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Introducing Protein Homeostasis and Glycogen Synthesis as Two Targets of Blue Light Radiation in *Lentinula edodes*

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Abstract

Introduction: There are documents about the biological effects of blue light radiation on different organisms. An understanding of the molecular mechanism of radiation effects on biological samples is an important event which has attracted researchers' attention. Determining the critical dysregulated proteins of *Lentinula edodes* following blue light radiation is the aim of this study.

Methods: 22 differentially expressed proteins of *L. edodes* in response to 300 lux of blue light were extracted from the related literature. Experimental, text mining and co-expression connections between the queried proteins were assessed via the STRING database. The maps were compared and the critical proteins were identified.

Results: Among the 21 queried proteins, six individuals including heat shock HSP70 protein, 20S proteasome subunit, 26S proteasome subunit P45, Aspartate aminotransferase, phosphopyruvate hydratase, and phosphoglucomutase were highlighted as the critical proteins in response to blue light radiation.

Conclusion: The finding indicates that protein homeostasis and glycogen synthesis are affected by blue light radiation. Due to the critical roles of proteins as enzymes and structural elements in life maintenance and involvement of glycogen synthesis in energy consumption, blue light radiation can be considered as a life promotional agent in future investigations.

Keywords: Blue light; Proteomics; Glycogen; Protein degradation; Co-expression

Introduction

Different wavelengths of emitted light affect the growth of plants and fungi, yet the molecular mechanism of this process is not clear enough. *Lentinula edodes* is a fungal species with therapeutic uses and is considered a shiitake mushroom from *Lentinus* family.[1] *L. edodes* is widely consumed in Northeast Asia and is the third most produced mushroom in the world.[2] Proponents of this fungus believe that it is effective in treating high blood pressure and atherosclerosis.[3] The developmental stages of this fungus are divided into 4 parts: the first stage is the vegetative mycelial growth stage which is accompanied by the colonization of the substrate; the second stage is the brown film layer formation stage due to light radiation; the third stage is the primordial formation stage, and the final stage is the fruit development stage.[4] The formation of a brown layer on the surface of mycelium always occurs on the developing bud of the fruit and prevents the growth of other bacteria and pathogenic agents on these surfaces.[5]

There are documents about the important roles of light in the promotion of vital activities of fungi. The light effects are induced via different types of proteins which are characterized as photoreceptors.[6] Investigations indicate that the red and blue photoreceptors of fungus trigger reactions for somatic cell growth and proliferation,[7] spore formation,[8] and the phenomena of phototropism and circadian processes.[9,10] Basically, blue

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light is an important environmental factor in primordial differentiation and fruit formation in fungi such as *Hypsizygus marmoreus*, *Pleurotus ostreatus*, and *Coprinus cinereus*.[11,12] Blue light induces fruit formation and pigmentation via photoreceptors.[13] Light as a whole is considered an important environmental factor in fungal growth and development[14] and regulates enzymatic activities.[15-17] Photoreceptors in the presence of light activate the light-sensitive genes by signal transduction phenomena.

One hundred species of fungi are known to be affected by red, blue, green, and near-purple wavelengths.[18,19] The main known sensor for blue light is the white collar-1/white collar-2 (WC-1/WC-2) complex, which is used in *Neurospora crassa* as a laboratory research model.[20] The cloned genes DST1 and DST2 in *C. cinereus* and PhrB and phrA in *L. edodes* and Slwc-1 in *Sparassis latifolia* have been identified as blue light receptors.[12,21-24] However, the molecular mechanism of the effect of blue light and the formation of brown films in *L. edodes* has not been fully elucidated, and this study investigated and introduced the critical proteins that are effective in metabolic circumstances, increasing growth and germination, and changing the morphology of fungi exposed to blue light. In this regard, proteomics combined with bioinformatics was applied to explore the critical targets (the genes and biological terms) of blue light in *L. edodes*.

Methods

Lentinula edodes is a mushroom used for food in northeast Asia. According to the report of Park and Jang,[25] the protein expression of samples that are radiated by 300 lux of blue light is compared with the samples in the absence of blue light (as controls). As it is described in this report, blue light radiation led to the dysregulation of 22 proteins (including 14 down-regulated and 8 up-regulated individuals) in *L. edodes*.

The 22 significant dysregulated proteins were assessed via the STRING database (https://string-db.org) to find the crucial ones.[26] In the first assessment, experimental connections between the proteins were evaluated and the linked proteins were determined. The connections from text mining were identified and the connected proteins were highlighted.

Since the co-expression relationship between the assessed proteins is an important process, these types of connections were investigated for the queried proteins. To find an overview of different types of interactions between the queried proteins, we constructed a network regarding co-expression, experimental, and text mining connections. The crucial proteins were identified and discussed based on the related biological terms.

Results

The 22 dysregulated proteins due to blue light radiation were assessed via the STRING database to find experimental connections. Since 2 isoforms of phosphoglucomutase were presented and "enzyme in the non-oxidative pentose phosphate pathway" was not recognized by STRING, the network (containing 20 elements) was formed from 9 isolated proteins, two paired individuals, and a main connected component including 9 proteins. The paired proteins and the connected 9 individuals are shown in Figure 1.

In the second evaluation, text mining connections between the queried proteins were determined. As it is shown in Figure 2, except for 8 proteins, the other 12 individuals were organized into two components including the main component (formed from 10 proteins) and two paired individuals.

Co-occurrence relationships between the queried proteins were investigated, and it appeared that there was no connection. The important process, the co-expression relationship between the analyzed proteins, was evaluated, and the resulting associations as a tetrad and two triples units were determined. As it is illustrated in Figure 3, three components including 10 proteins were constructed.

For better understanding, a network including co-expression, experimental, and text mining connections was constructed and analyzed. The result of this analysis is shown in Figure 4.

Discussion

Biomarker selection among the introduced differentially expressed genes or proteins is a well-known activity in biology and medicine.[27, 28] In the present study, the critical dysregulated proteins due to blue light radiation are determined in *L. edodes* under the described condition. Among the 22 queried proteins, two individuals are isoforms, and the total number of proteins is 21. Since "enzyme in the non-oxidative pentose phosphate pathway" was not recognized by the STRING database, 20 proteins were investigated via connections between them. As depicted in Figures 1-4, Testicular acid phosphatase like protein, acetyl-acetyl transferase, and ARD family are isolated in the entire analysis. It can be concluded that 17 proteins including T-complex protein 1, phosphoglucomutase, 26S proteasome subunit P45, phosphoserine aminotransferase, mitochondrial pyruvate dehydrogenase E1 component beta subunit, elongation factor EF-2, aspartate aminotransferase, homoserine dehydrogenase, ribose-5-phosphate isomerase, UDP-N-acetylglucosamine diphosphorylase, Aconitate hydratase, Heat shock HSP70 protein, phosphopyruvate hydratase, 20S proteasome subunit, creatinase aminopeptidase, seryl-tRNA synthetase, and 5-methyltetrahydropteroyltriglutamate-homocysteine s-methyltransferase are candidates for evaluation.

As it is shown in Figure 3, 10 proteins among the 17

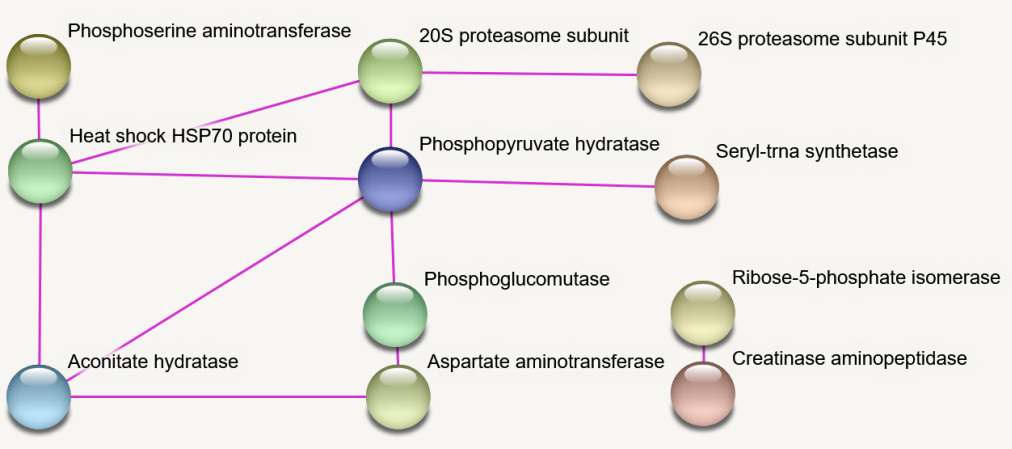

Figure 1. Experimental Connections Between 2 Paired and 9 Connected Proteins Among the 20 Queried Individuals. The figure is plotted by STRING

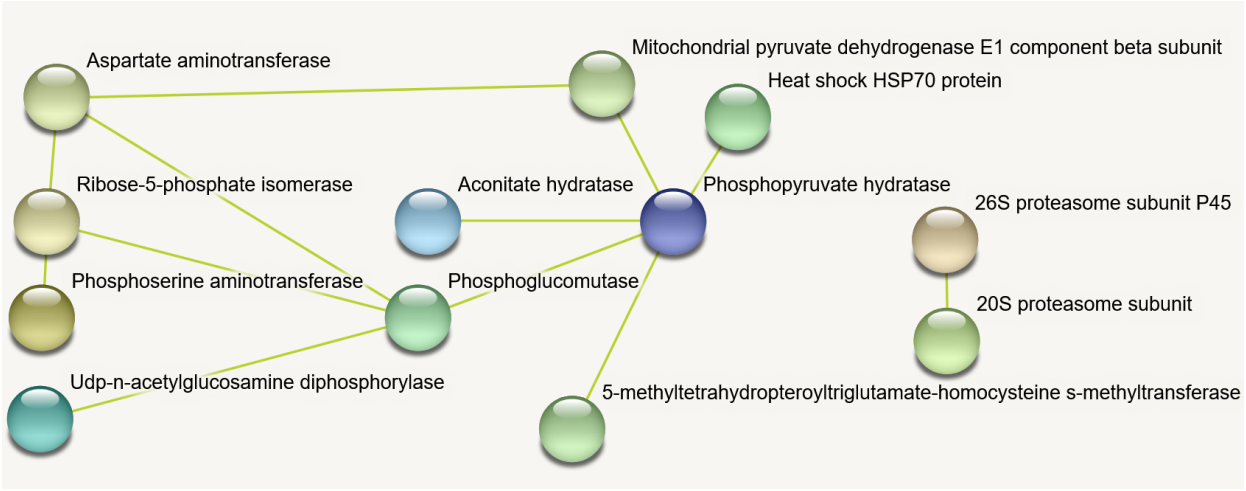

Figure 2. Text Mining Connections Between 2 Paired and 10 Connected Proteins Among the 20 Queried Individuals

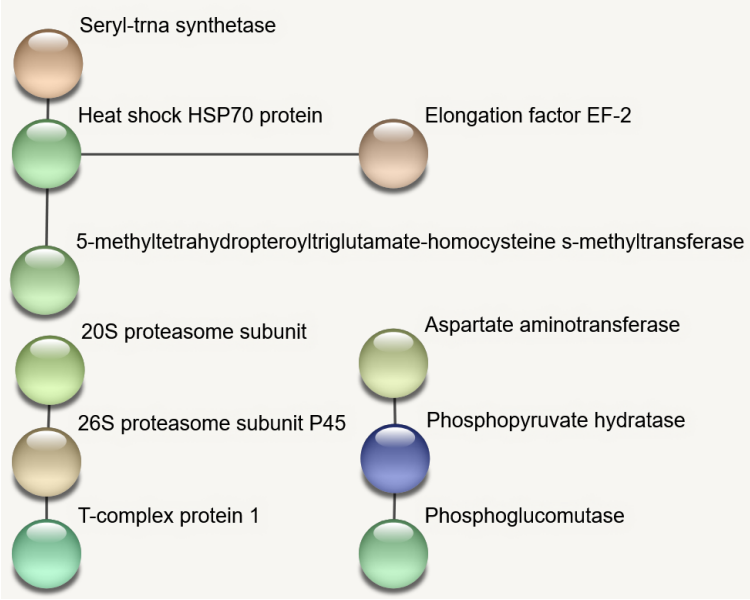

Figure 3. Co-expression connections between the investigated proteins.

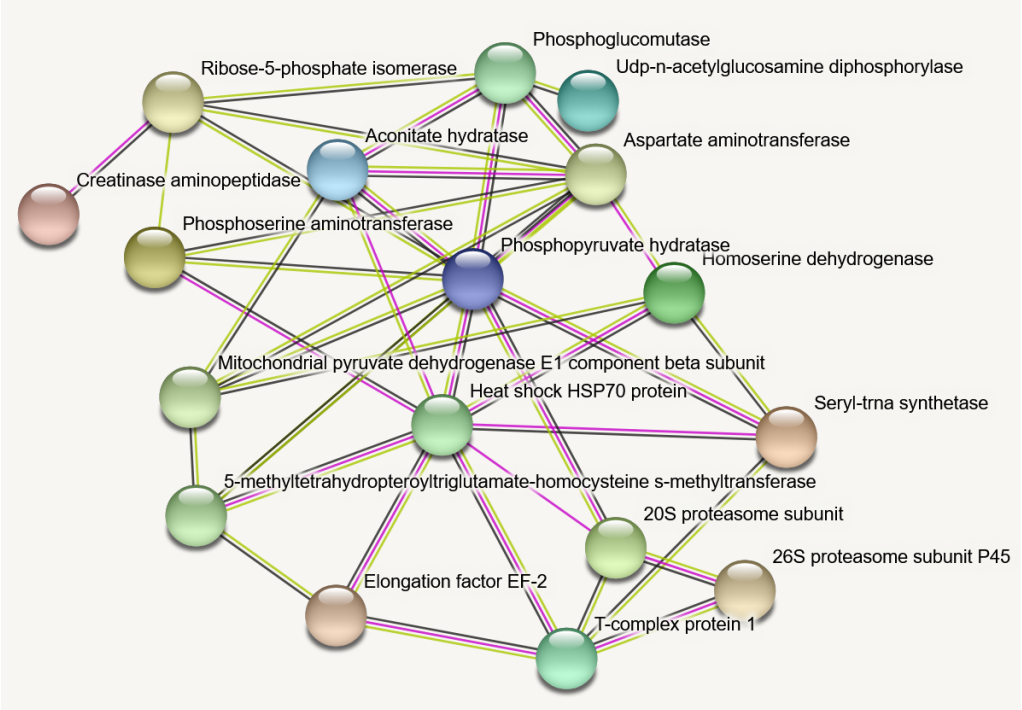

Figure 4. The Connected Queried Proteins Via Co-expression (Black), Experimental (Pink), and Text Mining (Green) Edges. 17 differentially expressed proteins among the 20 queried individuals are included in the network

analyzed individuals are connected via co-expression connection. As it has been reported, co-expression analysis is a well-known tool for biomarker prediction in biological and medical research.[29,30] Considering the data from Figure 1, elongation factor EF-2, 5-methyltetrahydropteroyltriglutamate-homocysteine s-methyltransferase, and T-complex protein 1 are not connected via experimental relationships. Regarding the results of text mining analysis, seryl-tRNA synthetase is not included in the text mining connection map. It seems that 6 proteins including Heat shock HSP70 protein, 20S proteasome subunit, 26S proteasome subunit P45, aspartate aminotransferase, phosphopyruvate hydratase, and phosphoglucomutase are the core of the dysregulated proteins in response to blue light. Except for the 20S proteasome subunit protein, the other 5 proteins are down-regulated.[25]

Proteasome as a multi-subunit protease is described as a large protein complex which is responsible for degrading intracellular proteins by using metabolic energy. Degradation of protein through the 26S ubiquitin-proteasome system is reported as the main function of the proteasome. This function is known to be responsible for protein degradation throughout homeostasis. Another important role of the proteasome which is attributed to the unbound 20S proteasome is the degradation of oxidized proteins.[31,32]

Another critical protein is heat shock HSP70 protein which belongs to the family of heat shock proteins. This family of heat shock proteins is involved significantly in protein homeostasis. As it has been reported, the HSP70 family improves cell survival following stress conditions such as hypoxia, elevated temperature, altered pH, oxidative stress, and heavy metals.[33]

Phosphoglucomutase (PGM)-1 catalyzes reversible conversion of glucose 1-phosphate to glucose 6-phosphate (a part of glycogenesis process). This enzyme is involved in the synthesis and breakdown of glycogen.[34] Another protein which is linked to phosphoglucomutase is phosphopyruvate hydratase (PPH). Based on the report of Yang et al, phosphopyruvate hydratase is an enzyme that participates in glycolysis.[35] Aspartate aminotransferase (AAT) is a member of the cluster that is highlighted in the Figure 3. An investigation indicates that AAT participates in glycolysis and plays a role in electron transfer from NADH.[36]

Analysis indicates that PGM, PPH, and AAT are involved in glycogen metabolism while 26S ubiquitin-proteasome, 20S proteasome subunit protein, and HSP70 play a role in protein homeostasis. As it was mentioned before, the second process (protein homeostasis) is linked to energy consumption. Since the proteins which are involved in glycogen synthesis are down-regulated, it can be concluded that the coupled processes are attenuated.

Conclusion

It can be concluded that blue light radiation affects protein homeostasis and the associated energy consumption processes. Since proteins administrate orders from DNA and glycogen synthesis is involved in energy consumption,

it seems blue light radiation is a suitable candidate for the promotion of biological processes. More investigations are required to explore the detail of the events.

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Conflict of Interests
The authors declare that they have no conflict of interest.

Ethical Considerations
Not applicable.

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