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Computational Approach to Validate Long-range Chromatin Association between Estrogen Receptor Alpha Proteins and Candidate Genes of Breast Cancer MCF-7 within Different Human Reference Genomes

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To investigate mechanism of estrogen receptor alpha (ER-α) associated with gene expression, In particular, we studied computational long-range effects by mapping estrogen receptor alpha binding sites (ER-αBSs) on 37 breast cancer candidate genes with the aim to reveal the most associated genes along the transcription start sites. Then, we compared result of the computational long-range chromatin interaction analysis with pair-end tag (ChIA-PET) on different human reference genome sequences 17 (hg17), 18 (hg18) and 19 (hg19) [1, 2].

By obtaining numerical coordinates of ER-αBSs, we could see a more completely computational result with ChIA-PET workflow on hg19 by detecting more number of ER-αBSs associated with breast cancer candidate genes within the same range of the transcription start sites. By investigating ER-α on different human reference genome sequences, we could determine coordinates of ER-αBSs can be altered to detect different positions of ER-αBSs based on association with breast cancer candidate genes such GREB1 and SGK3. In this study, we obtained 3500, 3488 and 3501 ER-αBSs respectively from hg17, hg18 and hg19. We found common 3487 ER-αBSs between hg17 and hg18, common 3425 ER-αBSs between hg17 and hg19, and common 3426 ER-αBSs between hg18 and hg19. However, we only found 3412 common ER-αBSs among hg17, hg18 and hg19. Therefore, within our comparative study, we could detect different positions and number of ER-αBSs associated with candidate genes on a single map, as we had not expected so far. To specifically differentiate the coordinates of ER-αBSs generated by computational ChIA-PET workflows on hg17, hg18, and hg19, we also reported all different coordinates of ER-αBSs associated with detectable breast cancer candidate genes.

Within our comparative study, we found that ChIA-PET workflow really depends on human reference genomes and this would lead to detect different numbers of ER-αBSs; moreover, different positions of ER-αBSs from breast cancer candidate genes can also be confirmed within our research study.

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