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Deciphering the functional characterization of *Bos taurus* p53 tumor suppressor protein through *in silico* platform

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Abstract
The present study was conducted to know the detail functional aspects and molecular interaction of p53 tumor suppressor protein of *Bos taurus* at Department of Veterinary Biochemistry, College of Veterinary Science & AH, Bhubaneswar from time period between September 2017 to February 2018. The P53 tumor suppressor protein plays a central role in the prevention of cancer in bovine by participating in the signaling pathway of apoptosis that protect against unnatural cell growth. Thus, a functional analysis of this protein is required to know the various interactions with other proteins and to find the conserved domain in its structure, for the development of putative therapeutic targets against the tumor. So in this study, the amino acid sequence of the bovine p53 was retrieved from NCBI site, the protein protein interaction was done to analyze the functional behavior of this protein through search tool for the retrieval of interacting proteins (STRING) platform. The conserved domain was searched for this protein on pfam database. It was found there were eleven nodes and 32 edges in its network and having strong interaction with MDM2 and CREBBP with score 0.998 but posses weak interaction with CDKN2A with a score of 0.991.It was observed DNA-binding domain is the important conserved domain present in this protein with no co expression with other proteins in *bos taurus*.

Keywords: p53 tumor suppressor protein, STRING, *Bos taurus*

1. Introduction
Apoptosis is one important biochemical process causing change in cell morphology, blebbing, cell shrinkage, chromatin condensation, nuclear and DNA fragmentation leading to programmed cell death in multicellular organism [1]. So for this process, several proteins are involved for initiation of either intrinsic or extrinsic pathway [2]. Among them, bovine tumor suppressor protein p53, one of important regulatory protein which can prevent the cell from replication by stopping the cell cycle at G1, or interphase, to give the cell, time to repair [3]. So there may be chance of tumerogenesis if any dysregulation of this p53 protein is occurred inside the body [4]. This signaling pathway is carried out by multiple molecular interactions between a numbers of proteins due to electrostatic forces including hydrophobic effect [5]. Now days, the protein protein interaction (PPI) studies have an important perspective in biochemistry, quantum chemistry, molecular dynamics that empowers the knowledge of different biochemical cascade in signaling pathway [6]. For this, the *insilico* tools are extensively used to simplify the difficulty task of visualizing these molecular interactions exist in the biochemical cascade [7]. Several properties such as allosteric sites and hotspots of the PPI are exploited for the development different drug strategies against the tumor in *Bos taurus* [8]. So there is a need of detail functional study of p53 protein with respect to the molecular interactions and the domain characteristics, for the development of a putative therapeutic target. So this present study would provide a better platform for the researchers to undertake modern biological research in molecular networks field related to this protein.

2. Materials and Methods
2.1 Retrieval of amino acid sequence of p53 protein
The amino acid sequence of p53 protein was retrieved from National Centre for Biotechnological Information (NCBI) with accession number GI/602333 under FASTA format

2.2 Development of p53 Protein interactions network through search tool for the retrieval of interacting proteins (STRING)

The protein interaction of p53 protein of *Bos taurus* was analyzed through the STRING 10.5 platform [9] under *insilico* approaches. The interaction network of this protein was created with different nodes and edges. The proteins which are correlated in the expression of p53 protein were analyzed in the Gene coexpresion viewer. Gene co occurrence Viewer was used to know the similarity of occurrence of other protein families with the p53 protein.

2.3 Determination of conserved Domains

The amino acids sequence was analyzed to know the conserved domain present in this protein with CD Blast (Basic Local Alignment Tool) under pfam database [10].

3. Results and Discussion

Protein-protein interactions (PPIs) are useful for understanding signaling cascades, predicting protein function, associating proteins with disease and fathoming drug mechanism of action [11]. The protein p53 of *Bos taurus* possesses the ability to interact with a variety of proteins. This present study showed the interactions of this protein that include physical and functional associations that contribute a particular score. The result of network association of this protein was shown in Fig 1. The result revealed that ten predicted functional interactions are existing in this network, which was chosen according to the highest score, shown in Table No 1. The top ten predicted protein interactions with p53 such as with MDM2, CREBBP, LOC784935, MDM4, TP53BP2, RPA1, BCL2 ATM PTEN and CDKN2A were found in this study. The interaction with MDM2 showed a highest confidence score (0.998) leaving weak interaction with CDKN2A with lowest confidence score (0.990) which is in accordance with the result of [12]. It may be due to the Mdm2 protein functionally inhibits p53 and targets the tumor suppressor protein for degradation [13]. However the CDKN2A protein protects the p53 protein in an uncontrolled manner leaving a lowest score in the functional interaction [14].

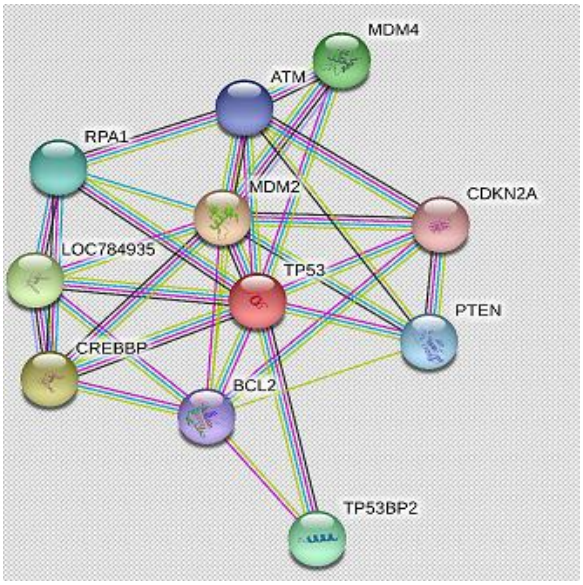

Fig 1: Showing the interaction of p53 protein to other proteins

Table 1: Showing the predicted functional partner of p53 protein in *Bos taurus*

Node 1	Node 2	Node 1 annotation	Node 2 annotation	Score
TP53	MDM2	Cellular tumor antigen p53	Mdm2, p53 E3 ubiquitin ligase	0.998
TP53	CREBBP	Cellular tumor antigen p53	CREB-binding protein	0.998
TP53	LOC784935	Cellular tumor antigen p53	Uncharacterized protein	0.997
TP53	MDM4	Cellular tumor antigen p53	Protein Mdm4	0.996
TP53	TP53BP2	Cellular tumor antigen p53	Uncharacterized protein	0.994
TP53	RPA1	Cellular tumor antigen p53	Replication protein A	0.992
TP53	BCL2	Cellular tumor antigen p53	Apoptosis regulator Bcl-2	0.991
TP53	ATM	Cellular tumor antigen p53	Serine-protein kinase ATM	0.991
TP53	PTEN	Cellular tumor antigen p53	Uncharacterized protein	0.991
TP53	CDKN2A	Cellular tumor antigen p53	Uncharacterized protein	0.990

The characteristics of the current protein network are given in the Table No 2. It was found that there are eleven nodes and thirty one edges indicating the number of proteins and number of protein protein associations respectively in the network. It might be due to all the interacting proteins are produced from a single protein coding gene locus and contribute to a shared function [15].

Table 2: Showing the Network statistics of p53 protein

Charactestics of Network	Values
Number of nodes	11
Number of edges	32
Average node degree	5.82
Avg. local clustering coefficient	0.81
Expected number of edges	14
PPI enrichment p-value	3.65e-05

The co expression study of all the interacted proteins was done in the suitable program and the result is shown in Fig No: 2. It was seen observed that none of these proteins are co expressed in *Bos taurus*, which indicates the genes are not correlated in expression across a large number of experiments [16].

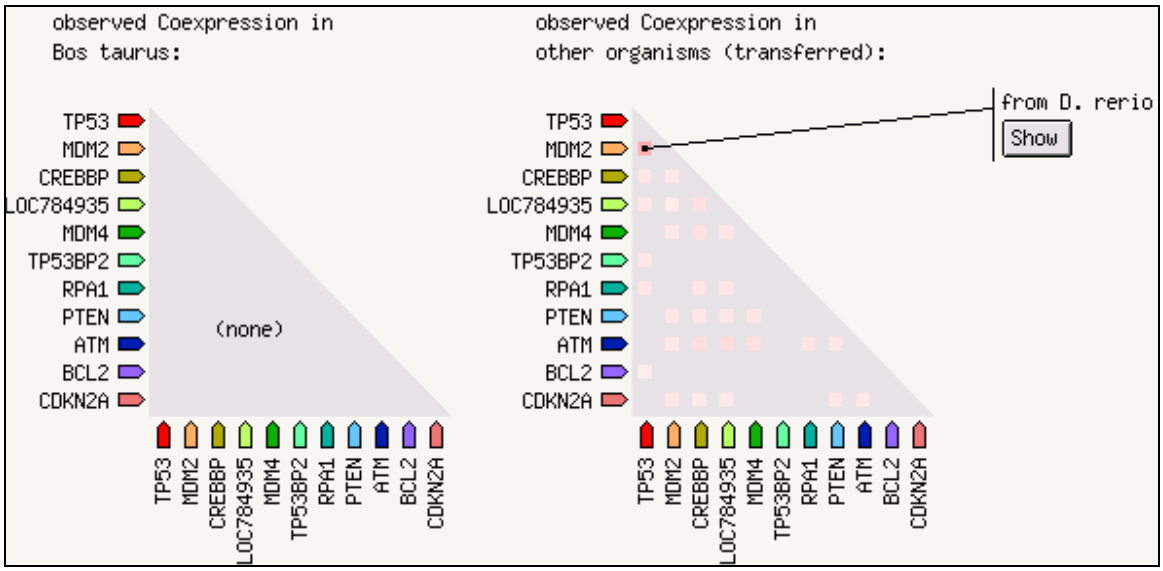

Fig 2: showing the co expression of the interacted proteins

The co ocurrence experiment study found that all the genes encoding these eleven proteins are coexisted in *Bos taurus*, shown in Fig No 3. All the proteins in this network are co-occurred in eukaryotes, prokaryotes and chordate, indicates there is much more similarity and correlation among the gene families [17].

Fig 3: showing the co occurrence of p53 protein across gene families

In this study, the domains present in the p53 protein were searched in pfam data base and the detail result as given in Table No 3.It was found that different conserved domains such as zinc finger, KIX, Histone acetylation protein, Creb Binding, SWIB/MDM2 are present in this protein. It may be due the involvement of this protein in various biochemical processes such as regulation of several pro-apoptotic gene, DNA repair and cell cycle mechanism [18].

Table 3: Showing the conserved domain present in the p53 protein in pfam database

	Protein Domain	Number	False discovery rate
PF02135	TAZ zinc finger	2	0.000244
PF02172	KIX domain	2	0.000244
PF06001	Domain of Unknown Function (DUF902)	2	0.000244
PF08214	Histone acetylation protein	2	0.000244
PF09030	Creb binding	2	0.000244
PF02201	SWIB/MDM2 domain	2	0.00122
PF00641	Zn-finger in Ran binding protein and others	2	0.00626
PF00569	Zinc finger, ZZ type	2	0.0182

4. Conclusion

This study can be concluded that the p53 protein has a major role in apoptosis pathway to prevent tumor formation in humans as well as animals. The protein protein interaction, vital for the cellular homestasis, is well observed in this protein with ten nodes in its network, leaving a suitable therapeutic target for the drug designer to prevent the tumor in bovine. So this study would provide a better platform for the researchers to exploit this p53 protein for further modern biological research.

5. References

1. Douglas G. Means to an End: Apoptosis and other Cell Death Mechanisms. Cold Spring Harbor, NY: Cold Spring Harbor Laboratory Press, 2011. ISBN 978-0-87969-888-1.
2. Böhm I, Schild H. Apoptosis: the complex scenario for a silent cell death. Molecular Imaging Biology. 2003; 5(1):2-14.
3. Bernstein C, Bernstein H, Payne CM, Garewal H. DNA repair/pro-apoptotic dual-role proteins in five major DNA

repair pathways: fail-safe protection against carcinogenesis. Mutation Research. 2002; 511(2):145-78.
4. Takaoka A, Hayakawa S, Yanai H, Stoiber D, Negishi H, Kikuchi H *et al*. Integration of interferon-alpha/beta signalling to responses in tumour suppression and antiviral defence. Nature. 2003; 424(6948):516-23, 53.
5. De Las Rivas J, Fontanillo C. June. Protein-protein interactions essentials: key concepts to building and analyzing interactome networks. PLoS Computational Biology. 2010; 6(6):e1000807.
6. Herce HD, Deng W, Helma J, Leonhardt H, Cardoso MC. Visualization and targeted disruption of protein interactions in living cells. Nature Communications. 2013; 4:2660.
7. Kohl M, Wiese S, Warscheid B. Cytoscape: Software for Visualization and Analysis of Biological Networks. Data Mining in Proteomics. Methods in Molecular Biology. 2011; 696:291-303.
8. Chen J, Sawyer N, Regan L. Protein-protein interactions: general trends in the relationship between binding affinity and interfacial buried surface area. Protein Science. 2013; 22(4):510–5.
9. Szklarczyk D, Franceschini A, Wyder S, Forslund K, Heller D, Huerta-Cepas J *et al*. STRING v10: protein-protein interaction networks, integrated over the tree of life. Nucleic Acids Research. 2015; 43:D447–52.
10. Marchler-Bauer A, Bo Y, Han L, He J, Lanczycki CJ, Shennan L *et al*. CDD/SPARCLE: functional classification of proteins via subfamily domain architectures. Nucleic Acids Research. 2017; 45(D):200-3.
11. Kotlyar M, Pastrello C, Pivetta F, Sardo AL, Cumbaa C, Li H *et al*. *In silico* prediction of physical protein interactions and characterization of interactome orphans. Nature Methods. 2015; 12:79-84.
12. Keller DM, Zeng SX, Lu H. Interaction of with cellular proteins. Methods. 2003; 234:121-33, 53.
13. Zhang P, Elabd S, Hammer S, Solozobova V, Yan H, Bartel F *et al*. TRIM25 has a dual function in the p53)/Mdm2 circuit. Oncogene. 2015; 34(46):5729-38.
14. Goldstein AM. Familial melanoma, pancreatic cancer and germline CDKN2A mutations. Human Mutation. 2004; 23(6):630.
15. Murakami Y, Tripathi LP, Prathipati P, Mizuguchi K. Network analysis and *in silico* prediction of protein-protein interactions with applications in drug discovery. Current Opinion in Structural Biology. 2017; 44:134-142.
16. Joshua SM, Eran S, Daphne K, Stuart KK. A gene-co expression network for global discovery of conserved genetic modules. Science. 2003; 302(5643):249-55.
17. Kim PJ, Nathan D. Price Genetic Co-Occurrence Network across Sequenced Microbes. PLOS Computational biology. 2011; 5:231-238.
18. Sahoo PR, Mohapatra S, Sahoo G, Behera PC. Deciphering physiochemical and structural characterization of p53 tumor suppressor protein in domestic animals through *in silico* approaches. International Journal of Chemical Studies. 2018; 6(2):254-257.