (Vousden and Lu, 2002). Protein (P53) germline mutation associated with high incidence of early set breast cancer and represent small proportion (<1%) of all breast cancer cases (Antoniou and Easton, 2006), while somatic mutation of p53 is more common (Borresen, 2003).

BRCA1 is another tumor suppressor gene because loss of its function lead to phenotype changes (Hall *et al.,* 2007). Life time risk of inheriting certain forms of breast and ovarian cancer greatly increased with BRCA1 gene mutation (Petruceli *et al.,* 2004). Carriers of BRCA1 mutation or deletion will develop breast cancer in younger age females and in percentage 25 to 35% (Casciato and Lowitz, 2000). BRCA1 ensure the stability of cell's genetic material (DNA) and assist preventing uncontrolled cell growth. Mutation in BRCA1 linked to the development of hereditary breast cancer (Kadouri *et al.,* 2007). Among women world wild, breast cancer is most common cancer and the leading cause of death in women aged 40-

49 years old (Black *et al.*, 2007). In Iraq following first and second Gulf war, its population exposed to high level of depleted uranium increasing the incidence three fold over the last ten years (Al-Azzawi, 2006). Among all new cancer cases in Iraqi females, breast cancer alone counted (31%) (Al Hasnawi and AL Mosawi, 2008). Many risk factors of breast cancer such as age, family history, menstrual history, genetic factors, age of menopause, and radiation exposure, are not modifiable while other risk factors such as the use of hormone replacement therapy, alcohol consumption, smoking and breast feeding are modifiable (Chlebowaski *et al.*, 2005). Lymphocytes, including T cells, T regulatory (T reg) cells, and natural killer (NK) cells, and cytokines that released are associated with both primary and secondary prevention of breast cancer. Cancer prognosis maybe related to the status of immune system function (Standish *et al.*, 2008).

1.2.Aims of study

This study aims to:

1- Evaluate the status of P53 and BRCA1 level in the serum of breast cancer women and the relative non breast cancer women.
2- Find out the level of (Total WBCs , Platelet , neutrophil and lymphocyte) in the serum of breast cancer women and the relative non breast cancer women .
3- Identify germline mutation of BRCA1 gene in tissue of breast cancer women .