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# INTERACTIONS OF BREAST CANCER GENES WITH RECEPTORS VIA DOCKING

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***Abstract:***Cancer has become more prevalent in present days. It is a condition where the cells grow uncontrollably and spread to various parts of the body due to gene mutations and environmental factors. Breast cancer is one of the most commonly identified cancers in women aging over 40 and above. Breast cancer is mainly caused by mutations in tumor suppressor genes –BRCA1 & BRCA2. Many diagnoses, treatments and therapies have come into existence in treating breast cancer but they have found to be recurring, and the final solution could be mastectomy. Bioinformatics is an interdisciplinary field where computational tools are used to interpret biological data helping the medical fraternity not only in laboratory diagnosis but in trying to know the interaction at the genetic level. In the present work I have identified the interacting receptors like ER, PR, HER2, RAD51, & XRCC3 with BRCA1 & BRCA2, and it is found that ER receptor interacts with BRCA2 with the help of docking tools, available in silico.

***Index Terms*** **- Breast Cancer genes (BRCA 1 & 2), Estrogen Receptor, Progesterone Receptor, Human Epidermal growth Factor Receptor 2(HER2), RAD51, XRCC3, Docking tools.**

## I. INTRODUCTION:

Cancer is a disease in which the cells of the body grow out of control and spread to other parts of the body. Human cells normally divide and replace old cells. This process breaks down in cancer, causing abnormal and damaged cells to grow and reproduce masses of tissue (Tumors), which can be benign or malignant.Some benign Tumors as in Brain can be fatal.Metastasis is the process wherein cancer spreads to other parts of the body, forming a new tumor.

"Drivers" are genetic changes that affect proto-oncogenes, Tumor suppressor genes, and DNA repair genes and contribute to cancer. Proto-oncogenes (HER2 gene, ras, Myc, and cyclin D) [1] that play a role in proper cell division if mutated can become cancer-causing genes (or oncogenes). Tumor suppressor genes involved in cell development (p53, Rb, VHL, BRCA1& BRCA2)[2] can cause cells to proliferate uncontrollably. Mutations in DNA repair genes, responsible for repairing damaged DNA, cause chromosomal alterations and malignancy of cells. By understanding genetic changes Scientists developed medicines targeting cancer-causing genes.[3]

Breast cancer is commonly diagnosed in women, and is the second leading cause of death from cancer. The breast milk-producing glands are anatomically located on the pectoralis major muscle & ligaments. Around fifteen to twenty lobes arrange to form breast. Each lobe is formed by lobules containing the glands responsible for milk production in response to prolactin.Breast cancer can be detected through routine screening, a breast lump, a change in shape or size or nipple discharge. Mastalgia is a common affliction. A physical examination, imaging, mammography, and tissue biopsy are required to diagnose breast cancer. Early detection increases the likelihood of survival. The Tumor is prone to lymphatic and haematological spread, leading to distant metastasis and a poor prognosis. [4]

Mutations in the Tumor suppressor genes BRCA1 and BRCA2, responsible for 5% to 10% of all breast cancer cases and cause hereditary breast and ovarian cancer syndrome, increase the risk of developing epithelial malignancies as well as other genetic or hereditary factors (HBOC). Ovarian and breast cancers are two cancers linked to BRCA1 and

BRCA2 [5]. Each person receives a copy of each gene from each parent. Only one copy of the gene increases the risk of developing HBOC. [6]

BRCA 1 AND 2 Tumor suppressor genes and their mutations are leading cause of breast cancer. BRCA1 is found on chromosome 17q12-21 and BRCA2 on chromosome 13q12-13, these are susceptibility genes. BRCA1 mutations are associated with ovarian cancer, while BRCA2 mutations with male breast cancer, ovarian, prostate, and pancreatic cancer. The isolation of these genes allows identification of genetic defect. [7]

**HORMONE THERAPY:** Hormones- the body chemicals produced by glands and circulated through the bloodstream, are linked to cancer growth. Hormone therapy inhibits the growth of cancer cells by removing or blocking hormones. Hormone therapyhas reduced using drugs, surgery, or radiation for treatment. Ovarian ablation stops the ovaries from producing estrogen, which promotes breast cancer growth. Early-stage and metastatic breast cancer are treated with tamoxifen-based therapy (type of hormone therapy).Agonist therapy for luteinizing hormone-releasing hormone (LHRH) reduces estrogen and progesterone levels. Aromatase inhibitors work by inhibiting aromatase enzyme, reducing estrogen levels. Aromatase inhibitors include anastrozole, letrozole, and exemestane. Other hormone therapies include megestrol acetate or anti-estrogen therapy (fulvestrant). [8]

**OTHER THERAPIES:**Breast cancer is treated in several ways.Surgery:Removal of cancerous tissue.Chemotherapy:kills cancer cells through medicines. Biological therapy: Works with body's immune system to fight cancer cells.Radiation therapy: Using high-energy rays to kill the cancer cells.[9]

## II. MATERIALS AND METHODS

This paper puts light on interactions between BRCA1, BRCA2 and hormone receptors such as (Estrogen, Progesterone, HER2) and DNA Repair Genes (RAD51, XRCC3) Receptors.

a) **BRCA1 GENE**: BRCA1 gene is involved in 40-45% of hereditary breast cancers, is rarely mutated in sporadic breast cancers, and plays a larger role in carcinogenesis. Because of protein-protein interactions, BRCA1 act as Tumor suppressor in cell cycle progression, DNA repair processes, DNA damage-responsive cell cycle checkpoints, regulation of a set of specific transcriptional pathways, and apoptosis [10]. The CDS of BRCA1 gene, having 1863 amino acids, with the accession number AAC37594 is extracted from the chromosome 13q12 of Homo sapiens.

b) **BRCA2 GENE:**The BRCA2 gene functioning as Tumorsuppressor prevents cells from rapidly growing, dividing, and repairs DNA damage caused by radiation and environmental exposures. It is essential for maintaining the genome stability of a cell. It aids in the regulation of cytokinesis. [11]. The CDS BRCA2 gene, having 3418 amino acids, with the accession number AAB07223.1, is extracted from chromosome 17 of Homo sapiens.

c) **ESTROGEN RECEPTOR:**Estrogen Receptors has two sub-types - ERα can be found in the mammary gland, uterus, ovary (thecal cells), bone, male reproductive organs (testes and epididymis), prostate (stroma), liver, and adipose tissue and ERβ is found in prostate (epithelium), bladder, ovary (granulosa cells), colon, adipose tissue, and immune system. ERα activation by estrogens is responsible for increased proliferation in breast cancers, but is countered by ERβ, which has an ant proliferative effect. Ductal breast cancer has a high level of ERα and low level of ERβ expression, whereas early-stage lobular breast cancer has abundant levels of both [12]. The CDS of ER Gene having 595 Amino Acids with the ACCESSION NO: AAA52399.1 is extracted from Homo sapiens.

d) **PROGESTERONE RECEPTOR:**Progesterone receptorsare ligand-activated transcription factors (TFs) that bind DNA at progesterone response elements and/or via tethering to other transcription factors (signal transducers and activators of transcription [STATs]. PR-A and -B can regulate sets of target genes (isoform-specific) and have both ligand-dependent and independent activities. PR-C isoform truncated in the DNA-binding domain by an AUG codon; inhibits PR-actions B's in the uterus. During puberty and pregnancy, progesterone acts as a breast mitogen, mediating the expansion of epithelial-derived mammary alveoli for lactation. Prior to pregnancy, PR-B, ER is required for mammary ductal elongation.[13] The CDS of PR Gene having 695 Amino Acids with the ACCESSION NO: BAC06585.1 is extracted from Homo Sapiens.

e) **HER2:**HER2, along with epidermal growth factor receptor, HER3, and HER4, is found on chromosome-17 and regulates normal cell proliferation, survival, and differentiation through different signal transduction pathways. The overexpression or amplification of the human epidermal growth factor receptor-2 gene is identified as HER2 activation mechanism in breast cancer. There are several HER2 kinase domains, whose mutations are oncogenic in nature [14]. The CDS of HER2 Gene having 1255 Amino Acids,with the ACCESSION NO: AAA75493is extracted from Homo sapiens.

f) **XRC33 and RAD51(DNA repair genes):**Double-strand break repair and homologous recombination are aided by DNA repair genes. During recombination repair, XRCC3 interacts and collaborates with RAD51. XRCC3 mutant cells have different homologous recombination (HR) product spectra, with longer gene conversion tracts, discontinuous tracts, and local rearrangements. Following phosphorylation, XRCC3, BRCA2, FANCD2, and FANCG form multiple pairwise interactions. These 4 proteins promote homologous recombination repair of damaged DNA [15]. Mutations in BRCA2 or XRCC3 genes lead to disruption in repair mechanism further leading to breast cancer. The CDS of both XRCC3 gene having 346 amino acids with ACCESSION NO: AAC04805.1 and RAD51 genehaving 339 Amino Acids with ACCESSION NO : CAG38796 were extracted from Homo sapiens.

The study of interactions between the BRCA genes and the receptors was done by the use of computational tools like:

- **NCBI:**NCBI stands for National Centre of Biotechnology Information. NCBI globally gathers all the information about molecular biology and was used to extract the ACCESSION numbers of the aforementioned proteins. NCBI's mission is to develop information technologies to aid in the understanding of fundamental molecular and genetic processes that control health and disease. [16]

- **SWISS-MODEL:**The SWISS-MODELbioinformatics tool was used for the process of homology modelling to build simple protein structures. The SWISS-MODEL server is designed to work with minimal user input, such as the amino acid sequence of a target protein in the simplest case. Because comparative modelling projects can vary in complex, some modelling projects may require additional user input. [17]

- **SWISS-PDB VIEWER:**Swiss-PdbViewer is widely used tool to view complex protein structures. BRCA1, BRCA2, Hormone Receptors, DNA Repairs Genes models were viewed through this tool. Swiss-PdbViewer (also known as DeepView) is anapplication with a user-friendly interface that allows to analyses multiple proteins at once. Proteins can be superimposed to determine structural alignments and compare active sites or other relevant parts. Working with Swiss model and Swiss-pdb viewer reduces the amount of time it takes to generate models.[18]

- **PSOPIA:** As this paper is based on Protien-Protien interaction, this tool helps in finding out the interactions of the previously mentioned genes with the help of its sequence. Using Averaged One-Dependence Estimators (AODE) and three features calculated for each protein pair, the proposed method can predict interactions between two proteins (of unknown structure). [19]

- **CLUSPRO:** ClusProtool has been used for protein–protein docking. The server (https://cluspro.org) provides a basic home page with only two files in Protein Data Bank (PDB) format to get started. It is one of the most widely used protein interaction tool using structures [20].

- **HEX8.0.0:** Hex, a molecular graphics programwas used for calculating and displaying possible docking modes for protein and DNA molecules in pairs. It also calculates protein in ligand docking if the ligand is rigid, and superposes pairs of molecules based on their 3D shapes alone.[21]

- **HDOCK:** HDOCK, a multi-component package which includes a number of third-party programs, was used for Docking Purpose. There can be a maximum of 20 jobs running at once, with hundreds more queued in the background. The docking process is quick, with a docking calculation taking about 10–20 minutes on average. [22]

# III. PROTOCOL:

To find out the interactions between the BRCA genes and the receptors, the following protocol was followed:

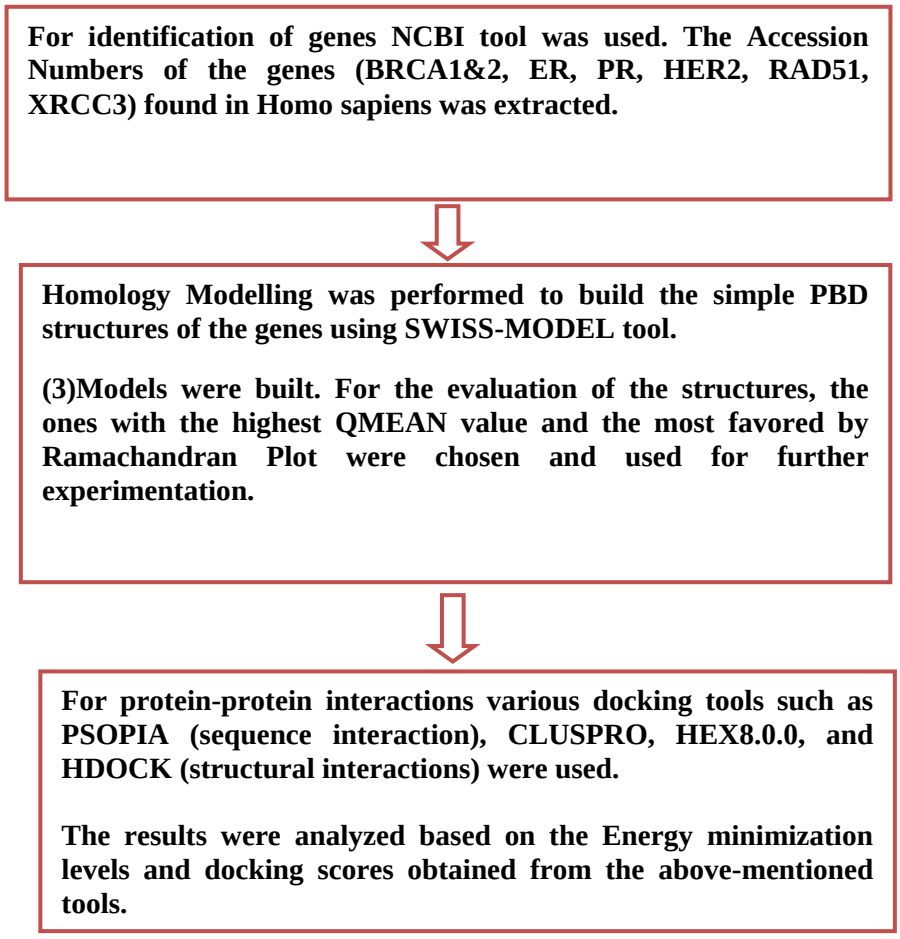



figure 1:

flow chart depicting protocol to identify the interactions between BRCA 1 & 2 genes with receptors showing the tools and methodologies performed

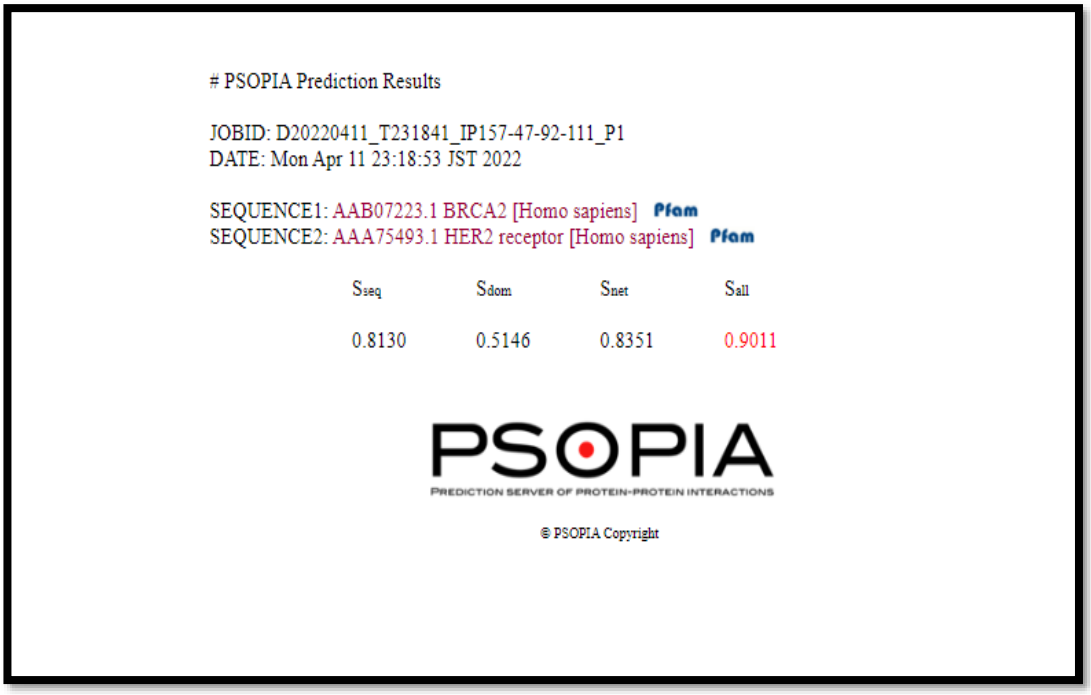
## IV. RESULTS (Tables and Figures):

The interactions were analyzed by the use of several in silico tools (Bioinformatics tools)and it has been found that ER genes have higher interaction with BRCA2 genes.

table 1:

showing the energy values and docking scores of the interactions between brca1&2 genes and various receptors using bioinformatics tools. the receptors having high affinity with the BRCA genes have been highlighted

| INTERACTIONS BETWEEN BRCA1&2 GENES AND RECEPTORS USING IN SILICO TOOLS | | | | | |
|---|---|---|---|---|---|
| **(A): PSOPIA: - ENERGY VALUES** | | | | | |
| **GENES** | **ER RECEPTOR** | **PR RECEPTOR** | **XRCC3** | **RAD51** | **HER2** |
| **BRCA1** | **0.2751** | **0.2926** | **0.2278** | **0.2427** | **0.2924** |
| **BRCA2** | **0.3525** | **0.3525** | **0.5577** | **0.5577** | **0.9011** |
| | | | | | |
| **(B): CLUSPRO: - ENERGY VALUES** | | | | | |
| **GENES** | **ER RECEPTOR** | **PR RECEPTOR** | **XRCC3** | **RAD51** | **HER2** |
| **BRCA1** | **-1028.1** | **-1086.2** | **-1146.2** | **-1189.8** | **-957.7** |
| **BRCA2** | **-1337.8** | **-1129.1** | **-1106.2** | **-1257.6** | **-1193.8** |
| | | | | | |
| **(C): HEX 8.0.0: - ENERGY VALUES** | | | | | |
| **GENES** | **ER RECEPTOR** | **PR RECEPTOR** | **XRCC3** | **RAD51** | **HER2** |
| **BRCA1** | **-45327.223** | **-11955.359** | **-55906.086** | **-44327.672** | **-38444.70** |
| **BRCA2** | **-44936.250** | **-36775.711** | **-80683.484** | **-9124.889** | **-54009.508** |
| | | | | | |
| **(D): HDOCK: DOCKING SCORES** | | | | | |
| **GENES** | **ER RECEPTOR** | **PR RECEPTOR** | **XRCC3** | **RAD51** | **HER2** |
| **BRCA1** | **-256.34** | **-271.08** | **-257.55** | **-245.58** | **-258.54** |
| **BRCA2** | **-327.91** | **-271.07** | **-300.50** | **-262.68** | **-270.75** |



# PSOPIA Prediction Results

JOBID: D20220411_T231841_IP157-47-92-111_P1
DATE: Mon Apr 11 23:18:53 JST 2022

SEQUENCE1: AAB07223.1 BRCA2 [Homo sapiens] Pfam
SEQUENCE2: AAA75493.1 HER2 receptor [Homo sapiens] Pfam

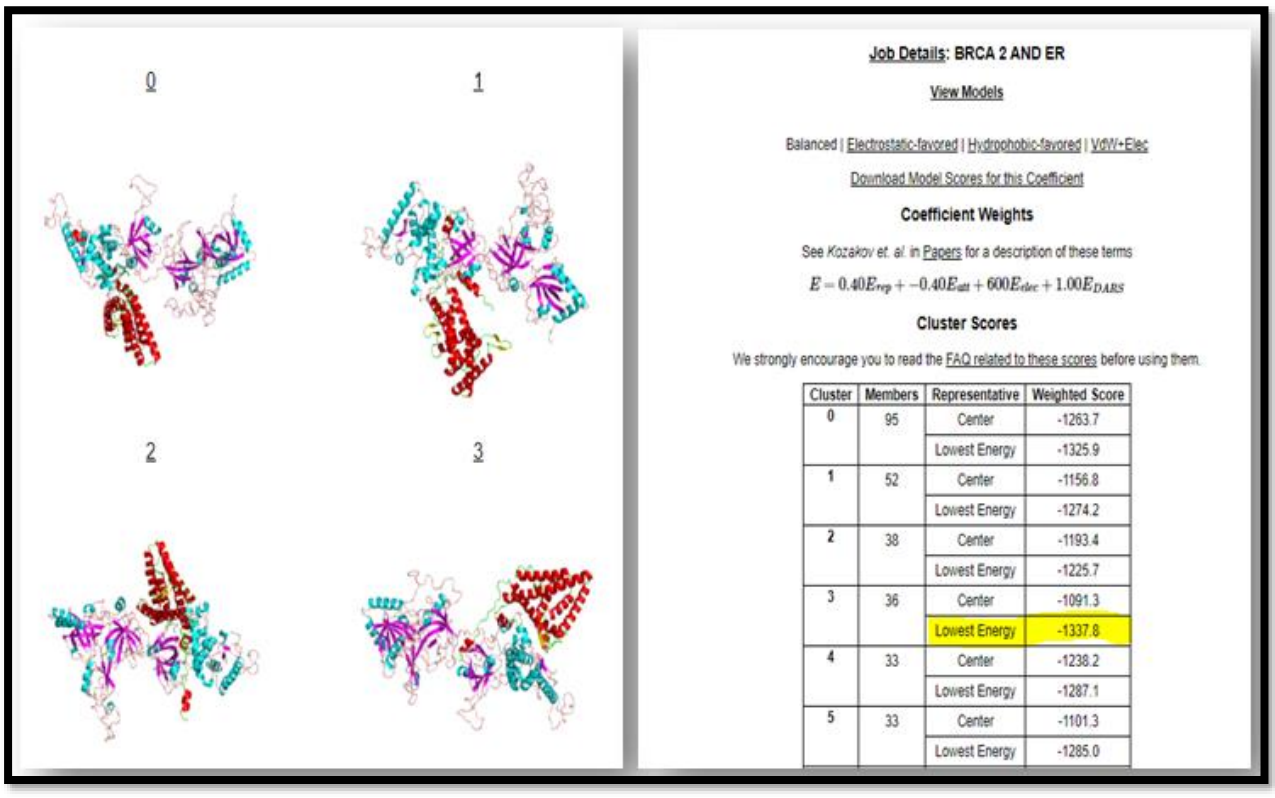
| $S_{seq}$ | $S_{dom}$ | $S_{net}$ | $S_{all}$ |
|---|---|---|---|
| 0.8130 | 0.5146 | 0.8351 | 0.9011 |

PSOPIA
PREDICTION SERVER OF PROTEIN-PROTEIN INTERACTIONS



figure 2: (corresponds to table1-a)

interaction of brca2 and her2 receptor using PSOPIA indicates that BRCA2 has high affinity with HER2 receptor (0.9011)




**Job Details: BRCA 2 AND ER**

View Models

Balanced | Electrostatic-favored | Hydrophobic-favored | VdW+Elec

Download Model Scores for this Coefficient

**Coefficient Weights**

See Kozakov et. al. in Papers for a description of these terms

$$E = 0.40E_{rep} + -0.40E_{att} + 600E_{elec} + 1.00E_{DARS}$$

**Cluster Scores**

We strongly encourage you to read the FAQ related to these scores before using them.

| Cluster | Members | Representative | Weighted Score |
|---|---|---|---|
| 0 | 95 | Center | -1263.7 |
| | | Lowest Energy | -1325.9 |
| 1 | 52 | Center | -1156.8 |
| | | Lowest Energy | -1274.2 |
| 2 | 38 | Center | -1193.4 |
| | | Lowest Energy | -1225.7 |
| 3 | 36 | Center | -1091.3 |
| | | Lowest Energy | -1337.8 |
| 4 | 33 | Center | -1238.2 |
| | | Lowest Energy | -1287.1 |
| 5 | 33 | Center | -1101.3 |
| | | Lowest Energy | -1285.0 |

figure 3: (corresponds to table1-b)

interaction of brca2 and er receptor using CLUSPRO indicates that BRCA2 has high affinity with er receptor (-1337.8)

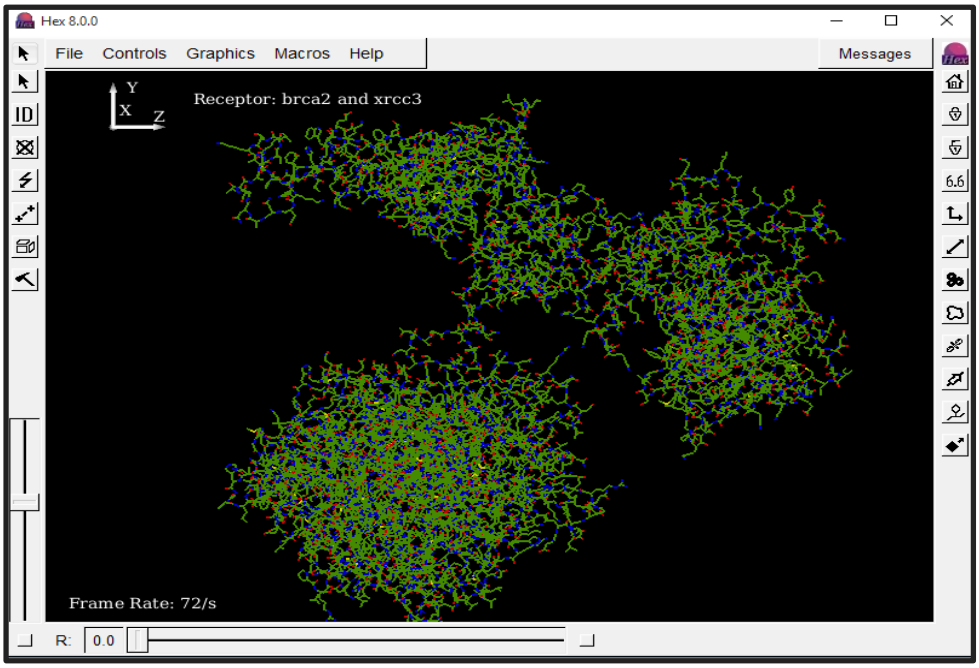


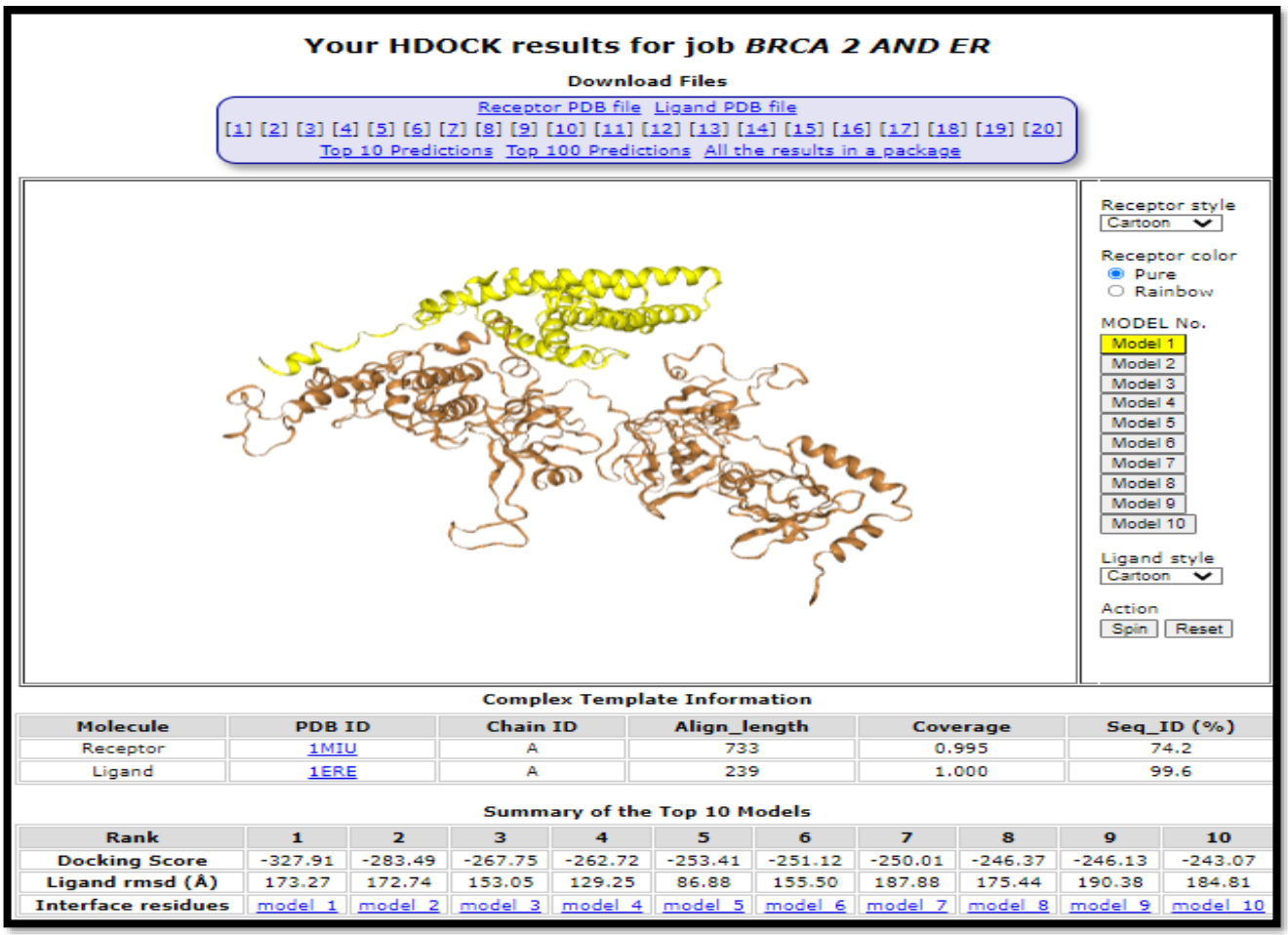

figure 4: (corresponds to table1-c)

docking of BRCA2 and XRCC3 receptor conducted using hex 8.0.0 and the energy minimization levels were later analyzed through SPDBV

| | | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| THR | C 287 | 0.320 | 1.988 | 2.727 | 1.121 | -29.15 | -9.07 | 0.0000 // E= -32.066 |
| TRP | C 288 | 3.206 | 6.471 | 8.903 | 5.928 | -67.13 | -8.04 | 0.0000 // E= -50.667 |
| ALA | C 289 | 0.263 | 1.393 | 0.901 | 0.130 | -28.96 | 13.98 | 0.0000 // E= -12.292 |
| ASN | C 290 | 1.018 | 5.800 | 2.699 | 0.600 | -38.78 | -160.66 | 0.0000 // E= -189.330 |
| GLN | C 291 | 1.122 | 5.068 | 1.717 | 0.500 | -48.65 | -168.14 | 0.0000 // E= -208.387 |
| LEU | C 292 | 1.522 | 6.249 | 3.602 | 1.180 | -30.32 | 4.67 | 0.0000 // E= -13.093 |
| LEU | C 293 | 0.195 | 3.785 | 1.839 | 0.638 | -36.20 | 4.64 | 0.0000 // E= -25.108 |
| VAL | C 294 | 0.506 | 1.602 | 2.441 | 0.683 | -30.20 | -10.66 | 0.0000 // E= -35.634 |
| ARG | C 295 | 1.428 | 2.848 | 10.004 | 0.921 | -57.27 | -273.64 | 0.0000 // E= -315.703 |
| LEU | C 296 | 0.552 | 4.433 | 1.586 | 0.329 | -44.88 | -14.12 | 0.0000 // E= -52.102 |
| LEU | C 297 | 0.468 | 3.575 | 2.437 | 0.383 | -41.83 | -13.45 | 0.0000 // E= -48.410 |
| ALA | C 298 | 0.323 | 0.436 | 2.240 | 0.019 | -30.42 | -10.76 | 0.0000 // E= -38.159 |
| ASP | C 299 | 0.821 | 2.521 | 6.214 | 1.123 | -26.94 | -14.92 | 0.0000 // E= -31.180 |
| ARG | C 300 | 1.203 | 3.476 | 2.559 | 0.778 | -36.91 | -261.69 | 0.0000 // E= -290.587 |
| LEU | C 301 | 1.025 | 7.676 | 4.550 | 0.335 | -36.73 | -19.01 | 0.0000 // E= -42.153 |
| ARG | C 302 | 2.225 | 4.146 | 5.466 | 0.341 | -23.56 | -251.77 | 0.0000 // E= -263.157 |
| GLU | C 303 | 0.748 | 3.348 | 3.358 | 0.093 | -18.47 | 12.56 | 0.0000 // E= 1.631 |
| GLU | C 304 | 0.346 | 2.912 | 3.821 | 0.208 | -18.46 | 9.54 | 0.0000 // E= -1.639 |
| GLU | C 305 | 0.373 | 6.458 | 4.779 | 0.261 | -29.32 | -11.53 | 0.0000 // E= -28.978 |
| ALA | C 306 | 0.188 | 2.598 | 0.819 | 0.379 | -16.60 | 5.90 | 0.0000 // E= -6.711 |
| ALA | C 307 | 0.254 | 1.681 | 2.403 | 0.218 | -13.12 | 9.70 | 0.0000 // E= 1.134 |
| LEU | C 308 | 0.830 | 9.406 | 2.559 | 0.128 | -17.81 | 48.70 | 0.0000 // E= 43.810 |
| GLY | C 309 | 0.508 | 2.497 | 2.907 | 0.017 | -16.74 | 36.47 | 0.0000 // E= 25.652 |
| CYSH | C 310 | 1.436 | 8.910 | 1.795 | 0.618 | -16.40 | 30.01 | 0.0000 // E= 26.373 |
| PRO | C 311 | 0.742 | 15.237 | 21.999 | 1.700 | -18.55 | -28.43 | 0.0000 // E= -7.300 |
| ALA | C 312 | 0.257 | 1.849 | 3.863 | 0.571 | -21.87 | -1.02 | 0.0000 // E= -16.348 |
| ARG | C 313 | 1.066 | 6.531 | 8.528 | 1.215 | -42.09 | -267.94 | 0.0000 // E= -292.685 |
| THR | C 314 | 0.543 | 1.330 | 2.088 | 0.576 | -29.12 | -21.24 | 0.0000 // E= -45.824 |
| LEU | C 315 | 0.721 | 2.536 | 4.807 | 0.593 | -37.70 | -6.24 | 0.0000 // E= -35.281 |
| ARG | C 316 | 1.300 | 2.823 | 5.559 | 1.230 | -39.97 | -277.46 | 0.0000 // E= -306.519 |
| VAL | C 317 | 0.813 | 1.687 | 3.859 | 0.652 | -34.14 | -0.22 | 0.0000 // E= -27.340 |
| LEU | C 318 | 0.358 | 2.738 | 3.103 | 0.324 | -31.81 | 4.31 | 0.0000 // E= -20.976 |
| SER | C 319 | 0.335 | 0.668 | 3.517 | 0.623 | -26.66 | -23.21 | 0.0000 // E= -44.723 |
| ALA | C 320 | 0.404 | 2.127 | 1.838 | 0.196 | -18.45 | 26.35 | 0.0000 // E= 12.472 |
| PRO | C 321 | 0.293 | 16.444 | 18.542 | 1.111 | -24.46 | -27.49 | 0.0000 // E= -15.557 |
| HISA | C 322 | 0.336 | 3.050 | 3.152 | 1.435 | -38.62 | 28.36 | 0.0000 // E= -2.287 |
| LEU | C 323 | 0.775 | 3.450 | 5.135 | 0.387 | -31.92 | 31.03 | 0.0000 // E= 8.857 |
| PRO | C 324 | 1.096 | 15.849 | 17.030 | 0.171 | -15.38 | -4.63 | 0.0000 // E= 14.140 |
| PRO | C 325 | 0.180 | 12.509 | 22.308 | 0.527 | -14.11 | -24.72 | 0.0000 // E= -3.298 |
| SER | C 326 | 0.426 | 0.986 | 4.533 | 1.013 | -18.52 | -26.70 | 0.0000 // E= -38.262 |
| SER | C 327 | 0.181 | 0.862 | 1.776 | 1.434 | -15.25 | -16.22 | 0.0000 // E= -27.215 |
| CYSH | C 328 | 0.341 | 1.596 | 9.715 | 0.569 | -23.12 | -6.09 | 0.0000 // E= -16.982 |
| SER | C 329 | 0.271 | 1.083 | 1.015 | 0.425 | -23.62 | -17.03 | 0.0000 // E= -37.852 |
| TYR | C 330 | 1.492 | 10.126 | 2.960 | 4.570 | -49.84 | -42.84 | 0.0000 // E= -73.536 |
| THR | C 331 | 0.752 | 3.548 | 7.848 | 0.677 | -26.97 | -14.71 | 0.0000 // E= -28.855 |
| ILE | C 332 | 1.088 | 3.099 | 3.959 | 0.852 | -20.97 | -1.50 | 0.0000 // E= -13.474 |
| SER | C 333 | 0.443 | 2.463 | 2.847 | 1.213 | -16.83 | -25.42 | 0.0000 // E= -35.283 |
| ALA | C 334 | 0.307 | 3.169 | 0.445 | 1.008 | -10.06 | 0.42 | 0.0000 // E= -4.712 |
| GLU | C 335 | 0.945 | 4.926 | 5.264 | 0.569 | -22.56 | 39.10 | 0.0000 // E= 28.244 |
| GLY | C 336 | 0.584 | 1.466 | 1.526 | 0.233 | -23.57 | 23.23 | 0.0000 // E= 3.465 |
| VAL | C 337 | 0.368 | 1.804 | 3.974 | 0.655 | -32.87 | 5.78 | 0.0000 // E= -20.290 |
| ARG | C 338 | 1.318 | 2.696 | 3.475 | 0.284 | -34.83 | -222.73 | 0.0000 // E= -249.794 |
| GLY | C 339 | 0.456 | 0.805 | 3.423 | 0.109 | -7.28 | 123.01 | 0.0000 // E= 120.524 |
| OXT | C 339 | 0.000 | 0.000 | 0.000 | 0.000 | -2.52 | -11.95 | 0.0000 // E= -14.466 |
| KJ/mol | | 1536.679 | 8822.537 | 9194.089 | 1723.712 | -49481.20 | -52479.30 | 0.0000 // E= -80683.484 |

figure 5: (corresponds to table1-c)

interaction of BRCA2 and XRCC3 receptor using swiss-pdb viewer (SPDBV) indicates energy minimization levels of the interaction (-80683.484)



Your HDOCK results for job *BRCA 2 AND ER*

Download Files

Receptor PDB file Ligand PDB file

[1] [2] [3] [4] [5] [6] [7] [8] [9] [10] [11] [12] [13] [14] [15] [16] [17] [18] [19] [20]

Top 10 Predictions Top 100 Predictions All the results in a package

Receptor style: Cartoon

Receptor color: Pure / Rainbow

MODEL No.: Model 1 | Model 2 | Model 3 | Model 4 | Model 5 | Model 6 | Model 7 | Model 8 | Model 9 | Model 10

Ligand style: Cartoon

Action: Spin Reset

Complex Template Information

| Molecule | PDB ID | Chain ID | Align_length | Coverage | Seq_ID (%) |
|---|---|---|---|---|---|
| Receptor | 1MIU | A | 733 | 0.995 | 74.2 |
| Ligand | 1ERE | A | 239 | 1.000 | 99.6 |

Summary of the Top 10 Models

| Rank | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 |
|---|---|---|---|---|---|---|---|---|---|---|
| Docking Score | -327.91 | -283.49 | -267.75 | -262.72 | -253.41 | -251.12 | -250.01 | -246.37 | -246.13 | -243.07 |
| Ligand rmsd (Å) | 173.27 | 172.74 | 153.05 | 129.25 | 86.88 | 155.50 | 187.88 | 175.44 | 190.38 | 184.81 |
| Interface residues | model 1 | model 2 | model 3 | model 4 | model 5 | model 6 | model 7 | model 8 | model 9 | model 10 |

figure 6: (corresponds to table1-d)

interaction of BRCA2 and er receptor using HDOCK indicates that ER receptor has high affinity with BRCA2 genes by analyzing the docking scores (-327.91)

## V. CONCLUSION:

The BRCA1 and BRCA2 genes are the tumor suppressor genes and the leading cause for Breast Cancer. The mutations in these genes are found to be the primary cause for the development of breast cancer. The interactions were analyzed to provide a better insight in understanding carcinogenesis. Several in silico tools (Bioinformatics tools) have been used to ascertain the interactions between BRCA genes, the Hormone Receptors and DNA Repair genes. The results were analyzed based on energy minimization values and the docking scores. The results indicate that ER genes have higher interaction with BRCA2 whereas the effects of other genes such XRCC3 and HER2 are significantly moderate.

Estrogen receptors are mostly found in the endometrium layer of the uterus, breast cells, and ovariancells and in males it is found in the ducts attached to testes. These receptors are activated upon binding of estrogen hormone, when the hormones bind to the specific receptors, they contribute to the growth of breast cells. Mutations in BRCA2 genes or ER can disrupt the cell growth pattern and lead to uncontrollable growth of cells which eventually, leads to breast cancer.

Further in vitro research is required to experimentally prove this interaction and can possibly stop the interactions using the gene editing tools(e.g., CRISPR). By blocking or preventing the interactions the carcinogenesis can be stopped. Thereby breast cancer can be possibly prevented in the potential cancer patients.

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