The transcription factor HOXC10 is upregulated during chemotherapy treatment and resistance in breast cancer

Hardik Panday

All India Institute of Medical Sciences

E-mail: hardik292@gmail.com

Breast cancer is the second leading cause of cancer deaths in women worldwide. Although chemotherapy is effective, resistance to drugs develops over time and can account for treatment failure in over 90% of metastatic breast cancer patients. HOX genes are homeobox-containing transcription factors well-known for their role in morphogenesis. However, accumulating evidence has emphasized their importance during carcinogenesis and metastasis. HOXC10, a protein in this family, was found to be overexpressed in a large subset of primary and metastatic breast cancer. The goal of this study is to understand the role of HOXC10 up-regulation in the response to chemotherapy. Cell survival assays after different chemotherapy drug treatment showed that overexpression of the exogenous HOXC10 in MCF10A cell lines reduced their susceptibility to most drugs, and vice versa, its knockdown in SUM159 cells increased their vulnerability to drug treatment. Further, HOXC10 expression increased upon DNA damage in vitro at the RNA and protein levels, and this upregulation was concentration and time dependent. Supporting the results, SUM159 and MDAMD231 xenografts that were treated with doxorubicin, etoposide, paclitaxel or carboplatin over weeks and that showed partial to no response tended to have a higher expression of HOXC10. Finally, HOXC10 was found to be significantly overexpressed in MCF7 isogenic cell lines gradually selected to be resistant to some chemotherapeutic drugs.We show for the first time that HOXC10, previously known to be involved in development, is upregulated upon DNA damage in breast cancer cell lines, and that this upregulation modulates the response of the cells to chemotherapy treatment. Further work should be done to investigate the mechanism of HOXC10 in DNA damage repair and survival pathways, and eventually the clinical and prognostic implication of its overexpression in breast cancer patients.