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Leveraging Computational Biology to Validate the Anticancer Efficacy of Jujube Against Tumor Protein 53-Mutated Mammary Carcinoma

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Abstract

The study aim is to evaluate the anticancer efficacy of *Ziziphus jujube*, a natural product, employing in silico analysis (TP53 as its mutation as human breast cancer); protein to protein contact; and molecular docking with TP53 and ligands that were derived from *Z. jujube*. For this purpose, we did SNPs analysis and get the diseased or deleterious SNPs of TP53 protein using different online tools like SIFT, Polyphen, Polyphen-2, fuNTRp, SNAP2 (to identify pathogenic SNPs), SNP&GO, PhD-SNP, PredictSNP, MAPP, SNAP, MetaSNP, PANTHER (disease-associated SNPs), Mu-Pro, I-Mutant, and CONSURF (to check protein stability) were used. Post-translational modifications (PTMs) were detected by Musitedeep, Protein secondary structure by SOPMA, Protein to protein interaction by STRING, and gene ontology by QuickGo and DAVID. For molecular docking with ligands obtained from Jujube from PubChem, the Autodock Vina in PyRx virtual screening tool PyRx 0.8 was used. In the results, most of the software showed 56 to 57 SNPs diseased and deleterious and in docking all the ligands (3-O-vanilloyl ceanothin acid, 3-O-protocatechuoyl ceanothin acid, Alphitolic acid, Betulinaldehyde, Betulinic acid, Ceanothic acid, Isoceanotic acid, Pomolic acid, Pomonic acid, Saponins, and Ursonic acid) were docked with TP53 with at least 6.5 to 7.4 binding energy. It was found hydrogen, conventional hydrogen, pi-pi

T shaped, and pi-sigma bonding in most of the interactions. In conclusion, the *Ziziphus jujube* has an anticancer activity for mammary carcinoma.
Keywords: Mammary carcinoma, TP53, *Ziziphus jujube, in-silico,* Phytochemicals, Anticancer

INTRODUCTION

Mammary carcinoma is a complicated and diverse disease that is the second greatest cause of cancer mortality (Ullah et al., 2021). The most prevalent disease diagnosed in both economically developed and developing nations is breast cancer in females (Bilal et al., 2021). The women who have germline mutations in the TP53 gene have a very great risk of breast cancer of up to 85 percent by old age e.g., sixty years. The average age at diagnosis for most of these breast cancers is thirty-four years (Schon & Tischkowitz 2018). A germline TP53 gene mutation is prevalent in 5-8 percent of mammary carcinoma patients under the age of thirty. Women with TP53 mutations are more likely to develop breast tumors that are hormone receptor-positive and/or HER2-positive (Kuba et al., 2021; Akbar et al., 2025).

In response to stimuli like radiation and chemotherapy, TP53 encodes the transcription factor p53, which starts the transcription of genes involved in processes including cell cycle arrest, apoptosis, metabolism, DNA repair, and cellular senescence (Kastenhuber & Lowe, 2017). Due to the majority of TP53 mutations in the DNA binding domain, the mutant p53 protein is transcriptionally inactive in response to stress (Tonnessen-Murray et al., 2016). Even though the level of p53 induction and particular targets that p53 transactivates depend on the kind of carcinoma, wild-type p53 activity is typically regarded to be associated with a good prognosis in cancer (Kastenhuber & Lowe, 2017). The KEGG pathway also talked about the role of TP53 in inducing mammary carcinoma. (Figure 1)

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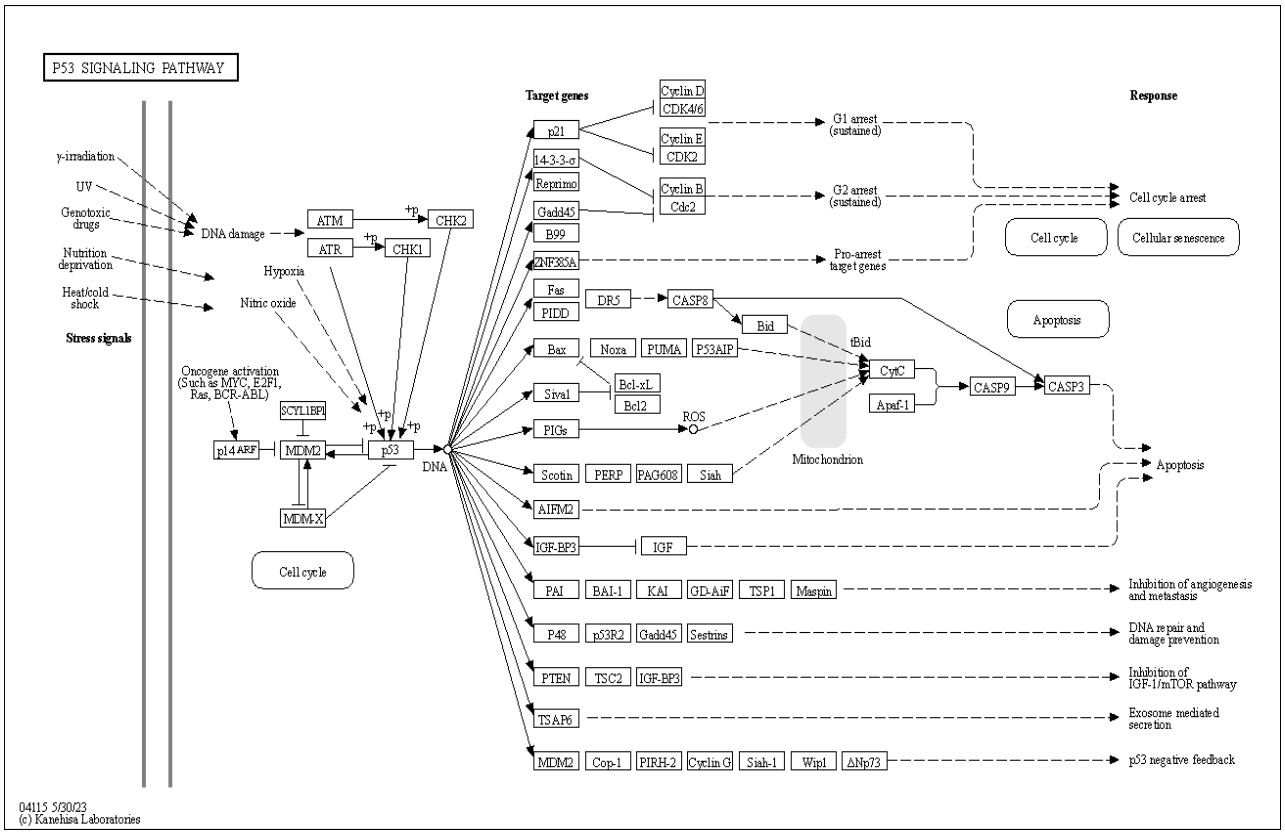

Figure 1: KEGG Pathway of TP53 Singling

To promote palliation for women whose disease cannot be cured, breast cancer therapies typically involve a multimodal strategy that includes medicinal, surgical, and radiological treatments. Chemotherapy, hormonal therapy, and targeted therapy are the main medical treatments for breast cancer today. These therapies are complicated, pricey, inefficient, and not universally accessible. Although estrogen dependence accounts for 70% of breast cancer cases, there are currently no primary preventative methods available (De Vargas et al., 2008). Therefore, the discovery of innovative anticancer drugs with fewer side effects derived from natural items, particularly plants, may offer an alternative and affordable therapeutic option (Krishnan et al., 2009).

It has been shown that plants are a source of clinically useful anticancer substances (Arivazhagan & Pillai, 2014). *Ziziphus jujube*, a member of the Rhamnaceae family of plants, is a common fruit that is mostly found in Asian countries like Iran, China, Pakistan, and India (Lakshmi & Subramanian, 2014). When fully grown, the fruit is wrinkled, crimson to purplish-black, and resembles a little date. The fruit has a solitary hard seed that resembles an olive stone. It is utilized as a delectable fruit and an efficient herbal medication with therapeutic benefits in a variety of illnesses, including cancer, gastrointestinal problems, liver issues, obesity, urinary issues, diabetes, skin infections, pharyngitis, and bronchitis (Sobhani et al., 2020). Verification of *Z. jujube*'s efficacy against cancer has taken a lot of time and effort. *Z. jujube* extracts have been found to

have anticancer effects on several tumor cell lines in earlier studies, either by themselves or in conjunction with other botanical formulations (Hoshyar et al., 2015). According to a study, *Ziziphus* possesses anticancer properties against the MCF-7 cell line (Batool et al., 2019; Farmani et al., 2016).

The present study aimed to examine the anticancer activity of *Z. jujube*, a natural product, using *in silico* analysis (TP53 as its mutation as human mammary carcinoma); protein to protein interaction and molecular docking with TP53 and ligands obtained from *Z. jujube*.

MATERIALS AND METHODS

Dataset of TP53 (Homo sapiens) Protein

The protein TP53 (protein sequence; NP NP_000537.3) in Fasta format, was collected from NCBI (http://www.ncbi.nlm.nih.gov/). UniProt (http://www.uniprot.org) provided the Protein IDs of the protein which is P04637.

Selection of harmful SNPs

SNPNEXUS a web-based tool (https://www.snp-nexus.org) is used for clarifications of known and new variations. SNPNEXUS has further SIFT and Polyphen servers that classified variants into deleterious and harmful. The input of SNPnexus was the rsIDs of protein. The output based on two servers helped to a screening of lethal nsSNPs. Polyphen-2, (http://genetics.bwh.harvard.edu/pph2/), fuNTRp (https://services.bromberglab.org/funtrp/), and SNAP2 (https://rostlab.org/services/snap2web/) server were used to predict the most pathogenic nsSNPs in TP53. The input was the sequence or UniProt accession no along with the position and name of individual residues of these proteins.

Identification of disease-related SNPs

SNP&GO (http://snps.biofold.org/snps-and-go/snps-and-go.html), PhD-SNP (https://snps.biofold.org/phd-sup/phd-snp.html), MetaSNP (http://snps.biofold.org/meta-snp/), PredictSNP (https://loschmidt.chemi.muni.cz/predictsnp1/), MAPP (http://mendel.stanford.edu/SidowLab/downloads/MAPP/), SNAP (https://www.rostlab.org/services/snap/), and PANTHER (http://www.pantherdb.org/tools/csnpScoreForm.jsp) servers were used to filter out disease-related nsSNPs from the neutral ones. The input was the amino acid sequence in FASTA format.

Protein stability and amino acid conservation affected by SNPs

MuPro (http://mupro.proteomics.ics.uci.edu/), I-Mutant 2.0 (http://gper2.biocomp.unibo.it/cgi/predictors/I-Mutant20/1-Mutant2.0.cgi) (Capriotti et al., 2005), tools were used to identify stability or disability of protein upon mutations. The input was the protein sequence of TP53.

The Bayesian technique was utilized to examine the conserved and exposed residues in both discussed proteins using Consurf (http://consurf.tau.ac.il).

Identification of Post Translation Modification (PTM) site & Molecular network interactions

The Musitedeep server (https://www.musite.net) was used to anticipate the TP53.

Prediction of Protein secondary structure

SOPMA (https://npsa-prabi.ibcp.fr/cgi-bin/secpred_sopma.pl) was used to forecast the secondary structure of the protein.

Protein-to-protein interaction (PPI)

STRING (https://string-db.org/) was use to protein-to-protein interaction (PPI)

Gene ontology

Gene ontology analysis has been done to observe the biological process (BP), cellular components (CC), and molecular functions (MF) of the protein TP53 using the websites QuickGo (https://www.ebi.ac.uk/QuickGO/annotations) and DAVID bioinformatics resources (https://david.ncifcrf.gov/).

Protein Modeling

Protein modeling was performed by Swiss-Model (https://swissmodel.expasy.org/). Models were designed of both proteins and the most suitable models were picked up for the next process.

Energy Minimization

The energy was minimized of selected wild and mutant models of both proteins by Chiron (https://dokhlab.med.psu.edu/chiron/login.php).

Docking

Accession of the target protein

The three-dimensional structure of TP53 was obtained in protein data bank file from Swiss-Model

Ligand selection

The chemical structures of ligands were obtained from PubChem (https://pubchem.ncbi.nlm.nih.gov/) database. The 3D structures were downloaded in SDF format and converted to PDB by Discovery Studio.

Target and ligand optimization

For docking analysis, PDB coordinates of the target protein and selected ligands molecule were optimized by Drug Discovery Studio version 3.0 software. These coordinates had minimum energy and stable conformation.

Analysis of target active binding sites

The active sites are the coordinates of the ligand in the original target protein grids, and these active binding sites of the target protein were analyzed using the Drug Discovery Studio version 3.0 and 3D Ligand Site virtual tools.

Molecular docking analysis

A computational ligand-target docking approach was used to analyze the structural complexes of the proteins with ligands to understand the structural basis of this protein target specificity. Initially, protein-ligand attraction was investigated for hydrophobic/ hydrophilic properties of these

complexes by the Platinum software web server. Finally, docking was carried out by PyRx. The energy of interaction of all ligands with both proteins one by one. The center of a selected grid of the protein was X= -5.3760, Y= -23.902, and Z= 4.0294 while the grid was set as X= 57.6559, Y= 47. 8367, and Z= 35.5463. The remaining parameters were set as default.

Software and PDB files

To examine the cross-docking of the binding orientation of substrates with tyrosinase protein, Autodock Vina in PyRx virtual screening tool PyRx 0.8 (http://pyrx.sourceforge.net) was chosen for this study.

Preparation of the ligand structures

The ligands were 3-O-vanilloyl ceanothin acid, 3-O-protocatechuoyl ceanothin acid, Alphitolic acid, Betulinaldehyde, Betulinic acid, Ceanothic acid, Isoceanotic acid, Pomolic acid, Pomonic acid, Saponins, and Ursonic acid.

RESULTS

From NCBI, TP53, 9478 single nucleotide polymorphisms (dbSNPs) for humans have been generated. From Ensembl 134284, there were 8076 in the 3'Downstream region, 4466 non-coding, 548 exonic, 93498 coding, 8202 in UTR region, 20042 in 5' upstream region, 3329 intronic, 3457 synonymous, 15570 non-synonymous, and 5393 in the 3' UTR 360 region (Figure S1A). Whereas, in RefSeq 77110, there were 895 in the 3'Downstream region, 58262 coding, 4969 in 3'UTR region, 10496 in 5' upstream region, 45812 intronic, 2189 synonymous, 10252 non-synonymous, and 1838 in 5' UTR region (Figure S1B). In UCSC 134292, there were 8084 in the 3'Downstream region, 4466 non-coding, 283 exonic, 93598 coding, 8202 in UTR region, 20042 in 5' upstream region, 74471 in intronic, 3457 in synonymous, 15570 in non-synonymous, and 5393 in the 3' UTR 360 region (Figure S1C). From CCDS 32080, there were 5600 in the 3'Downstream region, 18438 coding, 8042 in 5' upstream region, 9381 intronic, 1558 synonymous, 7499 non-synonymous, and 8042 in the 5' upstream region (Figure S1D).

Identification of Harmful SNPs in Proteins

SNPNEXUS was used to observe more than 10000 SNPs. By SIFT server it was examined that 8789 SNPs were deleterious with a score of less than 0.5. While 4626 SNPs were tolerable. SIFT identifies harmful SNPs based on the conservation of residue in matched sequence to closely linked sequence. The score in SIFT varies from 0 to 1. The algorithm predicts alterations in amino acids with a score less than 0.05 as deleterious and a score above 0.05 will be declared as tolerated (Figure S2A). In the Polyphen server, the alteration in amino acids has adverse effects on protein function. Its result was: probably damaging, possibly damaging, and or benign. In our results, 2087 SNPs were showing possibly damaging effects, 6963 were probably damaging, and 4543 SNPs were benign (Figure S2B).

Identification of pathogenic SNPs

After analyzing through SIFT and Polyphen, Polyphen-2 and SNAP2 were used further. The number of deleterious or diseased SNPs was 57, 10 were possibly damaged from Polyphen-2 and 46 were probably damaged, while 57 were effected by SNAP2. All the SNPs scored less than 1 at fuNTRp. (Table 1)

Table 1: Identification of most deleterious pathogenic SNPs

Sr. No	rsIDs	AA	Identification of pathogenic nsSNPs					
			SIFT		PolyPhen	PPH2	fuNTRp	SNAP2
			PREDICTION	SCORE E>0.5	PREDICTION	PREDICTION	PREDICTION	SCORE
1	rs786201057	T125R	Deleterious	0	Probably Damaging	Deleterious	**0.47**	effect
2	rs730881999	S127C	Deleterious	0	Probably Damaging	Deleterious	**0.53**	effect
3	rs863224683	L130F	Deleterious	0	Probably Damaging	Deleterious	**0.88**	effect
4	rs747342068	K132Q	Deleterious	0	Possibly Damaging	Deleterious	**0.72**	effect
5	rs1057519977	C141W	Deleterious	0	Probably Damaging	Deleterious	**0.75**	effect
6	rs587778718	P152H	Deleterious - Low Confidence	0	Probably Damaging	Deleterious	**0.83**	effect
7	rs587780068	R158C	Deleterious	0	Possibly Damaging	Deleterious	**0.66**	effect
8	rs1064795691	A161D	Deleterious - Low Confidence	0	Possibly Damaging	Deleterious	**0.78**	effect
9	rs397516436	R213G	Deleterious	0	Probably Damaging	Deleterious	**0.83**	effect
10	rs886039484	S215G	Deleterious	0	Probably Damaging	Deleterious	**0.89**	effect
11	rs765848205	M237R	Deleterious	0	Probably Damaging	Deleterious	**0.64**	effect
12	rs730882004	M237V	Deleterious - Low Confidence	0	Probably Damaging	Deleterious	**0.71**	effect
13	rs763098116	C238Y	Deleterious	0	Probably Damaging	Deleterious	**0.49**	effect
14	rs193920789	C238W	Deleterious	0	Probably Damaging	Deleterious	**0.62**	effect
15	rs375874539	C242W	Deleterious	0	Probably Damaging	Deleterious	**0.54**	effect
16	rs1057519982	C242G	Deleterious - Low Confidence	0	Probably Damaging	Deleterious	**0.85**	effect

17	rs985033810	G244V	Deleterious	0	Probably Damaging	Deleterious	**0.66**	effect
18	rs28934571	R249S	Deleterious	0	Probably Damaging	Deleterious	**0.46**	effect
19	rs121913343	R273C	Deleterious	0	Probably Damaging	Deleterious	**0.75**	effect
20	rs1057519983	C275R	Deleterious	0	Probably Damaging	Deleterious	**0.91**	effect
21	rs1131691029	A276P	Deleterious - Low Confidence	0	Probably Damaging	Deleterious	**0.75**	effect
22	rs886039483	Y126D	Deleterious	0.01	Possibly Damaging	Deleterious	**0.53**	effect
23	rs866775781	K132N	Deleterious - Low Confidence	0.01	Probably Damaging	Deleterious	**0.73**	effect
24	rs786203436	Y163N	Deleterious - Low Confidence	0.01	Probably Damaging	Deleterious	**0.81**	effect
25	rs483352697	R196L	Deleterious	0.01	Possibly Damaging	Deleterious	**0.61**	effect
26	rs879253894	P219S	Deleterious	0.01	Possibly Damaging	Deleterious	**0.74**	effect
27	rs530941076	Y220D	Deleterious	0.01	Probably Damaging	Deleterious	**0.62**	effect
28	rs786201592	E221K	Deleterious - Low Confidence	0.01	Probably Damaging	Deleterious	**0.53**	effect
29	rs1057519981	C238G	Deleterious	0.01	Probably Damaging	Deleterious	**0.6**	effect
30	rs587780074	M246R	Deleterious	0.01	Probably Damaging	Deleterious	**0.51**	effect
31	rs121912651	R248W	Deleterious - Low Confidence	0.01	Probably Damaging	Deleterious	**0.54**	effect
32	rs121912652	E258K	Deleterious	0.01	Probably Damaging	Deleterious	**0.9**	effect
33	rs17849781	P278S	Deleterious	0.01	Probably Damaging	Deleterious	**0.94**	effect
34	rs1064793881	G279E	Deleterious	0.01	Probably Damaging	Deleterious	**0.66**	effect
35	rs730882000	A159P	Deleterious	0.02	Probably Damaging	Deleterious	**0.76**	effect
36	rs1057520004	V216G	Deleterious	0.02	Probably Damaging	Deleterious	**0.92**	effect
37	rs970212462	G226V	Deleterious - Low Confidence	0.02	Probably Damaging	Deleterious	**0.5**	effect
38	rs1452189221	N247D	Deleterious - Low Confidence	0.02	Probably Damaging	Deleterious	**0.65**	effect

39	rs587781433	T256A	Deleterious	0.02	Probably Damaging	Deleterious	**0.88**	effect
40	rs1057520000	P151H	Deleterious - Low Confidence	0.03	Possibly Damaging	Deleterious	**0.76**	effect
41	rs1131691021	V172G	Deleterious - Low Confidence	0.03	Probably Damaging	Deleterious	**0.79**	effect
42	rs144340710	N235I	Deleterious	0.03	Probably Damaging	Deleterious	**0.65**	effect
43	rs121912656	G245V	Deleterious	0.03	Probably Damaging	Deleterious	**0.54**	effect
44	rs1057519987	F270L	Deleterious - Low Confidence	0.03	Probably Damaging	Deleterious	**0.54**	effect
45	rs1057519985	E286G	Deleterious	0.03	Probably Damaging	Deleterious	**0.86**	effect
46	rs1131691013	L130P	Deleterious	0.04	Possibly Damaging	Deleterious	**0.84**	effect
47	rs1131691034	K164N	Deleterious - Low Confidence	0.04	Possibly Damaging	Deleterious	**0.7**	effect
48	rs1057520001	S215R	Deleterious	0.04	Possibly Damaging	Deleterious	**0.61**	effect
49	rs730882026	Y236C	Deleterious - Low Confidence	0.04	Probably Damaging	Deleterious	**0.71**	effect
50	rs587782082	R249W	Deleterious	0.04	Probably Damaging	Deleterious	**0.67**	effect
51	rs55832599	R267W	Deleterious	0.04	Probably Damaging	Deleterious	**0.81**	effect
52	rs1057520005	V274F	Deleterious - Low Confidence	0.04	Probably Damaging	Deleterious	**0.82**	effect
53	rs786202082	A276D	Deleterious	0.04	Probably Damaging	Deleterious	**0.8**	effect
54	rs1064795369	C277G	Deleterious	0.04	Probably Damaging	Deleterious	**0.95**	effect
55	rs28934574	R282W	Deleterious	0.04	Probably Damaging	Deleterious	**0.69**	effect
56	rs1131691025	G262V	Deleterious	0.05	Probably Damaging	Deleterious	**0.87**	effect
57	rs587781525	D281V	Deleterious	0.05	Probably Damaging	Deleterious	**0.92**	effect

Disease Association of SNPs

All the SNPs were examined for disease association. There were 57, 56, and 57 SNPs predicted as diseased by SNP&GO, PhD-SNP, and Meta-SNP tools, respectively. There were 56, 57, and 57

SNPs predicted as deleterious by PredictSNP, MAPP, and SNAP respectively. 56 SNPs were predicted diseased by PANTHER. (Table 2)

Table 2: Disease-associated SNPs.

Sr.No	rsIDs	AA	Diseases associated nsSNPs						
			SNP&GO	PhD-SNP	PredictSNP	MAPP	SNAP	MetaSNP	PANTHER
			PREDICTION	PREDICTION	Prediction	Prediction	Prediction	Prediction	Prediction
1	rs786201057	T125R	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
2	rs730881999	S127C	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
3	rs863224683	L130F	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
4	rs747342068	K132Q	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
5	rs1057519977	C141W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
6	rs587778718	P152H	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
7	rs587780068	R158C	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
8	rs1064795691	A161D	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
9	rs397516436	R213G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
10	rs886039484	S215G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
11	rs765848205	M237R	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
12	rs730882004	M237V	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
13	rs763098116	C238Y	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
14	rs193920789	C238W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
15	rs375874539	C242W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
16	rs1057519982	C242G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
17	rs985033810	G244V	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
18	rs28934571	R249S	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
19	rs121913343	R273C	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
20	rs1057519983	C275R	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
21	rs1131691029	A276P	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
22	rs886039483	Y126D	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
23	rs866775781	K132N	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
24	rs786203436	Y163N	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease

25	rs483352697	R196L	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
26	rs879253894	P219S	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
27	rs530941076	Y220D	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
28	rs786201592	E221K	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
29	rs1057519981	C238G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
30	rs587780074	M246R	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
31	rs121912651	R248W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
32	rs121912652	E258K	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
33	rs17849781	P278S	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
34	rs1064793881	G279E	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
35	rs730882000	A159P	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
36	rs1057520004	V216G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
37	rs970212462	G226V	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
38	rs1452189221	N247D	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
39	rs587781433	T256A	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
40	rs1057520000	P151H	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
41	rs1131691021	V172G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
42	rs144340710	N235I	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
43	rs121912656	G245V	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
44	rs1057519987	F270L	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
45	rs1057519985	E286G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
46	rs1131691013	L130P	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
47	rs1131691034	K164N	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
48	rs1057520001	S215R	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
49	rs730882026	Y236C	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
50	rs587782082	R249W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
51	rs55832599	R267W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
52	rs1057520005	V274F	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
53	rs786202082	A276D	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
54	rs1064795369	C277G	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
55	rs28934574	R282W	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease

56	rs1131691025	G262V	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease
57	rs587781525	D281V	Disease	Disease	Deleterious	Deleterious	Disease	Disease	Disease

Protein stability and conservation of amino acids

In the protein, according to Mu-pro and I-Mutant, we didn't found the increasing stability but we observed from Consurf, T125R, S127C, L130F, K132Q, C141W, P152H, R158C, A161D, R213G, S215G, M237R, M237V, C238Y, C238W, C242W, C242G, G244V, R249S, R273C, C275R, A276P, Y126D, K132N, Y163N, R196L, P219S, Y220D, E221K, C238G, M246R, R248W, E258K, P278S, G279E, A159P, V216G, G226V, N247D, T256A, P151H, V172G, N235I, G245V, F270L, E286G, L130P, K164N, S215R, Y236C, R249W, R267W, V274F, A276D, C277G, R282W, G262V, D281V conserved and buried. (Figure 2; Table 3)

Figure 2: Evolutionary Conservation of amino acids

Table 3: SNPs with the highest Protein stability

Sr. No	rsIDs	AA	protein stability				Sequence Conservation
			Mu Pro		I Mutant		CONSURF
			PREDICTION	DETAL DELTA	STABILITY	RI	Conservation Score
1	rs786201057	T125R	DECREASE stability	-1.006	Decrease	2	9,e,f
2	rs730881999	S127C	DECREASE stability	-0.332	Decrease	2	9,b,s
3	rs863224683	L130F	DECREASE stability	-1.501	Decrease	4	8,b
4	rs747342068	K132Q	DECREASE stability	-0.604	Decrease	0	9,e,f
5	rs1057519977	C141W	DECREASE stability	-0.604	Decrease	4	8,b
6	rs587778718	P152H	DECREASE stability	-0.1309	Decrease	3	9,e,f
7	rs587780068	R158C	DECREASE stability	-1.274	Decrease	5	9,b,s
8	rs1064795691	A161D	DECREASE stability	-0.794	Decrease	3	8,b
9	rs397516436	R213G	DECREASE stability	-1.228	Decrease	2	9,e,f
10	rs886039484	S215G	DECREASE stability	-0.757	Decrease	8	9,b,s
11	rs765848205	M237R	DECREASE stability	-1.006	Decrease	2	6,b
12	rs730882004	M237V	DECREASE stability	-1.405	Decrease	1	6,b
13	rs763098116	C238Y	DECREASE stability	-0.332	Decrease	6	9,b,s
14	rs193920789	C238W	DECREASE stability	-1.235	Decrease	1	9,b,s
15	rs375874539	C242W	DECREASE stability	-0.825	Decrease	1	9,b,s
16	rs1057519982	C242G	DECREASE stability	-0.604	Decrease	8	9,b,s
17	rs985033810	G244V	DECREASE stability	-1.323	Decrease	7	9,e,f
18	rs28934571	R249S	DECREASE stability	-0.899	Decrease	4	9,e,f
19	rs121913343	R273C	DECREASE stability	-1.134	Decrease	4	9,e,f
20	rs1057519983	C275R	DECREASE stability	-0.856	Decrease	3	9,b,s
21	rs1131691029	A276P	DECREASE stability	-0.958	Decrease	2	9,b,s

22	rs886039483	Y126D	DECREASE stability	-1.405	Decrease	2	6,e
23	rs866775781	K132N	DECREASE stability	-0.825	Decrease	1	9,e,f
24	rs786203436	Y163N	DECREASE stability	-0.899	Decrease	2	8,e,f
25	rs483352697	R196L	DECREASE stability	-0.27	Decrease	2	9,b,s
26	rs879253894	P219S	DECREASE stability	-0.289	Decrease	9	8,e,f
27	rs530941076	Y220D	DECREASE stability	-0.856	Decrease	0	8,e,f
28	rs786201592	E221K	DECREASE stability	-0.8304	Decrease	6	9,e,f
29	rs1057519981	C238G	DECREASE stability	-1.501	Decrease	3	9,b,s
30	rs587780074	M246R	DECREASE stability	-1.274	Decrease	5	9,e,f
31	rs121912651	R248W	DECREASE stability	-0.794	Decrease	3	9,e,f
32	rs121912652	E258K	DECREASE stability	-0.27	Decrease	8	9,e,f
33	rs17849781	P278S	DECREASE stability	-0.91812	Decrease	9	9,e,f
34	rs1064793881	G279E	DECREASE stability	-0.91705	Decrease	9	9,e,f
35	rs730882000	A159P	DECREASE stability	-1.147	Decrease	3	8,b
36	rs1057520004	V216G	DECREASE stability	-1.134	Decrease	8	9,b,s
37	rs970212462	G226V	DECREASE stability	-0.122	Decrease	5	9,e,f
38	rs1452189221	N247D	DECREASE stability	-1.147	Decrease	4	9,e,f
39	rs587781433	T256A	DECREASE stability	-0.659	Decrease	9	9,b,s
40	rs1057520000	P151H	DECREASE stability	-1.323	Decrease	3	8,e
41	rs1131691021	V172G	DECREASE stability	-1.67	Decrease	7	8,b
42	rs144340710	N235I	DECREASE stability	-1.73	Decrease	3	8,e,f
43	rs121912656	G245V	DECREASE stability	-0.1309	Decrease	6	9,b,s
44	rs1057519987	F270L	DECREASE stability	-1.931	Decrease	7	8,b
45	rs1057519985	E286G	DECREASE stability	-0.91386	Decrease	6	9,e,f
46	rs1131691013	L130P	DECREASE stability	-1.235	Decrease	0	8,b

47	rs1131691034	K164N	DECREASE stability	-0.709	Decrease	6	9,e,f
48	rs1057520001	S215R	DECREASE stability	-1.931	Decrease	7	9,b,s
49	rs730882026	Y236C	DECREASE stability	-0.856	Decrease	3	9,e,f
50	rs587782082	R249W	DECREASE stability	-0.709	Decrease	5	9,e,f
51	rs55832599	R267W	DECREASE stability	-0.944	Decrease	8	7,e
52	rs1057520005	V274F	DECREASE stability	-0.289	Decrease	4	8,b
53	rs786202082	A276D	DECREASE stability	-0.8304	Decrease	2	9,b,s
54	rs1064795369	C277G	DECREASE stability	-0.91918	Decrease	1	9,b,s
55	rs28934574	R282W	DECREASE stability	-0.91493	Decrease	7	9,e,f
56	rs1131691025	G262V	DECREASE stability	-1.228	Decrease	8	9,e,f
57	rs587781525	D281V	DECREASE stability	-0.91599	Decrease	8	9,e,f

Post-translational modifications (PTMs)

In TP53, according to MustiDeep, there is 18 times Phosphorylation at amino acid number 7, 9, 15, 18, 20, 33, 36, 47, 55, 183, 185, 269, 284, 303, 314, 316, 327, and 392; 6 times Acetylation at 120, 305, 321, 373, 381, and 382; 6 times Methylation at 333, 335, 337, 370, 372, and 373; 1-time SUMOylation at number 386; 3-time Hydroxylation at number 75, 77, and 90; 2-time ubiquitination at number 291 and 292; and 9-time Glycosylation at number 9, 81, 90, 150, 239, 231, 232, 233, and 234. (Figure 3)

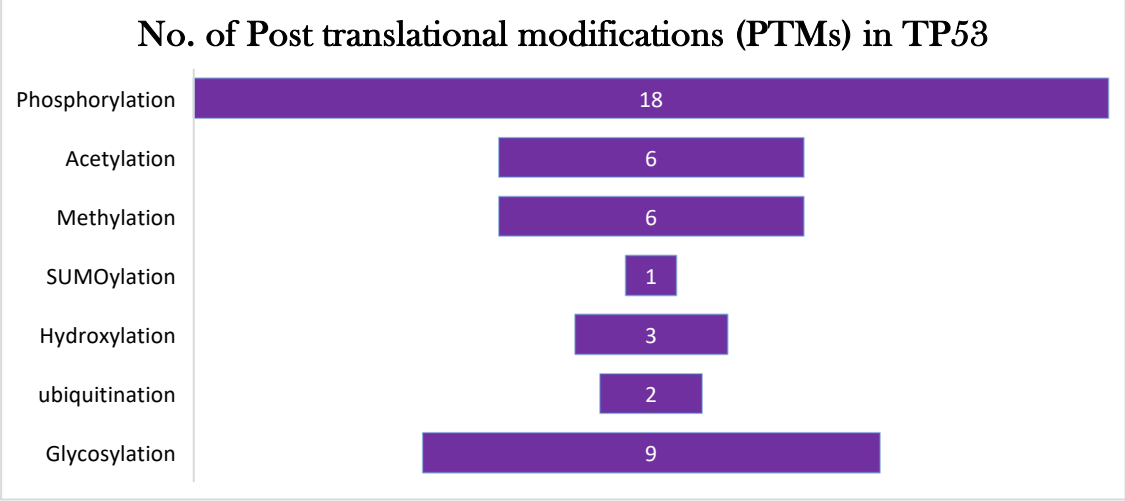

Figure 3: Post-translational modifications (PTMs) in TP53

Protein's secondary structure

According to SOPMA, the secondary structure of this protein consists of Alpha helix (Hh) was 78 (19.85%), Extended strand (Ee) was 71 (18.07%), Beta turn (Tt) was 14 (3.56%) and Random coil (Cc) was 230 (58.52%). (Figure 4)

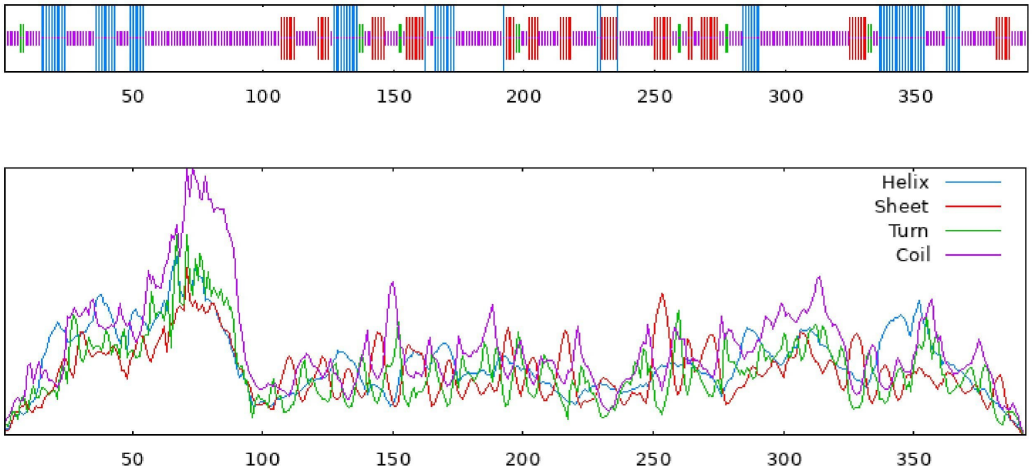

Figure 4: Secondary structure of TP53 protein

Protein to Protein Interaction (PPI)

TP53 has shown interaction with BARD1, AURKA, CDK2, MDM2, RPA1, EP300, SIRT1, DDX1, and CREBBP with score 0.7 to 0.9.

BARD1 heterodimer specifically mediates the formation of 'Lys-6-linked polyubiquitin chains and coordinates a diverse range of cellular pathways such as DNA damage repair, ubiquitination, and transcriptional regulation to maintain genomic stability. Plays a central role in the control of the cell cycle in response to DNA damage. Acts by mediating ubiquitin E3 ligase activity that is required for its tumor suppressor function. Also forms a heterodimer with CSTF1/CSTF-50 to modulate mRNA processing and RNAP II

Aurora kinase A; Mitotic serine/threonine kinase that contributes to the regulation of cell cycle progression. Associates with the centrosome and the spindle microtubules during mitosis and plays a critical role in various mitotic events including the establishment of mitotic spindle, centrosome duplication, centrosome separation as well as maturation, chromosomal alignment, spindle assembly checkpoint, and cytokinesis. Required for initial activation of CDK1 at centrosomes.

Cyclin-dependent kinase 2; Serine/threonine-protein kinase involved in the control of the cell cycle; essential for meiosis, but dispensable for mitosis. Phosphorylates CTNNB1, USP37, p53/TP53, NPM1, CDK7, RB1, BRCA2, MYC, NPAT, EZH2. Triggers duplication of centrosomes and DNA. Acts at the G1-S transition to promote the E2F transcriptional program and the initiation of DNA synthesis, modulates G2 progression; controls the timing of entry into

mitosis/meiosis by controlling the subsequent activation of cyclin B/CDK1 by phosphorylation, and coordinates the activation of cyclin.

E3 ubiquitin-protein ligase Mdm2; E3 ubiquitin-protein ligase that mediates ubiquitination of p53/TP53, leading to its degradation by the proteasome. Inhibits p53/TP53- and p73/TP73-mediated cell cycle arrest and apoptosis by binding its transcriptional activation domain. Also acts as a ubiquitin ligase E3 toward itself and ARRB1. Permits the nuclear export of p53/TP53. Promotes proteasome-dependent ubiquitin-independent degradation of retinoblastoma RB1 protein. Inhibits DAXX-mediated apoptosis by inducing its ubiquitination and degradation.

Replication protein A 70 kDa DNA-binding subunit; As part of the heterotrimeric replication protein A complex (RPA/RP-A), binds and stabilizes single-stranded DNA intermediates, that form during DNA replication or upon DNA stress. It prevents their reannealing and in parallel, recruits and activates different proteins and complexes involved in DNA metabolism. Thereby, it plays an essential role both in DNA replication and the cellular response to DNA damage. In the cellular response to DNA damage, the RPA complex controls DNA repair and DNA damage checkpoint activation.

Histone acetyltransferase p300; Functions as histone acetyltransferase and regulates transcription via chromatin remodeling. Acetylates all four core histones in nucleosomes. Histone acetylation gives an epigenetic tag for transcriptional activation. Mediates cAMP-gene regulation by binding specifically to phosphorylated CREB protein. Mediates acetylation of histone H3 at 'Lys-122' (H3K122ac), a modification that localizes at the surface of the histone octamer and stimulates transcription, possibly by promoting nucleosome instability.

NAD-dependent protein deacetylase sirtuin-1; NAD-dependent protein deacetylase that links transcriptional regulation directly to intracellular energetics and participates in the coordination of several separated cellular functions such as cell cycle, response to DNA damage, metabolism, apoptosis, and autophagy. Can modulate chromatin function through deacetylation of histones and can promote alterations in the methylation of histones and DNA, leading to transcriptional repression.

Probable ATP-dependent RNA helicase DDX5; Involved in the alternative regulation of pre-mRNA splicing; its RNA helicase activity is necessary for increasing tau exon 10 inclusion and occurs in an RBM4-dependent manner. Binds to the tau pre-mRNA in the stem-loop region downstream of exon 10. The rate of ATP hydrolysis is highly stimulated by single-stranded RNA. Involved in transcriptional regulation; the function is independent of the RNA helicase activity.

CREB-binding protein; Acetylates histones, giving a specific tag for transcriptional activation. Also acetylates non-histone proteins, like NCOA3 and FOXO1. Binds specifically to phosphorylated CREB and enhances its transcriptional activity toward cAMP-responsive genes. Acts as a coactivator of ALX1. Acts as a circadian transcriptional coactivator which enhances the

activity of the circadian transcriptional activators: NPAS2-ARNTL/BMAL1 and CLOCK-ARNTL/BMAL1 heterodimers (Figure 5).

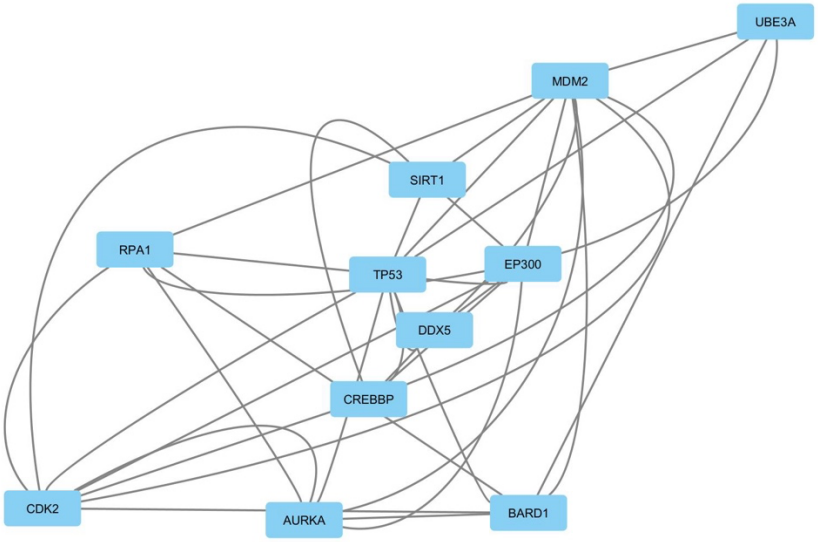

Figure 5: Protein-to-protein interaction (PPI) of TP53 protein

Gene ontology

According to gene ontology (QuickGo), there are top biological processes of TP53 are a response to stimulus, cellular process, biological regulation, regulation, cell communication, signaling, signal transduction, DNA damage response, intracellular signal transduction, cellular response to stress, and signal transduction by p53 class and biological regulation, its cellular components are intracellular anatomical structure and cellular anatomical entity while its molecular function proliferation, order to make tumor protein, and cell death (Figure 6).

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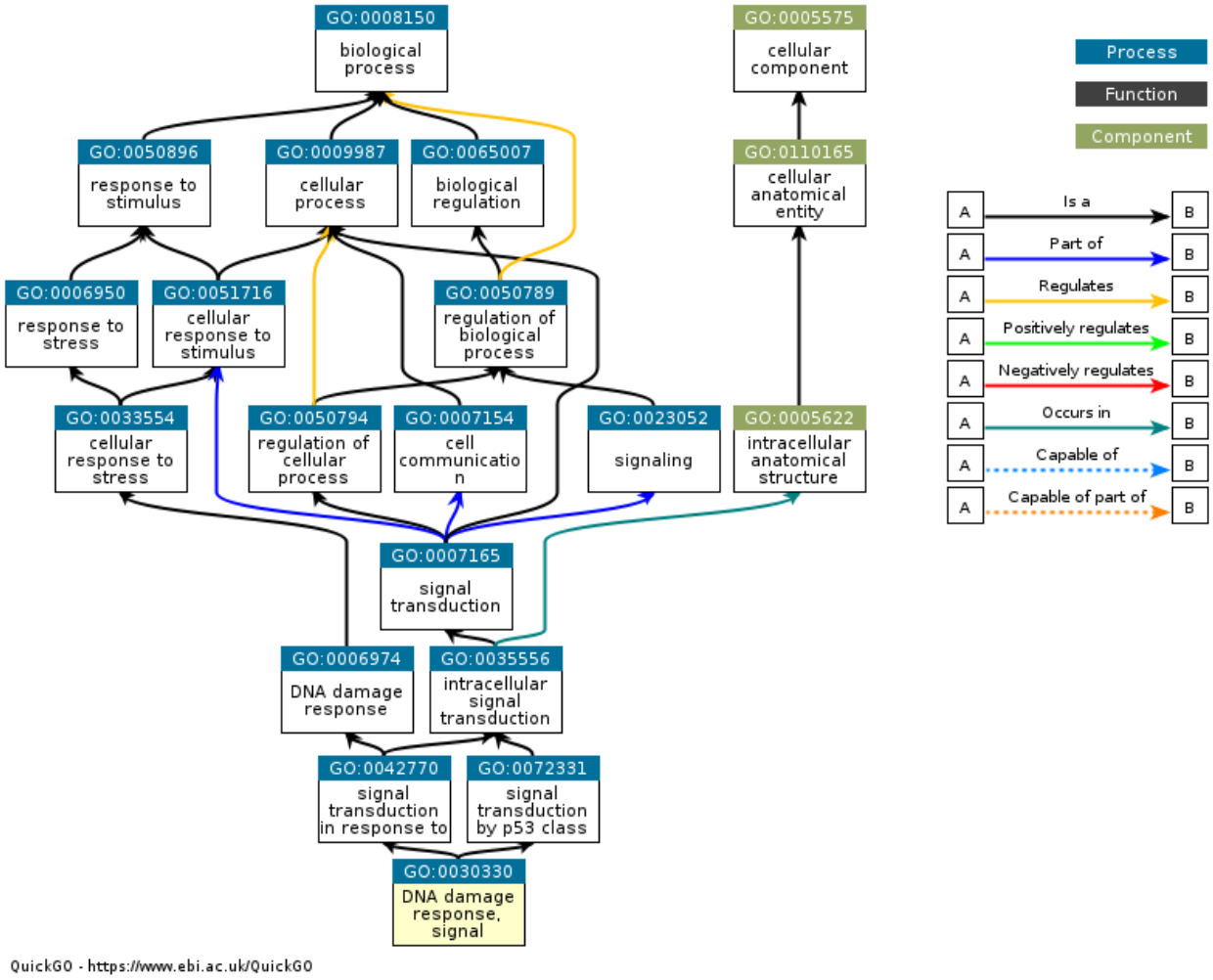

Figure 6: Gene Ontology analysis of TP53

According to DAVID bioinformatics resources, there 64, 14, and 29 are biological processes, cellular components, and molecular functions respectively. But we selected the top 4 from each for this study according to their gene count and p-value.

The top biological process including negative regulation of transcription (six genes), negative regulation of apoptotic (five genes), protein destabilization (four genes), and cellular response to DNA damage (four genes) and their p-value were 0.0000359, 0.0000585, 0.0000142, and 0.0000265 respectively.

The top cellular process includes Nucleoplasm (ten genes), Nucleus (ten gens), Cytosol (eight genes), and Cytoplasm (eight genes) with p-value 0.0000413, 0.0000156, 0.002257572, and 0.002510807 respectively.

The top molecular functions are protein binding (ten genes), metal ion binding (seven genes), p53 binding (five genes), and chromatin binding (four genes) with a p-value of 0.026322928, 0.0000465, 0.0000238, and 0.001132976 respectively (Table 4).

Table 4. Gene Ontology analysis of TP53

Category	Term	Count	P-Value	Genes
BP	negative regulation of transcription	6	0.0000359	CREBBP, CDK2, MDM2, EP300, SIRT1, TP53
BP	negative regulation of apoptotic	5	0.0000585	BARD1, MDM2, SIRT1, TP53, AURKA
BP	protein destabilization	4	0.0000142	CREBBP, MDM2, EP300, SIRT1
BP	cellular response to DNA damage	4	0.0000265	BARD1, RPA1, SIRT1, TP53
CC	Nucleoplasm	10	0.0000413	BARD1, CREBBP, DDX1, CDK2, MDM2, RPA1, EP300, SIRT1, TP53, AURKA
CC	Nucleus	10	0.0000156	BARD1, CREBBP, DDX1, CDK2, MDM2, RPA1, EP300, SIRT1, TP53, AURKA
CC	Cytosol	8	0.002257572	CREBBP, DDX1, CDK2, MDM2, EP300, SIRT1, TP53, AURKA
CC	Cytoplasm	8	0.002510807	BARD1, CREBBP, DDX1, CDK2, MDM2, EP300, SIRT1, TP53
MF	protein binding	10	0.026322928	BARD1, CREBBP, DDX1, CDK2, MDM2, RPA1, EP300, SIRT1, TP53, AURKA
MF	metal ion binding	7	0.0000465	BARD1, CREBBP, MDM2, RPA1, EP300, SIRT1, TP53
MF	p53 binding	5	0.0000238	CREBBP, MDM2, EP300, SIRT1, TP53
MF	chromatin binding	4	0.001132976	CREBBP, DDX1, EP300, TP53

Molecular Docking

When TP53 interacted with 3-O-vanilloyl ceanothin acid, we found a pi-pi T-shaped bond at TRP A:58, conventional hydrogen bonding at ARG A:22, and van der Waals forces around the complex. The TP53 and 3-O-protocatechuoyl ceanothin acid interaction results showed amide-pi stacked bonding at VAL A:9, pi-alkyl at PRO A:10 and ARG A:125, conventional hydrogen bond at ASP A:120 and SER A:173 and van der Waals forced around the complex (Figure 7)

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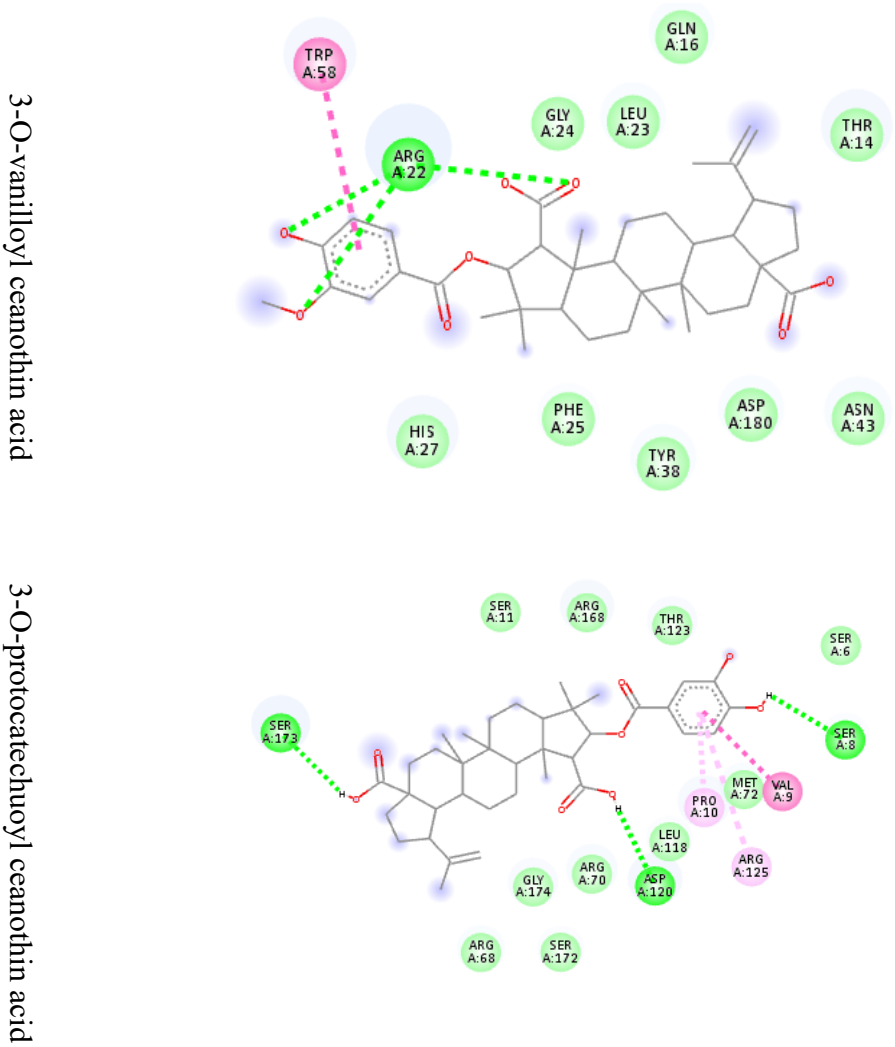

Figure 7: Docking of 3-O-vanilloyl ceanothin acid and 3-O-protocatechuoyl ceanothin acid

Alphitolic acid and TP53 complex showed a pi-sigma bond TRP A:58, conventional hydrogen bond at PHE A:25, and hydrogen bond at GLY A:24. When Betulinaldehyde was docked with protein, it showed a pi-sigma bond at TRP A:58 and conventional hydrogen bond at SER A:181 and ASN A:43 with unfavorable donor bonding (Figure 8)

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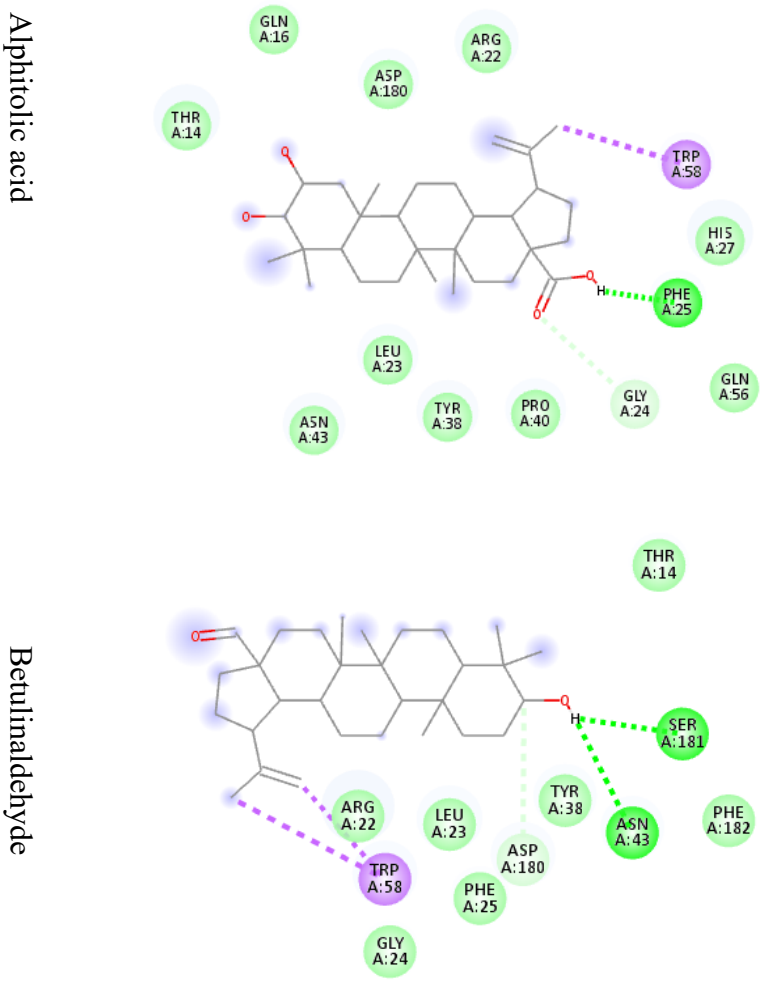


Figure 8: Docking of Alphitolic acid and Betulinaldehyde

There was hydrogen bonding at LEU A:23 and ARG A:22 in Ceanothic acid and alkyl bonding at LEU A:42&201 in Isoceanothic acid and there were van der Waals forces also found. Pomolic acid interacted with protein and it resulted in a sigma bond at TRP A:58 and ASP A:180 and LEU A:23 and van der Waal forces at different nodes (Figure 9)

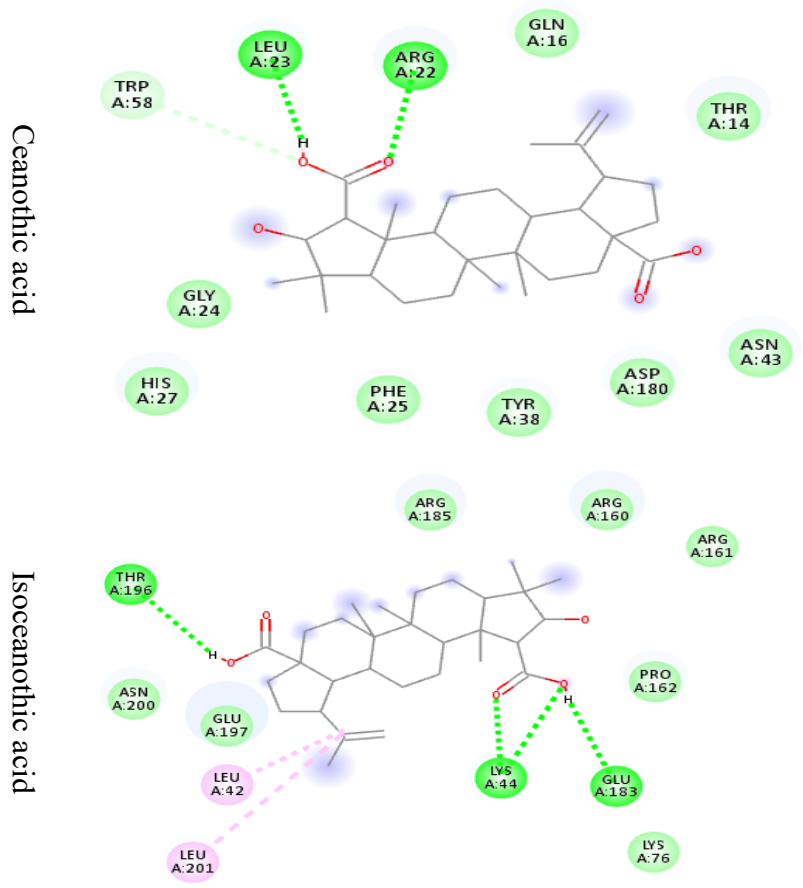
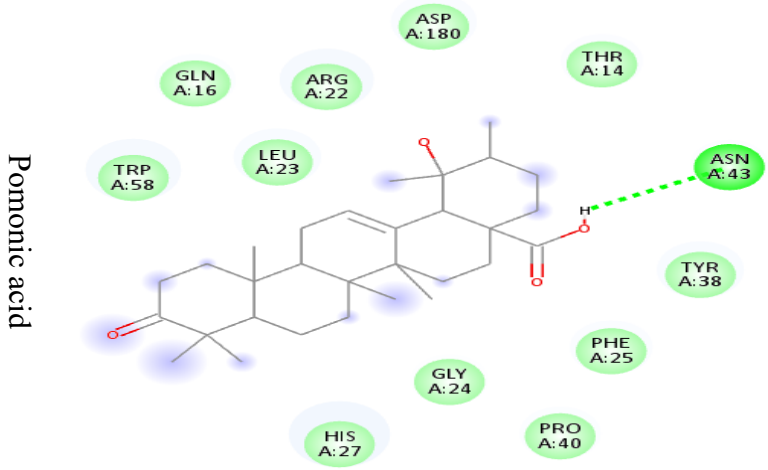


Figure 9: Docking of Ceanothic acid and Isoceanothic acid

Similarly, the interaction of Pomonic acid showed hydrogen bonding at ASN A:43 and also van der Waal forces at different nodes like Pomolic acid (Figure 10)



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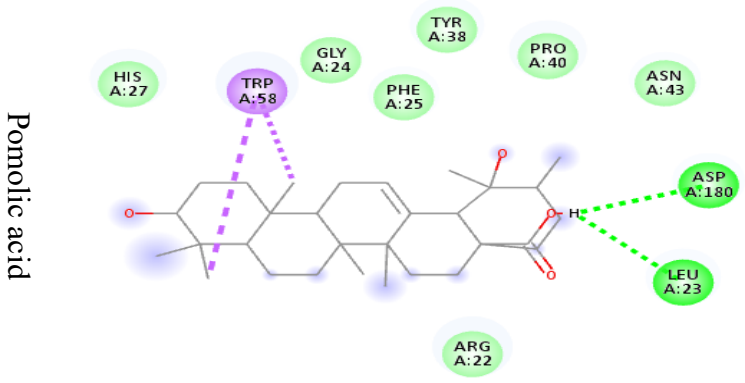
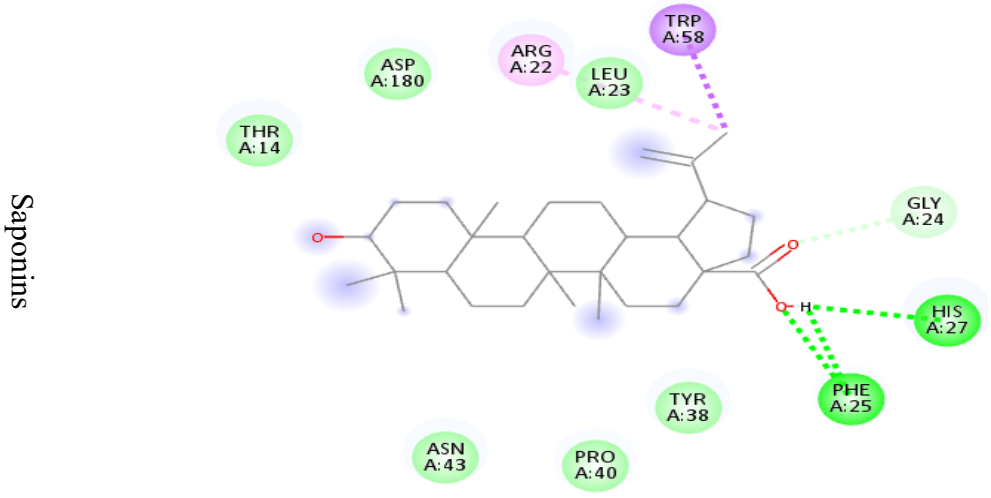


Figure 10: Docking of Pomonic acid Pomolic acid

Saponins when docked, it showed sigma, hydrogen, and alkyl bonding at TRP A:58, GLY A:24, and ARG A:22 respectively while reacted with Ursonic acid showed sigma, hydrogen, and conventional hydrogen bonding at TRP A:58, GLY A:24, and HIS A:27 respectively. Van der Waal forces were found around the all complexes. (Figure 11)



Ursonic acid

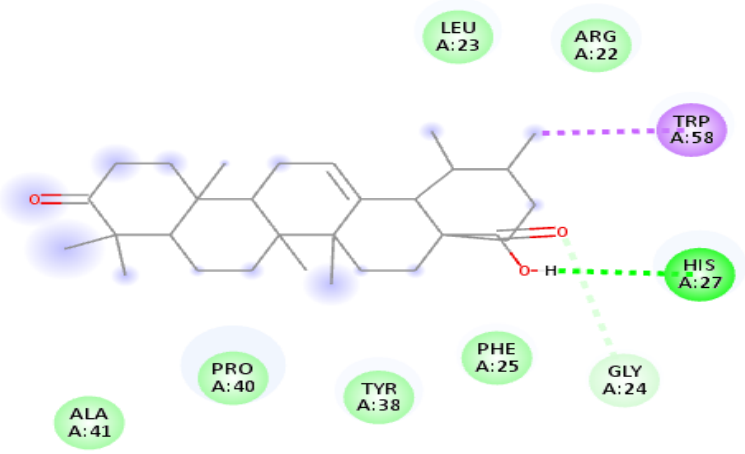


Figure 11: Docking of Saponins Ursonic acid

Betulinic acid showed hydrogen bond at PRO A:40 and GLY A:24, and conventional hydrogen bonding at SER A:181, ASP A:180, ASN A:43, ARG A:22&202, and ARG A:202 and van der Waal forces too (Figure 12).

Betulinic acid

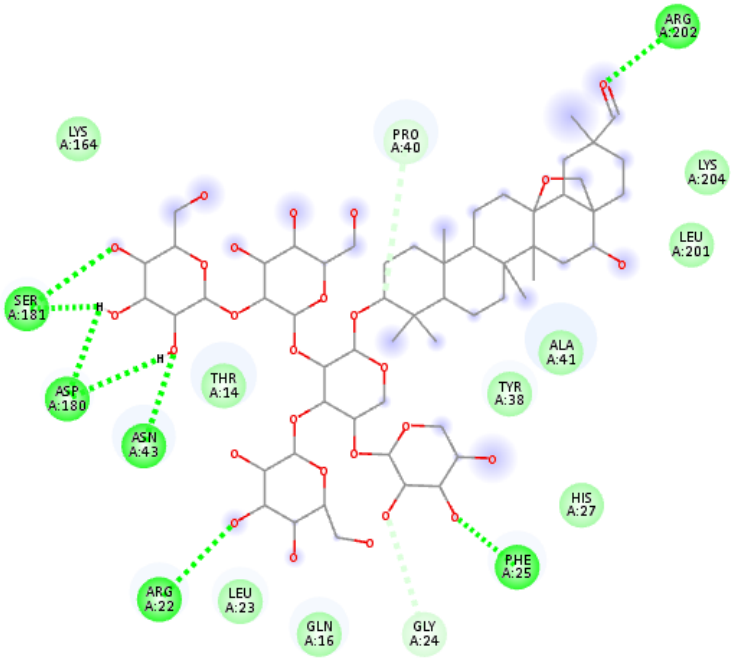


Figure 12: Docking of Betulinic acid

Table 5: Binding energy of ligands to protein while docking

Ligand	Binding Affinity	rmsd/ub	rmsd/lb
3-O-protocatechuoyl ceanothic acid	-7	30.487	27.695
3-O-Vanilloyl ceanothic acid	-6.9	28.114	23.376
Alphitolic acid	-6.6	3.915	2.661
Betulinaldehyde	-6.5	7.906	2.319
Betulinic Acid	-7.4	15.811	6.456
Ceanothic acid	-6.5	9.086	3.194
Isoceanothic acid	-6.7	22.013	19.177
Pomolic acid	-6.7	8.065	2.099
Pomonic acid	-7.2	8.477	2.598
Saponins	-6.8	8.321	1.895
Ursonic acid	-7	7.901	2.301

DISCUSSION

In a study BRCA1-associated RING domain protein 1 BARD1, which has the oncogenic role in breast cancer (Śniadecki et al., 2020), and in our study there 0.9 scored interaction of BARD1 and TP53 which predict its oncogenic role too. Other genes also have high interaction which showed oncogenic and proliferative parts in human cancer, especially mammary cancer. It has been discovered that AURKA and AURKB act as oncogenes to stimulate carcinogenesis in a variety of cancer types, especially breast cancer, including solid tumor and hematological malignancies, Additionally, in triple-negative breast cancer cell lines, cell lines with a p53 mutation and higher p53 expression are more responsive to ENMD-2076 than cell lines with lower p53 expression (Du et al., 2021). Increased CDK2 expression was discovered in the palbociclib-resistant breast cancer cell lines in a study of global gene expressions. Additionally, it was proposed that CDK2 is inhibited by p21 and p27 loss (Akli et al., 2011).

Studies conducted in vitro have shown that overexpressing MDM2 results in breast cancer cell lines being more aggressive, including having increased levels of cell invasion and motility as well as promoting the production and activity of MMP9 (Portman et al., 2020). According to research, RPA2-dependent tumorigenicity is achieved by increasing NF-B, a cell line, activity in breast cancer cells (Tang et al., 2017; Bilal et al., 2022). Multiple human cancers, including breast cancer and squamous cell carcinoma of the head and neck, have been linked to the EP300 mutation. Breast cancer mortality and recurrence risk are predicted to reduce by certain mutations in the EP300 gene (Zhu et al., 2020), In an in vivo experiment, it was demonstrated that SIRT1 influences activity to promote the development of breast cancer (Jin et al., 2018). DDX1 is a biomarker in mammary carcinoma (Taunk et al., 2012), and the most common changes in CREBBP are seen in

lung adenocarcinoma, colon adenocarcinoma, bladder urothelial carcinoma, follicular lymphoma, and breast invasive ductal carcinoma (Mei et al., 2017)

A study said that the following aspects of protein phosphorylation contribute to the occurrence and progression of cancer: inducing cancer cell proliferation, inhibiting cancer cell apoptosis, inducing cancer cell invasion and metastasis, inducing cancer cell angiogenesis, and inducing the proliferation of cancer stem cells (Liu et al., 2021; Bilal et al., 2022) and a range of processes, including changes in breast cancer mucin-type O-linked glycosylation, can lead to tumor development and progression. Changes in mucin-type O-linked glycosylation in the immune system can lead to new interactions between immune cells and lectins (Zhang et al., 2020) so, in our findings there are 18- and 9-times phosphorylation and glycosylation as PTMs in TP53 respectively.

In aid of this more PTMs which cause breast cancer that are acylation e.g., breast cancer is connected with lysine acetylation, which actively regulates the levels and functions of genes and proteins with tumor-promoting or tumor-suppressing actions, and plays essential roles in permitting malignant cells with cancer hallmarks (Guo et al., 2018). One of the heritable methylation marks associated with breast cancer risk was located close to the 5′ end of the gene Growth Regulation by Estrogen Breast Cancer 1 (Batra et al., 2021). SUMOylation plays a key role in several features of cell physiology, including cell cycle regulation, protein trafficking, and DNA damage repair. Consistently with this, the deregulation of the SUMO pathway is detected in different human pathologies, including mammary cancer (Rabellino & Khanna, 2020), and through the dynamic control of proteins relevant to cell development, proliferation, and survival, ubiquitination is essential for several cellular activities. (Wang et al., 2021; Bilal, 2021) and we found all these above-mentioned post-translational modifications in our results which predicted breast cancer.

Our selected ligands were 3-O-vanilloyl ceanothin acid docked with pi-pi T shaped and conventional hydrogen bonds with TP53 protein, 3-O-protocatechuoyl ceanothin acid blocked the binding site of this protein by amide-pi stacked and conventional hydrogen bond, there is again conventional hydrogen bond and pi-sigma bond with Alphitolic acid and Betulinaldehyde acid and the macromolecule, Betulinic acid interacts with hydrogen and conventional hydrogen bond, Ceanothic acid is reacted with hydrogen bonding while Isoceanotic acid has conventional hydrogen, hydrogen, and alkyl bond, and remaining Pomolic acid, Pomonic acid, Saponins, and Ursonic acid have also hydrogen, conventional hydrogen, and pi-sigma bonding for docking with TP53. The hydrogen bonds are very strong (Emsley, 1980), and as we found there is hydrogen bonding, in the form of pure hydrogen bonding, conventional hydrogen bonding, pi bonding (Cross et al., 1969), sigma bonding (Thompson et al., 1987) in every ligand and protein complex which block the binding site.

Conclusion

In conclusion, our results are consistent with the hypothesis that Jujube performs an anticancer and anti-tumor activity by preventing cell proliferation and inducing apoptosis. Its phytochemicals have effective breast cancer treatment.

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Data availability statement

Data will be available from the corresponding author upon reasonable request.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

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