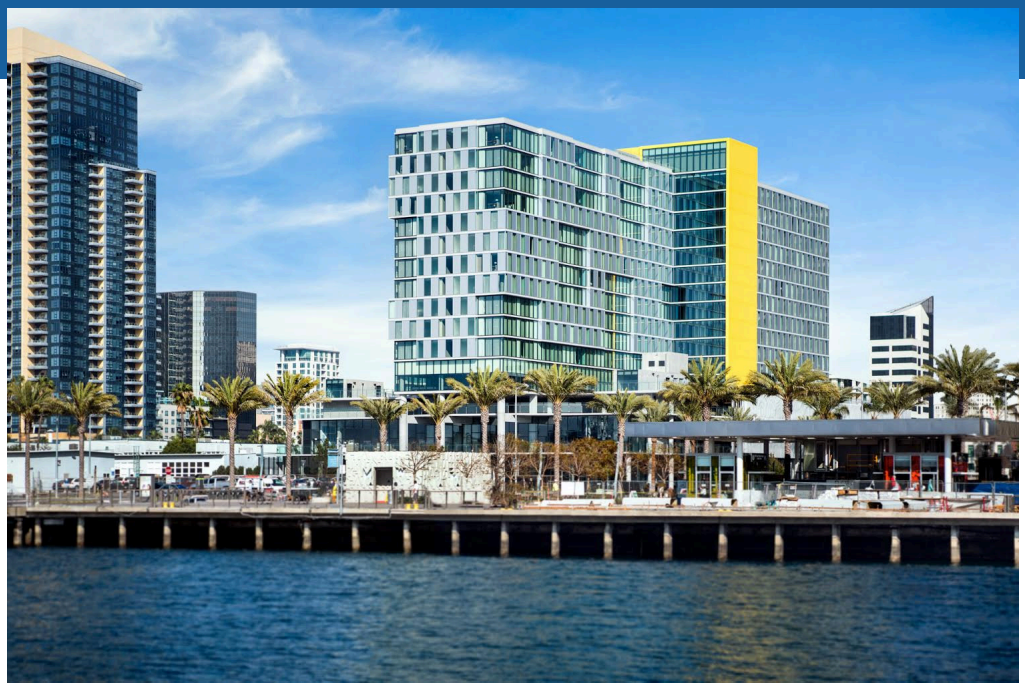
2017 ASP Presidential Evening Symposia:

'Photo-excited States: From Tissue Damage to Photomedicine'



Spring Hill Suites San Diego Downtown/Bayfront
900 Bayfront Court, San Diego, CA 92101

Welcome to San Diego, CA for the

2017 ASP Presidential Evening Symposia: 'Photo-excited States: From Tissue Damage to Photomedicine'.

This ASP focus symposium gathers basic and translational researchers that present cutting edge talks in high quality oral sessions held on two evenings:

Symposium I (Thursday, April 6, 2017, evening): **'Excited states in skin and other tissue damage: Photodamage, photocarcinogenesis, and photochemoprevention'**
This symposium examines the mechanistic role of excited states in mediating tissue damage (focusing on skin and solar exposure) and explores avenues for preventive and therapeutic intervention.

Symposium II (Friday, April 7, 2017, evening): **'Excited States in Photomedicine: From Mechanisms to Translation'**
This symposium will explore exciting new developments in the mechanisms and application of photoexcited states in medicine.

We hope for vibrant discussions during oral presentations and roundtable-style discussions.

We are looking forward to an exciting ASP focus meeting.

With our warmest regards,

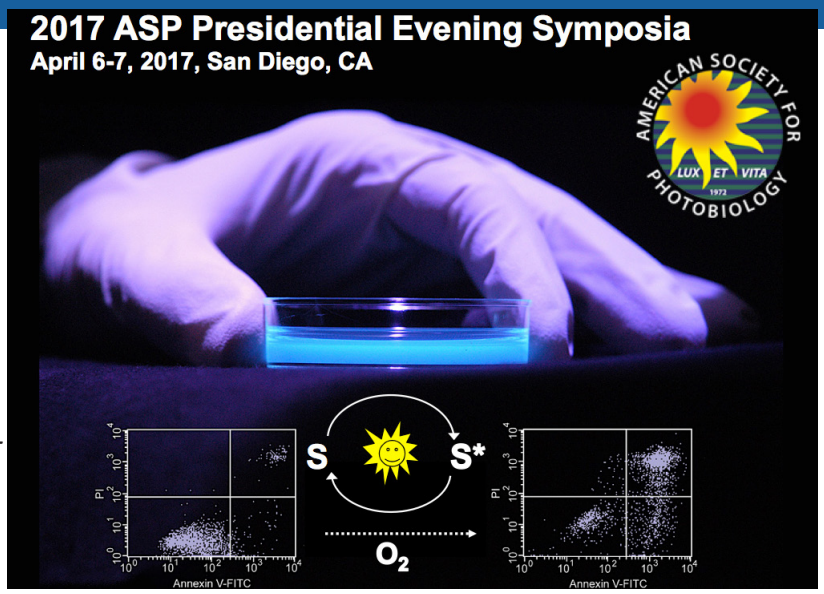
Georg T. Wondrak, *University of Arizona, ASP President*
Keith A. Cengel, *University of Pennsylvania, ASP Past president*
Yu-Ying He, *The University of Chicago, ASP President Elect*
Theresa M. Busch, *University of Pennsylvania, ASP Treasurer*

ASP Secretariat
Headquarters@photobiology.org

Symposium I (Thursday, April 6, 2017, evening)

'Excited states in skin and other tissue damage: Photodamage, photocarcinogenesis, and photochemoprevention'

6.30 - 10.00pm, Ted Williams Boardroom



6.30 - 7.00 pm
Evening reception with refreshments
'grab your dinner'

7.00 - 7.25 pm
1. Type I and II photosensitized oxidations: basic reactions and a novel lipophilic alkyl chain-pterin
Alexander Greer, Brooklyn College & The Graduate Center of the City University of New York, Brooklyn, New York, United States

7.25 - 7.50 pm
2. Mechanistic role of excited states in photodamage: nucleic acids as a target
Jean Cadet, Université de Sherbrooke, Sherbrooke, Québec, Canada

7.50 - 8.10 pm
3. Molecular actors in multiple roles: Endogenous photosensitizers and skin photodamage
Georg Wondrak, University of Arizona, Tucson, AZ, USA

8.10 - 8.25 pm
Refreshment Break

8.25 - 8.50 pm
4. Ultraviolet A-induced oxidation in cornea: characterization of the early oxidation-related events
Patrick J Rochette, Université Laval, Québec, Qc, Canada

8.50 - 9.15 pm
5. Chemiexcitation in Mammalian Cells: Beyond UV and Melanin
Douglas E. Brash, Yale School of Medicine, New Haven, CT, USA

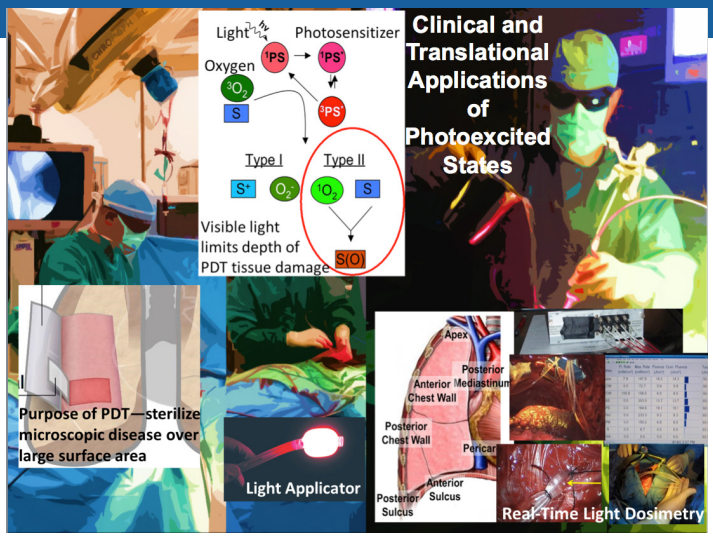
9.15 - 9.35 pm
6. Autophagy in UV-induced inflammation and tumorigenesis
Yu-Ying He, The University of Chicago, Chicago, IL, USA

9.35 - 10.00 pm
7. Molecular targets for skin cancer prevention
Zigang Dong, The Hormel Institute and University of Minnesota, Austin, MN, USA

Symposium II (Friday, April 7, 2017, evening)

'Excited States in Photomedicine: From Mechanisms to Translation'

6.30 - 10.00pm, Ted Williams Boardroom



6.30 - 7.00 pm
Evening reception with dinner buffet

7.00 -7.20 pm
1. Intraoperative PDT for Pleural Malignancies: Perspectives and Promise
Keith Cengel, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

7.20-7.45 pm
2. Translationally-relevant PDT Combinations: Mechanisms for Overcoming Molecular and Cellular Resistance and Enhancing the Tumoricidal Durability of Chemotherapeutics
Imran Rizvi, Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA

7.45-8.10 pm
3. Evidence for Peroxide Intermediates in Intralipid Photooxidations from 31P and 1H NMR Studies. Implications for Lipid Peroxidations, Superficial Photodynamic Therapy, and Tissue-Simulating Phantoms
Alexander Greer, City University of New York, Brooklyn College, Brooklyn, NY

8.10 -8.25 pm
Refreshment Break

8.25-8.50 pm
4. Antimicrobial Photodynamic Therapy
Thomas S Mang, University at Buffalo, Buffalo, NY

8.50-9.15 pm
5. Taking PDT from Bench to Bedside: Case Studies of AMD to Pancreatic Cancer
Tayyaba Hasan, Wellman Center, Harvard Medical School, Massachusetts General Hospital, Boston, MA

9.15-9.40 pm
6. Oxygen Sensing Phosphors – Translation from the Chemical Hood to Clinical Application
Conor L. Evans, Harvard Medical School, Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA

9.40-10.00 pm
7. Toward Clinical Translation of Physiologic Monitoring for Personalization of PDT
Theresa M. Busch, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

EXPLORE SAN DIEGO ON FOOT

When you stay at the Residence Inn & SpringHill Suites San Diego Downtown/Bayfront, you're just a short stroll away from vibrant shopping, dining, entertainment and nightlife. Whether you're exploring the historic, majestic ships on the bay, finding your favorite version of our famous fish tacos and West Coast IPAs, or dancing the night away in the Gaslamp Quarter, you'll soon discover why we earned our nickname of "America's Finest City."

POINTS OF INTEREST

1 B Street Cruise Ship Terminal - 5 minute walk
2 Coronado Ferry - 5 minute walk
3 Santa Fe Train Depot - 5 minute walk
4 Waterfront Park - 5 minute walk
5 America Plaza Trolley Station - 7 minute walk
6 USS Midway Museum - 8 minute walk
7 The Headquarters at Seaport - 10 minute walk
8 Maritime Museum - 10 minute walk
9 Little Italy - 10 minute walk
10 Seaport Village - 12 minute walk
11 Westfield Horton Plaza - 18 minute walk
12 Gaslamp Quarter - 20 minute walk
13 San Diego Convention Center - 20 minute walk

WANT YOUR INFO ON THE GO?

Stay connected during your vacation with these helpful smartphone apps:

San Diego Travel Guide
San Diego's Little Italy
Tap Hunter
Transit
Marriott

These attractions are recommendations based on positive feedback from previous guests. Although we provide a map for your convenience, we assume no responsibility for injury or damage that may occur while utilizing these routes.

SAN DIEGO DOWNTOWN/BAYFRONT

900 Bayfront Court
San Diego, CA 92101
RESIDENCE INN 619.831.0225 | ResidenceInnSanDiegoBayfront.com
SPRINGHILL SUITES 619.831.0224 | SpringHillSuitesSanDiegoBayfront.com

Residence Inn® Marriott

SPRINGHILL SUITES MARRIOTT

Type I and II photosensitized oxidation reactions: guidelines and mechanistic pathways

*Maurício da Silva Baptista[1] **Jean Cadet**[2] Paolo Di Mascio[1] Ashwini A. Ghogare[3,4] **Alexander Greer**[3,4] Michael R. Hamblin[5-7] Carolina Lorente[8] Silvia Cristina Nunez[9] Martha Simões Ribeiro[10] Andrés H. Thomas[8] Mariana Vignoni,8 and Tania Mateus Yoshimura[10]*

1 Instituto de Química, Universidade de São Paulo, São Paulo 05508-070, Brazil
2 Département de Médecine Nucléaire et de Radiobiologie, Université de Sherbrooke, Sherbrooke, Québec JIH 5N4, Canada
3 Department of Chemistry, Brooklyn College, 2900 Bedford Avenue, Brooklyn, New York 11210, United States
4 Ph.D. Program in Chemistry, The Graduate Center of the City University of New York, 365 Fifth Avenue, New York, New York 10016, United States
5 Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA 02114, United States
6 Department of Dermatology, Harvard Medical School, Boston, MA 02115, United States
7 Harvard-MIT Division of Health Sciences and Technology, Cambridge, MA 02139, United States
8 Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas (INIFTA), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), CCT La Plata-CONICET, Diagonal 113 y 64, 1900 La Plata, Argentina
9 Bioengineering Department, Unicastelo, Sao Paulo, Brazil 08230-030
10 Centro de Lasers e Aplicações, Instituto de Pesquisas Energéticas e Nucleares, IPEN-CNEN/SP, Av. Lineu Prestes, 2242, 05508-000, São Paulo, Brazil

E-mails: jean.cadet@usherbrooke.ca, and agreer@brooklyn.cuny.edu

ABSTRACT
Here, ten guidelines are presented for a standardized definition of type I and II photosensitized oxidation reactions. Because of varied notions of reactions mediated by photosensitizers, a checklist of recommendations is provided for their definitions. Type I and type II photoreactions are oxygen-dependent and involve unstable species such as the initial formation of radical cation or neutral radicals from the substrates and/or singlet oxygen ($^1O_2$ $^1\Delta g$) by energy transfer to molecular oxygen. In addition, superoxide anion radical ($O_2^{\bullet-}$) can be generated by a charge transfer reaction involving O_2 or more likely indirectly as the result of O_2-mediated oxidation of the radical anion of type I photosensitizers. In subsequent reactions, $O_2^{\bullet-}$ may add and/or reduce a few highly oxidizing radicals that arise from the deprotonation of the radical cations of key biological targets. $O_2^{\bullet-}$ can also undergo dismutation into H_2O_2, the precursor of the highly reactive hydroxyl radical ($^\bullet OH$) that may induce delayed oxidation reactions in cells. In the second part several examples of type I and type II photosensitized oxidation reactions are provided to illustrate the complexity and the diversity of the degradation pathways of mostly relevant biomolecules upon one-electron oxidation and singlet oxygen reactions.

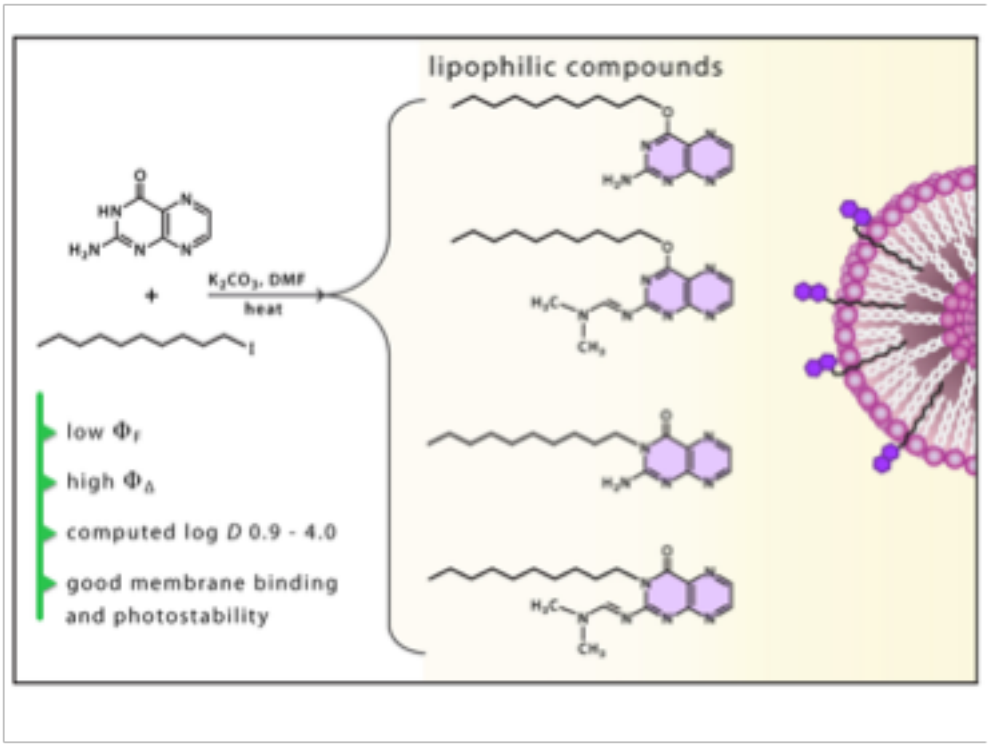
Decyl chain-pterin conjugates with lipophilic sensitizer properties

*Mariana Vignoni[1,2] Niluksha Walalawela[2,3] Sergio M. Bonesi[4] **Alexander Greer**[2,3] Andrés H. Thomas[1]*

1 Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas (INIFTA), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata (UNLP), CCT La Plata-CONICET, Casilla de Correo 16, Sucursal 4, (1900) La Plata, Argentina
2 Department of Chemistry, Brooklyn College, City University of New York, Brooklyn, New York 11210, United States
3 Ph.D. Program in Chemistry, The Graduate Center of the City University of New York, 365 Fifth Avenue, New York, New York 10016, United States
4 CIHIDECAR - CONICET, Departamento de Química Orgánica, FCEyN, Universidad de Buenos Aires, Pabellón 2, 3er Piso, Ciudad Universitaria, Buenos Aires, Argentina

E-mails: agreer@brooklyn.cuny.edu, and athomas@inifta.unlp.edu.ar

ABSTRACT
A new series of decyl chain [–(CH2)9CH3] pterin conjugates have been investigated by photochemical and photophysical methods, and with theoretical solubility calculations. To prepare the pterin products, a nucleophilic substitution (SN2) reaction was developed for the regioselective coupling of the alkyl chain to the O site over the N3 site. However, the O-alkylated pterin converts to N3-alkylated pterin under basic conditions, pointing to a kinetic product in the former and a thermodynamic product in the latter. Two additional adducts were also obtained from an N-amine condensation of DMF solvent molecule as by products. Comparison to natural pterins shows further utility of the new pterins, they had reduced fluorescence quantum yields (ΦF) due to deactivation of the singlet-excited state, and increased singlet oxygen quantum yields (ΦΔ). It is shown that the DMF condensed pterins were more photostable compared to the N3- and O-alkylated pterins bearing amine groups. The new pterins efficiently intercalate in large unilamellar vesicles, which is a good indicator of their potential use in biomembranes. Our study serves as a starting point where the synthesis can be expanded to produce novel lipophilic, photooxidatively active pterins.



Mechanistic role of excited states in photodamage: nucleic acids as a target

Jean Cadet
Département de médecine nucléaire et radiobiologie, Faculté de médecine et des sciences de la santé, Université de Sherbrooke, Sherbrooke, Québec, Canada J1H 5N4

Email: jean.cadet@usherbrooke.ca

ABSTRACT
DNA is the main cellular target of UVB photons and to a lesser extent of both the direct and sensitized effects of overwhelming UVA radiation. Major progress has been achieved in the last two decades on the experimental and computational assessment of photophysical features of pyrimidine and purine nucleobases thus providing suitable relevant information on the excited species involved in solar UV radiation induced damage to DNA. This has been complemented by the accurate measurement of the main DNA photoproducts in cells and human skin using quantitative HPLC analysis coupled with tandem mass spectrometry detection. They consist of three main classes of bipyrimidine lesions including cyclobutane pyrimidine dimers (CPDs), pyrimidine (6-4) pyrimidone photoproducts (6-4PPs) and their Dewar valence isomers (DEWs) together with oxidatively generated base modifications and DNA single strand breaks (SSBs). The UVB-induced formation of CPDs in DNA is mostly accounted for by a [2+2] photocycloaddition reaction. The formation of CPDs in TT tracts is a fast event that proceeds via $1\pi\pi^*$ excitons along a barrierless path. The mechanism of formation of 6-4PPs that involves a Paternó-Büchi cycloaddition pathway has been revisited. Thus it is now proposed that TT 6-4PP is generated via an oxetane intermediate through an excited charge transfer state with a significant energy barrier. The photoisomerization of 6-4PPs into related DEWs that involves an. electrocyclization reaction occurs significantly in DNA upon solar radiation exposure due to the predominant contribution of UVA photons. Interestingly evidence has been provided that CPDs are exclusively generated through direct interaction of UVA radiation with both isolated and cellular DNA. This is rationalized in terms of a charge transfer mechanism upon excitation of pyrimidine bases; however UVA photons are not enough energetic to promote the formation of 6-4PPs. It was recently shown that formation of CPDs is induced post UVB or UVA irradiation in melanocytes as a result of chemiexcitation. In addition photosensitized reactions mostly initiated by UVA radiation are able to damage DNA, mostly through the generation of singlet oxygen ($^1O_2$) formed by energy transfer from triplet excited endogenous sensitizers to molecular oxygen, the so-called “type II photosensitization mechanism”. The exclusive DNA $^1O_2$ oxidation product has been identified as 8-oxo-7,8-dihydroguanine. In addition oxidized pyrimidine bases and SSBs that arise from hydroxyl radical-mediated reactions are generated in low amounts as indirect effects of type I photosensitization mechanism.

Molecular actors in multiple roles: photodynamic and receptor-directed activities of endogenous photosensitizers in skin photodamage

Rebecca Justiniano, Jessica Perer, and ***Georg T. Wondrak***

Department of Pharmacology and Toxicology, College of Pharmacy and The University of Arizona Cancer Center, University of Arizona, Tucson, AZ 85724, USA

Email: wondrak@pharmacy.arizona.edu

ABSTRACT

Endogenous chromophores in human skin may serve as photosensitizers involved in skin photocarcinogenesis and photoaging. Absorption of solar photons, particularly in the UVA region, induces the formation of excited states of skin photosensitizers with subsequent generation of reactive oxygen species (ROS), organic free radicals, and other toxic photoproducts that might mediate skin photooxidative stress. It is now appreciated that structurally diverse cutaneous sensitizer chromophores may participate in photodamage as molecular actors in multiple roles beyond photodynamic activity. Recently, we have shown that the tryptophan-derivative 6-formylindolo[3,2-b]carbazole (FICZ), formed as a UVB-photoproduct and commensal microbial metabolite in human skin, displays activity as a nanomolar photosensitizer potentiating UVA- and visible light-induced oxidative stress and apoptogenicity in human primary epidermal keratinocytes, reconstructed epidermis and mouse skin. This photodynamic action of FICZ seems to synergize with its independent role as a high affinity ligand targeting the aryl hydrocarbon (dioxin) receptor (AhR) upstream of CYP1A1-dependent carcinogen activation. Likewise, we have identified the lipid peroxidation-derived malondialdehyde-protein adduct dihydropyridine (DHP)-lysine [(S)-2-amino-6-(3,5-diformyl-4-methyl-4H-pyridin-1-yl)-hexanoic acid] as a potent UVA-sensitizer in human skin that accumulates in response to acute UV exposure and during tumorigenic progression to squamous cell carcinoma (SCC). Strikingly, DHP [together with other cutaneous advanced glyoxidation-derived protein epitopes including CML (Nε-carboxymethyl-L-lysine)] displays activity as a potent RAGE (receptor for advanced glycation endproducts)-ligand, involved in inflammatory dysregulation and cutaneous tumorigenesis, suggesting a potential mechanistic overlap between DHP-photosensitizer and DHP-RAGE activities. Future research will determine the relative pathological impact of photodynamic versus receptor-directed activities of skin photosensitizer-chromophores on aging, inflammatory dysregulation, and carcinogenesis.

Ultraviolet A-induced oxidation in cornea: characterization of the early oxidation-related events

Patrick J Rochette[1,2,3] *and Corinne Zinflou*[1,2]

1 Axe Médecine Régénératrice, Centre de Recherche du CHU de Québec – Université Laval, Hôpital du Saint-Sacrement, Québec, Qc, Canada
2 Centre de Recherche en Organogénèse Expérimentale de l'Université Laval/LOEX, Université Laval, Québec, Qc, Canada.
3 Département d'Ophtalmologie et ORL - chirurgie cervico-faciale, Université Laval, Québec, Qc, Canada.

Email: patrick.rochette@orlo.ulaval.ca

ABSTRACT
Exposure to sunlight ultraviolet-A (UVA), the main component of solar UV reaching the eyes, is suspected to play an important part in the onset of ocular pathologies. UVA primary biological deleterious effects arise from the photo-induction of oxidative stress in cells. However, the molecular bases linking UVA-induced oxidation to UVA toxicity in eyes remain poorly understood, especially with regards to the cornea. To shed some light on this issue, we have investigated the susceptibility and response potential of the different corneal cellular layers (epithelium, stroma and endothelium) to UVA-induced oxidation. We have monitored UVA-induced immediate effects on cellular redox balance, on mitochondrial membrane potential, on 8-Hydroxy-2'-deoxyguanosine (8-OHdG) accumulation in cellular DNA and on S-glutathionylated proteins (PSSG) levels along whole rabbit corneas. Higher redox imbalance was observed in the posterior part of the cornea following irradiation. Conversely, UVA-altered mitochondrial membrane potentials were observed only in anterior portions of the cornea. UVA-induced 8-OHdG were found in nuclear DNA of epithelia, while they were found in both nuclear and mitochondrial DNA in stromal and endothelial cells. Finally, significantly higher levels of cytosolic PSSG were measured in epithelia and endothelia immediately after UVA exposure, but not in stromas. Taken together, our findings indicate that while corneal epithelial cells are subjected to important modifications in response to UVA exposure, they efficiently limit the early manifestations of UVA-induced toxicity. On the other hand, the corneal endothelium is more susceptible to UVA-induced oxidation-related toxicity.

Chemiexcitation in Mammalian Cells: Beyond UV and Melanin

Sanjay Premi[1], Leticia C. P. Goncalves[1], and ***Douglas E. Brash***[1,2]

Depts. 1Therapeutic Radiology and 2Dermatology, Yale School of Medicine

Email: douglas.brash@yale.edu

ABSTRACT

Mutations in sunlight-induced melanoma arise from cyclobutane pyrimidine dimers (CPDs), DNA photoproducts at thymine or cytosine usually created picoseconds after an ultraviolet (UV) photon is absorbed. In melanocytes, however, CPDs were generated for hours after UVA or UVB exposure. These "dark CPDs" constituted the majority of CPDs in cultured human and murine melanocytes and in mouse skin, and they were most prominent in skin containing pheomelanin, the melanin responsible for blonde and red hair.

The mechanism was discovered to be chemiexcitation – chemical excitation of an electron – a process familiar in fireflies and jellyfish but unknown in mammals. Dark CPDs arose when UV-induced superoxide and nitric oxide combined to form peroxynitrite, one of the few biological molecules capable of exciting an electron. Excitation occurred in fragments of melanin, creating a quantum triplet state that had the energy of a UV photon but induced CPDs by radiationless energy transfer to DNA. UVA and peroxynitrite also solubilized melanin and permeabilized the nuclear membrane, allowing melanin to enter. Melanin is evidently carcinogenic as well as protective. These findings may underlie the dependence of UV-induced and spontaneous skin cancers on melanin type, and they validate the long-standing suggestion that chemical generation of excited electronic states is important in mammalian biology.

Chemiexcitation should also occur in internal tissues because superoxide and nitric oxide arise during inflammation and ischemia-reperfusion injury, melanin is present in the eye and cochlea, and neuromelanin is present in regions of the brain that die in neurodegenerative diseases such as Parkinson's, Alzheimer's, and Down Syndrome. A Banbury Conference on Chemiexcitation in Human Disease was recently held at Cold Spring Harbor Laboratory, and the conference's assessment of the prospects, challenges, and goals of the new field of human excited-state biology will be summarized.

Autophagy in UV-induced inflammation and tumorigenesis

Lei Qiang[1], Ashley Sample[1], Christopher R. Shea[1], Keyoumars Soltani[1], Kay F. Macleod[2], and ***Yu-Ying He***[1]

1Department of Medicine, Section of Dermatology, 2The Ben May Department of Cancer Research, University of Chicago

Email: yyhe@medicine.bsd.uchicago.edu

ABSTRACT

Skin cancer is the most common cancer in the US. The incidence of skin cancer continues to rise at an alarming rate annually. Exposure to ultraviolet B radiation (UVB, 280-315 nm) from the sun is the major environmental risk factor for skin cancer. UV radiation causes DNA damage and lead to accumulation of oncogenic mutations. In addition, UV also damages self noncoding RNA to mediate acute the inflammatory response, collectively known as sunburn. In humans, sunburn sensitivity is positively associated with increased risk of skin cancer including both non-melanoma skin cancer and melanoma. However, the mechanism in regulating UV-induced inflammation is not well understood. Here we show the regulation of UV-induced inflammation and skin tumorigenesis by autophagy at the molecular, cellular, and organismal levels.

Molecular targets for skin cancer prevention

Zigang Dong

The Hormel Institute, University of Minnesota, 801 16th Ave NE, Austin, MN, U.S.

Email: zgdong@hi.umn.edu

ABSTRACT

Despite the intensive efforts and substantial advances that have occurred through focusing on improving treatment, cancer is still a leading cause of death worldwide. Many have argued that this could be avoided by focusing on cancer prevention, which has now entered the arena of targeted therapies. During the process of identifying preventive agents, dietary phytochemicals have emerged as modulators of key cellular pathways. By molecular modeling of the interactions of targeted proteins with these chemopreventive agents, we have provided knowledge for a better understanding of how these preventive agents work. Such knowledge will help the translation to new clinical practice of preventive medicine. We have studied and identified UV-induced signal transduction in skin carcinogenesis and identified signal transduction pathways (MAP kinases, S6 kinases) and transcriptional factors (AP-1, NF- κ B, NFAT, p53) as targets for prevention and therapy of skin cancer. We have identified tea polyphenols, resveratrol, aspirin, retinoids, myo-inositol, inositol hexaphosphate, and other natural compounds as chemopreventive agents for skin cancer.

Translationally-relevant PDT combinations: mechanisms for overcoming molecular and cellular resistance and enhancing the tumoricidal durability of chemotherapeutics

***Imran Rizvi**, Huang-Chiao Huang, Sriram Anbil, Shubhankar Nath, Joyce Liu, Emma Briars, Anne-Laure Bulin, Mans Broekgaarden, Michael Pigula, and Tayyaba Hasan*

Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA USA

Email: rizvi.imran@mgh.harvard.edu

ABSTRACT
Treatment resistance in cancer results in part from the underlying genetic and molecular diversity of cancer cells as well as the unrelenting ability of tumors to adapt to their environment. Targeting these adaptive mechanisms requires an understanding of the cellular and microenvironmental factors that modulate growth and allow cancer cells to survive under adverse conditions. The informed design of mechanism-based combinations is an increasingly important approach to effectively treat unresponsive populations of stubborn disease. The design of targeted photodynamic therapy (PDT)-based combinations is informed by the ability of PDT, a biophysical modality, to reverse chemoresistance, synergize with chemotherapeutics and biologics, and overcome compensatory survival pathways. PDT cooperates mechanistically with, and improves the efficacy of, traditional and emerging agents, while minimizing dose limiting toxicities. Improving the therapeutic index of conventional treatments is among the key reasons for including PDT as part of comprehensive management plans for cancer, particularly in complex disease sites. The role of PDT in overcoming resistance mechanisms, improving the efficacy and predictability of chemo- and targeted therapeutics, and enhancing the durability of outcomes in bioengineered and clinically relevant in vivo tumor models will be discussed.

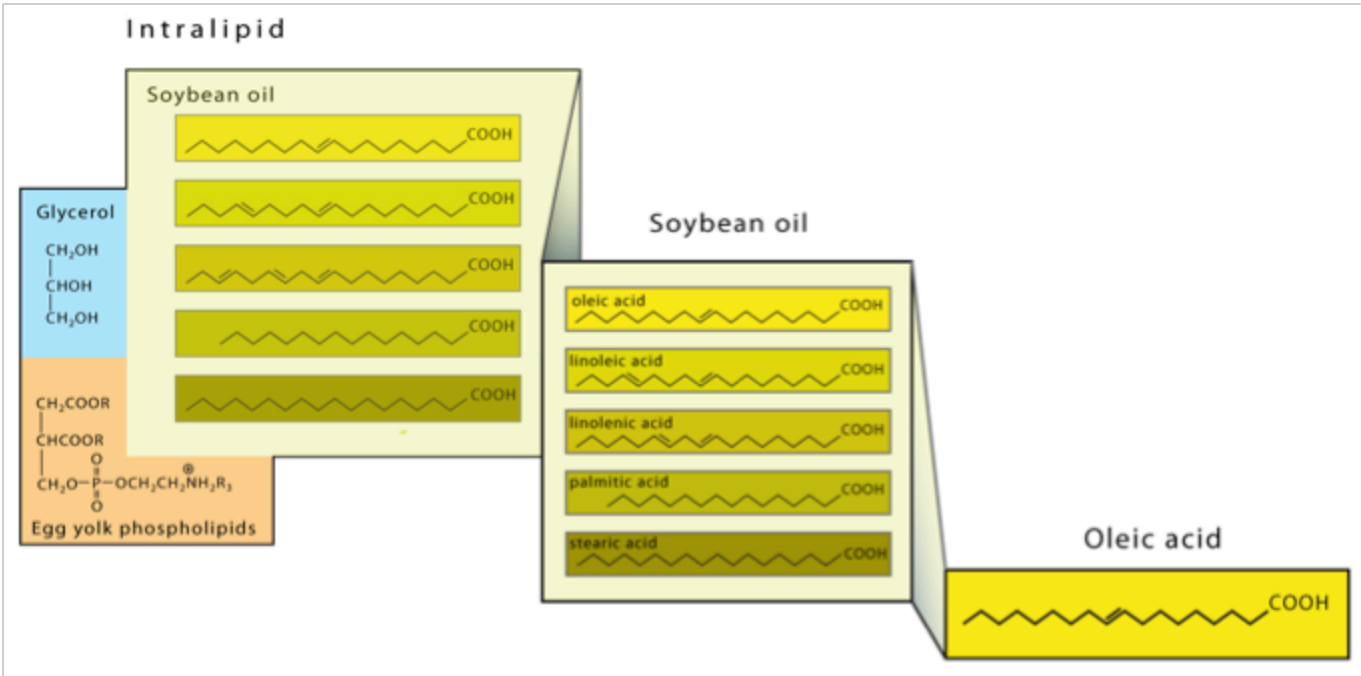
Intralipid Reaction with Singlet Oxygen: Relevance to Pleural Photodynamic Therapy

Prabhu Mohapatra[1,2] Callistus Chiemezie[1] Arina Kligman[1,2] Michele M. Kim[3,4] Timothy C. Zhu[3] and ***Alexander Greer***[1,2]

1 Department of Chemistry, Graduate Center, City University of New York, Brooklyn College. Brooklyn, New York 11210, United States.
2 Ph.D. Program in Chemistry, The Graduate Center of the City University of New York, 365 Fifth Avenue, New York, New York 10016, United States
3 Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA
4 Department of Physics and Astronomy, University of Pennsylvania, Philadelphia, PA

Email: agreer@brooklyn.cuny.edu

ABSTRACT
The reaction of singlet oxygen (1O2) with alkenes has been of interest, in which oxidation products arise. Despite many studies of 1O2 with alkenes, information is lacking on 1O2 reactions with intralipid®, a lipid emulsion used to help propagate light such as PDT in the pleural cavity, as light scattering media. Intralipid fluid is a 20% intravenous fat emulsion consisting of soybean oil (10%), and minor amounts of egg yolk phospholipids and glycerin. The soybean oil is linoleic acid, oleic acid, palimitic acid, linolenic acid. A recent study by Gemmell, et al. (J. Biophotonics 2017, 10, 320-326) has determined a decrease of 1O2 luminescence in intralipid fluid due to 1O2 quenching, other de-excitation pathways and/or diffusion of excitation and 1270 nm light. Deducing the compensation for the chemical removal of 1O2 by intralipid is important in quantitating singlet oxygen luminescence dosimetry (SOLD) measurements. Thus, we describe a study of the reaction of 1O2 with intralipid, and with model reagents soybean oil, and oleic acid. The peroxide products in the reactions were examined by a water-soluble phosphine trap (2'-dicyclohexylphosphino-2,6-dimethoxy-1,1'-biphenyl-3-sulfonate ion), and 1H and 31P NMR spectroscopy. The total quenching rate constant (kT) of 1O2 with intralipid will be measured.



Antimicrobial photodynamic therapy

Thomas S Mang PhD

Department of Oral and Maxillofacial Surgery, University at Buffalo, School of Dental Medicine, Buffalo, NY 14214

Email: tsmang@buffalo.edu

ABSTRACT

Antibiotic resistance continues to be a major healthcare concern and it is clear that this problem is reaching a critical stage worldwide. Significant levels of antibiotic resistance have been identified in a multitude of various pathogens including Methicillin-resistant Staphylococcus aureus (MRSA) common respiratory pathogens such as Streptococcus pneumoniae and Mycobacterium tuberculosis; and numerous multi-drug resistant Gram-negative bacteria such as Pseudomonas aeruginos, Escherichia coli, Klebsiella pneumoniae, and Acinetobacter baumannii among many others. Given the magnitude of this problem and the overall effect on morbidity and mortality, multidrug resistant organisms are a significant threat to the public healthcare system in this country as well as to those systems around the globe. Using various photosensitizers, multiple investigators have demonstrated that PDT can be used to inactivate some Gram-positive bacteria but are generally ineffective versus Gram-negative bacteria. Critical in the investigation of cell killing will not only be the ability of aPDT to inactivate the bacteria but the capability of the modality to destroy the biofilm in which they flourish. Results of studies conducted demonstrate that the ability to kill bacteria either in planktonic or biofilm cultures is dependent on multiple factors, which may include cell wall components, photosensitizer, and the substrata upon which the biofilm is grown. Multiple attenuated internal reflection infrared spectroscopy provides data demonstrating the level of loss of exopolysaccharides and amides suggesting induced biofilm fragmentation in aPDT treated biofilms corresponding with colony forming unit (CFU) assays demonstrating cell kill of greater than 3 logs. The demonstration of cell kill with biofilm destruction demonstrate that aPDT has the potential for use in the treatment of biofilm related infection in humans and suggests this technology warrants further analysis as a potential novel antimicrobial treatment.

Oxygen sensing phosphors – translation from the chemical hood to clinical application

Conor L. Evans, PhD

Harvard Medical School, Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA

Email: Evans.Conor@mgh.harvard.edu

ABSTRACT

Oxygen is critical for tissue survival and wound healing. The knowledge of tissue oxygenation and tissue oxygen consumption is critical for a host of applications, including in the management of burns, skin grafts and tissue transplants. However, the majority of clinical tools for measuring tissue oxygenation are complex, difficult to use, and require significant training. Portable and simple-to-use oxygen sensing tools are needed that allow for the non-disruptive, continuous monitoring of oxygenation across large areas of skin and wounds to guide care and therapeutic decisions. We have been working to develop a bandage that displays a map of tissue oxygenation that can be seen by eye and captured on a smartphone camera. This bandage has been tested in mouse and swine models of ischemia-reperfusion injury, full-thickness burns, skin grafting, and severe tissue inflammation and is now entering first-in-man clinical trials.

Toward clinical translation of physiologic monitoring for personalization of PDT

Theresa M. Busch, Department of Radiation Oncology,

University of Pennsylvania, Philadelphia PA

Email: buschtm@mail.med.upenn.edu

ABSTRACT

The cytotoxic action of photodynamic therapy (PDT) with many photosensitizers depends on the presence of molecular oxygen. Consequently, tumor physiologic properties such as oxygenation and blood flow can determine the efficacy of treatment. It is well established in animal models that PDT-induced changes in tumor oxygenation and blood flow will correlate with short and long-term treatment outcome. However, few have reported on clinical studies that investigate if physiologic properties of human tumors can associate with PDT outcome. We have investigated the association between lesion oxygenation and PDT outcome in patients treated on a Phase 1 trial of PDT with aminolevulinc acid (ALA) for high-grade dysplasia, carcinoma-in-situ, or early microinvasive squamous cell carcinoma of the head and neck. Results suggest that measurement of the physiologic properties of previously unresected lesions may play a role in identifying patients with the highest probability of benefiting from PDT. Together with pre-clinical data, these results support efforts toward developing real-time PDT dosimetry that adjusts illumination parameters during light delivery as a function of measured physiologic changes in the tumor microenvironment.

Symposium Participants

Douglas E. Brash; Department Therapeutic Radiology; Dermatology, Yale School of Medicine
Email: douglas.brash@yale.edu

Theresa M. Busch; Department of Radiation Oncology, University of Pennsylvania
Email: buschtm@mail.med.upenn.edu

Jean Cadet; Département de Médecine Nucléaire et de Radiobiologie, Université de Sherbrooke, Canada
Email: jean.cadet@usherbrooke.ca

Keith Cengel; University of Pennsylvania
Email: CengelASP@gmail.com

Jeff Cohen; AIRx Medical, Inc
Email: jcohen@airxmedical.com

Keith Cengel; Penn Radiation Oncology
Email: cengel@mail.med.upenn.edu

Zigang Dong; The Hormel Institute, University of Minnesota,
Email: zgdong@hi.umn.edu

Conor L. Evans, PhD; Harvard Medical School, Wellman Center for Photomedicine, Massachusetts General Hospital
Email: Evans.Conor@mgh.harvard.edu

Alexander Greer; Department of Chemistry, Brooklyn College, The Graduate Center of the City University of New York
Email: agreer@brooklyn.cuny.edu

Tayyaba Hasan; Wellman Center for Photomedicine, Massachusetts General Hospital, Harvard Medical School, Boston, MA USA
Email: thasan@mgh.harvard.edu

Yu-Ying He; Department of Medicine, Section of Dermatology; The Ben May Department of Cancer Research, University of Chicago
Email: yyhe@medicine.bsd.uchicago.edu

Derick Jones; University North Carolina, Greensboro
Email: ddjones4@uncg.edu

Thomas S Mang PhD; Bayer Consumer Health
Email: tsmang@buffalo.edu

Thomas Meyer; Department of Oral and Maxillofacial Surgery, University at Buffalo, School of Dental Medicine
Email: thomas.meyer3@bayer.com

Jessica Perer; University of Arizona Cancer Center
Email: jperer@email.arizona.edu

Rebecca Persinger; AirX Medical
Email: rpersinger@airxmedical.com

Imran Rizvi; Wellman Center, MGH, HMS
Email: rizvi.imran@mgh.harvard.edu

Patrick J Rochette; Axe Médecine Régénératrice, Centre de Recherche du CHU de Québec – Université Laval, Hôpital du Saint-Sacrement, Canada; Centre de Recherche en Organogénèse Expérimentale de l'Université Laval/LOEX, Université Laval, Canada; Département d'Ophtalmologie et ORL - chirurgie cervico-faciale, Université Laval, Canada
Email: patrick.rochette@orlo.ulaval.ca

Georg T. Wondrak; Department of Pharmacology and Toxicology, College of Pharmacy and The University of Arizona Cancer Center, University of Arizona
Email: wondrak@pharmacy.arizona.edu

American Society for Photobiology
1313 Dolley Madison Boulevard, Suite 402, McLean, Virginia 22101
703-790-1745
http://photobiology.org/