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Exploring the Reversible Effects of UV Laser Radiation on the Gene Expression Profiles of *Saccharomyces cerevisiae* Via Network Analysis

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Abstract

Introduction: The reversibility of biological processes is an important challenge in the study of environmental pollutants and also natural and artificial radiation**.** There are many pieces of evidence about the reversible and irreversible effects of UV radiation on the human body**.** Assessment of the reversibility of UV laser effects on *Saccharomyces cerevisiae* was the aim of this study.

Methods: Gene expression alteration in *S. cerevisiae* samples radiated by a 30s UV laser for 15, 30, and 60 minutes post-radiation times were investigated via network analysis to explore time-dependent reversible alteration in the gene expression profiles of the samples.

Results: 19 differentially expressed genes (DEGs) were identified as targeted genes for the samples which were harvested 60 minutes after radiation; network analysis revealed no significant alteration in biological processes.

Conclusion: It can be concluded that the gross effects of the UV laser on *S. cerevisiae* samples disappear after 60 minutes of radiation.

Keywords: Post-radiation time, Network analysis, *Saccharomyces cerevisiae*, Repair, Radiation

Introduction

The absorption of UV radiation by cells can affect the structure of DNA and genome.[1] Damage to nucleic acids and proteins is done either directly by energy absorption or indirectly by the generation of free radicals and single oxygen species.[2] UV induces cyclobutane pyrimidine dimers production lesions.[3] A Short wavelength is carcinogenic, and it is absorbed by DNA.[4] Excessive UV radiation causes different skin cancers and damage to the eye lens.[5] The laser is useful by providing high power, monochromatic, collimated light, and it causes high power to focus on a small area with a local fluence rate. Gasch et al are reported about the transcriptional profile alteration of hundred genes of irradiated cells as an environmental stress response.[6] Early changes in yeast transcriptome as a suitable biologic model subsequent to a short burst of laser energy were described by Hauser et al.[7] They mentioned the ability of yeast cells to respond to the UV-induced environmental insult by transcriptional responses which changed the following duration of radiation. However, modifying mechanisms are in place to minimize genome damage. Repairing the excision nucleotide (REN) could remove DNA damage from the transcriptionally silent genome. REN is a complex cellular response to prevent the loss of genetic information in damaged DNA.[8] For example, in individuals who suffer from *Xeroderma pigmentosum* as an autosomal recessive disease, UV-induced DNA damages could not be repaired because of the REN defect.[9] In *Saccharomyces cerevisiae* yeast as a biological model, short wave radiation causes damage to DNA which stimulate repair process.[10] DNA repair mechanisms as a survival factor in this regard is one of the scientists' interests.[11] The aim of this study was to investigate the time-dependent effects of the UV laser on the gene expression profile of *S. cerevisiae* by using the genomic data of a published document analyzed via network assessment. The results of this study can be useful in relation to an increase in knowledge about the

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application of UV radiation in the clinic.

Materials and Methods

We analyzed the results of a study by Hauser et al about the differentially expressed genes (DEGs) of *S. cerevisiae* samples which were exposed to a 30s UV laser and harvested 15 and 30 minutes after radiation (accepted papers by *Journal of Lasers in Medical Sciences*). On the basis of the methods of the paper published by Hauser et al, "The Explore One XP 355-1 UV laser (Spectra-Physics, Santa Clara CA) controlled by L-Win, a LabView-based graphical user interface" was used for the experiment.[7] More details of methods are described in the mentioned reference. In the present study, the gene expression profiles of the samples which were exposed to the 30s UV laser and harvested 60 minutes after radiation were analyzed, and the results were compared with the samples that were assessed previously. For better resolution, the samples that were radiated 30s and harvested 15, 30, and 60 minutes after radiation were categorized in three groups: group-1, group-2, and group-3 respectively.

Like the previously analyzed profiles, P value < 0.05 and ratio change > 2 were regarded to explore the significant DEGs. The number of significant DEGs of the three analyzed groups was compared. Maximum values of the fold change of the three groups of the samples were equated. The introduced significant DEGs interacted together via the STRING database and Cytoscape software to form a protein-protein interaction (PPI) network.[12] Due to weak interactions between the queried DEGs, 60 first neighbors (the optimum number of first neighbor genes that imply maximum interactions between queried DEGs) were added to the queried DEGs, and the network was reconstructed via undirected edges. The constructed network was visualized based on degree value and analyzed by "NetworkAnalyzer" plugin of Cytoscape. Similar to the previous two analyzed profiles, mean+ 2SD (standard deviation) was regarded as the cutoff of degree value to explore the possible hub nodes.[13,14] The central nodes were the hub nodes that appeared as top nodes based on betweenness centrality, closeness centrality, and stress.

Results

Data screening revealed that 19 significant DEGs (based on P value < 0.05 and ratio change > 2) were targeted genes by the UV laser. As it is depicted in Figure 1, the amounts of significant DEGs for groups 1 and 2 are 452 and 329 respectively. The reduction of DEGs (about 27%) in group 2 relative to group 1 and 94% in group 3 compare to group 2, is highlighted in Figure 1.

The alteration of the maximum value of fold change (based on the data from Hauser and colleagues' report[7] is presented in Figure 2. It is shown that the maximum values of fold change for groups 1-3 are 2193, 350, and 97 respectively, which are corresponded to severe attenuation

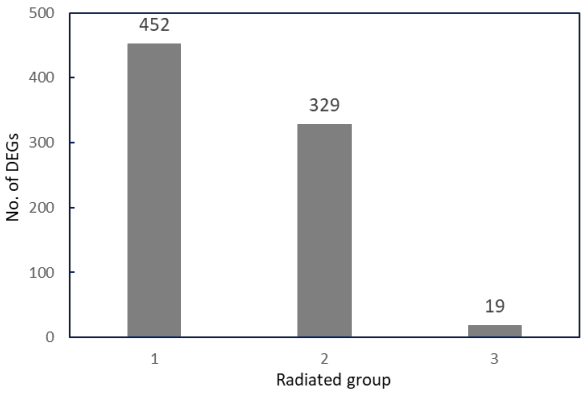

Figure 1. The number of differentially expressed genes for the three studied groups (1-3) that are exposed to a 30s UV laser and harvested 15, 30, and 60 minutes after radiation respectively.

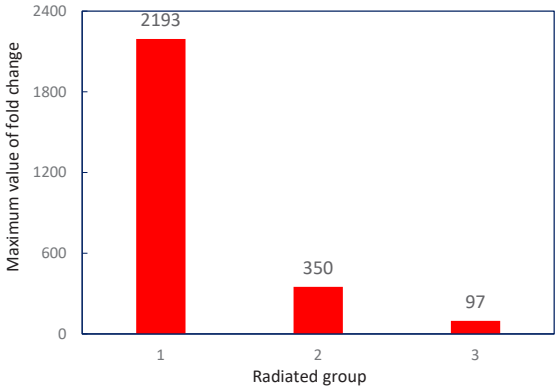

Figure 2. The maximum value of fold change for the groups (1-3) of the samples that are exposed to a 30s UV laser and harvested 15, 30, and 60 minutes after radiation respectively.

correlated with larger post-radiation times.

Interactions between the 19 DEGs are shown in Figure 3. It can be seen that the 19 nodes are connected with 4 edges. However, 12 nodes are isolated, and only 7 genes are connected as three sub-networks. Adding 60 first neighbors leads to constructing a network including 6 isolated nodes and a main connected component which contains 73 nodes (see Figure 4). The number of the central nodes of the networks of the three analyzed groups is presented in Figure 5. The findings indicated that there were 11, 9 and 0 central nodes for groups 1, 2 and 3 respectively.

Discussion

The reversibility or irreversibility of UV radiation is a challenge that has attracted researchers' attention for decades.[15,16] On the other hand, gene expression profile analysis as a suitable method is used to detect the molecular mechanism of UV radiation.[17] Here, the reversibility of gene expression alteration due to exposure to the UV laser was assessed via network analysis.

As it is shown in Figure 1, 1-hour post-radiation time attenuated the numbers of significant DEGs from 459 (related to 15-minutes post-radiation time) to 19. The

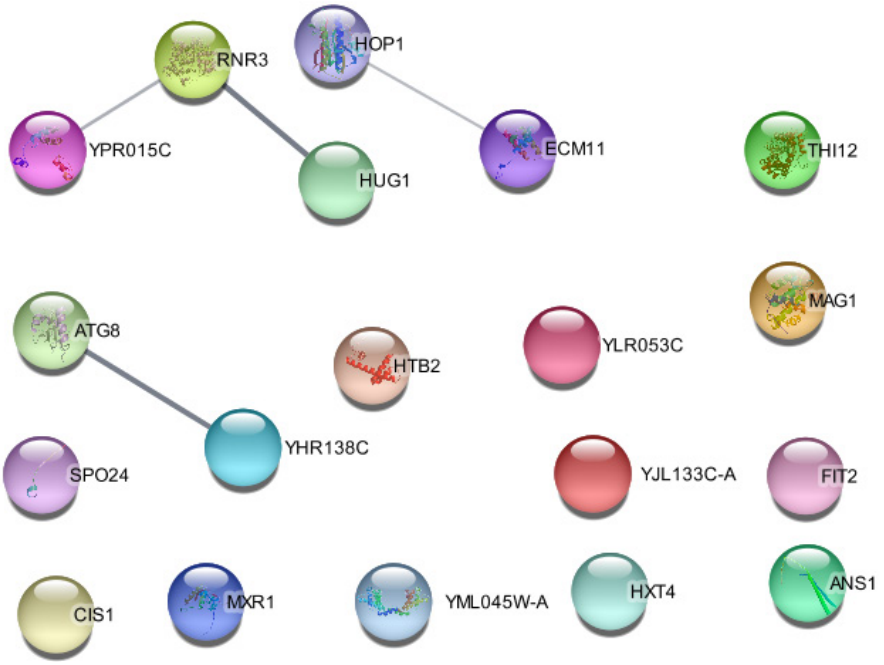

Figure 3. PPI network of the queried DEGs of *Saccharomyces cerevisiae* samples (group 3) which are exposed to a 30s UV laser and harvested 60 minutes after radiation.

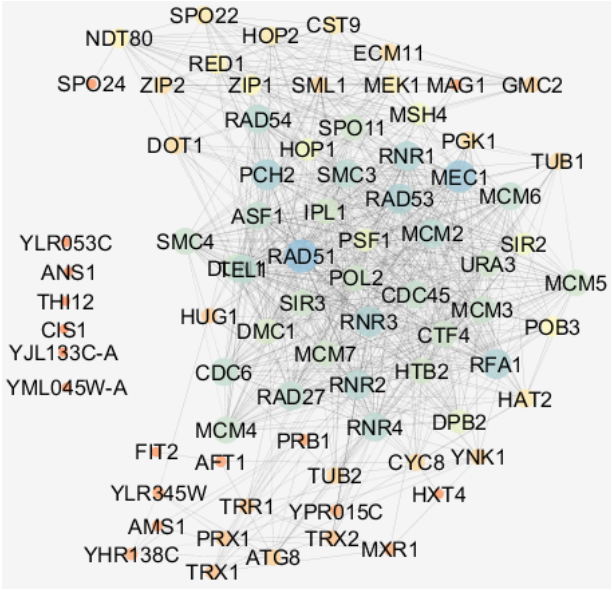

Figure 4. PPI network of the queried DEGs plus the 60 added first neighbors of *Saccharomyces cerevisiae* samples (group 3) which are exposed to a 30s UV laser and harvested 60 minutes after radiation. Color and size of the nodes are presented based on degree value.

findings indicated that the amounts of the significant DEGs were reduced by about 96%. It may be concluded that 4% of alterations remained and might be accompanied by biological effects. This idea was real when the range of the maximum value of fold change was reduced by about 96% (see Figure 2).

Network analysis revealed that the 19 significant DEGs for group-3 cannot interact with each other to form a scale-free network and are almost isolated from each other. As it is shown in Figure 3, there are only 4 edges

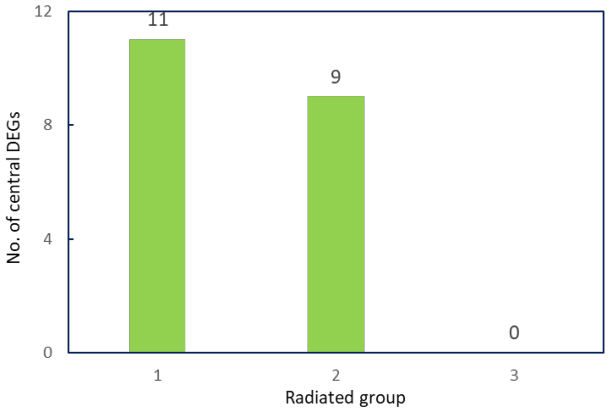

Figure 5. The number of the central genes of the analyzed networks of the studied groups 1-3 that are exposed to a 30s UV laser and harvested 15, 30, and 60 minutes after radiation.

between the 19 queried DEGs. It seems that network analysis cannot provide useful information about the characters of the queried DEGs.

Adding first neighbors is a useful method to make more interactions between the elements of a network.[18] Adding 60 first neighbors to the 19 queried DEGs led to constructing a more integrated unit (see Figure 4). It seems that this network contains a valuable finding about the role of the queried significant DEGs. Considering the criteria that the networks of groups 1 and 2 (related to 15 and 30 minutes respectively) were analyzed, network analysis indicated that there were no central nodes for this interactome unit (the network of group-3). As it is represented in Figure 5, numbers of central nodes of the network which was related to group 3 (the group which harvested after 1 hour of radiation) compared to groups 1

and 2 were reduced to zero.

It has been explored that doubling the time of the yeast cells is approximately 90 minutes[19]; therefore, 60-minute post-radiation time refers to maximum two generations of the studied yeast cells. There are experiments about the prevention of UV effects on *S. cerevisiae* by using different agents. Bisquert et al reported the preventive role of melatonin in *S. cerevisiae* versus UV radiation.[20] Li et al have investigated the repair of UV-induced DNA damages in *S. cerevisiae*.[21] Guo et al have studied the repair process in *S. cerevisiae* cells that were exposed to X-ray radiation. In this report, it was pointed to the enrichment of DEGs in detoxification and antioxidation activity categories of gene ontology at 1 hour.[22] Guintini et al studied the repair of telomeres after UV radiation on *S. cerevisiae*.[23] We highlighted telomeres as the targeted parts of *S. cerevisiae* in the previous investigations (In press data).

Conclusion

The findings indicated that UV laser effects on *S. cerevisiae* samples were repaired mostly after 1 hour of radiation. More investigation about the repair process in human cell lines such as fibroblast cells is suggested.

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Conflict of Interests

The authors declare they have no conflicts of interest.

Ethical Considerations

Not applicable.

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