



Identification of the effect of lycopene on the inhibition of yellow fever-causing flavivirus by studying microarray gene expression data

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Abstract

Introduction: Yellow fever virus causes systemic disease of the liver, kidneys, myocardium and hemorrhage, which are high incidence and mortality. Lycopene is one of the effective antioxidants used to prevent the growth of cancerous tumors. DNAJC14 protein is a variant of heat shock protein (chaperone) Hsp40. Hsp40 chaperone protein (DNAJC14) that when overexpressed was able to mediate protection from yellow fever virus (YFV)-induced cell death. In this study, to find a new treatment for yellow fever, the effect of lycopene on the expression of DNAJC14 gene involved in yellow fever was investigated.

Materials and Methods: In this project, using bioinformatics software, such as Matlab and Cytoscape, the effect of lycopene on the expression of DNAJC14 gene, as well as the relationship of this gene with different genes have been investigated. Big gene expression data in the NCBI database were used for this study.

Results: Analysis of microarray data showed that the expression level of DNAJC14 gene was increased under the influence of lycopene.

Conclusion: The lycopene combination can be used as a preventative and even treatment for yellow fever viral disease due to the effect DNAJC14 gene expression.

Keywords: Lycopene, Yellow fever, Bioinformatics, Co- expression, Microarray, Cytoscape

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Received: 2022.5.6, Accepted: 2022.6.7



Introduction

Flaviviruses of the Flaviviridae family are transmitted through arthropods and contribute to the astonishing number of significant human infections and deaths worldwide each year (1). Heat shock proteins are a family of highly conserved evolutionary proteins expressed in eukaryotes and prokaryotes. The expression of HSPs is increased in various cellular stresses, including heat stress, which occurs in the host organism as well as in pathogens in response to infection and inflammation (2). The DNAJC14 gene, which is a member of the Hsp40 family of chaperones, can inhibit the proliferation of flaviviruses (3). Overexpressed DNAJC14 is targeted to sites of yellow fever virus (YFV) replication complex (RC) formation, where it interacts with viral nonstructural (NS) proteins and inhibits viral RNA replication (4). Lycopene is a natural carotenoid and pigment that is made by plants and microorganisms to absorb light during photosynthesis. Vegetables and fruits that have a red color are important sources of lycopene, including tomatoes, watermelon, grapefruit, etc (5). In this study, to find a new, cheap and convenient method for the treatment of yellow fever, the effect of lycopene on the expression of DNAJC14 gene involved in yellow fever was investigated. Microarray has been one of the most widely used methods of generating Big data related to gene expression in genome performance projects. GEO (Gene Expression Omnibus) is one of the best repositories for gene expression databases located in the NCBI. Available microarray data includes raw data. Numerous software and hardware have been designed to use this data. Therefore, in proportion to the purpose of this research, these raw data have been used. In this study, we used the microarray data of a research project with access number 27140 (6). In the mentioned project, gene expression data of thousands of genes under the influence of lycopene were extracted as raw data and recorded in GEO. We analyzed the expression of DNAJC14 gene, which plays a key role in yellow fever, among a large number of genes and big data sets, and showed the results in the form of clustergram and histogram.

Materials and Methods

To receive gene expression data due to the effect of lycopene on DNAJC14 has been referred to the NCBI site. In the microarray project with access number GSE27140, the effect of lycopene consumption on gene expression in prostate cancer patients has been recorded as raw data on the NCBI section of GEO section. The GSE27140 project is a 2003 study of changes in the cox-2 and IGF-1 genes in patient with prostate cancer who were treated with lycopene (6). In the mentioned project, the expression of thousands of genes has been extracted and recorded in the form of raw data. We extract the DNAJC14 gene expression data by giving its special identification code (AA461486) from the data set which is registered as a matrix series on the NCBI website and import it into an Excel file. To get the p-value of analysis referred to GEO2R section at NCBI (Table 1). As described in GSE27140 research, gene expression data were obtained from microarray of prostate tissue biopsy in patients with prostate cancer. These patients underwent biopsy on the first day of the project and on the 90th day after treatment (6). By importing the given files in Excel format in MATLAB software and executing Syntax codes in MATLAB software, clustersgram (Figure 1) and histograms (Figure 2A & 2B) of DNAJC14 gene expression were extracted and displayed. And finally, we have used cytoscape software to demonstrate DNAJC14 co-expression with other genes (Figure 3).

Results

In Table 1, we have extracted and demonstrated the p-value of the gene analysis with its special code and symbol (p-vlue=0/000963). In the GEO dataset, the DNAJC14 gene is codenamed AA461486.

Table 1. DNAJC14 gene identification code and p-value.

ID	Adj.P.val	P.value	t	Logfc	Gene symbole
AA461486	0.2064	0.000963	-3.46	0.716	DNAJC14

After receiving the raw data related to the DNAJC14 gene from GEO dataset, we entered the data file as an excel file into the Matlab software, and by executing command codes to compare the expression of the desired gene on day 0 and day 90 after lycopene consumption, The result shown as a clustergram. As it

has been shown, the expression of this gene shows an increase compared to day zero (start of the study) (Figure 1).

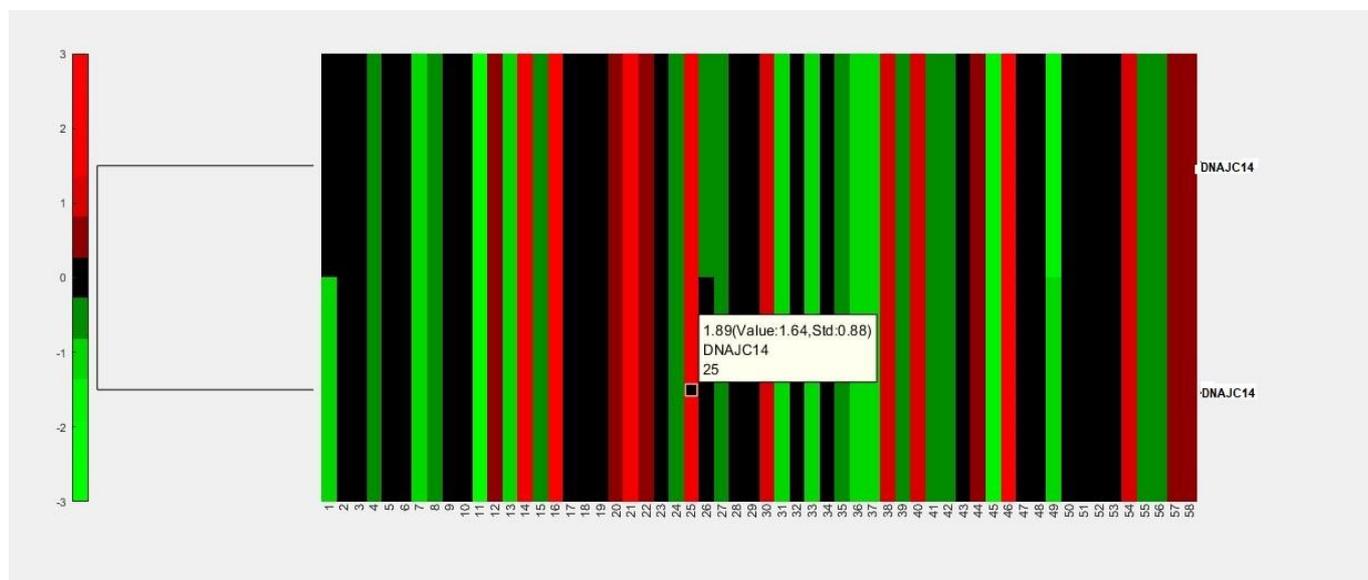


Figure 1. In this clustergram, 29 patients each have two samples of gene expression on day 0 and day 90 of the project. Horizontal odd numbers are gene expression on day 0 and horizontal even numbers are gene expression on day 90 of the project. Light green indicates the least and light red indicates the most expression.

In another method, using MATLAB software, the analysis result is shown as a histogram. Each bar is related to gene expression at day zero and day 90 after lycopene use. Gene expression has been shown to

increase after 90 days of lycopene use (Figure 2A & 2B). Comparison of histograms on day zero and day 90 showed increased DNAJC14 gene expression.

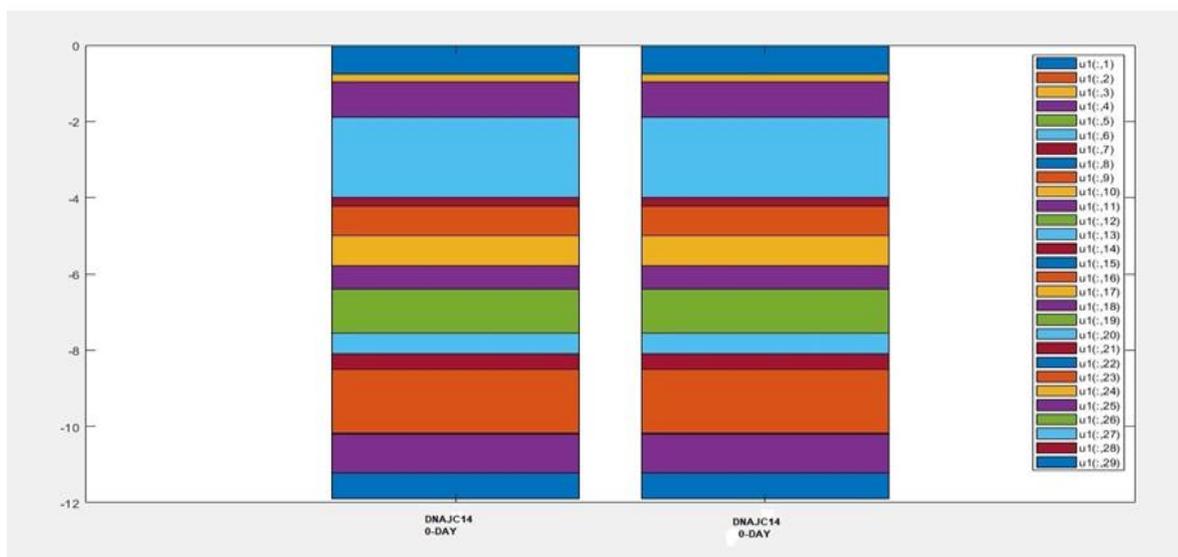


Figure 2A . The DNAJC14 gene expression histogram on day zero of the project, which is the range of gene expression between zero and minus 12.

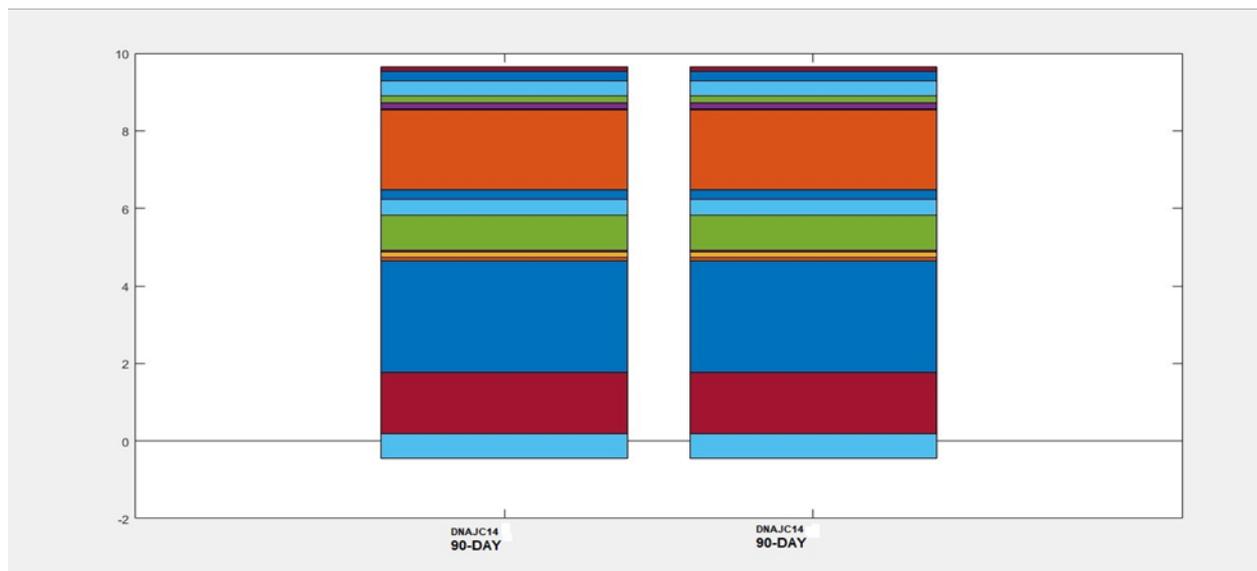


Figure 2B. The DNAJC14 gene expression histogram on day 90 of the project has a range of gene expressions ranging from an approximately negative one to positive ten.

Also, the relationship between DNAJC14 gene and other genes has been shown in terms of expression, using Cytoscape software(Figure 3). According to the results of the analysis by Cytoscape software, different

genes are co-expressed with DNAJC14 gene. Blue rectangles show related genes that are connected to DNAJC14 gene by bridges.

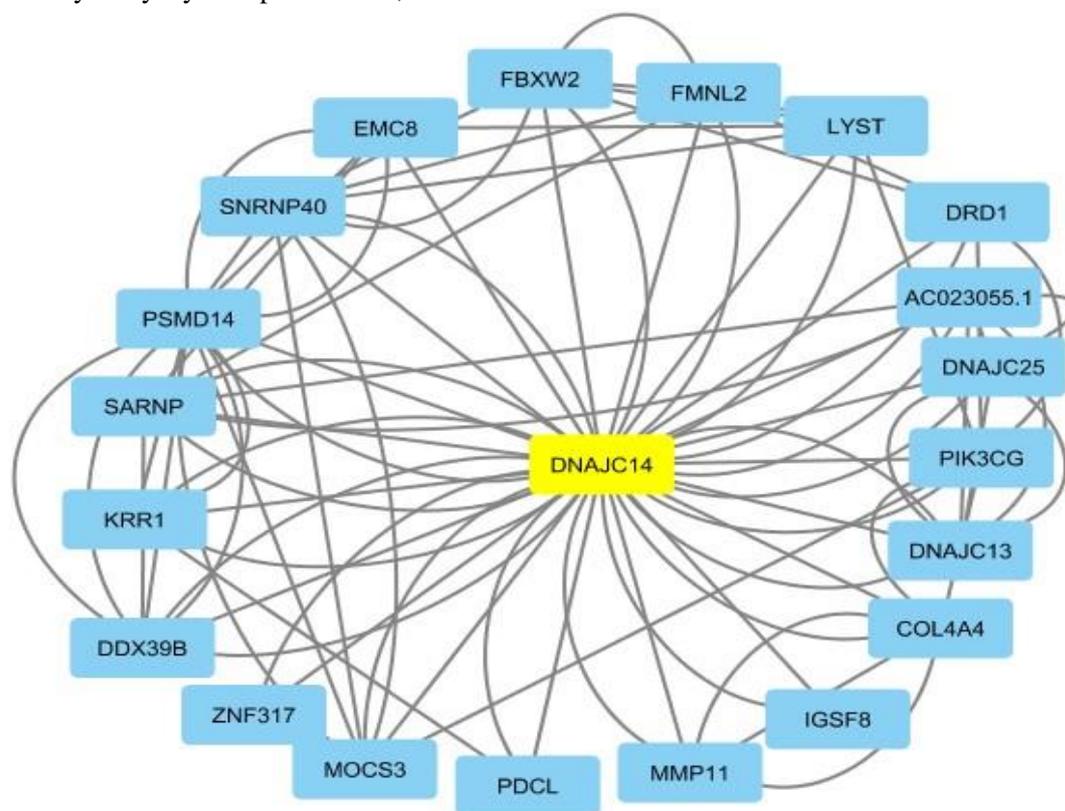


Figure 3. Co-Expression of DNAJC14 gene with other genes, in this form, genes that are linked to the DNAJC14 gene in terms of expression bind to the gene with the bridges.

Discussion

The causative agent of yellow fever is a virus (7). Vaccines are used to prevent (8) and Ribavirin drug is used to treat the disease (9). Vaccines are also used to increase the body's resistance and immunity against this virus (10). The compound studied in this study is lycopene, which is used to prevent the growth of cancerous tumors (5). HSPs are a family of highly conserved evolutionary proteins that are expressed in eukaryotic and prokaryotic organisms. In people who have a mutation in this gene and the gene has been turned off, the rate of virus replication is high, and disease and death are similarly high (3). DNAJC14 is an Hsp40 family member that broadly modulates flavivirus replication (11). This study found that lycopene significantly increased DNAJC14 gene expression. Comparing scientific documents, it was found that lycopene increases the level of DNAJC14 protein in cells by increasing the expression of a key gene involved in yellow fever, thus preventing the proliferation of disease-causing viruses. Taking a combination of lycopene is one of the simplest and easiest ways to increase the body's immunity against flaviviruses. By consuming and using foods containing this compound and even capsules and pills of this effective substance, yellow fever can be prevented rather, it treated yellow fever by consuming this nutrient and increasing the inductive expression of DNAJC14 gene through the use of lycopene. Due to the fact that the microarray data used in this study was obtained from a prostate biopsy in the study with the access number GSE27140 (6). Therefore, it is suggested that another study be performed by PCR method of biopsy of liver tissue of individuals and the result of the study be compared with the result of the present study.

Conclusions

This study showed that the lycopene, a carotenoid compound with antioxidant properties, has an additive effect on the expression of DNAJC14 gene. DNAJC14 protein belongs to the group of chaperones and prevents the proliferation of flaviviruses that cause yellow fever. As a result, the consumption of lycopene in fruits and vegetables such as tomatoes, carrots and cabbage can increase the immunity of the body cells by

increasing the expression of DNAJC14 protein against flaviviruses and yellow fever. And also help in the treatment of this disease if it is contracted. According to the results of this study, we can use lycopene as a low-cost and convenient treatment for yellow fever.

Conflict of interest

The authors declare that they have no conflicts of interest.

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