PHOTODYNAMIC THERAPY (PDT): PHYSICAL, BIOCHEMICAL AND CLINICAL ASPECTS

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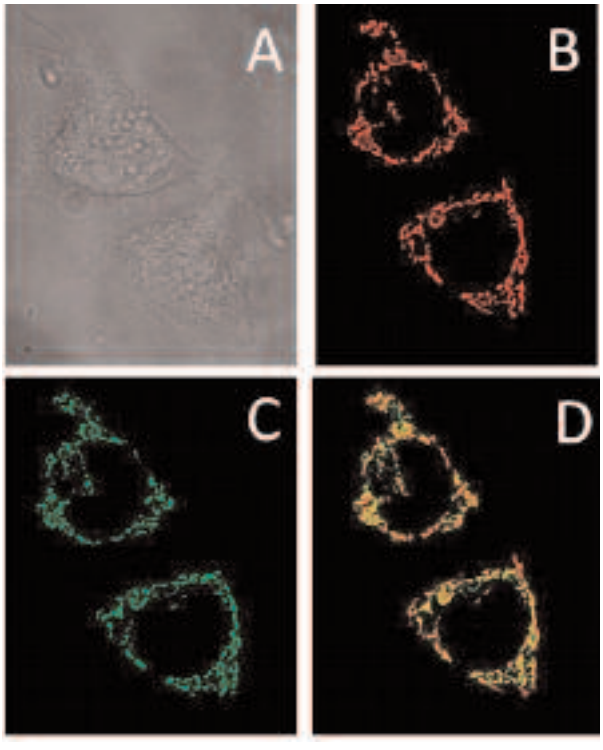

Micrographies of Hela cells: Transmitted light (A), fluorescence of PpNpNI (B), fluorescence of Rodamine 123 (C) and sobreposition of PpNpNI and Rodamine 123 (D).

The satisfactory outcome of a treatment by PDT depends on the interaction between light and living tissue, involving several processes that are usually dealt by professionals with expertise in different areas such as physics/photonics, chemistry/biochemistry and biology/medicine. These processes will be handled together on this project, by a team of researchers with multidisciplinary training. Our general aims are: i) to understand the physical, chemical, and biochemical mechanisms, ii) to synthesize, characterize and study activity of new potential drugs for PDT, iii) to propose low-cost clinical protocols using PDT for the treatment of cancer and infectious diseases; iv) to disseminate PDT to the various professionals in the health sciences, as well as to the general population. To achieve these goals, we propose the development of five sub-projects, which are: A) physical aspects that influence the efficiency in photodynamic PDT: penetration of light in living tissue and activation of photosensitizers; B) mechanisms in PDT: interaction of photo activated reactive species with biological systems; C) PDT *in vivo* and clinical trials; D) Synthesis of new molecules and photoactive nanomaterials; E) Development of tools to study photo damage in membranes. The mechanistic studies provide the necessary knowledge for the development of new drugs that will be synthesized and studied in the physical, chemical and medical aspects.

SUMMARY OF RESULTS TO DATE AND PERSPECTIVES

Interfaces are known to affect the mechanisms of photochemical reactions and the photochemical reactions are known to affect the properties of the membranes. Our research efforts are directed to investigate some mechanistic aspects of these processes. We have shown how interfaces of biomimetic systems, mitochondria and nanoparticles can modulate the competition between type I and type II reactions, allowing photosensitizers to produce either singlet oxygen or radical species and examples were published of how this knowledge can be used to study photo oxidation reactions. By looking at the membranes, we have shown the relationship between chemical structure, membrane binding and photodynamic efficiency in cells, revealing the mechanism for the increased photodynamic efficiency of amphiphic photosensitizers. We have also shown how photo oxidation affects the cooperative interaction between cytochrome-c and membranes.

In order to amplify the knowledge relating chemical structure with photo-activity, we have made affords to synthesize new molecular photo sensitizer and nanoparticles modified with photosensitizers. By studying the photo activity of these species, in biomimetic systems and cell cultures, we aim to propose relationships between intensity and localization of photo oxidation damage, and the mechanism of cell death. This knowledge is important, not only to propose better protocols to PDT, but also to understand sun damage in skin. Although the final goal is not to search directly for more efficient photosensitizers, we end up discovering molecules that are more efficient compared to those commercially available, which could improve PDT protocols. Some results have been published and a patent application is being analyzed in the patent office of USP.

The understanding of photochemical processes in interfaces and membranes is often limited because of the lack of experimental tools that can be used to answer questions relevant to processes occurring few nanometers away from an interface. We have contributed to scientific knowledge in this area by developing tools to study photo oxidation processes in interfaces by using Surface Plasmon Resonance (SPR) and Giant Unilamellar Vesicles (GUVs). A membrane biochip was developed using SPR and a method to study physical damage in membrane was implemented using GUVs.

If the basic science that is learned in our experimental laboratories can be used to treat patients, the society will feel the direct benefit of our research. Therefore, we have made efforts to develop inexpensive PDT protocols and to offer then as a free service in hospitals and specialized clinics. Nowadays we are supporting clinical trials in a specialized dermatological clinic called CEDERM in UNIFESP (dermatoses and osteomyalites), in the Hospital Emílio Ribas (Leishmaniose), Medicine School of USP and Hospital Pérola Baiton (HPV, gynecologic cancer) and Medicine School of ABC (Kaposi´s Sarcoma).

MAIN PUBLICATIONS

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