New Genetic Molecular Tools to Explore Breast Cancer Metastatic Potential

Thesis submitted to

Faculty of Science

In partial fulfillments required for M.Sc. degree in

Biochemistry

By

Bassant Safaa Mohamed Zaki Ezzat

B.Sc.

Biochemistry

Faculty of Science

Alexandria University

2007

Faculty of Science
Alexandria University
2012

Abstract

Signal transducer and activator of transcription 3 (STAT3) has been found constitutively activated in a wide variety of cancers and in recent years it has become an attractive therapeutic target. The aim of this study is to investigate the effect of a novel organotin supramolecular coordination polymer (C10) on breast cancer generally and on Stat3 signalling specifically. The potential influence of compound C10 in STAT3 signalling of breast cancer cells was evaluated by checking the status of STAT3 signalling and its downstream gene expression in two breast cancer cell lines (MDA-MB-231 and MDA-MB-157) with and without C10 treatment. The result shows that C10 decrease cell viability, induced apoptosis as indicated by accumulation of sub-G1 population, DNA fragmentation and cell shrinkage as well as it block constitutive Stat3 signalling in human breast cancer cell lines. The anti-apoptotic protein Bcl-2, which is encoded in target genes of Stat3, were down-regulated by C10 treatment followed by induction of apoptosis, suggesting that the antitumor cell activity of C10 is in part due to the blockade of Stat3-mediated dysregulation of growth and survival pathways. Moreover, compound C10 showed a significant reduction of β-catenin expression levels in both breast cancer cell lines. Furthermore, *in vivo*, the compound C10 suppressed tumor growth by 58% in animal model that developed mammary carcinoma. Taken together, compound C10 exhibits specific *in vivo* and *in vitro* antitumor effects suggesting that it is an effective STAT3 inhibitor.