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Role of Estrogen Receptor-alpha in Mammary Carcinoma by Single Nucleotide Polymorphisms and Molecular Docking: An In-silico Analysis

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Abstract : Estrogen receptor alpha, also known as estrogen receptor-1, is highly involved in risk of mammary carcinoma. The objectives of this study were to identify non-synonymous SNPs of estrogen receptor and their association with breast cancer and to identify the chemotherapeutic responses of phytochemicals against it via in-silico study design. For this purpose, different online tools. to identify pathogenic SNPs the tools were SIFT, Polyphen, Polyphen-2, fuNTRp, SNAP2, for finding disease associated SNPs the tools SNP&GO, PhD-SNP, PredictSNP, MAPP, SNAP, MetaSNP, PANTHER, and to check protein stability Mu-Pro, I-Mutant, and CONSURF were used. Post-translational modifications (PTMs) were detected by Musitedeep, Protein secondary structure by SOPMA, protein to protein interaction by STRING, molecular docking by PyRx. Seven SNPs having rsIDs (rs760766066, rs779180038, rs956399300, rs773683317, rs397509428, rs755020320, and rs1131692059) showing mutations on I229T, R243C, Y246H, P336R, Q375H, R394S, and R394H, respectively found to be completely deleterious. The PTMs found were 96 times Glycosylation; 30 times Ubiquitination, a single time Acetylation; and no Hydroxylation and Phosphorylation were found. The protein secondary structure consisted of Alpha helix (Hh) is (28%), Extended strand (Ee) is (21%), Beta turn (Tt) is 7.89% and Random coil (Cc) is (44.11%). Protein-protein interaction analysis revealed that it has strong interaction with Myeloperoxidase, Xanthine dehydrogenase, carboxylesterase 1, Glutathione S-transferase Mu 1, and with estrogen receptors. For molecular docking we used Asiaticoside, Ilekudinuside, Robustoflavone, Irinoticane, Withanolides, and 9-amin0-5 as ligands that extract from phytochemicals and docked with this protein. We found that there was great interaction (from -8.6 to -9.7) of these ligands of phytochemicals at ESR1 wild and two mutants (I229T and R394S). It is concluded that these SNPs found in ESR1 are involved in breast cancer and given phytochemicals are highly helpful against breast cancer as chemotherapeutic agents. Further in vitro and in vivo analysis should be performed to conduct these interactions.

Keywords : breast cancer, ESR1, phytochemicals, molecular docking
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