جامعة الإسكندرية
ALEXANDRIA
UNIVERSITY

Medical Research Institute
Department of Immunology and Allergy

The autophagic activities and cancer stem cells in breast cancer tumor microenvironment enriched with interleukin-6 monoclonal antibodies

A Thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy

In

Immunology and Allergy

Submitted by

Amira Mohamed Abdelfattah Moustafa Darwish

B. Sc. (Biochemistry/Chemistry),
Faculty of Science, Alexandria University, 2012
Master of Immunology and Allergy,
Medical Research Institute, Alexandria University, 2016

Medical Research Institute
Department of Immunology and Allergy
2023

ABSTRACT

Breast cancer is the leading cause of cancer deaths in women worldwide. Breast tumor microenvironment is recognized as an important factor in breast tumor development and progression, as well as a measurable parameter of treatment response. Chronic inflammation in the tumor microenvironment has been shown to promote tumor growth and induce resistance to chemo- and radiotherapy. Overexpression of the cytokine interleukin-6 (IL-6) in the tumor microenvironment has been observed in a variety of tumors, including breast cancer. In the tumor microenvironment, tumor cells and tumor-associated fibroblasts are the primary sources of IL-6 secretion.

In this study, we aimed to investigate the autophagic activities and level of cancer stem cells in breast cancer tumor microenvironment supplemented with anti-interleukin-6 monoclonal antibodies. The study was conducted on 20 patients with breast carcinoma who endue at modified radical mastectomy from the department of experimental and clinical Surgery, Medical Research Institute, Alexandria University. Sterile tumor samples were cultured in the presence and absence of appropriate concentration of anti-IL-6 monoclonal antibody. The levels of LC3B (specific marker of autophagy) and CD44 &CD24 (surface markers of cancer stem cells) were measured by double indirect immunofluorescence technique.

The levels of autophagy as well as both CD44 and CD24 in our own designed breast tumor tissue culture systems are significantly higher than that of the corresponding breast normal ones. These levels significantly decreased by neutralizing the IL-6 activities using anti-IL-6 mAbs.

No significant correlations were found between CD44 and CD24 levels in all tissue culture systems except in the anti-IL-6 mAb treated tumor / normal one. While negative correlations between CD44 and CD24 levels in the anti-IL-6 mAb supplemented tissue culture systems may be due to shift in the dynamic equilibrium between CSCs and NSCCs

No significant correlation was found between the autophagy level and either CD44 or CD24 levels in almost all tissue culture systems except the anti-IL-6 mAb tumor tissue culture ones.

Accordingly, neutralization of IL-6 within breast cancer TME may represent a potential promising immunotherapeutic strategy of the disease through reduction of both autophagic activity and stemness of the tumor tissue.