STRENGTH DEVELOPMENT OF EPOXY GROUTS FOR PIPELINE REHABILITATION

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Abstract

The solute carrier (SLC) 16A gene family comprises of 14 members and encodes monocarboxylate transporter, mediating the absorption of monocarboxylic compounds such as lactate, thyroid hormone, and several amino acids. As their function become more prominent in the field of physiological function, activity, disease pathophysiology, the study of their structure are few, moreover several type of MCT is underlooked. Through using phylogenetic tree, homology modeling, and gene ontology, this study aims to initiate our understanding on its evolution and structural function.

Keywords: Monocarboxylate Transporters, Phylogenetic Tree, Solute Carrier 16A gene family, gene ontology, homology modelling

1.0 INTRODUCTION

Within human, solute carrier (SLC) *SLC16A* gene family comprises of 14 members and encodes for monocarboxylate transporters (MCTs) [1][2]. MCTs is commonly recognized due to its detrimental roles as carriers of high-energy metabolites such as lactate and pyruvate [3]. However, MCTs roles is wider since its mediate the absorption and distribution of monocarboxylic compounds across plasma membranes, including amino acids such as L-phenylalanine and L-tyrosine and thyroid hormones [4]. Thus it playing a significant role on metabolic diseases such as cancer, fatigue, exercise induced hyperinsulinism and severe x-linked psychomotor retardation [5][6]. Doherty & Cleveland (2013) has described that by inhibiting MCT4 to uptake lactate, a cancer growth can be inhibited. In addition to that, MCTs play significant role in sports and nutrition, especially on exercises and fasting period [7].

Despite its vast of function, a study on MCTs structure and functional characterization are still lacking and didn't cover all MCTs. Among them, only MCT 1,2,3,4,8, and 10 has been studied intensively while the rest still remain a puzzle [8]. Thus this study aims to initiate study on its structure function and their closeness within each other through phylogenetic construction using MEGA X homology modeling using Phyre2, gene function interpretation using Gene Ontology (GO), and information enrichment from The Human Protein Atlas [9][10][11].

2.0 METHODOLOGY

2.1 Data Retrieval

Amino Acid FASTA sequence was retrieved from NCBI on protein database with "monocarboxylate" and "*Homo sapiens*" as keyword. The data gathered were compiled within one fasta file.

2.2 Phylogenetic Tree Construction

Multiple Sequence Alignment was conducted within MEGA X using MUSCLE. Then the aligned file undergo benchmarking. From it, maximum likelihood and LG+G model was chosen since it performed the best. During the phylogenetic tree construction, 1000 bootstrap was chosen.

2.6 Homology Modelling, Gene Ontology, and Databases

Using Phyre2, Amino Acid Sequence was inserted one by one with intensive as its modelling mode. Gene Ontology was accessed through The Human Protein Atlas to further analyze the result of phylogenetic tree and inferring the homology modelling result.

3.0 RESULTS AND DISCUSSION

Among 14 sequences, MCT9 sequence is the only one that was retrieved from third party data since there is no reference sequence for it. The retrieved sequence is listed within Table 1

Table 1 FASTA file accession number.

MCT no	Accession Number	MCT no	Accession Number
1	NP_001159968.1	8	NP_006508.2
2	NP_004722.2	9	CAD80155.1 TPA
3	NP_037488.2	10	NP_061063.2
4	NP_004198.1	11	NP_699188.2
5	AQN67655.1	12	NP_998771.3
6	NP_001258694.1	13	NP_963860.1
7	NP_004685.2	14	NP_689740.2

Figure 1 presents the bootstrapped phylogenetic tree of MCTs. This result is against phylogenetic tree constructed by Fisel *et al.* (2018), where in their work, MCT5 was shown as having closer relationship with MCT12. But it is supportive against Halestrap, 2011 where it have a similar result with our phylogenetic tree. The differences may occur due to different selection of FASTA file. However, our analysis on Homology Sequencing based on Phyre2 result show that MCT 5 and 12 supposed to be not within the same ancestry line if we would consider the main template of its structure prediction (Table 2). Table 2 shows the result of Phyre2 structure prediction in respect of its model, confidence, and template. There we can see that MCT5 and MCT12 has a distinctive recognized template. Thus making both supposed to be not closely related.

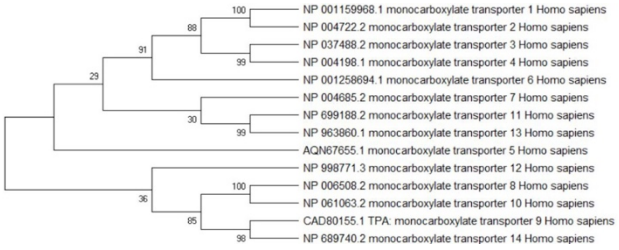

Figure 1: Bootstrapped Tree of MCTs

Table 2 Result of Homology Modelling in Phyre

No	modelled	confidence	Main Template
1	99%	>90%	d1pw4a (100%)
2	99%	>90%	d1pw4a (100%)
3	97%	>90%	d1pw4a (100%)
4	99%	>90%	d1pw4a (100%)
6	93%	>90%	d1pw4a (100%)
7	98%	>90%	c6e9oA (100%)
11	97%	>90%	c6e9oA (100%)
13	100%	>90%	c6e9oA (100%)
5	77%	>90%	c6exsA (99.7%)
12	90%	>90%	d1pw4a (100%)
8	84%	>90%	d1pw4a (100%)
10	90%	>90%	d1pw4a (100%)
9	98%	>90%	c6e9oA (100%)
14	98%	>90%	c6e9oA (100%)

Table 2 showcase the recognition of MCT as a family transporter according to its template: d1pw4a is a domain template of MFS general substrate transporter, c6e9oA is a cluster of membrane protein, and c6exsA is a cluster of membrane protein. From the modelled result it show that available database still unable to determine strongly the structure of MCT 5, followed by MCT 8.

Table 3 present Human Genome Atlas information in respect to the MCTs information of its expression as either protein or RNA and its Main location. The respected substrate of each MCT was obtained from Fisel *et al.* (2018). Unfortunately, the information within Human Protein Atlas is unable to discuss the gap between MCT5 and MCT12. However it shows that both were expressed as RNA, meaning the sequence may have closer relation. Considering MCT 1-3, the closer relation might means that they perform function in similar organelle but might not the expression.

Table 2 Expression, Main Location, and Responsible Substrate of each MCT

No	Exp.	Main Location	Substrate
1	protein	Plasma Membrane (E) Cell Junctions (E)	ß-hydroxybutyric acid
2	RNA	Plasma Membrane (A)	acetoacetic acid
3	protein	Plasma Membrane (S) Nuclear Membrane (A)	pyruvic acid
4	protein	Microtubules (A) Cytosol (A) Cytokinetic Bridge (A)	L-lactic acid
6	protein	Vesicles (A)	-
7	protein	Nucleoplasm (A) Plasma Membrane (S)	-
11	RNA	-	pyruvic acid
13	RNA	Golgi Apparatus (S)	-
5	RNA	-	-
12	RNA	Mitochondria (A)	creatine
8	protein	Focal Adhesion Sites (A) Intermediate Filaments (A)	tetraiodothyronine triiodothyronine
10	protein	Vesicles (A) Cell Junctions (A)	L-tryptophan L-tyrosine L-phenylalanine
9	protein	Nucleus (A) Cell Junctions (A)	L-carnitine
14	protein	Endoplasmic Reticulum (A)	-

In general, MCT have a beta-helix shape that support its function as a transporter as shown with MCT1 model (Figure 2).

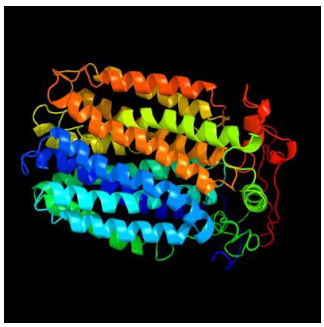

Figure 2: MCT1 model

4.0 CONCLUSION

MCTs family still has an unraveling understanding of its function, especially MCT5, however with the usage of Phylogenetic Tree and Structural Bioinformatic Tools we can infer its relation within each other and predict its function.

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