THESIS ABSTRACT

Investigating the role of Notch and related signaling pathways in Breast cancer patients

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Background: Breast cancer is the most common cancer in women worldwide. Cancer Stem Cells play an important role in the processes of drug resistance and metastasis. Studies showed that behavior and biology of B.C differ in different racial groups, emphasizing the importance of understanding the biology of the disease in each population separately. Aim: Here we investigated the differential expression of a number of CSCs regulating genes in Egyptian and British patients. we have studied the influence of cancer therapy on the expression levels of these genes. Materials and Methods: CSCs were isolated from a total of 24 B.C patients from Egypt and England, using Anoikis resistance assay. RNA was extracted, its concentration and quality were measured by nano drop, bioanalyzer and qPCR) and cDNA was then synthesized. qPCR arrays harboring primers specific for (Notch1, Notch4, Nanong, JAG1, PARP1, HIF1A, SP1, STAT1, NFKB1, DNMT1, DNMT3B) were designed. The differential gene expression between; Egyptian untreated vs British untreated, Egyptian treated vs British treated, Egyptian untreated vs Egyptian treated, and British untreated vs British treated was detected using $\Delta\Delta$ Ct method. **Results**: We have detected which genes of the genes under study are differentially expressed between Egyptians and British patients. we determined which genes in both racial groups may be responsible for CSCs resistance to therapy. Conclusion: Our study strongly confirms the racial variation in B.C biology and is the first study to show that CSCs signaling pathways are behind this variation. More importantly, we detected which genes showed be targeted to sensitize CSCs to therapy in Egyptian patients.

Keywords: Breast cancer; NOTCH; PARP1; Stem cells

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