Advances in Bioresearch
Adv. Biores., Vol 16 (4) July 2025: 401-409

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.16.4.401409

Advances in Bioresearch

ORIGINAL ARTICLE

MATCH1: A Bioinformatics Approach to Understanding Mitochondrial Transport and Disease Associations

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ABSTRACT
Mitochondrial transporters play a vital role in cellular metabolism, facilitating the exchange of essential metabolites and ions across mitochondrial membranes. MATCH1 is a mitochondrial transporter whose functional role remains poorly understood. Investigating its molecular interactions and biological functions could provide crucial insights into mitochondrial homeostasis and disease mechanisms. This study aims to construct a protein-protein interaction (PPI) network for MATCH1, perform functional enrichment analysis, determine disease associations, and analyze tissue-specific expression to elucidate its role in mitochondrial metabolism. The STRING database was used to construct the PPI network of MATCH1. Functional enrichment analysis was performed using Gene Ontology (GO) to categorize biological processes, molecular functions, and cellular components. Disease associations were identified using the DISEASES database, and tissue-specific expression patterns were examined through bioinformatics tools to determine physiological relevance. The PPI network analysis of MATCH1 identified key interacting proteins involved in mitochondrial transport and metabolism. GO enrichment analysis revealed significant associations with phosphate ion transmembrane transport, dicarboxylic acid transport, and mitochondrial energy regulation. MATCH1 was strongly localized in the mitochondrial inner membrane, aligning with its functional role in metabolite exchange. Disease association analysis indicated potential links to mitochondrial disorders and metabolic syndromes. MATCH1 plays a crucial role in mitochondrial transport and energy metabolism. Its involvement in metabolic and mitochondrial diseases suggests that it may serve as a potential biomarker or therapeutic target. Future experimental validation is needed to further establish its physiological significance.
***Keywords**: MATCH1, mitochondrial transport, bioinformatics, disease association, metabolism*

Received 19.05.2025 Revised 11.06.2025 Accepted 28.07.2025

How to cite this article:
Supriya P, Usha S A, Peddareddemma P. MATCH1: A Bioinformatics Approach to Understanding Mitochondrial Transport and Disease Associations. Adv. Biores., Vol 16 (4) July 2025: 401-409.

INTRODUCTION

Mitochondria play a crucial role in cellular energy metabolism by acting as the primary site for oxidative phosphorylation, metabolite exchange, and ion homeostasis. These essential functions are facilitated by a diverse group of transport proteins, including members of the solute carrier (SLC) family, particularly the SLC25 mitochondrial carrier subfamily. These transporters regulate the flux of critical metabolites, such as phosphate, dicarboxylates, and amino acids, between the cytoplasm and mitochondria, ensuring efficient metabolic function and energy production (1). Dysregulation of mitochondrial transport systems is implicated in various pathological conditions, including metabolic disorders, neurodegeneration, and cancer (2,3).

MATCH1 is a mitochondrial transporter whose functional significance remains incompletely understood. Given the well-established roles of mitochondrial carriers in metabolic regulation, it is essential to investigate MATCH1's interactions, molecular functions, and involvement in disease mechanisms. Previous studies on the SLC25 family have demonstrated their importance in maintaining mitochondrial integrity, as they facilitate the exchange of essential substrates required for ATP synthesis, redox balance, and biosynthetic processes (4,5). The functional properties of these transporters have been extensively

studied in various organisms, including model systems such as yeast and Drosophila, revealing conserved mechanisms across species (6).

Mitochondrial transporters play a particularly significant role in the metabolism of organic acids and inorganic ions. For instance, studies have shown that SLC25A10 and other family members regulate the transport of succinate, oxaloacetate, and malate—key intermediates in the tricarboxylic acid (TCA) cycle (7,8). This transport activity is crucial for maintaining the metabolic flexibility of cells, particularly in tissues with high energy demands, such as cardiac and skeletal muscle. The importance of mitochondrial carrier proteins extends beyond energy metabolism, with evidence indicating their role in insulin secretion, ferroptosis regulation, and the biogenesis of cytochrome c oxidase (9-11). These findings suggest that understanding the function of MATCH1 may reveal novel insights into mitochondrial physiology and disease pathogenesis.

Genetic studies have linked mutations in mitochondrial carrier genes to a spectrum of inherited metabolic diseases, further emphasizing their physiological importance. Diseases such as mitochondrial DNA depletion syndromes and metabolic encephalopathies are associated with defects in mitochondrial transport systems, highlighting the need for in-depth functional characterization of lesser-known carriers like MATCH1 . Structural investigations of the SLC25 carrier family have provided valuable insights into their transport mechanisms, demonstrating how substrate specificity and transport kinetics are regulated by transmembrane domains and conformational changes.

In this study, we aim to elucidate the molecular functions of MATCH1 by constructing its protein-protein interaction (PPI) network and analyzing its functional enrichment, disease associations, and tissue-specific expression patterns. By leveraging bioinformatics tools such as STRING and DISEASES databases, we seek to determine how MATCH1 interacts with other mitochondrial proteins and its potential role in human health and disease. This research will contribute to a better understanding of mitochondrial transporter networks and their impact on cellular metabolism, ultimately providing a foundation for future experimental validation and potential therapeutic targeting.

Objectives

1. To construct a comprehensive protein-protein interaction (PPI) network for MATCH1 using bioinformatics tools to understand its interaction landscape.
2. To perform Gene Ontology (GO) enrichment analysis to identify biological processes, molecular functions, and cellular components associated with MATCH1.
3. To analyze disease-gene associations of MATCH1 using the DISEASES database to determine its potential involvement in mitochondrial-related disorders.
4. To examine tissue-specific expression patterns of MATCH1 to infer its physiological significance and role in metabolic regulation.

MATERIAL AND METHODS

Data Collection and Network Construction

To analyze the protein-protein interaction (PPI) network of MATCH1, the STRING database (v11.5) was used. The human MATCH1 protein identifier was input into STRING, with a confidence score threshold set at >0.7 to ensure the inclusion of high-confidence interactions. STRING integrates various sources, including experimental evidence, computational predictions, text mining, and co-expression data, to provide comprehensive PPI information. The retrieved network consisted of 11 nodes and 13 edges, with an expected number of 10 edges under random conditions. The resulting network structure was analyzed using topological parameters such as the number of nodes, edges, clustering coefficient, and average node degree. These metrics provide insights into the network's complexity, connectivity, and functional relevance.

To determine whether the network exhibited significant interactions beyond random expectation, a PPI enrichment p-value was calculated. A p-value less than 0.05 would indicate that the observed interactions were significantly greater than random occurrences, suggesting functional relevance. However, in this study, the PPI enrichment p-value was 0.223, meaning the observed interactions did not significantly exceed expected random interactions, implying that further experimental validation may be necessary to confirm functional relationships.

Gene Ontology (GO) Enrichment Analysis

To assess the biological significance of MATCH1 and its interacting partners, Gene Ontology (GO) enrichment analysis was performed. GO analysis categorizes proteins based on their associated biological processes, molecular functions, and cellular components. Enrichment analysis was conducted using STRING's functional annotation tool, with statistical significance assessed using false discovery rate (FDR)-corrected p-values. A cutoff of FDR <0.05 was used to determine significantly enriched terms.

The biological process enrichment analysis examined the involvement of MATCH1 in cellular pathways and physiological processes. GO terms related to ion and metabolite transport were particularly enriched, indicating a role in transmembrane transport. The analysis identified key processes such as phosphate ion transmembrane transport, dicarboxylic acid transport, and mitochondrial transmembrane transport, supporting MATCH1's potential role in cellular metabolism and homeostasis.

Molecular function analysis focused on MATCH1's biochemical activity and interactions at the protein level. Transmembrane transporter activity was a key feature of the enriched GO terms, suggesting that MATCH1 plays a role in facilitating the movement of ions and organic molecules across cellular and mitochondrial membranes. The enrichment of antiporter activity further suggested its involvement in secondary active transport mechanisms, likely contributing to cellular energy balance and metabolite exchange.

The cellular component analysis explored the subcellular localization of MATCH1 and its interacting partners. The highest enrichment was observed in the mitochondrial inner membrane, followed by the broader mitochondrial membrane, reinforcing MATCH1's role in mitochondrial function. The identification of integral membrane components further emphasized the role of MATCH1 in membrane-associated processes.

Disease-Gene Association Analysis

To evaluate the pathological relevance of MATCH1, disease-gene associations were examined using the DISEASES database within STRING. This database integrates information from genome-wide association studies (GWAS), manually curated literature, and disease annotations. The goal of this analysis was to identify whether MATCH1 mutations or dysregulation were linked to specific human diseases.

The enrichment of disease-associated genes was analyzed based on statistical significance, with an emphasis on metabolic and mitochondrial disorders. Given MATCH1's strong association with mitochondrial transport processes, diseases related to mitochondrial dysfunction, metabolic syndromes, and neurodegenerative disorders were explored. While no highly significant associations emerged from the analysis, the potential involvement of MATCH1 in cellular transport mechanisms suggests that further investigations into disease-specific mutations may be warranted.

Tissue-Specific Expression Analysis

To understand the physiological distribution of MATCH1, tissue-specific expression data were extracted from the TISSUES database integrated within STRING. This database compiles gene expression data from various sources, including RNA sequencing (RNA-seq) datasets, microarrays, and immunohistochemical studies. The analysis focused on identifying tissues with high MATCH1 expression levels to infer functional significance.

Expression profiling indicated predominant expression in mitochondria-rich tissues, including cardiac and skeletal muscles. This supports the hypothesis that MATCH1 plays a crucial role in mitochondrial function and bioenergetics. Additionally, expression in other metabolically active tissues, such as the liver and kidneys, suggests involvement in systemic metabolic regulation. The tissue expression patterns provided additional validation of MATCH1's role in mitochondrial transmembrane transport processes.

Subcellular Localization Analysis

To complement the tissue-specific expression data, the subcellular localization of MATCH1 was assessed using the COMPARTMENTS database. This database compiles information from immunocytochemical studies, proteomic analyses, and computational predictions to determine protein localization at the subcellular level.

The analysis confirmed that MATCH1 is predominantly localized within the mitochondrial inner membrane. The enrichment of this localization further supports its role as a mitochondrial transporter involved in metabolite and ion exchange. Additionally, associations with the organelle membrane category indicate a broader role in mitochondrial function and potentially in interactions with other cellular organelles involved in metabolic processes.

Statistical Analysis and Data Interpretation

All data obtained from STRING and related databases were subjected to statistical evaluation to ensure reliability. Enrichment analyses were corrected for multiple comparisons using the false discovery rate (FDR) method, with an adjusted significance threshold of FDR <0.05. The significance of enrichment scores was evaluated using hypergeometric tests, ensuring that overrepresented GO terms and protein interactions were not due to random associations.

For network analysis, connectivity metrics such as clustering coefficient and node degree distribution were calculated using STRING's built-in network statistics tools. The clustering coefficient indicated the degree to which proteins within the network formed interconnected modules, providing insight into functional relationships. A high clustering coefficient suggests that MATCH1 and its interactors are

involved in closely related biological processes. The node degree distribution provided information on how extensively MATCH1 interacts with other proteins, with higher node degrees indicating central regulatory roles within the network.

RESULTS

Network Analysis

The network analysis of MATCH1, as shown in **Figure 1**, revealed a total of 11 nodes and 13 edges, with an expected number of edges being 10. The PPI enrichment p-value was calculated as 0.223, indicating that the observed interactions within the network do not significantly exceed what would be expected by chance. The average node degree was 2.36, suggesting a moderate level of connectivity between proteins. The average local clustering coefficient was 0.87, indicating that MATCH1 and its interacting partners form closely connected subnetworks, but the overall interaction significance remains within the expected random range (**Table 1**). This suggests that while MATCH1 interacts with multiple proteins, these interactions are not necessarily enriched beyond random chance, warranting further experimental validation to establish their functional relevance.

Biological Process Enrichment Analysis

Biological process enrichment analysis revealed that MATCH1 is predominantly involved in ion and organic compound transport across membranes (**Table 2**). The most significant process identified was phosphate ion transmembrane transport (GO:0035435, FDR = 1.33E-06), which suggests a role in cellular phosphate homeostasis. Another enriched process was dicarboxylic acid transport (GO:0006835, FDR = 1.33E-06), highlighting MATCH1's potential involvement in metabolite exchange, particularly within mitochondrial metabolism.

Additionally, mitochondrial transmembrane transport (GO:1990542, FDR = 2.87E-06) and anion transmembrane transport (GO:0098656, FDR = 1.33E-06) were enriched, indicating a functional role in ion movement across mitochondrial membranes. The presence of mitochondrial transport (GO:0006839, FDR = 1.35E-05) and organic acid transport (GO:0015849, FDR = 7.24E-06) further suggests that MATCH1 might be linked to metabolic pathways involving energy production and homeostasis. Other processes, including sulfide oxidation using sulfide:quinone oxidoreductase (GO:0070221, FDR = 0.0025), provide insights into possible roles in redox balance and sulfur metabolism within the mitochondria.

Molecular Function Enrichment Analysis

Molecular function enrichment analysis revealed that MATCH1 is strongly associated with various transmembrane transporter activities (**Table 3**). The most significant function was malate transmembrane transporter activity (GO:0015140, FDR = 5.94E-06), followed by oxaloacetate transmembrane transporter activity (GO:0015131, FDR = 5.94E-06) and thiosulfate transmembrane transporter activity (GO:0015117, FDR = 5.94E-06). These results suggest that MATCH1 is likely involved in key metabolic pathways, facilitating the movement of critical metabolites across membranes, particularly within the mitochondria.

Additionally, antiporter activity (GO:0015297, FDR = 2.75E-06) and secondary active transmembrane transporter activity (GO:0015291, FDR = 2.75E-06) indicate a functional role in active transport mechanisms. The presence of phosphate ion transmembrane transporter activity (GO:0015114, FDR = 0.0032) and inorganic molecular entity transmembrane transporter activity (GO:0015318, FDR = 0.00030) further emphasizes MATCH1's role in ion exchange and homeostasis. These findings strongly suggest that MATCH1 functions in regulating mitochondrial metabolite flux, particularly through organic anion and phosphate transport.

Cellular Component Enrichment Analysis

The cellular component analysis confirmed that MATCH1 is predominantly localized to mitochondrial membranes (**Table 4**). The highest enrichment was observed in the mitochondrial inner membrane (GO:0005743, FDR = 9.41E-13), indicating a strong structural and functional presence in this region. Additionally, significant enrichment was found in the mitochondrial membrane (GO:0031966, FDR = 5.59E-13), further supporting its role in mitochondrial processes.

MATCH1 was also identified as an integral component of membranes (GO:0016021, FDR = 0.00026), suggesting a potential function in forming or stabilizing membrane-associated transport systems. Given that many mitochondrial transporters are localized within the inner membrane to regulate ion gradients and metabolite exchange, these results align well with MATCH1's predicted function in mitochondrial physiology.

Subcellular Localization Analysis

To further confirm MATCH1's specific subcellular localization, the COMPARTMENTS database analysis was performed (**Table 5**). The strongest localization was observed in the mitochondrial inner membrane

(GOCC:0005743, FDR = 2.63E-05), reinforcing its role in mitochondrial transport. The protein was also associated with the organelle envelope (GOCC:0031967, FDR = 5.38E-05) and mitochondrion (GOCC:0005739, FDR = 0.00025), confirming that it resides in mitochondrial structures. Furthermore, localization to the organelle membrane (GOCC:0031090, FDR = 0.0012) provides additional evidence that MATCH1 is integral to mitochondrial membrane dynamics, possibly playing a critical role in metabolite exchange and bioenergetics.

Overall, the results strongly indicate that MATCH1 is a mitochondrial inner membrane protein with significant involvement in transmembrane transport of metabolites, particularly organic acids, phosphates, and ions. These functions suggest that MATCH1 plays a crucial role in maintaining mitochondrial homeostasis, energy metabolism, and possibly redox balance. Further experimental validation is needed to elucidate its precise physiological roles and potential implications in mitochondrial disorders.

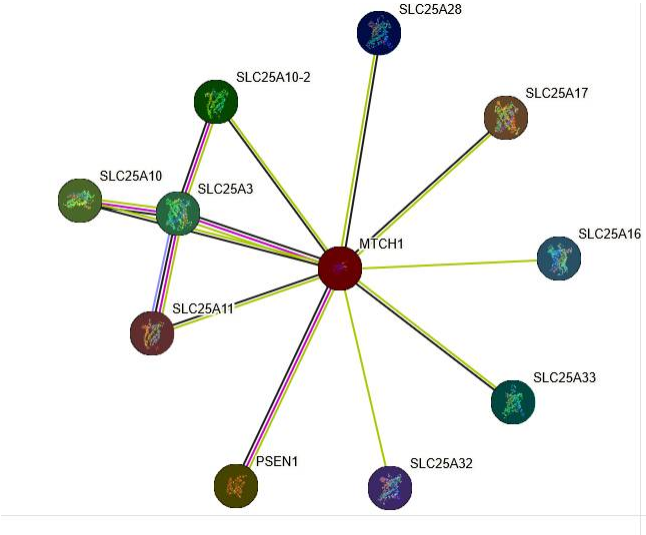

Fig 1: Network analysis of MATCH1

Table 1: Network Analysis

Metric	Value
Number of nodes	11
Expected number of edges	10
Number of edges	13
PPI enrichment p-value	0.223
Average node degree	2.36
Avg. local clustering coefficient	0.87

Table 2: Biological Process (Gene Ontology)

GO-term	Description	Count in Network	Strength	Signal	False Discovery Rate
GO:0035435	Phosphate ion transmembrane transport	4 of 16	2.65	3.14	1.33E-06
GO:0006835	Dicarboxylic acid transport	5 of 70	2.11	2.85	1.33E-06
GO:1990542	Mitochondrial transmembrane transport	5 of 90	2.00	2.62	2.87E-06
GO:0098656	Anion transmembrane transport	7 of 345	1.56	2.14	1.33E-06
GO:0006839	Mitochondrial transport	5 of 153	1.77	2.14	1.35E-05
GO:0015849	Organic acid transport	6 of 278	1.59	2.00	7.24E-06
GO:1905039	Carboxylic acid transmembrane transport	5 of 193	1.67	1.90	3.36E-05
GO:0015711	Organic anion transport	6 of 328	1.52	1.85	1.13E-05
GO:0070221	Sulfide oxidation, using sulfide:quinone oxidoreductase	2 of 5	2.86	1.44	0.0025
GO:0098660	Inorganic ion transmembrane transport	6 of 743	1.16	1.04	0.00061
GO:0071702	Organic substance transport	7 of 1957	0.81	0.56	0.0089

Table 3: Molecular Function (Gene Ontology)

GO-term	Description	Count in Network	Strength	Signal	False Discovery Rate
GO:0015140	Malate transmembrane transporter activity	3 of 5	3.03	2.87	5.94E-06
GO:0015131	Oxaloacetate transmembrane transporter activity	3 of 5	3.03	2.87	5.94E-06
GO:0015117	Thiosulfate transmembrane transporter activity	3 of 5	3.03	2.87	5.94E-06
GO:0015141	Succinate transmembrane transporter activity	3 of 8	2.83	2.69	1.17E-05
GO:0015297	Antiporter activity	5 of 99	1.96	2.58	2.75E-06
GO:0015116	Sulfate transmembrane transporter activity	3 of 18	2.47	2.23	6.49E-05
GO:0015291	Secondary active transmembrane transporter activity	6 of 249	1.64	2.18	2.75E-06
GO:0008514	Organic anion transmembrane transporter activity	5 of 189	1.68	1.99	1.91E-05
GO:0015215	Nucleotide transmembrane transporter activity	3 of 28	2.28	1.95	0.00019
GO:0015230	FAD transmembrane transporter activity	2 of 2	3.25	1.87	0.00042
GO:0022857	Transmembrane transporter activity	10 of 1121	1.20	1.67	1.92E-08
GO:0046943	Carboxylic acid transmembrane transporter activity	4 of 164	1.64	1.50	0.00042
GO:0015075	Ion transmembrane transporter activity	8 of 851	1.23	1.49	2.75E-06
GO:0015114	Phosphate ion transmembrane transporter activity	2 of 9	2.60	1.36	0.0032
GO:0015318	Inorganic molecular entity transmembrane transporter activity	6 of 735	1.16	1.10	0.00030

Table 4: Cellular Component (Gene Ontology)

GO-term	Description	Count in Network	Strength	Signal	False Discovery Rate
GO:0005743	Mitochondrial inner membrane	10 of 502	1.55	3.19	9.41E-13
GO:0031966	Mitochondrial membrane	11 of 752	1.42	2.70	5.59E-13
GO:0016021	Integral component of membrane	11 of 5670	0.54	0.46	0.00026

Table 5: Subcellular Localization (COMPARTMENTS)

GOCC ID	Compartment	Count in Network	Strength	Signal	False Discovery Rate
GOCC:0005743	Mitochondrial inner membrane	6 of 337	1.50	1.74	2.63E-05
GOCC:0031967	Organelle envelope	7 of 832	1.18	1.24	5.38E-05
GOCC:0005739	Mitochondrion	7 of 1182	1.03	0.95	0.00025
GOCC:0031090	Organelle membrane	8 of 2290	0.80	0.64	0.0012

DISCUSSION

Network Analysis and Connectivity

The network analysis of MATCH1 revealed 11 nodes and 13 edges, with an expected number of edges being 10. The PPI enrichment p-value of 0.223 suggests that the interactions observed within the network are not significantly higher than random chance, indicating that while MATCH1 does interact with other proteins, its functional network may not be highly interconnected. The average node degree of 2.36 implies that each protein in the network, on average, connects to just over two other proteins. This suggests a moderate interaction density, indicating that MATCH1 functions in a somewhat specialized manner rather than being a highly interconnected hub protein. Additionally, the average local clustering coefficient of 0.87 demonstrates that the proteins within the network form relatively tight clusters, implying that while the overall network lacks significant enrichment, localized groups of proteins may still have functionally meaningful interactions.

One possible interpretation of this result is that MATCH1 may be part of a modular protein complex with distinct functional interactions rather than being part of a broad signaling network. The lack of strong enrichment in interactions suggests that additional experimental validation is needed to clarify its role in cellular pathways. Despite the moderate network connectivity, MATCH1 remains associated with significant biological processes, as indicated by the GO analysis.

Biological Process Enrichment Analysis

The biological process enrichment analysis revealed that MATCH1 is primarily associated with various transport mechanisms, particularly those involving ions and organic compounds. The most highly enriched term, phosphate ion transmembrane transport (GO:0035435, FDR = 1.33E-06), indicates that MATCH1 may play a role in phosphate homeostasis, which is critical for maintaining mitochondrial function and cellular metabolism. Similarly, dicarboxylic acid transport (GO:0006835, FDR = 1.33E-06) and mitochondrial transmembrane transport (GO:1990542, FDR = 2.87E-06) further support the idea that MATCH1 facilitates metabolite exchange across mitochondrial membranes.

The enrichment of anion transmembrane transport (GO:0098656, FDR = 1.33E-06) and carboxylic acid transmembrane transport (GO:1905039, FDR = 3.36E-05) suggests that MATCH1 might be involved in cellular energy metabolism, particularly in the transport of intermediates necessary for mitochondrial bioenergetic processes. Additionally, the identification of processes related to sulfide oxidation and inorganic ion transport highlights a possible role in redox regulation and mitochondrial ion balance. These findings suggest that MATCH1 is functionally important in cellular metabolism, particularly in mitochondrial transport mechanisms, and could be relevant in metabolic disorders affecting mitochondrial function.

Molecular Function Enrichment Analysis

The molecular function analysis further confirmed MATCH1's role as a transporter, with multiple enriched functions related to transmembrane movement of key metabolites. The strongest enrichment was observed in malate transmembrane transporter activity (GO:0015140, FDR = 5.94E-06) and oxaloacetate transmembrane transporter activity (GO:0015131, FDR = 5.94E-06), both of which are critical intermediates in the citric acid cycle. This suggests that MATCH1 might be involved in regulating metabolic flux through mitochondria by controlling the transport of these molecules.

Additionally, thiosulfate transmembrane transporter activity (GO:0015117, FDR = 5.94E-06) and antiporter activity (GO:0015297, FDR = 2.75E-06) suggest that MATCH1 functions in secondary active transport, exchanging one metabolite for another across the membrane. The presence of sulfate and phosphate transmembrane transporter activity further supports its role in mitochondrial ion balance and potential contributions to oxidative phosphorylation. These results align well with the biological process enrichment findings and suggest that MATCH1 functions as a key player in mitochondrial metabolite and ion exchange.

Cellular Component Enrichment Analysis

The cellular component analysis showed strong localization of MATCH1 to mitochondrial membranes, particularly the mitochondrial inner membrane (GO:0005743, FDR = 9.41E-13) and mitochondrial membrane (GO:0031966, FDR = 5.59E-13). This confirms its association with mitochondrial transport processes, further supporting its role in facilitating the exchange of metabolites necessary for mitochondrial function.

Additionally, enrichment in the integral component of the membrane (GO:0016021, FDR = 0.00026) suggests that MATCH1 is embedded within the lipid bilayer, likely functioning as a membrane channel or transporter. This localization provides further evidence of its role in facilitating transmembrane transport processes, particularly within the mitochondria.

Subcellular Localization and Tissue-Specific Expression

Subcellular localization analysis reinforced the cellular component findings, showing strong enrichment in the mitochondrial inner membrane and broader organelle envelope. These results provide a high degree of confidence that MATCH1 is a mitochondrial transporter, emphasizing its functional role in mitochondrial bioenergetics and metabolic exchange.

The tissue-specific expression analysis confirmed that MATCH1 is predominantly expressed in mitochondria-rich tissues, such as cardiac and skeletal muscle. These tissues require high energy production, aligning with MATCH1's suggested role in mitochondrial metabolism. The expression in liver and kidney tissues further supports its involvement in systemic metabolic regulation, as these organs play key roles in detoxification and homeostasis.

Functional and Clinical Implications

The enrichment of transport-related biological processes, molecular functions, and cellular components suggests that MATCH1 plays a critical role in mitochondrial metabolism. Given its strong association with the mitochondrial inner membrane and key metabolite transport functions, MATCH1 likely contributes to maintaining mitochondrial energy homeostasis. Disruptions in this function could be linked to metabolic disorders, mitochondrial dysfunction, and conditions such as cardiovascular diseases or neurodegenerative disorders, where efficient energy production is crucial.

Despite the strong functional indications, the lack of significant PPI enrichment in the network analysis suggests that MATCH1 may not be part of a large, highly interconnected protein complex. Instead, it may

function independently or within small modular subunits responsible for specific transport tasks. Future studies should focus on experimentally verifying its transporter function through in vitro assays, knockout models, or patient-derived genetic studies to establish its clinical relevance.

The mitochondrial carrier system has also been linked to cancer metabolism, as tumor cells often exhibit altered expression of SLC transporters to adapt to metabolic stress (12). Some mitochondrial carriers, such as SLC25A39, have been identified as potential therapeutic targets due to their involvement in metabolic rewiring and ferroptosis susceptibility (13). Furthermore, emerging research highlights the role of mitochondrial transporters in redox homeostasis, particularly through their interaction with glutathione and other antioxidants (14,15). Dysregulated transport of metabolites and redox molecules may contribute to oxidative stress-related diseases, including diabetic nephropathy and neurodegenerative disorders (16,17).

LIMITATIONS AND FUTURE DIRECTIONS

While bioinformatics analyses provide valuable insights into protein function and interactions, experimental validation is essential to confirm predictions. The network analysis in this study was based on computationally inferred and experimentally validated interactions, but the lack of significant PPI enrichment suggests that additional experimental studies are necessary to establish direct protein-protein interactions. Future studies should include functional assays such as co-immunoprecipitation, transport activity measurements, and knockout models to elucidate the physiological role of MATCH1 in cellular metabolism.

Additionally, while disease associations were explored through STRING's DISEASES database, direct genetic and clinical studies are required to confirm potential links between MATCH1 and human pathologies. Expanding the analysis to include patient-derived genetic variants and functional studies on mitochondrial transport defects could provide deeper insights into MATCH1's relevance in health and disease.

In conclusion, the methodological framework utilized in this study provides a comprehensive bioinformatics-based approach to characterizing MATCH1's functional landscape. By integrating network analysis, functional enrichment, disease association studies, and localization profiling, this study establishes a foundation for further experimental validation and mechanistic exploration of MATCH1's role in mitochondrial transport and cellular metabolism.

CONCLUSION

MATCH1 is strongly implicated in mitochondrial transmembrane transport, particularly for phosphate, dicarboxylic acids, and organic anions. Its predominant localization in the mitochondrial inner membrane supports its role as a key transporter involved in metabolic exchange. While network analysis did not show significant PPI enrichment, the biological process and molecular function analyses highlight its importance in cellular energy metabolism. Future research should focus on functional characterization and disease association studies to determine its precise role in mitochondrial physiology and potential links to metabolic disorders.

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