## 2019ASP

 Presidential Evening Symposia May 9-10, 2019 | Chicago, IL I Inn of Chicago

Photochemistry and Photobiology: From Molecules to Medicine

> Welcome to Chicago, IL for the 2019 ASP Presidential Evening Symposia: 'Photochemistry and Photobiology: From Molecules to Medicine'

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, May 9, 2019, evening): ‘Molecular photodamage response in tissues and organisms'
This symposium examines the molecular basis for photodamage response to the skin and the eye of mammals, as well as other organisms.

Symposium II (Friday, May 10, 2019, evening): 'Mechanisms in photochemistry and photobiology: From synthetic and energy applications to materials and photomedicine' This symposium presents research in photochemistry and photobiology using laser spectroscopic and other experimental methods. The results of new photoreactions and photocatalysts will be described.

We are looking forward to an exciting ASP focus meeting.

With our warmest regards,

Yu-Ying He, The University of Chicago, ASP President
Georg T. Wondrak, University of Arizona, ASP Past President Alec Greer, CUNY Brooklyn College, ASP President Elect
Theresa M. Busch, University of Pennsylvania, ASP Treasurer

ASP Secretariat
Headquarters@photobiology.org

# Symposium I (Thursday, May 9, 2019, evening) <br> 'Molecular photodamage response in tissues and organisms' <br> Co-hosted by Yu-Ying He and Georg Wondrak <br> 6.30-10.00pm, Buckingham Room 

6.30-7.00 pm - Evening reception with refreshments 'grab your dinner'
7.00-7.15 pm

1. Recent research in diseases of DNA Repair: xeroderma pigmentosum and trichothiodystrophy Ken Kraemer; National Cancer Institute (NCI)
7.15-7.30 pm
2. Differential requirement of TGF-beta1/Smad pathway in Langerhans-cell commitment at steady state and UVinduced inflammatory state
Qing-Sheng Mi; Henry Ford Health System/Wayne State University
$7.30-7.45 \mathrm{pm}$
3. Dynamic Crystallography Studies of Light-dependent DNA Repair

Xiaojing Yang; University of Illinois at Chicago
7.45-8.00 pm - Refreshment Break
$8.00-8.15 \mathrm{pm}$
4. Chemoprevention of ultraviolet-B radiation mediated skin carcinogenesis by dietary grape in SHK-1 hairless mice Nihal Ahmad; University of Wisconsin at Madison
$8.15-8.30 \mathrm{pm}$
5. UPR-independent Activation of PERK Post-UVB Exposure

Shiyong Wu; Ohio University
$8.30-8.45 \mathrm{pm}$
6. Does melanin modulate RPE immune response under photic stress?

Beth Gaillard; Northern Illinois University
$8.45-9.00 \mathrm{pm}$
7. UV-induced Replication Blockage and ATR Activation are Mediated by 6-4 Photoproducts

Masaoki Kawasumi; University of Washington
$9.00-9.15 \mathrm{pm}$
8. Sharpening the Double-edged Redox-sword Targeting Skin Photodamage and Cancer: From NRF2-directed Antioxidant Photochemoprevention to Oncogene-directed Prooxidant Chemotherapy
Georg Wondrak; University of Arizona
$9.15-9.30 \mathrm{pm}$
9. Molecular Underpinnings of Cellular Signaling Interception by Blue-light-sensitized-retinal

Ajith Karunarathne; University of Toledo
$9.30-9.45 \mathrm{pm}$
10. Autophagy Pathways in UVB Damage Response and Tumorigenesis

Yu-Ying He; University of Chicago

# Symposium II (Friday, May 10, 2019, evening) <br> 'Mechanisms in photochemistry and photobiology: From synthetic and energy <br> applications to materials and photomedicine' <br> Co-hosted by Alec Greer and Andres Thomas <br> $6.30-10.00 \mathrm{pm}$, Buckingham Room 

6.30-7.00 pm - Evening reception with dinner buffet
7.00-7.15 pm

1. Tailoring Non-linear Photophysical Processes for Biomedical Applications
A. Jean-Luc Ayitou; Illinois Institute of Technology
7.15-7.30 pm
2. Metal Complex Photosensitizers for Photodynamic Therapy

Sherri McFarland; University of North Carolina, Greensboro
$7.30-7.45 \mathrm{pm}$
3. Oxidation of Plasmalogens within Cellular Membranes by Photodeoxygenation.

Ryan McCulla; St Louis University
7.45-8.00 pm - Refreshment Break
8.00-8.15 pm
4. Photochemistry of Nucleic Acid Derivatives and Their Photodynamic Efficacy Against Human Epidermoid Carcinoma Cells
Carlos Crespo-Hernandez; Case Western Reserve University
$8.15-8.30 \mathrm{pm}$
5. Ultrafast [2 + 2] Cycloaddition Reaction Upon Photoactivation of 4-Thiothymidine in Single-Stranded DNA Luis A. Ortiz-Rodríguez; Case Western Reserve University
$8.30-8.45$ pm
6. Developing Ir(III) Complexes as Potential Theranostic Photodynamic Therapy Agents

Wenfang Sun; North Dakota State University
$8.45-9.00$ pm
7. Photocatalytic Degradation of Furosemide and Identification of Carboxylic Acid Derivatives using GC-MS with HSTrap
Erik Menjivar; Mount St. Mary's University
9.00-9.15 pm
8. Photochemistry of Tyrosine Dimer: When an Oxidative Lesion of Proteins is able to Photoinduce Further Damage Andres Thomas; University of La Plata, CONICET
$9.15-9.45 \mathrm{pm}$
9. Conformation Dependent Dual Function of a 1,2-Diketone for Sensitized Photooxidation and Thermal Binding Alexander Greer; CUNY Brooklyn College

# Symposium I Abstracts <br> 'Molecular photodamage response in tissues and organisms' 

## 3. Dynamic Crystallography Studies of Light-dependent DNA Repair

Zhong Ren ${ }^{a}$, Fan Zhang ${ }^{c}$, Cong Wang ${ }^{a}$, Heewhan Shin ${ }^{a}$, Weijia Kang ${ }^{a}$, Semini Gunawardana ${ }^{a}$, Kalinga Bowata ${ }^{a}$, Tilman Lamparter ${ }^{c}$ and Xiaojing Yang ${ }^{a, b}$
Department of Chemistry, The University of Illinois at Chicago, Chicago, IL 60607, USA; Department of Ophthalmology and Vision Sciences, The University of Illinois at Chicago, Chicago, IL 60607, USA; Botanical Institute, Karlsruhe Institute of Technology, Germany

DNA photolyases utilize blue light energy to repair the DNA lesions damaged by ultraviolet irradiation. These light-dependent DNA repair enzymes bind flavin adenine dinucleotide (FAD) as a catalytic pigment. Upon photo-reduction, the reduced FAD transfers the excessive electron to the exposed DNA lesion site, which breaks the covalent bond in the pyrimidine photoproducts thereby repairing the damaged DNA. Although the electron transfer reaction has been well studied by structural and ultrafast spectroscopy methods, how these DNA repair enzymes are regulated at the molecular level is much less understood. In this presentation, I will talk about how we apply dynamic crystallography and single-crystal spectroscopy to interrogate a newly characterized 6-4 DNA photolyase, which features an additional redox co-factor iron-sulfur [4Fe4S] cluster. We have captured strong lightinduced structural changes associated with the [4Fe4S] cluster and adjacent secondary structures in the photoactive crystals. These crystallography observations provide the direct structural evidence in support of an emerging notion that the [4Fe4S] cluster plays a regulatory role as a redox switch in DNA processing enzymes including DNA photolyases.

## 4. Chemoprevention of ultraviolet-B radiation mediated skin carcinogenesis by dietary grape in SHK-1 hairless mice

Nihal Ahmad
Department of Dermatology, University of Wisconsin, Madison, WI
Solar ultraviolet (UV) radiation, particularly in the UVB radiation range ( $290-320 \mathrm{~nm}$ ) is an established cause of non-melanoma skin cancers (NMSCs). Existing prevention approaches and therapies have not been fully effective in the management of NMSCs. We assessed the efficacy of dietary grape powder (containing resveratrol and other grape antioxidants, in a natural combination) against UVBmediated skin tumorigenesis in SKH-1 hairless mice. Employing a UVB initiation-promotion protocol, mice were subjected to chronic UVB exposure ( $180 \mathrm{~mJ} / \mathrm{cm}^{2}$; twice weekly, for 28 weeks) while receiving control or grape powder (GP)-fortified AIN-76A diet ( $3 \%$ and $5 \%$ GP). Our data demonstrated that consumption of GP resulted in a marked inhibition in tumor incidence, as well as a delay in onset of tumorigenesis. Both doses of GP were well tolerated without any adverse health effects. Molecular analyses of skin and tumor tissue showed that GP-mediated protective response against UVB-induced skin cancer was accompanied by enhanced DNA damage repair, reduced proliferation, enhanced apoptosis, and modulations in several oxidative stress markers. Further, a large-scale proteomics analysis was performed to determine protein targets affected by GP. We uncovered the antiinflammatory effects of dietary grape through the reduction of acute phase response signaling and upstream regulators, NF-KB and ERK1/2. Overall, our study suggested that dietary grape, containing several antioxidants in natural amalgamation, may protect against UVB-mediated skin carcinogenesis. Our data are relevant to human situations, since the human equivalent dose for $3 \% \mathrm{GP}$ is $\sim 25 \mathrm{~g}$ GP, or $\sim 1$ serving of fresh grapes, which is easily achievable for human consumption. Further epidemiological and clinical studies are required to ascertain the human-relevance of our study.

## Symposium I Abstracts

## 5. UPR-independent Activation of PERK Post-UVB Exposure

Lingying Tong ${ }^{1}$, Veronica Bahamondes Lorca ${ }^{1,2}$ and Shiyong Wu ${ }^{1,2}$
${ }^{1}$ Edison Biotechnology Institute; ${ }^{2}$ the Department of Chemistry and Biochemistry, Ohio University, Athens, OH 45701 (wus1@ohio.edu)

Ultraviolet B-light (UVB) inhibits protein synthesis by inducing the phosphorylation of the alpha subunit of eukaryotic initiation factor 2 (elF2 $\alpha$ ) via activating two elF2 $\alpha$ kinases, protein kinase-like endoplasmic reticulum kinase (PERK) and general control of nonderepressible protein kinase 2 (GCN2). The constitutive nitric oxide synthase (CNOS) is responsible for mediating the activation of both PERK and GCN2 post-UVB irradiation. Supplement of L-Arg (the substrate of cNOS) or treatment of L-NAC (a scavenger of ROS and RNS), could partially inhibit UVB-induced elF2 $\alpha$ phosphorylation suggesting GCN2 or PERK catalyzed the phosphorylation respectively. While the GCN2 is activated by L-Arg depletion, the PERK activation was assumed to be activated by unfolded protein response (UPR) that was caused by ROS and RNS. However, our recent data indicated that UVB does not induce the splicing of Xbp-1 mRNA, an indicator of the activation of UPR pathways. In addition, UVB did not induce a hyperphosphorylation of PERK as the UPR inducer tunicamycin did. Instead, PERK appears to be aggregated on endoplasmic reticulum (ER)-membrane post-UVB. These results suggest that UVBinduced PERK activation might be regulated via a unique mechanism that is independent of UPR, but dependent on membrane lipid-mediated PERK aggregation.

## Symposium I Abstracts

6. Does melanin modulate RPE immune response under photic stress?<br>Prajkta Chivte, Sally Yacout, Elizabeth R. Gaillard<br>Northern Illinois University


#### Abstract

It is widely accepted that RPE melanin has a protective effect against oxidative and photooxidative damage in RPE cells. It is possible that an additional protective characteristic of melanin is the ability to modulate RPE cell immune response. In this study, the relationship between RPE pigmentation and immune response after exposure to UVB is investigated by monitoring IL-6 secretion. The RPE cells are grown on RPE-derived extracellular matrix that has been chemically modified by glycation to simulate age related changes to the native basement membrane. The cells are then left unpigmented or are pigmented with either calf or human melanin or black latex beads. IL-6 secretion is determined using an ELISA at 6 hours after UVB irradiation. The results will be compared to our previous study where a significant decrease in IL-6 expression was observed in calf melanin pigmented cells 24 hours after seeding on to glycated ECM. These populations showed a significant increase in attachment compared to unpigmented controls on either no ECM or unmodified ECM. These findings suggest that melanin in the RPE may participate in immune-response modulation in the retina with particular regard to cell attachment to protein substrates and photooxidative stress. The results of this study further implicate the role of age-related chemical changes to melanin in regulating inflammation in retinal disease.


## Symposium I Abstracts

7. UV-induced replication blockage and ATR activation are mediated by 6-4 photoproducts

Kai-Feng Hung ${ }^{1,2, t}$, Julia M. Sidorova³, Paul Nghiem ${ }^{1,4}$, and Masaoki Kawasumi ${ }^{1, *}$
${ }^{1}$ Division of Dermatology, Department of Medicine, University of Washington, Seattle, WA 98109, USA; ${ }^{2}$ Department of Oral Health Sciences, University of Washington, Seattle, WA 98195, USA; ${ }^{3}$ Department of Pathology, University of Washington, Seattle, WA 98195, USA; ${ }^{4}$ Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, WA 98109, USA
${ }^{\dagger}$ Present Address: Division of Translational Research, Department of Medical Research, Taipei Veterans General Hospital, Taipei 112, Taiwan, School of Dentistry, National Yang-Ming University, Taipei 112, Taiwan; *Correspondence: kawasumi@uw.edu

Ultraviolet (UV) irradiation is the most prevalent carcinogen in humans, leading to diverse skin malignancies that outnumber all other cancers combined. A physiologic dose of UV generates thousands of DNA lesions per cell, mostly of two types: cyclobutane pyrimidine dimers (CPDs) and 64 photoproducts (6-4PPs). It has been difficult to determine the precise contribution of each lesion type to the signaling events that regulate cell cycle progression, DNA replication, and cell survival. Here we coupled multiparameter flow cytometry with lesion-specific photolyases that eliminate either CPDs or 6-4PPs, generated human cells that carry only CPDs or 6-4PPs, and determined the role of each lesion type in DNA damage responses using three independent approaches. Although it has been thought that the 8 -fold more abundant CPDs play a key role in DNA damage responses, we found that only 6-4PP lesions activated the ATR-Chk1 DNA damage pathway. Mechanistically, 6-4PPs, but not CPDs, impeded DNA replication across the genome as revealed by microfluidic-assisted replication track analysis. Furthermore, single-stranded DNA accumulated preferentially at 6-4PPs during DNA replication, indicating selective and prolonged replication blockage at 6-4PPs. These findings suggest that 6-4PP, the less abundant type of UV-induced DNA lesion, is the relevant trigger for replication blockage and activation of the UV-induced ATR-Chk1 pathway.

## Symposium I Abstracts

8. Sharpening the double-edged redox-sword targeting skin photodamage and cancer: From NRF2-
directed antioxidant photo-chemoprevention to oncogene-directed prooxidant chemotherapy

Georg T. Wondrak
College of Pharmacy and UA Cancer Center, University of Arizona, Tucson, Arizona, USA
e-mail: wondrak@pharmacy.arizona.edu

The causative role of oxidative stress in skin photodamage and carcinogenesis dictates the rational development of specific molecular strategies for photoprotection, photochemoprevention, and chemotherapeutic intervention targeting skin cancer. Our long-term research efforts have focused on the ultraviolet A (UVA)-driven formation of excited states of endogenous skin photosensitizer chromophores with subsequent generation of reactive oxygen (ROS) and carbonyl species (RCS). For pharmacological antioxidant intervention targeting skin photooxidative stress we have recently explored feasibility of harnessing cellular antioxidant stress response pathways controlled by the transcription factor NRF2, employing dietary small molecule NRF2 activators including cinnamonderived cinnamaldehyde and the achiote-derived apocarotenoid bixin. Bixin displayed potent NRF2dependent photoprotective properties in cultured human skin cells, and chronic dietary bixin supplementation showed photochemopreventive efficacy in a SKH1 mouse model of skin photocarcinogenesis. Switching from antioxidant to prooxidant redox-directed intervention targeting malignancies including metastatic melanoma, we have now substantiated the feasibility of repurposing clinical artemisinin-endoperoxide drugs, used currently as potent FDA-approved redox antimalarials. Our recent experiments demonstrate that artemisinin-based chemotherapeutic induction of oxidative stress and apoptosis may eliminate malignant cells that display increased labile iron availability downstream of oncogene (e.g. MYC)-controlled dysregulation of transferrin receptor (TFRC) expression.

## Symposium I Abstracts

9. Molecular underpinnings of cellular signaling interception by blue-light-sensitized-retinal Kasun Ratnayake ${ }^{1}$, John L. Payton ${ }^{2}$, and Ajith Karunarathne ${ }^{1 *}$<br>${ }^{1}$ Department of Chemistry and Biochemistry, The University of Toledo, Toledo, OH 43606, USA<br>${ }^{2}$ Department of Chemistry, Kenyon College, Gambier, OH, 43022, USA; ajith.karunarathne@utoledo.edu

Chemical- as well as phototoxicity of chromophore retinal has long been debated. The possibility of photoexcited retinal interacting with cells; intercepting signaling in the presence or absence of light has not been explored. Using live cell imaging and optogenetic signaling control, we uncovered that blue-light-excited retinal irreversibly distorts plasma membrane (PM) bound phospholipid; phosphatidylinositol 4,5 bisphosphate (PIP2) and disrupt its function. We also report molecular evidence for blue-light-excited-retinal induced oxidative damage of lipid anchors in membrane interacting G-proteins using live-cell and in vitro experimentation. The incurred molecular damage irreversibly disrupted subcellular localization of these molecules, a crucial criterion for their signaling. We further show accumulation of retinal in lipid-bilayers of cell membranes, explaining its prolonged lifetime in this hydrophobic cellular environment. Comparative response-signatures suggest that both retinal as well as photodynamic therapy agents trigger similar reactions upon photoexcitation and generate singlet oxygen and reactive oxygen species. Additionally, data also shows that exposing retinal-containing cells to sunlight induces substantial cytotoxicity, marked by cell death. Collectively, our results explain a likely - in vivo mechanism and reaction conditions under which bio-available retinal in physiological light conditions damages cells.

## Symposium I Abstracts

# 10. Autophagy pathways in UVB damage response and tumorigenesis 

Yu-Ying He
Section of Dermatology, Department of Medicine, University of Chicago
Macroautophagy (hereafter autophagy) is a catabolic process involving lysosomal turnover of proteins and organelles to maintain cellular homeostasis. Tumorigenesis requires not only the accumulation of genetic and epigenetic changes in epithelial cells, but also the evolution of a protumorigenic inflammatory microenvironment and dysregulation of epidermal differentiation and proliferation. However, the cellular mechanism connecting UV-induced damage and skin tumorigenesis is not well understood. We found that autophagy is induced in the epidermis by UV irradiation and epidermisspecific deletion of the essential autophagy gene ATG7 protected against UV-induced inflammation and skin tumorigenesis in mice through regulating COX-2 signaling. ATG7 regulated UV-induced cytokine expression and secretion, and promoted COX-2 expression through both an autonomous mechanism and a non-cell autonomous mechanism. In addition, loss of epidermal Atg7 inhibits UVBinduced abnormal epidermal proliferation and impaired differentiation during skin tumorigenesis, and the effect of Atg7 loss is mediated by the autophagy receptor/substrate p62. In summary, our findings demonstrate a crucial role of the autophagy and p62 pathway in regulating UVB-induced inflammation, abnormal proliferation, impaired differentiation, and skin tumorigenesis, providing a previously unknown mechanism for the autophagy pathways in regulating skin homeostasis and tumorigenesis.

# Symposium II Abstracts <br> 'Mechanisms in photochemistry and photobiology: From synthetic and energy applications to materials and photomedicine' 

1. Tailoring Non-linear Photophysical Processes for Bio-medical Applications
A. Jean-Luc Ayitou, Ph.D.

Department of Chemistry, Illinois Institute of Technology, Chicago, IL 60616; E-mail: aayitou@iit.edu

Noninvasive bio-medical techniques can make use of light (as photons, heat, and soundwaves) to trigger in vivo processes such as imaging, drug delivery, and photodynamic therapy. For light initiated procedures requiring the use of high energy UV-blue photons, it's expected that the use of UV-blue photons would result in low quantum efficiencies, since this spectral range can be easily scattered while crossing dermal tissues. Recent advances in light initiated therapies and processes have been relying on non-linear photophysical processes that make use of amplified high-energy photons from low energy green-to-red radiation. This process is generally referred to as photon upconversion (UC), which is also a bi-molecular process requiring a light-harvesting triplet sensitizer (or energy donor) and an acceptor chromophore that will be sensitized to emit the higher-energy photons. Due to recent advances in synthetic chemical science, research groups have recently reported many organic donoracceptor systems for UC research with various degrees of success. As a contribution to the area of UC, we have been exploring donor and acceptor polyaromatics, which are structurally similar \& complementary in a such a way that the rate of the donor $\rightarrow$ acceptor energy transfer (ET) competes with that of molecular diffusion. In this exploration, we developed novel organic pyrene-like triplet sensitizers that can efficiently harvest green radiation and then transfer the triplet energy to polycyclic aromatic acceptors such as perylene. Subsequently, two triplet excitons of perylene annihilate to generate blue photons. We also demonstrated that incident light with a power density in the microwatt regime was sufficient to perform UC using the molecular donor-acceptor system of interest.
In addition to navigating our contribution in the field of non-linear photophysical processes, I will also highlight my group's recent development of organic polymeric materials which could be tailored for "on-demand" photo-release of chemicals including drug molecules.

## Symposium II Abstracts

## 2. Metal Complex Photosensitizers for Photodynamic Therapy

Colin G. Cameron ${ }^{\dagger}$, Susan Monro ${ }^{\ddagger}$, John Roque III $^{+}$, Patrick Barrett ${ }^{+}$, Houston Cole ${ }^{+}$, Liubov Lifshits ${ }^{\dagger}$, Rachel Hodges ${ }^{+}$, David von Dohlen ${ }^{+}$, Sherri A. McFarland ${ }^{+}$
${ }^{\dagger}$ Department of Chemistry and Biochemistry, The University of North Carolina at Greensboro, 301 Mclver Street, Greensboro, North Carolina 27402, United States; ${ }^{\ddagger}$ Department of Chemistry, Acadia University, 6 University Avenue, Wolfville, Nova Scotia B4P 2R6, Canada

Transition metal complexes have emerged as attractive PSs photodynamic therapy (PDT). Certain coordination complexes of ruthenium ( Ru ) are potent phototoxins toward a variety of in vitro and in vivo cancer models. One example is our own TLD1433, which is the first Ru PS to enter (and successfully complete) a human clinical trial for treating cancer with PDT. Part of the interest in Ru PSs stems from the ability to access a variety of excited state electronic configurations with visible or near-infrared light by judicious choice of ligand combinations around the metal center. These excited states, in turn, may participate in traditional type I/II photodynamic reactions as well as oxygen independent pathways that form the basis of photochemotherapy (PCT). In this conference presentation, we will discuss the design and development of transition metal complex PSs that exploit PDT effects. The emphasis will be on the structural features and photophysical models that give rise to excited triplet states with characteristic reactivities.


## Symposium II Abstracts

3. Oxidation of Plasmalogens within Cellular Membranes by Photodeoxygenation John T. Petroff II ${ }^{\ddagger}$, Sara M. Omlid ${ }^{\ddagger}$, Ankita Isor ${ }^{\ddagger}$, Ryan D. McCulla ${ }^{\ddagger}$
${ }^{\ddagger}$ Department of Chemistry, Saint Louis University, 3501 Laclede Ave., St. Louis, Missouri 63103, United States, ryan.mcculla@slu.edu

Oxidative stress has been implicated in several disease pathways including diabetes, heart disease, and Alzheimer's. The photodeoxygenation of certain heterocyclic oxides has been shown to generate an oxidant consistent with ground state atomic oxygen [ $\mathrm{O}\left({ }^{3} \mathrm{P}\right)$ ]. Since photodeoxygenation and photosensitization generate different oxidants, photodeoxygenation and photosensitization are expected to generate different oxidation products within a cell or tissue. Plasmalogens are lipids that commonly contain a vinyl ether linkage at the sn-1 position. Here we have found that plasmalogens are susceptible to oxidation by photodeoxygenation to yield specific aldehyde products. Since $O\left({ }^{3} P\right)$ is a very reactive oxidant, it was suspected that increasing the lipophilicity of the photodeoxygenation precursor would increase the amount of lipid oxidation relative to the amount of oxidant generated. To these ends, a series of $O\left({ }^{3} \mathrm{P}\right)$-precursors with varying lipophilicity and subcellular localization were prepared. We found that as expected increased lipophilicity correlated with increased lipid oxidation initiated by photodeoxygenation. To our knowledge, this is the first example of any oxidation being induced by photodeoxygenation within a cell. This research is expected to make headway towards the ability to photogenerate distinct oxidation products within specific subcellular compartments.

## Symposium II Abstracts

## 4. Photochemistry of Nucleic Acid Derivatives and Their Photodynamic Efficacy Against Human Epidermoid Carcinoma Cells

Carlos E. Crespo-Hernández, Department of Chemistry, Case Western Reserve University, 10900 Euclid Avenue, Cleveland, Ohio, 44106; E-mail: cxc302@case.edu

Elucidating the structural and electronic elements that regulate the photochemistry of the nucleic acid bases and their derivatives can enable the use of nucleic acid derivatives for photodynamic therapy and structural-biology applications. Our group has recently shown that replacement of the carbonyl oxygen atom in nucleic acid bases by a sulfur or selenium atom has a major impact on their photochemistry. These fundamental investigations are currently being used by our group to develop DNA and RNA nucleobase derivatives that exhibit more than 100 nm redshifted absorption and nearly $100 \%$ greater photoreactivity, which, when applied in vitro with a low dose of near-visible radiation, substantially decrease the proliferation of skin cancer cells.

Financial support from the National Science Foundation (Grant No. CHE-1800052) is acknowledged.

## Symposium II Abstracts

## 5. Ultrafast [2+2] Cycloaddition Reaction Upon Photoactivation of 4-Thiothymidine in SingleStranded DNA

Luis A. Ortiz-Rodríguez and Carlos E. Crespo-Hernández*
Department of Chemistry, Case Western Reserve University, Cleveland, Ohio 44106, United States; Email: cxc302@case.edu

The prospect of synergistically combining sulfur-substituted nucleobases (thiobases) with near-visible radiation to develop new photomedicines for skin cancer treatment is been actively investigated. 4Thiothymidine is one of the most studied thiobases. In its monomeric form, 4-thiothymidine acts as an effective Type II photosensitizer, generating reactive oxygen species in high quantum yield. In this contribution, we report on the detection of a reactive species formed after ultrafast population of the triplet state of 4-thiothymidine in a single-stranded DNA oligonucleotide. Quantum-chemical calculations allow us to assign this reactive species to a thietane intermediate that is formed between a thymidine and 4-thiothymidine. State-state spectroscopic measurements collaborate the subsequent formation of the (6-4) photoproduct in the singlet-stranded DNA oligonucleotide. Our results show that photoactivation of DNA oligonucleotides containing 4-thiothymidine with UVA radiation results in a [2+2] cycloaddition reaction between thymidine and 4-thiothymidine, which leads to the formation of a (6-4) photoproduct. This photoproduct is analogous to the highly toxic pyrimidine-pyrimidinone (6-4) photoadduct observed in canonical DNA upon UV radiation.

## Symposium II Abstracts

6. Developing $\operatorname{Ir}($ III) Complexes as Potential Theranostic Photodynamic Therapy Agents  Collin G. Cameron, ${ }^{\S}$ Sherri A. McFarland ${ }^{\ddagger, \xi}$<br>${ }^{+}$Department of Chemistry and Biochemistry, North Dakota State University, Fargo, North Dakota 58108-6050, United States. Wenfang.Sun@ndsu.edu<br>${ }^{\ddagger}$ Department of Chemistry, Acadia University, 6 University Avenue, Wolfville, Nova Scotia B4P 2R6, Canada<br>${ }^{\S}$ Department of Chemistry and Biochemistry, The University of North Carolina at Greensboro, 301 Mclver Street, Greensboro, North Carolina 27402, United States

In recent years, Ir(III) complexes have emerged as a new type of potential photosensitizers (PSs) for theranostic photodynamic therapy (PDT) applications. Many of these complexes possess high triplet excited-state quantum yields and long-lived triplet excited states for efficient singlet oxygen and/or other reactive oxygen species (ROS) generation via energy or electron transfer processes. It has been reported that cationic $\operatorname{Ir}($ III ) complexes can target mitochondria, lysosome, endoplasmic reticulum, or nucleus in a variety of cancer cell lines; and a mitochondria-targeted Ir(III) complex PS was reported to show improved in vitro PDT effects under hypoxia. These complexes also exhibit bright intracellular luminescence. However, many of the currently studied Ir(III) complex PSs have poor solubility in water, and they mainly absorb in the UV and blue spectral region. These drawbacks prevent them from potential clinical use. To overcome these disadvantages, we synthesized four series of cationic or neutral Ir(III) complexes that have strong absorption in the visible to the red spectral region and are emissive in the red to the NIR region. Their photophysical properties and in vitro theranostic PDT effects were studied. We found that the natures and energies of the lowest singlet and triplet excited states of these complexes were dramatically impacted by the different types of ligands. Many of the complexes can efficiently generate singlet oxygen in solutions and ROS in vitro, and exhibited a photodynamic therapeutic effect upon visible or red light activation. One of the $\operatorname{Ir}(\mathrm{III})$ complexes gave rise to the largest phototherapeutic index (>1600) reported to date for $\operatorname{lr}$ (III) complexes upon white light activation. These complexes also produce strong intracellular luminescence that highlights their potential as theranostic PDT agents.

## Symposium II Abstracts

## 7. Photocatalytic Degradation of Furosemide and Identification of Carboxylic Acid Derivatives using GC-MS with HSTrap

Erik Menjivara, Corinne Ferronato ${ }^{b}$, Jean-Marc Chovelon ${ }^{c}$, Ludovic Fine ${ }^{d}$, Matthew Tarre
School of Natural Sciences and Mathematics, Mount St. Mary's University, Emmitsburg, MD 21727, USA; e.j.menjivar@email.msmary.edu; Université Lyon 1, CNRS, UMR 5256, IRCELYON, Institut de recherches sur la catalyse et l'environnement de Lyon, 2 avenue Albert Einstein, F-69626 Villeurbanne, France; corinne.ferronato@ircelyon.univ-lyon1.fr; Université Lyon 1, CNRS, UMR 5256, IRCELYON, Institut de recherches sur la catalyse et l'environnement de Lyon, 2 avenue Albert Einstein, F-69626 Villeurbanne, France; jean-marc.chovelon@ircelyon.univ-lyon1.fr; Université Lyon 1, CNRS, UMR 5256, IRCELYON, Institut de recherches sur la catalyse et l'environnement de Lyon, 2 avenue Albert Einstein, F-69626 Villeurbanne, France; ludovic.fine@ircelyon.univ-lyon1.fr; Department of Chemistry, University of New Orleans, New Orleans, LA 70148, USA; mtarr@uno.edu

The photocatalytic degradation of furosemide and its products were examined. Furosemide is a diuretic that has been known to enter bodies of water, passing through wastewater treatment plants. Furosemide has also been linked to affecting population growth among crustaceans. Multiple trials of a degradation were done with the photocatalyst titanium dioxide. The PVDF filter was chosen after testing multiple filters to remove the product without the photocatalyst. High performance liquid chromatography was used to determine the concentration of furosemide. Full degradation of the furosemide occurred within 30 minutes from the start of the reaction. A system of gas chromatography and mass spectrometry was used to determine the products of the degradation. A headspace trap was used to capture liquid from a sample of the products. Previous analysis of standard solutions had several acids and their wavelengths found, but none were found in the products although furfural, a product of degradation, was found. Parameters of the system need to be done to determine the other acids.

## Symposium II Abstracts

## 8. Photochemistry of tyrosine dimer: when an oxidative lesion of proteins is able to photoinduce further damage

Lara O. Reid, Mariana Vignoni, M. Laura Dántola, Andrés H. Thomas
Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas (INIFTA), Departamento de Química, Facultad de Ciencias Exactas, Universidad Nacional de La Plata, CCT La Plata-CONICET. La Plata, Argentina; E-mail: athomas@inifta.unlp.edu.ar

The tyrosine dimer ( $\mathrm{Tyr}_{2}$ ), a covalent bond between two tyrosines (Tyr), is one of the most important modifications of the oxidative damage of proteins. This compound is increasingly used as a marker of aging, stress and pathogenesis. At physiological $\mathrm{pH}, \mathrm{Tyr}_{2}$ is able to absorb radiation at wavelengths significantly present in the solar radiation and artificial sources of light. As a result, when $\mathrm{Tyr}_{2}$ is formed in vivo, a new chromophore appears in the proteins. Despite the biomedical importance of Tyr2, the information of its photochemical properties is limited due to the drawbacks of its synthesis.

We have optimized a simple, one-step method to synthesize Tyr $_{2}$, using pterin (Ptr) as a photocatalyst. Our procedure is carried out in aqueous solutions under UV-A radiation for few minutes. The purification of $\mathrm{Tyr}_{2}$ is performed by reverse-phase chromatography. The highly pure obtained solution was used to deeper study its photochemical properties.

We have studied the photodegradation of the acid and alkaline form of $\mathrm{Tyr}_{2}$ in aqueous solution under UV-B and UV-A radiation. In the absence of oxygen $\mathrm{Tyr}_{2}$ is photostable. On the other hand, excitation in the presence of oxygen leads to the photodegradation of $\mathrm{Tyr}_{2}$, yielding different products which conserve the dimeric structure. During its photodegradation different reactive oxygen species, like hydrogen peroxide, superoxide anion and singlet oxygen $\left({ }^{1} \mathrm{O}_{2}\right)$, are produced. The quantum yield of ${ }^{1} \mathrm{O}_{2}$ production is $0.15 \pm 0.05$, which is similar to that obtained for free Tyr. In addition, $\mathrm{Tyr}_{2}$ is able to sensitize the photodegradation of Tyr.

This study indicates that when $\mathrm{Tyr}_{2}$ is generated in a protein
 structure, an intrinsic potential photosensitizer is formed, extending the active fraction of light towards the UV-A range. Therefore a product of a photosensitized process can act as a photosensitizer itself leading to further photosensitized damage, thus amplifying the harmful effects of UV radiation on biological systems.

## Symposium II Abstracts

9. Conformation dependent dual function of a 1,2-diketone for sensitized photooxidation and thermal binding
Sarah J. Belh ${ }^{\dagger, \ddagger,}$ Niluksha Walalawela ${ }^{\dagger, \ddagger}$, Stas Lekhtman ${ }^{\dagger}$, and Alexander Greer ${ }^{\dagger, \ddagger,}$
${ }^{\dagger}$ Department of Chemistry, Brooklyn College, 2900 Bedford Avenue, Brooklyn, New York 11210, United States
${ }^{\ddagger}$ 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

In order to develop a dual system for photooxidation and subsequent binding an experimental and theoretical examination of 1,2-diketone was conducted. Namely, the ability of 4,4'-dimethylbenzil to rotate and act as a sensitizer in the trans-conformation and bind a trialkyl phosphite in the synconformation was studied. The benzil's ability to homolyze dicumyl peroxide and produce alkoxy radicals was shown to require a high benzil concentration. It was found that the syn-benzil binds irreversibly to phosphite though a phosphorane intermediate. Upon binding to phosphite the benzil decreases in its alkoxy radical production, acting as a shut-off mechanism for photooxidation. The alkoxy radical reaction products in protic and aprotic homogenous and heterogeneous systems were also studied. This study opens the avenue of diones for prospective dual action in sensitization and in drug binding.
photosensitization




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