

Predicted Biological Mechanism and Gene Networking of Associated Putative Genes in Gout Using *in silico* Analysis

Muhammad Danish Waldan Azhan, Wan Rohani Wan Taib*, Imilia Ismail

School of Biomedicine, Faculty of Health Sciences, Universiti Sultan Zainal Abidin, Gong Badak Campus,
21300 Terengganu, Malaysia

Corresponding author: wanrohani@unisza.edu.my

Received: 25th July 2022

Accepted: 23rd August 2022

Published: 30th October 2022

Abstract

Gout is associated with disturbed metabolic pathways which is hyperuricemia, due to the unbalanced state of purine nucleotide metabolism or excretion of uric acid by the kidney (1). Differentially targeted genes should be evaluated on their metabolic pathways and gene networking to investigate the potential biomarkers in developing the personalized medicine for gout. The study was opted to determine the differentially target genes with the regulatory mechanisms by using *in silico* analysis. Ten target genes were engine-searched from the published articles such as from PubMed, google scholar, ResearchGate, and Science Direct. The information from the articles were stratified according to populations in a mutual or close genetic entities from year 2012 to 2018. The ten chosen putative genes associated with gout were *SLC2A9*, *ABCG2*, *SLC22A12*, *SLC22A11*, *SLC17A1*, *SLC17A2*, *SLC17A3*, *SLC17A4*, *SLC16A9*, and *SLC5A6* which were determined their biological mechanism and gene networking by using bioinformatic tools such as the Gene Ontology Resource, STRING, and Reactome Pathway. The significant associations of the putative genes with the biological mechanism and gene networking are determined based on the p-value and FDR value. The ten chosen putative genes showed significant association with the biological mechanisms and gene networking. The result from Gene Ontology Resource database showed high significant association between the putative genes and the biological processes, molecular functions, cellular components (p-value < 0.05) as depicted in Table 1.0. The highly significant associated biological processes were the organic anion transport (9.14E-19, 7.16E-15), anion transport (2.93E-17, 1.53E-13) and urate metabolic processes (2.98E-20, 4.67E-16) along with their respective raw p-value and FDR value. Then, the highly significant associated molecular functions were the active transmembrane transporter activity (5.04E-15, 2.47E-11), symporter activity (1.16E-13, 1.90E-10) and secondary active transmembrane transporter activity (1.80E-14, 4.40E-11) along with their respective raw p-value and FDR value. While the highly significant associated cellular components were the plasma membrane region (7.26E-09, 4.90E-06), apical plasma membrane (4.48E-13, 9.08E-10) and apical part of cell (1.64E-12, 1.66E-09) along with their respective raw p-value and FDR value. Next, the result from STRING database as depicted in Figure 1.0 were highly significant in which all the putative genes had networking among them, such that six out of ten putative genes had the highest gene networking among the others; *SLC2A9*, *SLC22A11*, *SLC22A12*, *SLC16A9*, *ABCG2*, *SLC17A1*, and followed by the other four genes which had less gene networking; *SLC17A2*, *SLC17A3*, *SLC17A4*, and *SLC5A6*. As for the Reactome Pathway database, the result as depicted in Table 2.0 showed high significant association between the putative genes and the pathways (p-value <

0.05). The highly significant pathways were the transport of small molecules ($1.00\text{E-}08$, $3.34\text{E-}07$), SLC-mediated transmembrane transport ($1.96\text{E-}08$, $3.34\text{E-}07$) and organic anion transport ($8.36\text{E-}06$, $9.19\text{E-}05$) along with their respective raw p-value and FDR value.

Table 1: Top 3 highly associated significant results from Gene Ontology Resources

Biological Process		
GO biological process	raw P-value	FDR
Organic anion transport	$9.14\text{E-}19$	$7.16\text{E-}15$
Anion transport	$2.93\text{E-}17$	$1.53\text{E-}13$
Urate metabolic process	$2.98\text{E-}20$	$4.67\text{E-}16$
Molecular function		
GO molecular function	raw P-value	FDR
Active transmembrane transporter activity	$5.04\text{E-}15$	$2.47\text{E-}11$
symporter activity	$1.16\text{E-}13$	$1.90\text{E-}10$
secondary active transmembrane transporter activity	$1.80\text{E-}14$	$4.40\text{E-}11$
Cellular component		
Go cellular component	raw P-value	FDR
Plasma membrane region	$7.26\text{E-}09$	$4.90\text{E-}06$
Apical plasma membrane	$4.48\text{E-}13$	$9.08\text{E-}10$
Apical part of cell	$1.64\text{E-}12$	$1.66\text{E-}09$

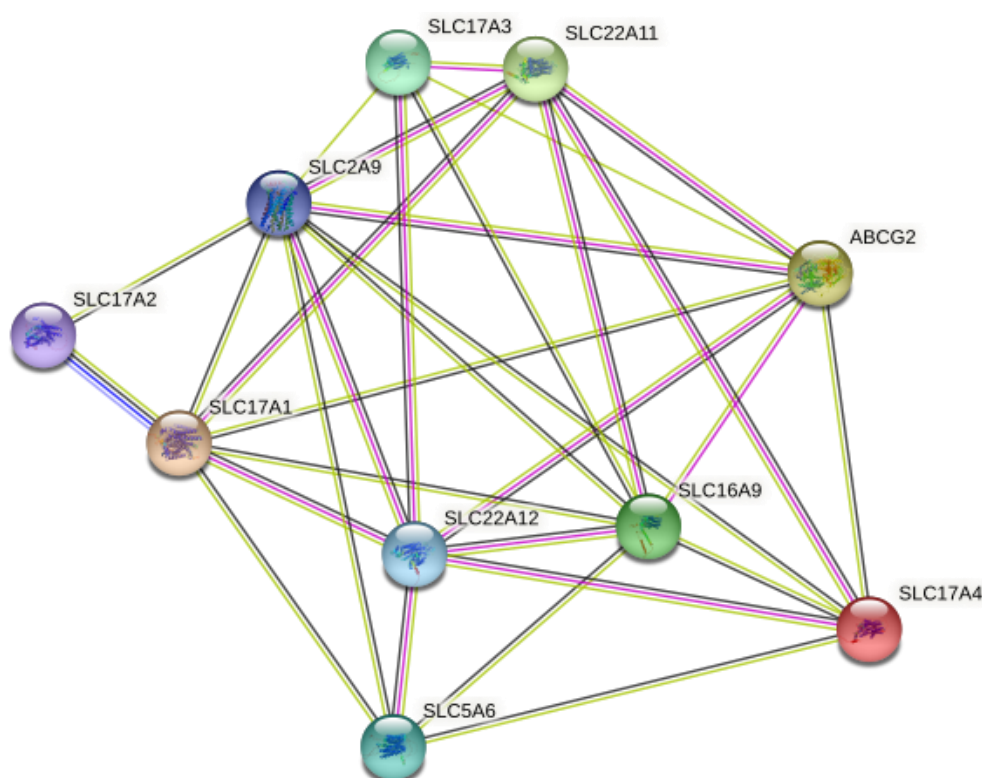


Figure 1: Result from STRING

Table 2: Top 3 highly associated significant results from Reactome Pathway

Pathway name	Entities p Value	Entities FDR
Transport of small molecules	1.00E-08	3.34E-07
SLC-mediated transmembrane transport	1.96E-08	3.34E-07
Organic anion transport	8.36E-06	9.19E-05

In conclusion, the study revealed the role of putative targeted genes in the biological mechanism in gout pathogenesis has provides insight of the potential biomarkers in developing the personalized medicine better treatment for gout patient in ensuring better patient healthcare.

Keywords

Gene networking, Gout, Predicted biological mechanism,

Acknowledgement

This study is supported by Fundamental Research Grant Scheme (FRGS/1/2021/SKK0/UNISZA/02/3).

References

1. George C. and Minter DA (2021). Hyperuricemia. Retrieved from StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing: https://www.ncbi.nlm.nih.gov/books/NBK459218/#_ncbi_dlg_citbx_NBK459218