Controlled Photosensitizer-free Singlet Oxygen Release for Biomedical Applications

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***Abstract*—Numerous studies have been published that discuss the triggering of apoptosis and the enhancement of mitochondrial respiration through laser illumination and singlet oxygen production in different cells and tissues. However, a significant gap in understanding remains, and it is crucial to pinpoint the precise mechanisms of laser irradiation effects. In this paper, we share our findings in exploring this area.**

***Index Terms*—$^1O_2$, photosensitizer-free generation**

I. Introduction

Molecular oxygen and reactive oxygen species (ROS) are crucial in controlling fundamental cellular functions under both normal and pathological conditions. Recently, the active study of the ROS physiological role has attracted particular interest in the singlet form of oxygen ($^1O_2$). $^1O_2$, an electronically excited and less stable form of triplet oxygen ($^3O_2$), can be generated through thermal, enzymatic, or photochemical methods. It has also been recently discovered that $^1O_2$ can be directly excited from its main form using light at specific wavelengths (see Fig. 1) [1], [2]. This capability of direct optical generation (photosensitizer-free) with control of the $^1O_2$ production by altering laser light power, exposure time, and other laser characteristics holds significant promise for advancements in redox biology and clinical medicine.

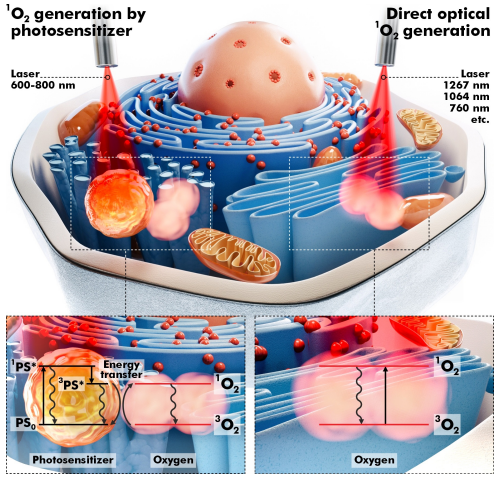

Fig. 1. Primary methods for generating $^1O_2$. Left part: the photodynamic mechanism involves a transferring energy to molecular oxygen from photosensitizer singlet and triplet excited states ($^1PS^*$ and $^3PS^*$). Right part: $^1O_2$ is directly generated through laser illumination. The wavelengths 760, 1064, and 1267 nm represent the peaks of oxygen light absorption.

II. Photosensitizer-free Generation of Singlet Oxygen

In our exploration of initiating apoptosis via laser-induced $^1O_2$, we examined B16 melanoma cells and human skin fibroblasts [3]. Our findings confirmed that 1267nm laser illumination is highly selective for $^1O_2$ generation without producing other ROS (superoxide anion O_2^- and hydrogen peroxide H_2O_2), and activating lipid peroxidation. While $^1O_2$ did not alter mitochondrial membrane potential ($\Delta\Psi m$) in control fibroblasts, it led to oscillations in $\Delta\Psi m$ and full mitochondrial depolarisation in melanoma cells by triggering the opening of the permeability transition pore (PTP). This effect led to an increase in apoptosis in melanoma cells without affecting the necrosis rate in fibroblasts, suggesting that $^1O_2$ can specifically initiate apoptosis in cancer cells through opening the PTP, without leading to fibroblast death.

Additionally, we proposed several methods to detect $^1O_2$ and assessed the production efficiency at different laser irradiation parameters [4]. We employed a chemical "trap" (L-histidine) and a fluorescent probe (SOSG) for detection. This work covered laser wavelengths of 1267, 1244, 1122, and 1064 nm. The 1267 nm wavelength was the most efficient in generating $^1O_2$, with 1064 nm showing nearly comparable efficiency. The 1244 nm wavelength also produced a measurable amount of $^1O_2$. We found that increasing laser exposure time was more effective for generating $^1O_2$ than increasing the power.

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