



PHOTO: IPA 2019 WORLD CONGRESS, BOSTON (USA)

International Photodynamic Association (IPA) Newsletter: Winter Lights

12/31/18

IN THIS ISSUE

Featured in This Issue

edited by [Huang Chiao (Joe) Huang and Pilar Acedo Nuñez]

President's note

Dear Colleagues

First, my best wishes to you and your family for 2019! May you have a happy, healthy and peaceful year. This quarter's Newsletter is a mix of good and sad news.

The sad news is that in the death of Tom Dougherty, we lost a luminary in the field of PDT. Tom worked tirelessly to promote PDT and along with Professor Hayata of Japan and others, founded the IPA that we are trying to build and sustain. There is an obituary by David Kessel, on Tom's passing in this Newsletter. You will learn more about his life and work at the IPA Boston 2019 when we kick off the conference with a session that pays tribute to Tom and his contributions from people who worked closely with him.

The good news is that we will meet soon at the 17th World Congress of the IPA, from June 28-July 4, 2019, at the Boston Marriott in Cambridge. The preparations are well advanced and I thank those of you who made suggestions to help shape the program. At your suggestion, the Plenary speakers include experts in some aspect of cancer biology but not necessarily practitioners of PDT. The plenary topics include the role of tumor microenvironment, immunology development and challenges, a Nobel Laureate lecture on evolutionary biology, and challenges in macromolecular targeting approaches. Both academic and industry leaders will be presenting these lectures and I look forward to seeing as many of you as possible.

Please submit your abstracts! January 9, 2019 is the deadline. We are not allowed to issue letters for visa support without the abstracts being accepted. I will try to expedite the process but please do submit as soon as you can so these letters can be issued. I want to see you here in Boston!! As I said this is my last major activity with the IPA and would love to see a lot of you. Please sign up for special events at the Congress. Several workshops and a PDT school are planned.

Poster awards and travel grants will also be available. Make use of these perks! I am working hard to raise more funds so a maximum number of people can receive assistance and awards. A group email detailing the events should have gone out and I hope you will take the time to read it.

As in the past years, the IPA will present awards for a variety of activities. Please participate in it. Carolyn Cross chairs it again this year but feel free to ask to join the committee or nominate a colleague or yourself! Ask for information if you need. Participate.

And now I come to the topic of the IPA: building and sustaining it. The elections for Board membership are approaching and very soon you will receive the election materials. PLEASE PARTICIPATE in whatever form is realistic for you. The senior members are always happy to help but new blood is needed on the Board for a boost. I will certainly continue to assist in whatever form I can but hope that the leadership will be new and energetic!

Please join me in thanking the Newsletter Editors, Huang Chiao (Joe) Huang and Pilar Acedo for doing all the work on this and Vandana Grover in helping frame it and distribute it in the fabulous form that we see. She also provides IPA news via social media which gives us significant exposure. Thanks to those of you who have offered to take on specific tasks that we hope to be hearing about in the next few months. Your help in service to our Association and providing news such as awards, grants and other recognitions would be appreciated by all.

Again, my best wishes to all for the coming year and hope to see a lot of you in Boston in 2019! We have made special efforts to order good weather for you and I am sure you will enjoy our fair city if you were to join us.

Tayyaba Hasan, Ph.D.

President, IPA Board of Directors | IPA Congress 2019



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IPA World Congress, Boston, USA
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Dr. Thomas Dougherty obituary

by [David Kessel]

The death of Tom Dougherty in October 2018 ended a career that had provided the major influence for bringing PDT into the realm of cancer therapy. Tom was initially looking for a method to sensitize malignant tissues to ionizing radiation, but soon realized that a method first described in 1900 could be used to sensitize such tissues to light. Initial studies by Samuel Schwartz and Robert Lipson at the Mayo Clinic had indicated the ability of porphyrins to preferentially accumulate in sites of neoplasia. Efforts to attract interest and support for further studies were unsuccessful until Tom initiated pre-clinical and clinical programs at the Roswell Park Cancer Institute in the 1970s.

He and a group of associates eventually received FDA approval for the procedure (1994). Groups in Japan, China, England and elsewhere began developing PDT for clinical management of cancer. The Japanese group organized the first IPA meeting in 1986. Meetings have been held every two years since then. PDT has been shown useful for a variety of indications, including the eradication of spurious blood vessels that occur in the retina. When recounting the history of PDT, it is important to note that none of these accomplishments would have occurred without Tom's early efforts at bringing PDT into clinical usage.

We can seldom point to a single person who establishes a field. It seems likely that anesthesia and antibiotics would have been discovered without Thomas Morton and Alexander Fleming. Whether PDT would have developed to the extent it has today without the efforts of Tom Dougherty is unclear. His influence on the field was perhaps best summed up by Nancy Oleinick, an investigator at Case Western Reserve in Cleveland and the first person to identify apoptosis as a major route to PDT-induced cell death. She remembered Tom as "a superb scientist, a gentleman, a visionary, and a cheerleader for PDT". There is no doubt that Tom left the world a better place for his having been there.



**Thomas J Dougherty
1933 - 2018**



First IPA meeting held in Tokyo

Featured Research Published by IPA Members

edited by [Pilar Acedo Núñez and Huang Chiao (Joe) Huang]

Interstitial PDT of Locally Advanced Cancer

Gal Shafirstein and his colleagues at Roswell Park Comprehensive Cancer Center in Buffalo (New York), have reported that it is critically important to exceed a threshold light irradiance during interstitial PDT (I-PDT) of experimental locally advanced tumors in order to achieve a high cure rate (*Irradiance Controls Photodynamic Efficacy and Tissue Heating in Experimental Tumors: Implication for Interstitial PDT of Locally Advanced Cancer*. British Journal of Cancer 2018; 119: 1191-1199).

The Shafirstein group found that although high intratumoral irradiances alone can be associated with significant light-induced tissue heating in large experimental mouse tumors, I-PDT with the addition of Photofrin® resulted in significantly ($p < 0.05$) greater cure rates of up to 90%. I-PDT treatment conditions established in mice were successfully translated to locally advanced tumors implanted in the neck of rabbits. A proof of concept that this I-PDT regimen can be implemented in the treatment of a patient with locally advanced head and neck cancer is included in the BJC supplement. This translational paper highlights, for the first time, the importance of delivering a threshold intratumoral light irradiance in I-PDT. It provides guidelines to use I-PDT in clinical settings.

Sunlight Active Formulated Extract (SAFE)

An Egyptian Innovation for Malaria Vector Control, by Prof. Mahmoud H. Abdel-Kader

Malaria is a major life-threatening disease that affects all age groups of people. It remains the main cause of poverty and underdevelopment, and one of the main obstacles in the face of economic growth.

Despite the efforts of the World Health Organization (WHO) since 1905 to eradicate the disease, it still results in massive economic and human losses, especially in Sub-Saharan Africa and in some rural areas of Asia and Latin America. According to the WHO, it is expected that there will be a continued role for DDT in malaria control until equally cost effective alternatives are developed.

There are some implemented strategies for malaria vector control, which are considered effective but costly. Those include controlling the disease transmitter, chemoprevention, and case management.

Controlling the disease transmitter involves the usage of insecticide-treated mosquito nets (ITNs) and Indoor Residual Spraying (IRS). Chemoprevention, on the other hand, is used to prevent blood contamination for a person subjected to the infection.

Finally, case management involves diagnosing and treating the infected case, which makes the diagnostic stage and diagnostic tools very important.

The use of photochemical process as a tool to control the population of several types of insects has been examined in laboratory studies. Compounds of plant origins have been isolated, identified and studied as photo toxins against a wide range of pests including insects, fungi and weeds. Among the main classes studied recently are Chlorophyllin and Pheophorbide as photoparasitocides.

SAFE, is an innovative modality for malaria vector control. The scientific idea behind SAFE is eliminating the malaria mosquito from the source, through cutting its life cycle by getting rid of the larvae living in stagnant water by using photo-oxidation modality. The process involves utilization of sunlight and chlorophyll derivatives (extracted from plants) which are sprayed in swamps so that the mosquito larva might feeds on. A photochemical reaction in the larvae induces oxidative stress in the larvae body which eventually leads to the organism's death within only two hours as shown by the field application results.

Fortunately, SAFE was highly effective as it ensures up to 95-100% mortality of mosquito larvae and no harm was shown to other beneficial organisms.

The novelty of using SAFE lies in developing a new ecologically safe modality using natural plant extracts and sunlight which

exist in all countries suffering from malaria. The advantages of SAFE involve; the safety of the photosensitizer used, low cost, easy to apply in the field, highly effective as they ensure high mortality rate of the mosquito larvae, and most importantly; they are FDA approved for use as food additives.

The SAFE innovation has been recognized from the WHO after studying its submitted dossier for over a year. The product SAFE was discussed in the 3rd WHO Vector Control Advisory Group (VCAG) meeting held at WHO/HQ. VCAG's assessment of the file concluded that; based on the evidence presented, SAFE falls within a previously defined paradigm (larvicides). In addition, any product falling within already defined paradigms do not need to demonstrate public health efficacy through community trials.

Large scale field implementation strategy for using SAFE in malaria vector control has already been developed in Ethiopia, and Al-Neil Al-Azrak (Sudan), after the successful achievements obtained in small scale field trials. Those trials were carried out on larvae in sewage routs as well as infested swamps.

Two complementary methods have been used in this study to evaluate the effect of chlorophyll derivatives as photo pesticide against *Anopheles gambiae* and *Culex pipiens* (either in laboratory or in infected swamps). The first method investigated the effect of external factors namely chlorophyll derivatives concentration, light dose and exposure time, in which results were revealed as percent of survival of the larvae. The second method investigated the internal factor, which is the accumulation inside the organs and tissues of the larvae.

Regarding the effect of chlorophyll derivatives application in sewage routes and infested swamps, a jump in the percent of mortality was observed. This result was mainly affected by the used critical concentration of chlorophyll derivative, the high sensitivity to low light doses, and the long exposure time as allowed by the long sunny days (which could compensate for a lower dose other than the critical dose).

As for the behavior of chlorophyll derivative distribution inside the body organs of the larvae, Confocal Laser Scanning Microscope (CLSM) technique was used. It provided the best information represented by fluorescence images, fluorescence spectra and lifetime measurement. The fluorescence spectra measurement inside the tissues of

Anopheles larvae is a quantitative method for estimation of the accumulated chlorophyll derivative at any time of incubation and after light exposure. Lifetime measurements of spots inside the larvae were determined to be 1.5 ± 1.04 ns for the 5 hours incubation period and 11.9 ± 3.3 ns for 15 hours incubation period. This difference may be attributed to the different ratio of aggregated and non-aggregated forms of chlorophyll derivatives.

These are very essential measurements for field application to optimize the parameters of the photochemical process for the target species and avoid the beneficial micro-organisms living in the same infested swamp.

In conclusion, this work introduces an innovative modality for malaria vector control, which combines efficiency and low cost with the highest levels of human safety and environmental friendliness.

Future PDT by Harubumi Kato. Past president of IPA and Emeritus Professor of Tokyo Medical University

Basic investigation through innovative ideas is important for the development of PDT, but a more important issue is to apply them as clinical treatment for patients. Thirty-eight years have already passed since the first therapeutic success of PDT in treating early stage central type squamous cell carcinoma of the lung. PDT for endoscopically detected early stage cancers of the lung, esophagus, stomach and cervix showed highly curative results in the 1980's. For almost a half century, many kinds of cancer patients have been treated by PDT; however, this treatment has not been recognized as a major therapy for cancer patients. The reasons were the difficulty of early detection and changes in the rates of occurrence of different types of cancer. For example, in lung cancer, the occurrence of central type lung cancer, which is well indicated for PDT, decreased significantly in recent years, while peripheral type lung cancer has rapidly increased throughout the world. However, in some countries, smoking, air pollution and environmental conditions still induce a high occurrence of central type lung cancer. In these countries, PDT is still highly effective in treating patients, if it is detected at an early stage.

The advantages of PDT are that it is a less invasive, safe and low-cost treatment, and moreover it is a highly effective treatment for early stage cancers.

In order to recognize PDT as one of the major treatments for cancer patients, it is necessary to establish guidelines to evaluate the response to PDT. The classification into completely curable diseases, diseases of adjuvant therapy with surgery, improvement of symptoms, progression-free survival with chemotherapy and/or radiotherapy in different organs is easy to understand for clinical doctors and patients, and this measure could help to develop better PDT in future. International criteria for recording PDT, which include devices, photosensitizers, and photoradiation energy as therapeutic methods, diagnostic imaging, pathological and cytological diagnosis, molecular pathogenesis and clinical stage are necessary for the establishment of guidelines. This is not easy, but we have to do this important work to obtain recognition for PDT in cancer therapy under the IPA.

For promotion of the IPA it is also necessary to develop a new ideal PDT. PDT for peripheral lung cancer, which is increasing significantly throughout the world as described above, is one of the promising therapeutic methods. Early detection of peripheral lung cancer is easily achieved by CT screening. There are still some problems to overcome in establishing a pre-therapeutic definitive diagnosis and in the evaluation of therapeutic results, however, it will not take a long time to develop these technologies.

In Japan, the clinical trial of PDT for peripheral early stage lung cancer is now ongoing through the support of the government. With government approval in the near future, this will be good news (the gospel) for patients with lung cancer throughout the world.

Although photo-immunotherapy for cancer therapy has been topical in recent years, this therapy is no different from traditional PDT, a concept that was advanced 100 years ago and discussed for long time. It has been reported that PDT is immunogenic. This therapy is photodynamic therapy by molecular targeted TKI antibody conjugated photosensitizer and light photoradiation. The phase II clinical trial for head and neck cancer was reported to be showing good results. While it is very good and welcome to be promoting PDT, there seems to be some

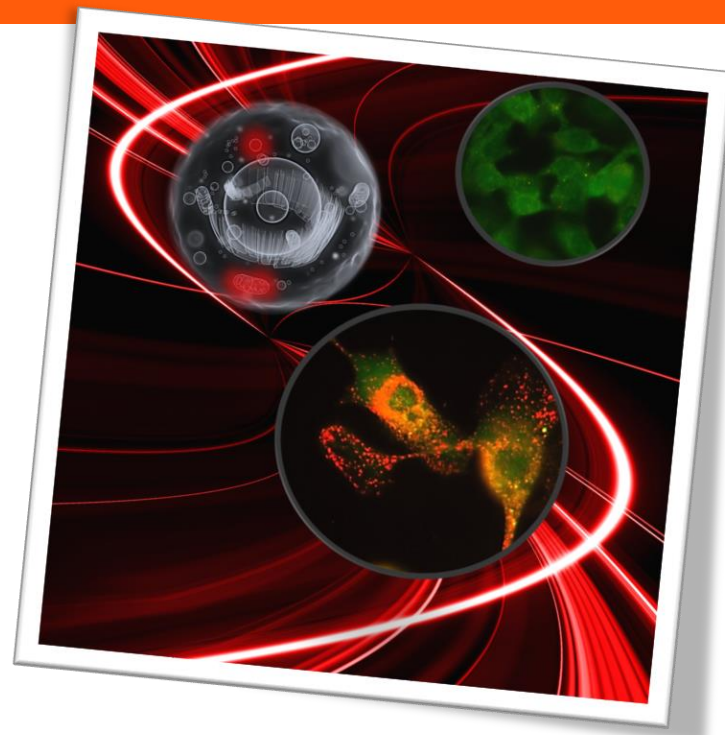
incongruity between the therapeutic mechanism and the naming of the therapy.

As a cancer treatment, in order to achieve precision PDT, cancer pathogenesis should be investigated. One of the methodologies is the investigation by proteogenomics. Identification of neoantigens and the development of appropriate antibodies is necessary for antibody-PDT, and moreover Kinase inhibitor-PDT, immunological regulatory T-cell targeted PDT and immunological checkpoint targeted PDT could be promising for specific immunological PDT in advanced diseases in future. Thus, PDT could transfigure and become a mainstream therapy by means of the various devices of PDT in future.

How precise can be the damage induced by photosensitized oxidations?

by Mauricio S. Baptista

edited by [Huang Chiao (Joe) Huang and Pilar Acedo]



Photosensitized oxidations, which are reactions provoked by the interaction of light with photosensitizer (PS) molecules, are being used in medical technologies, such as photodynamic therapy, in order to trigger oxidation of biomolecules and consequently to eliminate cancer cells or pathogens. Damage in cytoplasmic or organelle membranes is key to modulate the mechanism as well as the overall efficiency of regulated cell death.¹⁻³

There are two major mechanisms of photosensitized oxidations, called type I and type II, representing respectively, the direct oxidation of biological targets (direct-contact reactions) and the oxidations mediated by diffusing species, such as singlet oxygen.⁴

Nevertheless, the detailed molecular steps leading to biological injury remains largely uncharacterized and it is not clear how precise can be the spatial damage induced by the photosensitized oxidation reactions. In case of direct-contact reactions, the damage is performed precisely in the place where the excited species are generated and for type II processes, singlet oxygen or other diffusing species can carry out oxidation potentials hundreds of nanometers or micrometers away from the point of light absorption.

In a recent publication, we demonstrated that for a PS to fully compromise membrane function, it needs to be sacrificed through contact-dependent reactions, forming lipid-truncated aldehydes, which are the active agents causing membrane leakage.⁵ Therefore, relevant damage that definitively changes the outcome of cells are precisely the locus of PS location, and therefore, justifies the search for molecular-specific oxidation-induced photodamage.

Also, PS regeneration should be exploited as an effective tool to maximize the effects of photosensitized oxidations.

FOR MORE INFORMATION

Content:

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PHOTO: Produced by Waleska K. Martins.

2019 IPA World Congress, Boston, USA (June 28 - July 4, 2019)

by IPA and David Kessel

The 17th meeting of the IPA is approaching. It might be interesting to look back on the preceding meetings over the years. Tom Dougherty had organized a series of conferences in both Buffalo and Washington, D.C. (1975-78) to discuss progress in the field. David Kessel had obtained a substantial award from the NIH to put together a meeting at the Washington Hilton in 1980. PDT was making an appearance at national and international conferences. A Japanese group led by Prof. Hayata at Tokyo Medical College decided to formalize the approach and put on the first IPA meeting in Tokyo (1986) at the Keio Plaza Hotel. A welcoming committee along with a ceremonial dinner was hosted by Dr. Hayata.

John Carruth invited Princess Anne to speak at the 1988 meeting in London. The 1990 conference was organized by Tom Dougherty in Buffalo. IPA has now met in such diverse places as Shanghai, Munich, Melbourne, Seattle, Seoul, Coimbra and Rio. Perhaps the most elaborate conference was held in Vancouver (2001) when QLT got involved and staged an elaborate series of events at several sites including the Vancouver Aquarium and a private club where photography was discouraged.

At the Shanghai meeting (2007) competition for next site was eliminated when the Board decided it was time to get back to the US and that David Kessel should organize the 2009 meeting. Prof. Kessel contacted the group that had put on the very successful Vancouver meeting but they asked for an 'up front' guarantee of \$600,000. The fall-back position was letting SPIE do it in Seattle on a 'cost-plus' agreement where they would accrue any profit and absorb any loss.

The Munich meeting (2005) was a high-tech event with guards at every door and transponders built into badges so that the pathway of each participant could be tracked. In contrast, the SPIE staff at Seattle consisted of exactly two people, one of whom left after the second day. SPIE organizes a meeting somewhere on the globe every few days and has the system down to an exact science.

The Boston meeting (actually Cambridge) will be held at Kendall Square, avoiding the nontrivial costs at Boston hotels. K Sq is a sight to see. Prof. Kessel mentioned to the IPA: *"When I was a student at MIT (right up the street), this was a desolate area filled with cheap diners, vacant lots, laundries, pawn shops and a decrepit subway stop. Today, K Sq is filled with a magnificent array of shops, restaurants, hotels, research outfits and remarkable architecture. Have a look on Google Maps. Last time I visited MIT and was emerging from the Kendal Square subway, I wasn't certain where I was and had to consult a compass to find my way to the Institute".*

The International Photodynamic Association World Congress has been bringing together researchers and clinicians in all fields of photodynamic therapy (PDT) and photodiagnosis (PD) since 1986. Every two years, the IPA organizes a conference to foster scientific development and contribute to clinical practice. The 17th IPA World Congress will be held at the Marriott Cambridge, MA, June 28 - July 4, 2019. We welcome you to Boston in 2019.

For information about the IPA and past conferences, please visit the IPA website or email info@ipaboston2019.org.

For discounted registration, become an IPA member:
www.internationalphotodynamic.com/membership

Abstracts Due
9 January 2019

Manuscripts Due
5 July 2019

Photodynamic Therapy (PDT) Sessions
PDT in Clinical Practice: A Look at Current Oncology Trials
Nanotechnology in PDT
Photo-immunology and PDT-Induced Immunology
PDT Mechanisms: Tumor Microenvironment and Cell Death Pathways
Challenges in PDT Dosimetry and Technology
Fluorescence Guided Resection and PDT imaging
Antimicrobial and Anti-infective PDT

Role of PDT in Gastroenterology, Pulmonology, Head and Neck Cancers, Dermatology, and Gliomas

Development Opportunities

Networking Events, Mentoring Lunches with Faculty, Grant Writing Workshops, Careers in Industry, Panel Trainee.

Travel grants are available.

Social Events

Welcome Reception, Gala Dinner, Tours, Awards, and more!!!

Symposium Chair Tayyaba Hasan

Wellman Ctr. for Photomedicine



Resources and Opportunities

by [IPA]

Looking to reach photobiologists and related professionals on a regular basis? Put your message in their e-mail inboxes with IPA triennial e-newsletters. IPA Newsletter reaches more than 400 members with member news. Contact [Vandana Grover](#).

Opportunities

We are seeking for 2019 International Photodynamic Association (IPA) conference sponsorship. If you have questions about 2019 IPA conference

sponsorship, please contact the Finance Committee Chair of IPA Congress 2019: [Professor Huang Chiao \(Joe\) Huang @ hchuang@umd.edu](#).

International Photodynamic Association (IPA) Newsletter: Winter Lights

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WISHING YOU A VERY HAPPY NEW YEAR 2019

