Transcriptional signature of histone deacetylases in breast cancer

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Breast cancer is the leading cancer in women worldwide. In Egypt, Breast cancer is ranked the first among females, representing about 32% of all cancer cases. Its incidence is anticipated to 3-fold increase by 2050. One of the major challenges of breast cancer management is the heterogeneity (clinicopathological and genetic status) between tumors. Thus, characterizing the critical biomarkers, their role in carcinogenesis and drug response as well as their use as targets for diagnosis and therapy is pivotal to breast cancer management. Epigenetic alterations are frequent in breast cancers, prompting much interest in their clinical significance and whether manipulating these alterations could be adopted as therapeutic strategies. Histone acetylation is a relatively well known histone modification that regulates gene transcription. The opposing actions of two types of enzymes, Histone Acetyltransferases (HATs) and Histone Deacetylases (HDACs) modulate the acetylation status of the histones. Typically, the euchromatic regions of the genome are actively transcribed are enriched with acetylated histones, supporting a critical role for modified histones in regulating gene expression and cellular growth. An enormous work has been done to investigate the expression of HDACs in cancer with emphasis on breast cancer and their role as a biomarker of disease outcome. In addition, several studies addressed the effects of Histone Deacetylase Inhibitors (HDACIs) as an adjuvant therapy. However, Transcriptional profile of the whole HDACs in human breast cancer tissue has not been characterized yet. Through accomplishment of this project, we will be able to characterize the expression profile of HDACs in 50 breast cancer patients, using quantitative real time polymerase chain reaction (qRT-PCR) to quantify mRNA expression levels of different HDACs in breast cancer in comparison to normal breast tissue. Moreover, correlation between the expression profile of different members of HDACs and clinicopathological criteria of cancer will also be attempted through assessment and collection of all available Tumor data including, age of onset, Tumor size, nodal status, metastasis, histopathological type and staging and depth of penetration. Hereafter, HDACs role as biomarkers of breast cancer will be evaluated. Moreover, the relation between our identified transcriptional profile and previously characterized translational profile will allow more understanding of the biological process in carcinogenesis. This will be the first study where full transcriptional signature of HDACs in breast cancer is conducted. The successful completion of this project will provide the first HDACs transcriptomic profile of Egyptian Breast cancer patients along with data that can serve as the basis for identification of predictive markers in patients. This project will not only allow us to answer essential molecular biology question about breast cancer but will also allow us to develop new targeted and curative therapeutic regimens for these patients as it will assist in identification of certain selective HDACIs that can be used in trials of breast cancer management.

Biography

Sahar El Shafei has completed her BSc and worked as a Demonstrator in the Department of Human Genetics Medical Research Institute in 1984 and then started working as an Assistant Lecturer of Human Genetics Medical Research Institute in 1988 and became a Lecturer of Human Genetics at Medical Research Institute in 1995. She was awarded the scientific title of Assistant Professor of Human Genetics at Medical Research Institute in 2003 and scientific title of Professor in 2009. She was the Co-Principal Investigator of a project from Science and Technology Developmental Fund. She is currently a Professor and Head of Human Genetics Department at Medical Research Institute, Alexandria University, Egypt

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