Hypothesis

Demystifying the Biophoton-Induced Cellular Growth: A Simple Model

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Abstract

Background: None-Chemical Distant Cellular Interactions (NCDCI) are among the unexplained issues in cell biology. One example of such interactions is the biophoton-induced growth. In this process, photon emissions from one cell can induce mitosis in other cells while they are chemically separated. This effect is evident among many species. Hypothesis: It is hypothesized that some simple but universal molecular pathways, which include photoreceptor proteins, modulators of cell cycle and circadian rhythm, can explain this phenomenon. Particularly, existing experimental data has been used to support the hypothesis that exposure of cellular structures to visible light photons deactivates the cryptochrome protein and this deactivation disinhibits cell growth. This disinhibition happens through the influx of Ca\(^{2+}\) cations and subsequent activation of the downstream mitogenic pathways. Conclusion: While the existing lines of evidence are mixed and equivocal, current hypothesis provides a testable framework for further experimental investigation. The present model and its predictions can be used as a well-documented platform to address the mechanisms of None-Chemical Distant Cellular Interactions in biological systems.

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Ultra-weak photon emission in biological objects

In 1920’s, A. G. Gurwitsch was the first cell biologist who discovered the phenomenon of the ultra-weak photon emission (UPE) during the period of the cell division of onion root tips (1). This phenomenon is also known as mitogenetic radiation, dark luminescence, low level chemoluminescence and biophoton emission (2). The emission of mitogenic radiations are often attributed to de-excitation of the free radicals in biological objects. This mechanism has been supported by experimental evidence such as increased biophoton emission by reducing the antioxidants in tissue (3) or increased biophoton emission by reducing the antioxidants in tissue (4). This relationship has been supported by several lines of evidence over recent years. Table 1 presents an outline of such supporting evidence.

None-Chemical Distant Cellular Interaction, an explanatory gap

Along with the discovery of biophoton emissions, several studies suggested the “intercellular communication” as the biological role of the biophoton emission. In fact, Gurwitsch himself was the first one to report that the onion roots can induce mitosis in each other only by emitting biophotons (1). This early discovery was followed by a load of subsequent studies demonstrating the
same effect in yeast cells (10), pig’s neutrophils (11), developing tissues (12) and paramecium (13). A short list of similar reports is presented in Table 2 while a comprehensive review has been provided in (14). Although mechanism for biophoton emission is well documented, plausible models for biophonic communication are still lacking. In particular, biophoton-induced mitosis is among unexplained issues. Therefore, the main aim of the present work is to propose a simple model to possibly explain the mechanism of “biophoton-induced mitosis”.

The hypothesis

Literally, the term “biophoton” indicates the source of a photon and these photons do not seem to have fundamental differences with other photons emitted from different sources. Considering this, the present paper tries to suggest possible cellular pathways which may underpin the photon-induced growth. It is hypothesized that biophoton emissions from one cell can deactivate a flavin-binding photoreceptor in the other. This deactivation will result in an influx of Ca\(^{2+}\) ions which induce mitosis through Ca\(^{2+}\)-Calmodulin-related cascades in the receiver cell. Figure 1 is a schematic representation of this hypothesis.

Photons can induce growth, regardless of their origin

Photon induced growth is ubiquitous among living organism, especially in plant tissues. Early observations of this phenomenon in plants belong to the last decades of the 19th century (20). In the upcoming years of the 20th century, the similar observation was made in animal cells and was referred to as LASER wound-healing (21). The nature photoreceptor proteins mediating this effect in plants was not explained until 1993 (22). These proteins are phototropines (23), photoactivated adenyl cyclase (24) and cryptochromes (25). However, the counterpart proteins in the animal cells which mediate the same effect have remained unknown.

Mediators of light-induced growth, cryptochrome pathway, cell and circadian cycle

Among all above photoreceptor proteins, cryptochrome (Cry) is a particularly interesting. Cry protein highly similar to photolyase proteins which repair DNA by breaking the UV-induced pyrimidine dimers through a light-induced process. Both Cry and Photolyase proteins use Flavin Adenine Dinucleotide (FAD) as their cofactor. However, Cry proteins - except the DASH Cry in some species - do not have the capability of DNA repair. Since the knockdown of Cry in mouse completely abolishes the circadian clock (26, 27), the main function of Cry proteins is assumed to be the regulation of the circadian clock. It is remarkable that Cry regulates the circadian rhythms in a “light independent” manner. This fact questions the benefit of conserving the photoreception capability of Cry in evolution and the answer to this question is still unknown. Hence, there might be other conceivable functions for Cry. To identify possible roles of photoreception capability in Cry, inspecting the intertwined relationship between the circadian cycle and cell cycle seems warranted (28).

Possible pathway for biophoton-induced growth: cryptochrome

As mentioned above, Cry proteins are the major regulators of the circadian rhythm while they can also affect the cell cycle. Cry proteins inhibit cAMP production (29, 30) which is a secondary messenger allowing Ca\(^{2+}\) channels opening. Therefore, it is conceivable that Cry protein can suppress the inward flow of Ca\(^{2+}\) but the pivotal interaction that bridges the gap in the cycle is the interaction between Cry proteins and photons.

It is known that light emission causes ubiquitination and subsequent proteolytic degradation of Cry in drosophila (31, 32) and this

### Table 1. A short list of evidence establishing the relationship between free radicals and biophoton emission

<table>
<thead>
<tr>
<th>Finding</th>
<th>Year</th>
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<tbody>
<tr>
<td>Direct relationship between the intensity of biophotons and neural metabolic activity in rat hippocampal slices (5).</td>
<td>1995</td>
</tr>
<tr>
<td>Association between spontaneous biophoton emission from rat's brain and cerebral energy metabolism and oxidative stress (6,7).</td>
<td>1999</td>
</tr>
<tr>
<td>Use of Biophoton emission based imaging to measure oxidative stress(8n).</td>
<td>2006</td>
</tr>
<tr>
<td>Biophoton emission as an indicator of dehydration induced oxidative stress (10n).</td>
<td>2008</td>
</tr>
</tbody>
</table>
Discussion and Conclusion

It is hypothesized that photon emission, regardless of its origin (biological/non-biological) can affect the cell growth through Cry proteins. Some other characteristics of Cry can be used to support the current hypothesis. First, any mechanism which mediates the biophoton/photon induced growth should exist in a wide variety of species. Cry proteins are expressed in animal cells, plants, fungi (34), and even some bacterial species (35, 36). Therefore, it fulfills the first criterion. Secondly, the gene expression profile of the Cry protein in human and mouse shows that it is being expressed in all investigated tissues (37). Hence, ubiquity of Cry protein makes it a possible candidate for mediation of a ubiquitous process. However, these evidences cannot guarantee that the Cry mediates all existing biophotonic communications. In Arabidopsis thaliana, Cry knock-out mutants show the light induced Ca\(^{2+}\) influx while phototropin knock-out mutants cannot demonstrate this effect (38). Consequently, it seems that the light-dependent Ca\(^{2+}\) influx is mediated through the phototropin proteins rather than cryptochromes in this plant. Thus it is possible that biophotonic communication in some plants happens through other proteins. Additionally, the interaction between Cry protein and cell cycle is another complicated issue that should be considered. The main interaction site between Cry and cell cycle is the G2/M transition checkpoints. It is reported that Cry proteins promote G2/M transition through inhibition of wee1 gene expression (39). On the other hand, Cry proteins cause degradation of Bmal proteins. Bmal proteins enhance the expression of the wee1 gene and act against Cry by inhibiting the cell proliferation. Based on such evidence, Cry can promote cell proliferation which turns to be completely against the current hypothesis.

Fortunately, since Bmal mutant cell lines do not show a higher proliferation rate or promotion of spontaneous cancer comparing with wild types, the interaction between Cry and cell cycle does not seem to have a significant impact on cell growth. Moreover, both Cry and Bmal mutant cells lead to low proliferative rates which questions the impact of the Cry on cell proliferation again. Therefore, the cell cycle interactions of the Cry seem to be still away from a comprehensive understanding.

In summary, the current hypothesis asserts that a simple photochemical cycle including cryptochrome, cAMP and Ca\(^{2+}\) may possibly answer a century-old question. However, only if the predictions of the hypothesis come true, it can be

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Table 2. Several samples of the light-growth interactions in biological systems.

<table>
<thead>
<tr>
<th>Finding</th>
<th>Year</th>
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<tr>
<td>Biophoton emission changed protein secretion, lipid peroxidation and ultra-weak photon emission in detector cells of mammary gland tissue (15)</td>
<td>1993</td>
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<tr>
<td>Decreased adhesive capability of pseudomonas fluorescens cells through biophotonic communication (16)</td>
<td>2000</td>
</tr>
<tr>
<td>Increased growth rate in Escherichia coli bacterial colonies through vis-IR photons (17)</td>
<td>2003</td>
</tr>
<tr>
<td>Germinating Fucus-zygotes direct their growth with biophoton emissions (18)</td>
<td>2005</td>
</tr>
<tr>
<td>Proliferation induction with electromagnetic emission between osteoblast cells (19)</td>
<td>2007</td>
</tr>
</tbody>
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Figure 1. Schematic representation of the hypothesis.
accounted as plausible. Some predictions of this hypothesis are outlined below:

• There is a positive correlation between photon/biophoton emission and cAMP concentration in the cell.
• Biophoton-induced mitosis should be inhibited by Ca²⁺ channel blockers.
• Knock-down Cry1 and Cry2 cells cannot show the so-called “biophotonic communication”.
• Since blue light has the peak absorbance for Cry, blue light photons are the most effective “mitogenic” photons and they can accelerate light-induced wound healing.

It is noteworthy to mention that if the current hypothesis will be confirmed, it will help to determine the types of tissues that phototherapy has its peak efficacy based on the tissue’s cry gene expression profile.

Acknowledgment

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References

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