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Original Article

COMPUTATIONAL IDENTIFICATION OF PUTATIVE DRUG TARGETS IN *MALASSEZIA GLOBOSA* BY SUBTRACTIVE GENOMICS AND PROTEIN CLUSTER NETWORK APPROACH

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ABSTRACT

Objective: Yeast commonly causes superficial mycoses similar to the dermatophytes. Superficial mycoses were reported with an estimated incidence of ~140,000,000 cases/year worldwide and most frequently caused by *Malassezia globosa* and *Malassezia furfur*. Treatment available for these conditions is limited and with side effects. Moreover, termination of the treatment may result in the reoccurrence of the disease. The objective of this research was to identify the putative drug targets using computational approaches.

Methods: The analysis of genome sequence improves the understanding of diseases which leads to better treatment. Comparison of the genome of the pathogen with the host at the molecular level is suitable for performing the sequence based prediction of protein-protein interaction network, which also forms the basis of drug target identification leading to the discovery of new drugs for the improved treatment.

Results: Out of 100 pathways of *M. globosa*, 95 were common to the host and 5 were unique to the pathogen. Total common and unique targets from common pathways are 1704 and 300, respectively. A unique target from unique pathways and 147 from common pathways were non-homologous targets. From this, 46 targets were screened out as essential and processed in the next phase to identify the clustered targets which resulted with three clusters based on their biological role and subcellular location.

Conclusion: In this study, putative drug targets were identified in *M. globosa* using *in silico* approaches of subtractive genomics and cluster network which will help in the next level of drug discovery such as lead identification for the novel targets.

Keywords: *Malassezia globosa*, *Homo sapiens*, Comparative genomics, Protein-protein interactions, Drug targets

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INTRODUCTION

Now fungi are becoming ubiquitous in the environment and fungal infections are increasing at an alarming rate causing significant health problems [1]. The growing populations of immune compromised individuals with highly susceptibility to fungal pathogens have become a common cause of morbidity and mortality [2]. Fungal infections can be divided into systemic and superficial mycoses. Systemic or deep mycoses are able to infect internal organs. Superficial mycoses affect external part of the skin and hair, and these infections are the most common fungal diseases which affect approximately 25% of the general population worldwide [3]. Members of the genus *Malassezia* have become noticed as opportunistic yeasts of increasing importance in recent years by dermatologists and mycologists [4-7]. Out of 14 recognized species of *Malassezia* [8], a small genome size, spanning ~9 Mb, *Malassezia globosa* is associated with skin diseases [9] such as pityriasis versicolor [10], seborrhoeic dermatitis and dandruff [11]. Treatment involves the use of ketoconazole, selenium sulfide, zinc pyrithione, ciclopirox olamine, climbazole [12] but termination of the treatment often leads to the reoccurrence of the symptoms [13].

Microorganisms are becoming resistant to multiple antibiotics, making the infections tough to eradicate [14]. Novel antimicrobials are therefore needed to combat infections. Target identification is the foremost important step in drug discovery as this whole process depends on the target and also important to battle against diseases and drug resistant microorganisms. Traditional method of drug discovery is time-consuming, labour intensive, cost effective and yield few drug targets. Novel therapeutics in areas with a high medical need is based on innovative putative drug targets, a key focus for both the pharmaceutical industry and academic research. Thus the focus in drug development has been shifted to computational subtractive genomic approach for identifying pathogen specific drug targets. Targeting the pathogen's metabolic enzymes (targets) affect only the pathogen and not the host. Exploiting the metabolic differences between the host and the pathogen avoids host-drug interactions, i.e. the problem of cross-reactivity and side effects are minimized by non-homologous proteins. Advances in computational methods, availability of complete genome and significant information in databases such as metabolic pathways, enzymes and various tools come in handy. Glycolytic pathway involved enzymes were reported as potential targets against fatal disease causing parasitic organism, *Trypanosoma brucei* [15]. Blocking the enzymes involved in the aspartate pathway by phytocompounds is lethal to the microorganism [16]. Lacking literature about metabolic pathway analysis based potential drug targets in *M. globosa* enhanced the focus on identifying the same.

MATERIALS AND METHODS

Identification of common and unique metabolic pathways

Available computational tools encompass various *in silico* based approaches to identify new protein targets, of which, metabolic pathway/metabolic network analysis emerged as an efficient method to identify candidate metabolic enzymes as targets. KEGG (Kyoto Encyclopedia of Genes and Genomes), a manually curated database makes a clear understanding of the biological system of any sequenced organisms. Metabolic pathways of the *M. globosa* and the *Homo sapiens* were retrieved from the KEGG database and manual comparison was done to find out the unique and common pathways of the pathogen (http://www.genome.jp/kegg).

Mining of suitable proteins

The sequences of the protein pertaining to both pathways were retrieved from the UniProt (http://www.uniprot.org) database and subjected to BLAST (Basic Local Alignment Search Tool) and sequence similarity search was performed against the host proteome database. The main objective of this step is to define the non-homologous proteins of the pathogen as it's likely to prevent

the cross-reactivity of drug compounds with the human host proteins [17]. 'Expect' value (e-value) fixed was <0.005 and a minimum bit score was> 100 to exclude the homologous sequences. Proteins which showed "hits" with the above mentioned cut-off values were considered as non-homologous proteins [18-20] and subjected to further screening process where remaining were excluded from the list.

Essentiality assessment of *M. globosa* proteins

DEG (Database of Essential Genes) is a database of indispensable genes from bacteria, archaea, and eukaryote organisms which support their cellular life. In order to identify the essential proteins of *M. globosa*, the resultant non-homologous were subjected to the protein BLAST tool and similarity search was performed against the essential eukaryotes [21] with an e-value <0.0001, bit score >100 [22] and identity greater than 30% [23].

Network based targets

Selected indispensable proteins are then subjected to STRING (Search Tool for the Retrieval of Interacting Genes/Proteins) database to construct protein-protein interaction network (http://string.embl.de) [24]. Interactors with confidence score greater than or equal to 0.700 alone included here in the protein network [25] and with low and medium confidence score were eliminated to avoid false positives and false negatives. Target protein with more interactors is considered as a metabolically active protein which could be an appropriate drug target [26, 27]. The interaction network was analyzed using Cytoscape 2.8.1 [28], a package for biological network visualization and analysis. MCODE (Molecular COmplex Detection) plugin detects highly interconnected regions in the network. The optimized parameters in MCODE to analyze network includes loops, degree cutoff 2 and node score cut off 0.2, haircut, node density cutoff (0.1), k-core-2, maximum depth (100) were used to produce the best network [29].

Other Important criteria to be a drug target

The subcellular localization of the eukaryotic targets was identified by support vector machine method (SVM), ESLpred is an elegant approach (http://www.imtech.res.in/raghava/eslpred/submit.html) [30]. All the identified potential drug targets were further evaluated for its druggability by searching them against DrugBank [31] and Therapeutic Target Database (TTD) [32].

RESULTS AND DISCUSSION

Common and unique targets

Identification of putative drug targets from annotated metabolic pathways available in KEGG using subtractive genomics/ proteomics has been widely used by several researchers in bacterial pathogens [33-38]. Metabolic pathways that are present in both the host and the pathogen are identified as common pathways and those which are present only in infection causing organism but not in the host as unique pathways. Out of 100 pathways of *M. globosa* taken for the present analysis, 95 pathways are common and 5 are unique to the pathogen. The same number of unique pathways were reported from *Mycoplasma hyopneumoniae* in the process of identifying the drug and vaccine targets [39]. Each common pathway of the *Homo sapiens* and the pathogen retrieved from pathway database were compared manually and identified the common and unique targets.

In the present study, the total number of common and unique targets from common pathways are 1704 and 300, respectively. Out of 1704 common targets, 705 are involved in metabolism, 802 in genetic information processing, 17 in environmental processing and 180 in cellular processes. Total numbers of unique targets from common pathways include 177 in metabolism, 9 in genetic information processing, 53 in environmental processing and 61 in cellular processes. Five unique pathways of *M. globosa* are carbapenem biosynthesis, various types of N-glycon biosynthesis, C-5 branched dibasic acid metabolisms, methane metabolism, sesquiterpenoid and triterpenoid biosynthesis. In this study, unique pathways have 29 enzymes of which 28 enzymes are involved in common pathways which is in accordance with the report [40] which stated that common drug targets are also involved in the pathway unique to the pathogens of bacterial meningitis. Also, the number of drug targets identified from the common pathways of *M. globosa* were more than that identified among *Streptococcus pneumonia, Neisseria meningitidis, Haemophilus influenzae* type b and *Staphylococcus aureus* causing bacterial meningitis.

Non-homologous and essential targets

In this phase, non-homologous targets were segregated from homologous targets in the common pathways to avoid the undesirable cross reaction of the drug, thereby preventing its binding to the homologous proteins in the host, and its essentiality represents a good alternative for the development of new antifungal drugs [41]. Conserved genes in different genomes often turn out to be essential [42, 43]. The products of essential genes that are indispensable for the growth, replication, viability or survival are important to develop drugs against the pathogen with a novel mode of action [44]. In *M. globosa*, a total of 147 non-homologous targets from common pathways were identified. Two unique targets were identified from unique pathways of which one target was found to be present in common pathways and the other is non-essential hence not included in the novel drug target identification. Out of 147 targets from common pathways, only 46 targets were found to be essential and the remaining were found to be non-essential [table 1].

Based on the theory that similar proteins which are essential in one eukaryotic genome may be essential for another eukaryote, hits found with DEG database with the mentioned cut-off values were expected to represent the crucial conserved essential proteins of the selected organism while remaining proteins were not, therefore excluded from the list of probable drug targets. A study showed that 57 potential drug targets from eight human fungal pathogens (*Candida albicans*, *Aspergillus fumigatus*, *Blastomyces dermatitidis*, *Paracoccidioides brasiliensis*, *Paracoccidioides lutzii, Coccidioides immitis*, *Cryptococcus neoformans* and *Histoplasma capsulatum)*, which did not include *Malassezia* sp., of which only 10 were conserved as essential targets [45].

Clustered targets

Unlike the usual computational approaches, the other strategy to tackle a pathogen at the metabolic level is to identify the pathogen specific interacting enzymes [46]. Many functions within a cell are carried out by interactions between proteins being depicted by protein-protein interaction network that communicates associations between proteins. The network that finds hubs are the highly interconnected proteins or clusters playing an important role in the biological network as it is more likely to be an essential one than proteins having smaller links [47]. In the present study, 46 essential proteins of *M. globosa* studied using STRING database revealed low (<0.004), medium (0.400-0.700) and high confidence protein-protein interactions (≥0.700). The interactors with confidence score ≥0.700 alone were used which goes in line with the target identification pipeline for *Mycobacterium tuberculosis* [48] and five non-interacting proteins of *M. globosa* (MGL_1691, MGL_2217, MGL_ 2793, MGL_1167 and MGL_2547) were excluded while selecting enzymes involved in the metabolic network as potential drug targets [fig. 1]. K-core clustering is the parameter that amplifies highly interconnected regions and removes less connected proteins that are usually a part of biomolecular interactions [49].

Interacting proteins with high confidence scores were visualized using MCODE plugin to predict protein-protein complex data set. This approach isolated densely connected regions or clusters in three steps namely (i) vector (nodes-proteins) weighting, (ii) complex prediction i.e. the protein with highest clustering density is used to seed a complex and (iii) optional post processing to filter or add proteins to the resulting complex according to certain connectivity criteria [29]. Finding precisely the important interacting enzymes as network clusters provides insights into the functions of unknown proteins [50] and as tools in the exploration of potential drug targets [46]. Indeed, the network view is increasingly being taken in many areas of applied biology including drug discovery [51, 52].

Table 1: Essential proteins of *Malassezia globosa*

S. No	Name of the pathways	Name of the pathogen's enzyme	MGL Seq ID	DEG ID
	Metabolism			
1	Glycolysis/Gluconeogenesis/ Pentose phosphate pathway/Fructose and Mannose Metabolism	hexokinase	MGL_2217	DEG20090714 DEG20010617
2	Starch and Sucrose Metabolism	trehalose 6-phosphate synthase/phosphatase	MGL_1326	DEG20030078
3	Starch and Sucrose Metabolism	trehalose 6-phosphate synthase/phosphatase	MGL_2848	DEG20030078
4	Starch and Sucrose Metabolism	trehalose 6-phosphate synthase	MGL_1842	DEG20030078
5	Starch and Sucrose Metabolism/MAPK signaling pathway	1,3-beta-glucan synthase	MGL_0311	DEG20080016 DEG20091251 DEG20090795 DEG20090494
6	Amino Sugar and Nucleotide Sugar Metabolism	chitin synthase	MGL_1195	DEG20010039 DEG20020057
7	Nitrogen Metabolism	carbonic anhydrase	MGL_1814	DEG20090940
8	Glycerolipid Metabolism/ Glycerophospholipid Metabolism	glycerol-3-phosphate O-acyltransferase/dihydroxyacetone phosphate acyltransferase	MGL_2378	DEG20090920
9	Glycerophospholipid Metabolism Glycine, Serine and Threonine Metabolism	CDP-diacylglycerol---serine O-phosphatidyl transferase	MGL_2439	DEG20091203
10	Glycine, Serine and Threonine Metabolism	homoserine kinase	MGL_3519	DEG20090876
11	Glycine, Serine and Threonine Metabolism/Cysteine and Methionine metabolism/Lysine Biosynthesis	aspartate kinase	MGL_4205	DEG20090951
12	Glycine, Serine and Threonine Metabolism/Cysteine and Methionine metabolism/Lysine Biosynthesis	aspartate-semialdehyde dehydrogenase	MGL_3740	DEG20091259
13	Cysteine and Methionine metabolism	homoserine O-acetyltransferase	MGL_2541	DEG20080024
14	Cysteine and Methionine metabolism	homoserine O-acetyltransferase	MGL_3917	DEG20080024
15	Valine, Leucine and Isoleucine biosynthesis/Pantothenate and CoA Biosynthesis	ketol-acid reductoisomerase	MGL_3299	DEG20010747
16	Valine, Leucine and Isoleucine biosynthesis Pantothenate and CoA Biosynthesis	dihydroxy-acid dehydratase	MGL_3741	DEG20010579
17	Histidine Metabolism	phosphoribosyl-ATP pyrophosphohydrolase/phosphoribosyl-AMP cyclohydrolase/histidinol dehydrogenase	MGL_2613	DEG20030044
18	Histidine Metabolism	phosphoribosylformimino-5-aminoimidazole carboxamide ribotide isomerase	MGL_2036	DEG20030128
19	Histidine Metabolism	HisF/His H/glutamine amidotransferase/cyclase	MGL_0140	DEG20030249
20	Histidine Metabolism	imidazoleglycerol-phosphate dehydratase	MGL_3523	DEG20080003
21	Histidine Metabolism	histidinol-phosphatase (PHP family)	MGL_3105	DEG20091091
22	Phenyl Alanine, Tyrosine and Tryptophan Biosynthesis	pentafunctional AROM polypeptide	MGL_3989	DEG20090474 DEG20030155
23	Phenyl Alanine, Tyrosine and Tryptophan Biosynthesis/Glycine, Serine and Threonine Metabolism	tryptophan synthase	MGL_0012	DEG20080034 DEG20090244
24	Phenyl Alanine, Tyrosine and Tryptophan Biosynthesis	anthranilate synthase/indole-3-glycerol phosphate synthase/phosphoribosyl anthranilate isomerase	MGL_0538	DEG20091201 DEG20030117 DEG20090948
25	Phenyl Alanine, Tyrosine and Tryptophan Biosynthesis	chorismate synthase	MGL_1168	DEG20091208 DEG20030052
26	Phenyl Alanine, Tyrosine and Tryptophan Biosynthesis	anthranilate phosphoribosyltransferase	MGL_1155	DEG20091019
27	Phenyl Alanine, Tyrosine and Tryptophan Biosynthesis	chorismate mutase	MGL_0402	DEG20090359
28	Thiamine Metabolism	hydroxymethylpyrimidine/phosphomethylpyrimidine kinase	MGL_1338	DEG20090945
29	Riboflavin Metabolism	GTP cyclohydrolase II	MGL_1904	DEG20090158
30	Riboflavin Metabolism	2,5-diamino-6-(ribosylamino)-4(3H)-pyrimidinone 5'-phosphate reductase	MGL_2361	DEG20010061
31	Riboflavin Metabolism	3,4-dihydroxy 2-butanone 4-phosphate synthase	MGL_0570	DEG20090968 DEG20010261
32	Riboflavin Metabolism	6,7-dimethyl-8-ribityllumazine synthase	MGL_0356	DEG20090651
33	Riboflavin Metabolism	riboflavin synthase	MGL_0273	DEG20010082 DEG20091197
34	Vitamin B6 Metabolism	5'-phosphate synthase pdxT subunit	MGL_1990	DEG20030345
35	Nicotinate and Nicotinamide Metabolism	nicotinate phosphoribosyltransferase	MGL_3226	DEG20090331
36	Biotin Metabolism	biotin synthase	MGL_1037	DEG20030139
37	Folate Biosynthesis	2-amino-4-hydroxy-6-	MGL_1723	DEG20090637

		hydroxymethyldihydropteridine diphosphokinase/dihydropteroate synthase		DEG20010889
38	Folate Biosynthesis	para-aminobenzoate synthetase	MGL_0916	DEG20030117 DEG20090948 DEG20091201
39	Terpenoid Backbone Biosynthesis	phosphomevalonate kinase	MGL_2793	DEG20010822
Genetic Information Processing				
40	Basal Transcription Factors	transcription initiation factor TFIIF subunit alpha	MGL_2547	DEG20091239
41	Ribosome	small subunit ribosomal protein S10	MGL_1513	DEG20010163 DEG20090970
42	Ribosome	large subunit ribosomal protein L28	MGL_3122	DEG20090779
43	Protein export	signal peptidase complex subunit 3	MGL_1691	DEG20010691 DEG20090095
Environmental Information Processing				
44	MAPK signaling pathway	osomolarity two-component system, phosphorelay intermediate protein YPD1	MGL_3758	DEG20010156
45	MAPK signaling pathway	osomolarity two-component system, response regulator, SSK1	MGL_0602	DEG20010520
Cellular Processes				
46	Endocytosis	ADP-ribosylation factor GTPase-activating protein 2/3	MGL_1167	DEG20090514

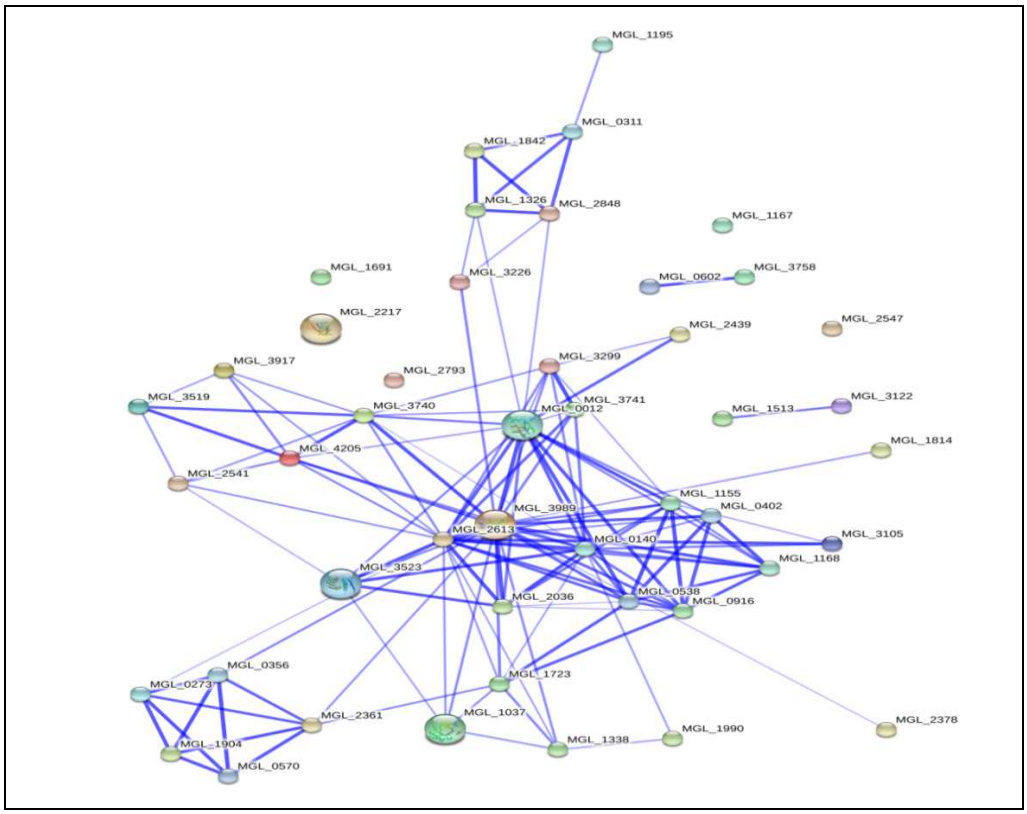

Fig. 1: Interacting and non-interacting proteins of *Malassezia globosa*

Four clusters were resulted from the entire network as the objective is to group proteins that are related by functions and have a significant biological process. High score of a cluster represents an important network region because the components of this molecular complex function towards the same biological goal that provides another level of functional annotation [47]. Even the node of the least score cluster found to be significant in some case [53]. Here, the first cluster involves most enzymes that participate in amino acid biosynthesis, an important pathway in identifying putative drug targets since the amino acid biosynthesis pathway had been already validated by the pathway comparison between aspergillosis causing pathogen and human proteins which revealed eight enzymes as potential targets for drug design where most of them were from this pathway [54]. Also, one of these clustered targets (MGL_0916) found to be participating in the metabolism of co-factor and vitamins, especially in the folate biosynthesis. The first cluster score is greater than 5 with 7 nodes (interactors) and 21 edges (interactions). The clustered targets given in the order of node IDs namely para-aminobenzoate synthetase, glutamine amidotransferase, anthranilate phosphoribosyl transferase, anthranilate synthase/ indole-3-glycerol phosphate synthase/phosphoribosyl anthranilate isomerase, phosphorribosyl-ATP pyrophosphohydrolase/ phosphoribosyl-AMP cyclohydrolase/ histidinol dehydrogenase, tryptophan synthase, pent-afunctional AROM polypeptide were predicted to be present in mitochondria, a specialized organelle that regulate metabolism.

Fungal pathogen specific mitochondrial proteins play a key role in virulence, adaptation to stress, cell wall synthesis and antifungal drug tolerance. Further, lacking homologs in human is an added advantage of antifungal therapy as stated by Calderone *et al.* [55].

The cluster2 consists of 5 nodes and 7 edges with the cluster score of 3.3. Targets namely 3,4-dihydroxy 2-butanone 4-phosphate synthase, GTP cyclohydrolase II,6,7-dimethyl-8-ribityllumazine synthase, 2,5-diamino-6-(ribosylamino)-4(3H)-pyrimidinone 5'-phosphate reductase and riboflavin synthase of this cluster belong to the pathogen pathway of metabolism of co-factor and vitamins. The subcellular location of these targets varies viz MGL_0570 and MGL_1904 were predicted as nuclear, MGL_0356 as cytoplasmic, MGL_2361 as mitochondrial and MGL_0273 as extracellular enzymes. The cluster3 with the score 2.4 includes 4 nodes and 6 edges, and these targets are involved in carbohydrate metabolism and signal transduction pathway. Likewise, in another analysis, six targets from the carbohydrate metabolism and some more targets from the other pathways were reported as essential for the bacterial organism surveillance and multiplication [56], and enzymes involved in carbohydrate metabolism as important drug targets in *Leishmania* parasites [57]. The cellular location of three enzymes (MGL_2848=trehalose 6-phosphate synthase/phosphatase; MGL=trehalose 6-phosphate synthase/phosphatase; and MGL=trehalose 6-phosphate synthase) predicted to be nuclear except MGL_0311 (1,3-beta-glucan synthase), an extracellular enzyme.

The least score (1.5) of this analysis is for cluster4 with the equal number of nodes and edges (3) and the targets were identified as cytoplasmic proteins such as aspartate kinase, homoserine kinase and aspartate-semialdehyde dehydrogenase involved in amino acid metabolism. In the study of infectious pathogens such as *Chlamydophila pneumoniae, Porphyromonas gingivalis* and *Helicobacter pylori* causing Atherosclerosis, a total of 14 interacting drug targets were predicted [58].

In addition, the other vital properties which are significant to be potential drug targets are druggability, molecular weight and sub-cellular localization of these clusters [59] and the results of this study is given in table 2. The non-hit proteins of drug bank and therapeutic target database could be novel targets. In the present study, 2 proteins with hits were considered as druggable and the remaining may be the novel putative drug targets as stated in an earlier report [60]. Even lower molecular weight protein helped in mapping the small molecule binding and aids more specifically in developing the high-affinity inhibitors [61]. Here, molecular size of the enzymes found to be greater than 100 are more likely to represent essential and considered as significant drug targets [62].

Enzymes from different metabolic pathways are important to identify novel drug targets. Eighty-six targets from amino acid metabolism and forty-one from vitamin and cofactor biosynthetic pathways and forty-eight from carbohydrate metabolism were identified as potential drug targets in *Mycobacterium tuberculosis* through the computational analysis [63]. Researchers interested in virology created the Chikungunya database containing its virulent strains and the role of drug target in the infection [64]. Targets are helpful in finding out suitable ligands or hits against disease causing organisms as in the case of *Klebsiella pneumonia* [65] and *Mycobacterium tuberculosis* [66]. Mahendran *et al.* [67] reported nine enzymes from the investigation of metabolic pathways where targets lacking three-dimensional structure were modeled *in silico* and identified potential ligands against *Treponema pallidum*. From the present analysis, 19 targets have been suggested as potential drug targets to combat infections caused by *M. globosa.*

Table 2: Clustered targets of the pathogen

Cluster	Score	Nodes	Edges	Node Identifications	Subcellular location of the protein	Molecular size	Existing/Novel drug targets	Pathways Involved
1	5.25	7	21	MGL_0916	Mitochondria	464	No hits	Metabolism of co-factor and vitamins and amino acid metabolism
				MGL_0140	Mitochondria	576	No hits	
				MGL_1155	**Mitochondria**	**413**	**Yes**	
				MGL_0538	Mitochondria	502	No hits	
				MGL_2613	Mitochondria	884	No hits	
				MGL_0012	Mitochondria	660	No hits	
				MGL_3989	Mitochondria	1611	No hits	
2	3.333	5	10	MGL_0570,	Nuclear	172	No hits	Metabolism of co-factor and vitamins
				MGL_1904,	Nuclear	455	No hits	
				MGL_0356,	**Cytoplasmic**	**171**	**Yes**	
				MGL_2361,	Mitochondria	245	No hits	
				MGL_0273	Extracellular	293	No hits	
3	2.4	4	6	MGL_0311,	Extracellular	1311	No hits	Carbohydrate metabolism and signal transduction pathway
				MGL_2848,	Nuclear	1317	No hits	
				MGL_1842,	Nuclear	523	No hits	
				MGL_1326	Nuclear	680	No hits	
4	1.5	3	3	MGL_4205,	Cytoplasm	502	No hits	Amino acid metabolism
				MGL_3519,	Cytoplasm	355	No hits	
				MGL_3740	Cytoplasm	367	No hits	

Bold indicates existing druggable targets

CONCLUSION

Synthetic antifungal compounds which are the leading candidates among various treatment options have poor clinical efficacy as they are unable to prevent the recurrence. Such complications prompted the search of new antifungals to treat the clinical condition caused by *M. globosa*. Computational method reduces time in the identification of putative drug targets from important pathways. Designing target based drug reduces off-target side effects. Therefore the current research work focused on identifying the potential drug targets in *M. globosa* which may be the first study that would be helpful to explore new and efficient compounds in target based drug discovery for the treatment of the organism. Here, a total of 19 drug targets that include 2 druggable and 17 novel putative drug targets were identified by comparative genomics and cluster network approach thereby opening a new area in antifungal drug discovery through an interdisciplinary endeavour.

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CONFLICT OF INTERESTS

No conflict of interest

AUTHOR CONTRIBUTION

Both authors contributed equally to this work

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