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In silico analysis of Translationally-Controlled Tumour Proteins of social amoeba *Dictyostelium discoideum*

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Abstract- Translationally-Controlled Tumour Protein (TCTP) is an evolutionarily conserved protein throughout eukaryotic species. It is a multifunctional protein, involved in diverse biological mechanisms, e.g. cell growth, cell proliferation, cell cycle, cell death, stress and immune responses. It is identified as an apoptosis-inhibitory protein, hence associated with tumour progression. Expression is controlled both at transcriptional and translational levels. Dysregulation of TCTP leads to a range of diseases. TCTP in *Dictyostelium discoideum* has two isoforms called TPT1 and TPT2. Our previous findings showed the involvement of TPT1 in growth and development-related functions. Studying the roles of TPT proteins is crucial for comprehending their biology in its whole. In this study, we focus on *in silico* aspects of *Dd*TPTs. This study explores the TPT proteins at molecular levels of organisation and their functional interacting partners alongside human TCTP. The fundamentally conserved mechanisms are suggested by the common interacting partners and shared homology between *Dd*TPTs and human TCTP.

Key words: TCTP, *Dictyostelium, in-silico,* Interactions

INTRODUCTION

Translationally-controlled tumour protein (TCTP), also known as TPT1, P23, fortilin, HRF (Histamine-Releasing Factor), is a multifunctional protein with higher degree of conservation in eukaryotic organisms, sharing similarities with proteins found in plants and animals.[1] TCTP is reported to be cytoplasmic whereas some reports suggest its nuclear localisation.[2,3] TCTP is a housekeeping gene and is widely expressed in a variety of tissues and cell types. It is both extracellular and intracellular, and it has been linked to numerous biological processes that include the regulation of apoptosis, cell proliferation, cell cycle, stress responses, and even the allergic response.[4,5] TCTP is associated with tumours due to its higher expression in several cancer cell-types.[6] TCTP was shown to be the most pronouncedly downregulated gene in tumour reversion.[7]

TCTP knockout mouse embryos died due to reduced cell numbers and higher apoptosis at 9.5-10.5 embryonic stage day.[8] TCTP mutant mice exhibit defects in neuronal and glial differentiation during CNS development.[9] However, *in vitro* research using mouse embryonic fibroblast (MEF) cells showed that TCTP is not essential for the survival of the cell.[8] According to Choi *et al*. (2017)[10], TCTP is essential for *Drosophila* organ growth as well as DNA repair and chromatin remodelling. TCTP has been investigated as a stress hallmark protein that shields cells from heat stress.[10,11]

In *Arabidopsis thaliana,* the two *tctp* genes present are not redundant and have partially different activities;

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*At*TCTP1 is an essential regulator of mitosis, whereas *At*TCTP2 is involved in plant growth and development.[12] *Trypanosoma brucei* possesses two isoforms of TCTP (TCTP1 and TCTP2) that are uniquely expressed at distinct periods of the life cycle.[13]

Dictyostelium discoideum is a lower eukaryote having two distinct phases in its life cycle: vegetative phase (in nutrient-rich conditions), and multicellular development phase (in nutrient-starved conditions). Growth and development are independent processes in *D. discoideum. Dictyostelium* has two isoforms of TCTP known as TPT1 and TPT2. We have investigated the role of TPT1 in our earlier work[14], where we showed its involvement in cell growth and proliferation. TPT1 was also seen to be implicated in *Dictyostelium* developmental processes like cell-differentiation and patterning ultimately affecting the size and viability of fruiting body.[14] Our unpublished studies on TPT2 also suggest its role in similar cellular and developmental processes.

Present study involves the *in-silico* approach to find the homology between *Dictyostelium* TPTs (TPT1 and TPT2) and human TCTP (*Hs*TCTP). We have explored the sequence and structural differences between *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2 proteins at 1°, 2° and 3° levels along with their interacting partners using various bioinformatics and computational biology tools. The *in-silico* knowledge is crucial as it serves as a powerful tool for forecasting the therapeutic potential. Uncontrolled cell proliferation and loss of apoptosis are traits of cancerous cells.[15] TCTP controls both these processes thus, could be a potential target in cancer cell therapy. It is important to study the basic biology of this protein in lower eukaryotes like *Dictyostelium* to better understand its function.

MATERIALS & METHODS

Sequence Retrieval & domain prediction- Protein sequences of *Dictyostelium discoideum* TPTs were retrieved from dictyBase.org online resource (http://www.dictybase.org). The protein sequence of human TCTP *(Homo sapiens)* was retrieved from NCBI (National Institutes of Health) database (https://www.ncbi.nlm.nih.gov/). Domain architecture of *Dd*TPTs and human protein was deduced by Simple Modular Architecture Research Tool (SMART)[16] (http://smart.embl-heidelberg.de/).

Multiple sequence alignment- The retrieved protein sequences from human TCTP and *Dictyostelium* TPT proteins were aligned using multiple sequence alignment program Clustal Omega at EBI server (https://www.ebi.ac.uk/jdispatcher/msa/clustalo).

Construction of Phylogenetic tree- The *Dd*TPT orthologues were searched by Basic Local Alignment Search Tool (BLASTp) at NCBI (https://blast.ncbi.nlm.nih.gov/Blast.cgi), UniProt and dictyBase. The retrieved FASTA amino acid sequences were pasted into a text document file format. For multiple sequence alignment, ClustalW program was used under MEGAX. The aligned file was saved in mega format. A phylogenetic tree was constructed using MEGAX Phylogeny construction using Neighbour-joining statistical method with bootstrap replicate value as 1000. The evolutionary distances were computed using Poisson correction method of substitution.

Secondary structure prediction- For the prediction of secondary structures of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2, the FASTA sequences of given proteins were entered on PHYRE2 at Protein Fold Recognition server (http://www.sbg.bio.ic.ac.uk/phyre2/html/page.cgi). The retrieved structures were then analysed.[17]

Structural alignment of 3D protein structures- The three-dimensional protein structures were retrieved from UniProt (https://www.uniprot.org/) in PDB file format. X-ray structure of *Hs*TCTP (PDB id: 1YZ1) and Alpha fold predicted structures of *Dd*TPT1 (UniProt id: Q54RX6), *Dd*TPT2 (UniProt id: Q54RX1) were used for the study. The PDB files were then opened in PyMol TM 3.0.4 and then superimposed (*Hs*TCTP & *Dd*TPT1), (*Hs*TCTP & *Dd*TPT2), and (*Dd*TPT1 & *Dd*TPT2) to identify similarities and differences in tertiary protein structures. Misaligned sequences were selected and marked. RMSD values were noted.

Identification of functional partners- The functional partners of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2 were identified using STRING, Protein-Protein Interaction Networks Functional Enrichment Analysis (https://string-db.org/). The primary protein sequences were loaded and predicted functional partners were identified. The bitmap image generated was used for demonstration.

RESULTS & DISCUSSION

Identification of TCTP homologues in *D. discoideum* and conserved residues in primary sequence- *Dictyostelium* orthologs of TCTP: TPT1 and TPT2; gene id: DDB_G0282853 and DDB_G0282861 are located on Chromosome 3 coordinates no. (6303739 to

6304648, Watson strand and 6318668 to 6319252, Crick strand). TCTP is a small multifunctional protein. A sequence of *Hs*TCTP contains 172 amino acids (19.5 kDa), while a sequence of *Dd*TPT1 contains 174 amino acids (19 kDa) and *Dd*TPT2 includes 194 amino acids (22 kDa). To identify its functional domain, the domain analysis was performed using SMART (Simple Modular Architecture Research Tool). The FASTA protein sequence of human TCTP (*Hs*TCTP), and *Dictyostelium* TPTs (*Dd*TPT1 and *Dd*TPT2) were used for the analysis. Domain architecture analysis shows both human and *Dictyostelium* TPTs have a single domain (Figure. 1A).

A multiple sequence alignment between amino acid sequences of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2 was performed to find the sequence similarity and conserved residues (Figure. 1B). The primary sequences of *Dd*TPT1 and *Dd*TPT2 are 40.68% and 31.76% identical to human TCTP. Conserved residues showed identity between social amoeba and *Homo sapiens*. According to sequence search, the important residues have remained constant throughout evolution. It is counterintuitive that TCTP plays a role in the mTORC1 signalling pathway given that prior studies have shown that Glutamate12 (Glu12), which is found in the loop region of *Drosophila* TCTP, is an essential residue for Rheb (Ras homologue enrichment in brain) activity that triggers TOR (Target of Rapamycin). Therefore, the prospect of Rheb function in lower eukaryotes is opened by the conservation of Glu12 in *Dd*TPTs.[14] According to sequence and phylogenetic analyses, *Dd*TPTs are conserved proteins in eukaryotes. In the several species under investigation, residues crucial for microtubules and Ca^{2+} binding are likewise conserved. On the other hand, the Plk-phosphorylated Ser46 and Ser64 residues are unique to mammalian TCTP and are not conserved in lower eukaryotes.[14] The phylogenetic analyses revealed *Dictyostelium* family share a separate clade and fall closest to *Plasmodium falciparum* and *Saccharomyces* species (Figure. 1C).

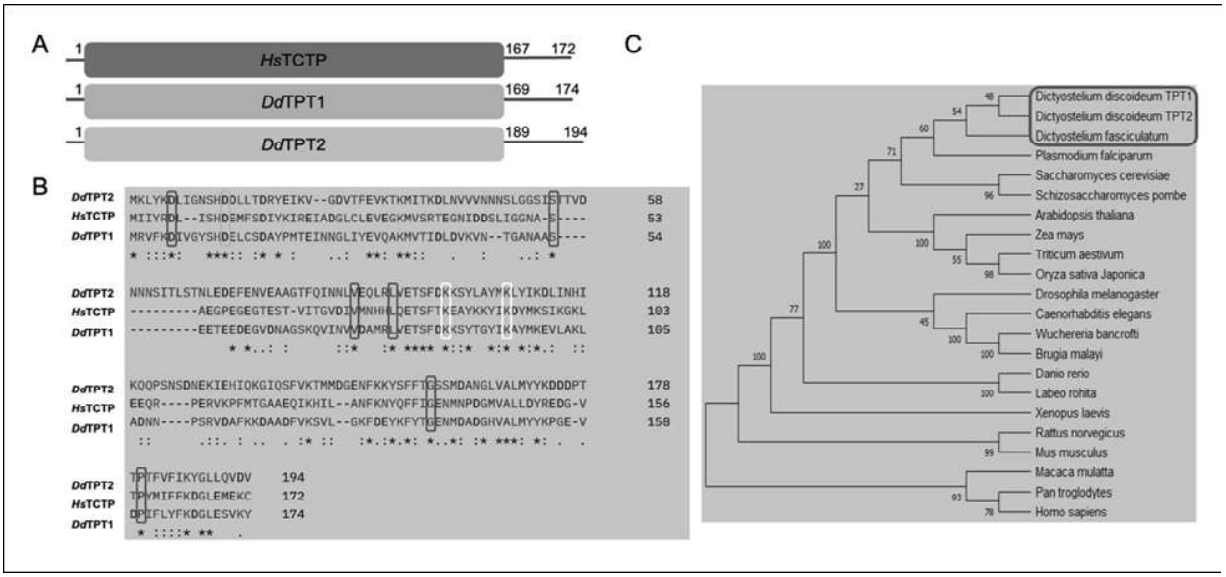

Figure 1: Identification of TCTP domain and protein sequence alignment of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2. (A) TCTP is a small protein containing a single domain. Domains of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2 are identified by SMART. **(B)** Multiple sequence alignment of primary protein sequences from human and *Dictyostelium* TPTs performed by Clustal Omega. Sequences used in this study are *Dictyostelium discoideum* (DDB_G0282853, DDB_G0282861), and *Homo sapiens* (Uniprot id: P13693). Identical [*], 90% conserved [:], and 50% conserved [.] amino acid residues are indicated in multiple sequence alignment. Residues shown in rectangular boxes are involved in different functions which are conserved from lower to higher organisms. Residues crucial for Rheb interaction are shown, while residues involved in microtubules and Ca^{2+} are highlighted in white colour box. **(C)** *Dictyostelium discoideum* TPTs share homology with known TCTP proteins from various organisms. The phylogenetic tree generated by MEGAX using Clustalw as multiple sequence alignment tool. The *Dictyostelium* species fall in a separate clade where *Plasmodium falciparum* is their closest relative. The other close clade belongs to *Saccharomyces* species while human, monkey and mouse appear farthest. [*Dictyostelium discoideum* TPT1, *Dictyostelium discoideum* TPT2, *Dictyostelium fasciculatum, Plasmodium falciparum, Saccharomyces cerevisiae, Saccharomyces pombe, Arabidopsis thaliana, Zea mays, Triticum aestivum, Oryza sativa Japonica, Drosophila melanogaster, Caenorhabditis elegans, Wuchereria bancrofti, Brugia malayi, Danio rerio, Labeo rohita, Xenopus laevis, Rattus norvegicus, Mus musculus, Macaca mulatta, Pan troglodytes, Homo sapiens]*.

Homology modeling of *Dd*TPTs with *Hs*TCTP- In addition to providing information regarding protein activity, relationships and functions, protein secondary structure prediction is an important initial step towards tertiary structure prediction. The polypeptide backbone of local conformation proteins is referred to as protein secondary structure. There is one irregular secondary structure type, the coil region (C) and two regular secondary structure states: α-helix (H) and β-strand (B).[18] A comparative protein secondary structure models were generated for *Dictyostelium* and human TCTP by Phyre2 to study the resemblance and differences between the structures (Figures 2A-C). *Hs*TCTP contains 21% α-helix and 36% β-strand region whereas 17% region was identified as disordered. In case of *Dd*TPT1, there are 22% α-helix regions and 32% β-strand along with 15% disordered structures. While secondary structure of *Dd*TPT2 includes the highest percentage of disordered regions; 24% and lesser α-helix; 20% and 32% β-strand (Table-1). Both human and *D. discoideum* TPTs showed 2 α-helix and multiple β-strand (10-12). α-helices and β-strand are marked as H1, H2 and B1-B12 (Figure. 2). The positions of H1 and H2 were conserved in *Hs*TCTP and *Dd*TPT1, whereas α-helix positions in *Dd*TPT2 are different (Table-2). Similarly, numerous β-strand are present in secondary structure of TCTP, their positions are marked in (Table-3). First three β-sheets are present between first 2-25 amino acids. The positions of β-strand in *Dd*TPT1 are mostly like *Hs*TCTP.

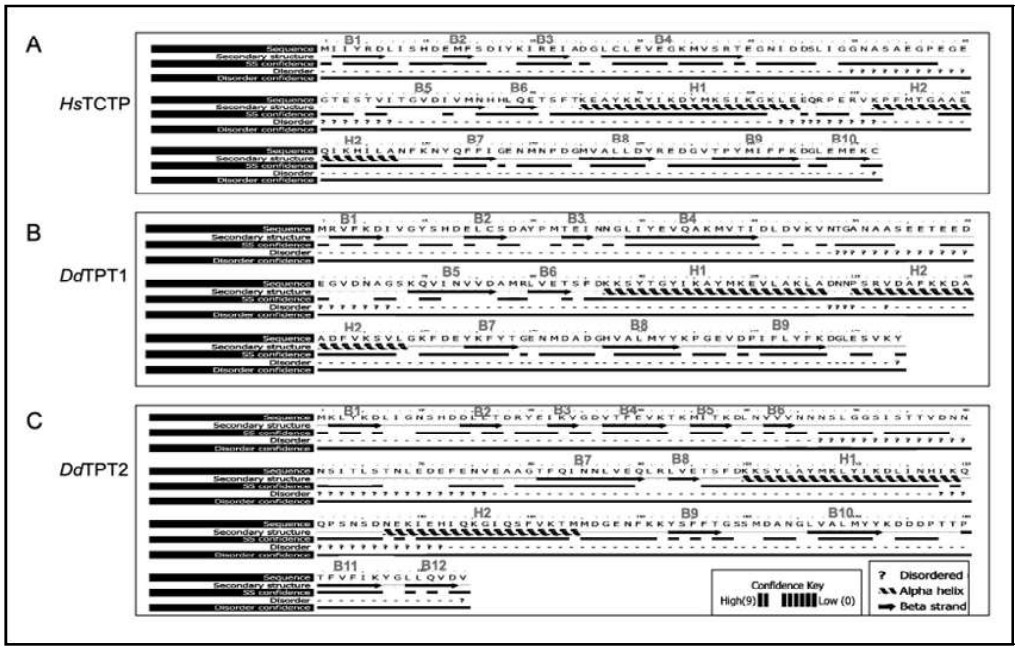

Figure 2:The secondary structure of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2 predicted by Phyre2 software (Protein Homology/ analogY Recognition Engine V 2.0) and compared with *Hs*TCTP. (A) The secondary structure of *Hs*TCTP comprises 2 α-helices and 10 β-strands. **(B)** The secondary structure of *Dd*TPT1 holds 2 α-helices and 9 β-strands. **(C)** *Dd*TPT2 comprises 2 α-helices and 12 β-strands. The α-helices are identified as H (1,2) and β-strands are marked as B (1-12). The positions of α-helix and β-strands are given in Tables 2 & 3.

Table 1- The percentage of secondary structures: α-helix, β-strand and disordered structures in *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2

Features	*Hs*TCTP	*Dd*TPT1	*Dd*TPT2
Disordered structures (%)	17	15	24
α-helix (%)	21	22	20
β-strand (%)	36	32	32

Table 2- Positions of α-helices (H1, H2) in secondary protein sequence of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2

α-helix (H) positions	*Hs*TCTP	*Dd*TPT1	*Dd*TPT2
H1	85-104	87-106	100-119
H2	112-127	110-128	127-144

Table 3- Positions of β-strands (B1-B12) in the secondary protein sequence of *Hs*TCTP, *Dd*TPT1 and *Dd*TPT2.

β-strands (B) positions	*Hs*TCTP	*Dd*TPT1	*Dd*TPT2
B1	2-6	2-6	2-6
B2	12-14	14-17	14-17
B3	20-23	23-25	22-24
B4	27-39	29-40	27-32
B5	66-75	69-76	35-38
B6	78-80	80-83	42-44
B7	133-137	134-138	81-90
B8	145-151	147-153	93-95
B9	157-164	159-166	153-157
B10	166-171	-	166-172
B11	-	-	180-186
B12	-	-	189-193

Determination of the tertiary structure of a protein is important to understand its biological functions. *Hs*TCTP and *Dd*TPTs tertiary structures are shown in (Figures. 3A-C). The *Dictyostelium* TPT1 and TPT2 structures are superimposed with human TCTP and unaligned sequences from structures are marked (Figure. 3D-F). For *Hs*TCTP and *Dd*TPT1, most unaligned sequences fall in β-strands and loop regions marking conserved α-helical areas as observed in secondary structure (Figure. 3D). The calculated RMSD value is 0.826. The superimposed structure of *Dd*TPT2 with human TCTP revealed their H1 region does not align and the unaligned *Dd*TPT2 sequences belong to β-strand and loop regions. The calculated RMSD value is 1.0 (Figure. 3E). The similarity search between tertiary structures of *Dd*TPT1 and *Dd*TPT2 revealed overlapping α-helical regions and unaligned regions mostly belonging to β-strand and loop regions, the calculated RMSD value is 0.653 (Figure. 3F). RMSD values are depicted in (Table- 4).

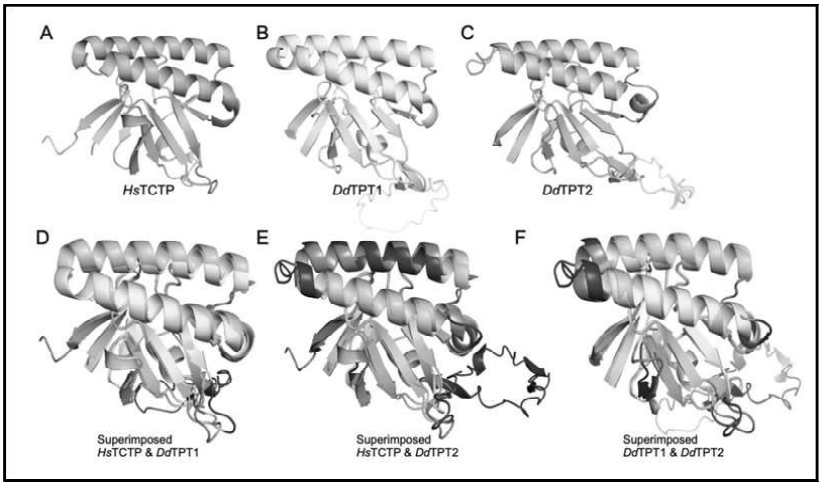

Figure 3:Comparison between tertiary structures of TCTP proteins (*Hs*TCTP, *Dd*TPT1 and *Dd*TPT2) using PyMol™ software. Tertiary protein structures were downloaded from PDB (Protein Data Bank) and represented as **(A)** *Hs*TCTP **(B)** *Dd*TPT1 and **(C)** *Dd*TPT2. Tertiary models of TCTP contain two α-helices and various numbers of β-sheets along with loops representing disordered secondary structures. Next, the structures were superimposed using PyMol to mark differences between the functional protein models of the three. **(D)** Superimposed protein model of *Hs*TCTP and *Dd*TPT1 where mismatched regions are observed for *Hs*TCTP and *Dd*TPT1. **(E)** Superimposed protein model of *Hs*TCTP and *Dd*TPT2 where mismatched regions are observed for *Hs*TCTP and *Dd*TPT2 region. **(F)** Superimposed protein model of *Dd*TPT1 and *Dd*TPT2 where mismatched regions are observed for *Dd*TPT1) and *Dd*TPT2 region. RMSD values are mentioned in Table-4.

Table 4- RMSD values are mentioned below

RMSD values	*Hs*TCTP + *Dd*TPT1	*Hs*TCTP + *Dd*TPT2	*Dd*TPT1 + *Dd*TPT2
	0.826	1.0	0.653

Functional interacting partners of *Dd*TPTs- Since most proteins in a cell function as a component of a complex with other proteins, it is crucial to identify the functional interacting partners of proteins. Comprehending the interplay between proteins is essential for understanding their roles in cellular processes. Understanding the mechanisms that initiate and advance diseases is made easier by the examination of these networks. InterProScan revealed both human and *Dictyostelium* TCTP proteins to be involved in Ca^{2+} binding and microtubule stabilisation and homologous to Mss4-like superfamily. It functions as a growth-regulating protein implicated in the TSC1-TSC2-mTOR pathway or a guanine nucleotide dissociation inhibitor for the elongation factors EF1A and EF1B.[19] Functional partners of *Hs*TCTP and *Dd*TPTs are identified in this study using STRING program and compared (Figure. 4). Common interacting partners involve its guanine nucleotide exchange factor, *Hs*EEF1β, *Dd*EF1β (Elongation factor 1β), which with EF-1-delta stimulate the exchange of GDP bound to EF-1α to GTP. Another common interacting partner is RPLP0 (60S acidic ribosomal protein P0); Ribosomal protein P0 is the functional equivalent of *E. coli* protein L10 which helps the ribosome interact with translational factors that are bound to GTP. Other common interacting partners include NACs and various ribosomal small and large subunit proteins. NACs are nascent polypeptide-associated complex subunits, which prevent inappropriate targeting of non-secretory polypeptides.

Additionally, *Hs*TCTP interacts with PELO (Protein pelota homolog); required for normal chromosome segregation during cell division and genomic stability (by similarity), and RACK1 (Receptor of activated protein C kinase 1, N-terminally processed); scaffolding protein involved in the recruitment, assembly and/or regulation of a variety of signalling molecules. *Dd*TPT1 and *Dd*TPT2 share common interacting partners and interact with each other. Moreover, *Dd*TPT1 interacts with efa1G; a Glutathione S-transferase domain-containing protein. *Dd*TPT2 interacts with P-type ATPase (DDB_G0267924); and belongs to the cation transport ATPase (P-type) family.

Functional annotations of the above TCTPs show their involvement in Ca^{2+} ion-binding, metal ion-binding and cation-binding. The common functions of *Hs*TCTP and *Dd*TPT1 include their involvement in cellular processes and developmental processes. There are various other functions *Hs*TCTP and *Dd*TPT1 are involved in; those are depicted in (Table-5).

In silico study on *Dd*TPT1 and its functional annotations validated the role of TPT1 shown in our previous study *i.e.,* cell proliferation, growth, pinocytosis, cell type differentiation, cell patterning and developmental processes.[14] Our unpublished work on *Dd*TPT2 also suggests its role in such processes. For this reason, *in silico* research is fundamental for *in vivo* studies.

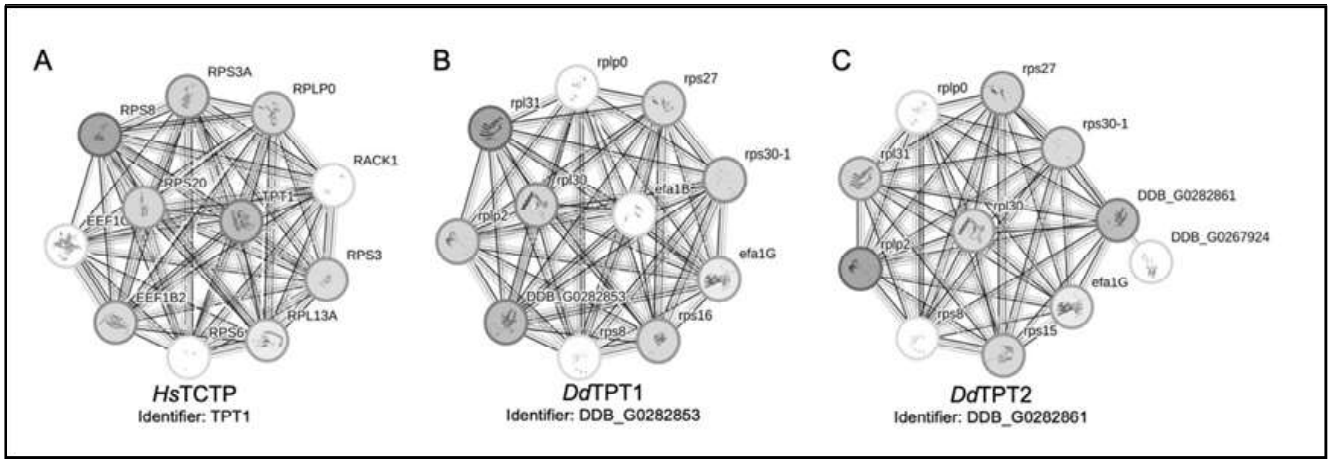

Figure 4: Functional partners of TPTs are identified using STRING analysis. Human TCTP (*Hs*TCTP) and *Dictyostelium discoideum* TPTs (*Dd*TPT 1 & 2) shared a list of functionally common interacting partners *i.e.*, GDP to GTP exchange protein, large and small ribosomal proteins, elongation factors, ribosomal protein P0, nascent polypeptide associated complex (NAC) **(A)** *Hs*TCTP, identifier: TPT1 **(B)** *Dd*TPT1, identifier: identifier: DDB_G0282853 **(C)** *Dd*TPT2, identifier: DDB_G0282861.

Table 5- List of functional annotations of human and *Dictyostelium* TPT1

*Dd*TPT1	*Hs*TCTP
Endocytosis	Cellular ion homeostasis
Pinocytosis	Response to external stimulus
Macropinocytosis	Response to virus
Vesicle-mediated transport	Regulation of signal transduction
Asexual reproduction	Regulation of cell communication
Anatomical structure development	Regulation of signalling
Cell differentiation	Regulation of biological process
Establishment of localization	Regulation of cell death
GTP hydrolysis & joining of 60s ribosomal subunit and Translational elongation	Negative regulation of apoptotic process
Ribosome and Translation elongation factor activity	Chemical homeostasis

CONCLUSION

Amino acid sequences of *Dd*TPTs hold conserved residues for Rheb interactions, Ca^{2+} and microtubule binding. At secondary level, *Dd*TPTs contain 2 α-helix regions like *Hs*TCTP and varied number of β-strands (9 & 12). The positions of α-helix and β-strands are more conserved in *Dd*TPT1. Compared to *Dd*TPT2, the tertiary structure of *Dd*TPT1 is more effectively overlaid on *Hs*TCTP. The common functional partners of STRING analysis revealed the conserved functions of TCTP in lower eukaryote *D. discoideum* and humans. Our data suggests that *Dd*TPT1 is more similar to *Hs*TCTP.

REFERENCES

1. **Amson R., Pece S., Marine J. C., Di Fiore P. P., & Telerman A. 2013.** TPT1/TCTP-regulated pathways in phenotypic reprogramming. *Trends Cell Biol*. **23:** 37-46. 10.1016/j.tcb.2012.10.002.
2. **Li F., Zhang D., & Fujise K. 2001.** Characterization of fortilin, a novel antiapoptotic protein. *J. Biol. Chem*. **276:** 47542-47549. 10.1074/jbc.M108954200.
3. **Arcuri F., Papa S., Carducci A., Romagnoli R., Liberatori S., Riparbelli M. G., Sanchez J. C., Tosi P., & Del Vecchio M. T. 2004.** Translationally controlled tumor protein (TCTP) in the human prostate and prostate cancer cells: expression, distribution, and calcium binding activity. *Prostate*. **60:** 130-140. 10.1002/pros.20054.
4. **Rho S. B., Lee J. H., Park M. S., Byun H. J., Kang S., Seo S. S., Kim J. Y., & Park S. Y. 2011.** Anti-apoptotic protein TCTP controls the stability of the tumor suppressor p53. *FEBS Lett*. **585(1):** 29-35. doi: 10.1016/j.febslet.2010.11.014.
5. **Bommer U. A., Heng C., Perrin A., Dash P., Lobov S., Elia A., & Clemens M. J. 2010.** Roles of the translationally controlled tumour protein (TCTP) and the double-stranded RNA-dependent protein kinase, PKR, in cellular stress responses. *Oncogene*. **29(5):** 763-73. doi: 10.1038/onc.2009.380.
6. **Gnanasekar M., Dakshinamoorthy G., & Ramaswamy K. 2009.** Translationally controlled tumor protein is a novel heat shock protein with chaperone-like activity. *Biochem Biophys Res Commun*. **386(2):** 333-7. doi: 10.1016/j.bbrc.2009.06.028.
7. **Tuynder M., Susini L., Prieur S., Besse S., Fiucci G., Amson R., & Telerman A. 2002.** Biological models and genes of tumor reversion: cellular reprogramming through tpt1/TCTP and SIAH-1. *Proc Natl Acad Sci U S A*. **99:** 14976-14981. 10.1073/pnas.222470799.
8. **Chen S. H., Wu P. S., Chou C. H., Yan Y. T., Liu H., Weng S. Y., & Yang-Yen H. F. 2007.** A knockout mouse approach reveals that TCTP functions as an essential factor for cell proliferation and survival in a tissue-or cell type–specific manner. *Mol Biol Cell*. **18:** 2525-2532. 10.1091/mbc.e07-02-0188.
9. **Chen S. H., Lu C. H., & Tsai M. J. 2020.** TCTP is Essential for Cell Proliferation and Survival during CNS Development. *Cells*. **9(1):** 133. doi: 10.3390/cells9010133.
10. **Choi K. W., Hong S. T., & Le T. P. 2017.** Function of Translationally Controlled Tumor Protein in Organ Growth: Lessons from *Drosophila* Studies. TCTP/tpt1-Remodeling Signaling from Stem Cell to Disease. 173-191. 10.1007/978-3-319-67591-6_8.

11. **Burgess A., Labbe J., Vigneron S., Bonneaud N., Strub J., Van Dorsselaer A., Lorca T., & Castro A. 2008.** Chfr interacts and colocalizes with TCTP to the mitotic spindle. *Oncogene*. **27:** 5554-5566. 10.1038/onc.2008.167.

12. **Toscano-Morales R., Xoconostle-Cázares B., Cabrera-Ponce J. L., Hinojosa-Moya J., Ruiz-Salas J. L., Galván-Gordillo S. V., Guevara-González R. G. & Ruiz-Medrano R. 2015.** *At*TCTP2, an *Arabidopsis thaliana* homolog of Translationally Controlled Tumor Protein, enhances *in vitro* plant regeneration. *Front plant Sci*. **6:** 468. 10.3389/fpls.2015.00468.

13. **Jojic B., Amodeo S., & Ochsenreiter T. 2018.** The translationally controlled tumor protein TCTP is involved in cell cycle progression and heat stress response in the bloodstream form of *Trypanosoma brucei. Microb Cell*. **5:** 460. 10.15698/mic2018.10.652

14. **Kumar R., Maurya R., & Saran S. 2020.** Investigating the role of translationally control tumor protein in growth, development and differentiation of *Dictyostelium discoideum*. *Front Cell Dev Biol*. **8:** 742. 10.3389/fcell.2020.00742

15. **Nagano-Ito M., & Ichikawa S. 2012.** Biological effects of Mammalian translationally controlled tumor protein (TCTP) on cell death, proliferation, and tumorigenesis. *Biochem. Res. Int*. **2012:** 204960. doi: 10.1155/2012/204960.

16. **Schultz J., Copley R. R., Doerks T., Ponting C. P., & Bork P. 2000.** SMART: a web-based tool for the study of genetically mobile domains. *Nucleic Acids Res*. **28(1):** 231-4. doi: 10.1093/nar/28.1.231. PMID: 10592234; PMCID: PMC102444.

17. **Kumar R., Rafia S., & Saran S. 2014.** Cloning, expression and characterization of the ornithine decarboxylase gene from *Dictyostelium discoideum*. *Int. J. Dev. Biol*. **58(9):** 669-76. doi: 10.1387/ijdb.140174ss. PMID: 25896203.

18. **Ma Y., Liu Y., &Cheng J. 2018.** Protein Secondary Structure Prediction Based on Data Partition and Semi-Random Subspace Method. *Sci Rep*. **8(1):** 9856. doi: 10.1038/s41598-018-28084-8.

19. **Huang J., & Manning B. D. 2008.** The TSC1-TSC2 complex: a molecular switchboard controlling cell growth. *Biochem J*. **412(2):** 179-90. doi: 10.1042/BJ20080281.

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