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Genomic characterization of ERa-driven super-enhancers at CUEDC1 region in MCF-7 cells

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Breast cancer is the most common malignant cancer type among women. Annually, two million new cases are diagnosed, most of which are expressing ERa. ERa molecules induce the formation of super-enhancers (SEs), which are clusters of putative enhancers in close genomic proximity and associated with various histone modifications. By having higher density of transcriptional regulators, they could increase transcriptional output of many genes, such as CUEDC1. Activation of the latter is required for proliferation of breast cancer cells. However, SEs' role in cancer is still under investigation. Here, we are seeking a genomic characterization of the ERa-driven SEs in the breast cancer-driven MCF-7 cell line. For this, MCF-7 cells were cultured and treated with estradiol (E2) 100 μ M. Then chromatin immunoprecipitation (ChIP) assays were conducted and coupled with qPCR. ERa and H3K27 acetylation fold enrichment of four selected SE constituents, located at the CUEDC1 gene region, were evaluated in E2-treated cells over control. Our study demonstrates that after estradiol treatment and within a SE region, one enhancer, called mother enhancer, has stronger activity than the others, known as daughter enhancers. At the same time, presence of the mother enhancer is not only detectable prior to any specific treatment, but also its activity is significantly higher after activation with estradiol. This is due to the presence of a strong, canonical estrogen response element. Upon estradiol treatment, H3K27 acetylation levels at the mother enhancer region are significantly higher than those at daughter enhancer regions as ERa-driven SE region becomes more open and more transcriptional regulators are recruited. Our practical result conforms to the former findings (Bojcsuk D et al NAR, 2016) which were obtained by using bioinformatics tools. Hence, this study might give a better understanding for one of ERa molecular mechanisms that are associated with high risk of breast cancer.

Noura Faraj is the recipient of a CPP Fee Waiver.