CELLULAR MECHANISMS OF LOW POWER LASER THERAPY

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Abstract: Cytochrome *c* oxidase is discussed as a possible photoacceptor when cells are irradiated with monochromatic red to near-IR radiation. Five primary action mechanisms are reviewed: changes in the redox properties of the respiratory chain components following photoexcitation of their electronic states, generation of singlet oxygen, localized transient heating of absorbing chromophores, NO release from catalytic center of cytochrome c oxidase, and increased superoxide anion production with subsequent increase in concentration of the product of its dismutation, H_2O_2. A cascade of reactions connected with alteration in cellular homeostasis parameters (pH_i, $[Ca_i]$, cAMP, E_h, [ATP] and as well as NF - κB, AP-1) is considered as a photosignal transduction and amplification chain in a cell (secondary mechanisms).

INTRODUCTION

The most frequently used mechanism of photon energy conversion in laser medicine is heating. Average heating of irradiated samples occurs with all methods of tissue destruction (cutting, vaporization, coagulation, ablation). Many of these surgical laser techniques are reviewed elsewhere. At low light intensities the photochemical conversion of the energy absorbed by a photoacceptor prevails. This type of reaction is well known for specialized photoacceptors such as rhodopsin or chlorophyll. In medicine light absorption by non-specialized photoacceptor molecules (i.e., molecules that can absorb light at certain wavelengths, but that are not integral to specialized light-reception organs) is used rather extensively. The absorbing molecule can transfer the energy to another molecule, and this activated molecule can then cause chemical reactions in the surrounding tissue. This type of reaction is successfully used in photodynamic therapy (PDT) of tumors. Alternatively, the absorbing molecule in a light-activated form can take part in chemical reactions, as occurs in treatment of skin diseases with psoralens and UVA radiation (PUVA). Importantly, in both PDT and PUVA therapy the photoabsorbing molecules are artificially introduced into a tissue before irradiation.

Irradiation of cells at certain wavelengths can also activate some of the native components. In this way specific biochemical reactions as well as whole cellular metabolism can be altered. This type of reaction is believed to form the basis for low-power laser effects. One should note that light-therapy methods based on photochemical conversion of photoabsorbing molecules are not laser-specific methods. Conventional light sources generating the appropriate wavelength can also be used (as is done in PUVA and UV therapy). Laser sources are just handy tools providing many practical advantages (e.g., efficient fiber-optic coupling to irradiate interior body parts, high monochromaticity and easy wavelength tunability, simplicity of use and electrical safety in the case of semiconductor lasers).

PHOTOACCEPTORS AND PRIMARY REACTIONS

Biological responses of cells to visible and near-IR (laser) radiation occur due to physical and/or chemical changes in photoacceptor molecules, components of respiratory chains like NADH-dehydrogenase and cytochrome *c* oxidase [1,2].

As a result of the photoexcitation of electronic states, the following physical and/or chemical changes can occur: alteration of redox properties and acceleration of electron transfer, changes in biochemical activity due to local transient heating of chromophores, one-electron auto-oxidation and O_2^- production (and subsequent production of H_2O_2), NO release, $^1O_2$ production and photodynamic action. It is not excluded that different reaction pathways can provide the same result: a change in mitochondrial redox activity.

There are no grounds to believe that only one of these processes occurs when a cell is irradiated. An important question for the future is which of these reactions is responsible for a certain low-power laser effect. However, recent experimental results of measurements of redox absorbance changes of living cells after

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irradiation [3,4] clearly indicate that a mechanism based on changes in redox properties of terminal enzymes of respiratory chains might be crucial.

SECONDARY REACTIONS

The primary physical and/or chemical changes induced by light in photoacceptor molecules are followed by a cascade of biochemical reactions in the cell that do not need further light activation and occur in the dark (photosignal transduction and amplification chains). These reactions are connected with changes in cellular homeostasis parameters. The crucial step here is thought to be an alteration of the cellular redox state: a shift towards oxidation is associated with stimulation of cellular vitality, and a shift towards reduction is linked to inhibition. It was shown that cells with a lower than normal intracellular pH, in which the redox state was shifted in the reduced direction, were more sensitive to the stimulative action of light as compared to cells in which the respective parameters were optimal or near optimal. Recall here a change in action spectrum recorded after a decrease of partial pressure of oxygen before irradiation and as well as the results of a set of experiments where the irradiation effects were modified by various chemicals[1].

CONCLUDING REMARKS

Light action on the redox state of a cell via the respiratory chain also explains the diversity of low-power laser effects. Beside explaining many controversies in the field of low-power laser effects (i.e., the diversity of effects, the variable magnitude or absence of effects in certain studies), the proposed redox-regulation mechanism may be a fundamental explanation for some clinical effects of irradiation, for example, the positive results achieved in treating indolent wounds, chronic inflammation, and ischemia, all characterized by acidosis and hypoxia.

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