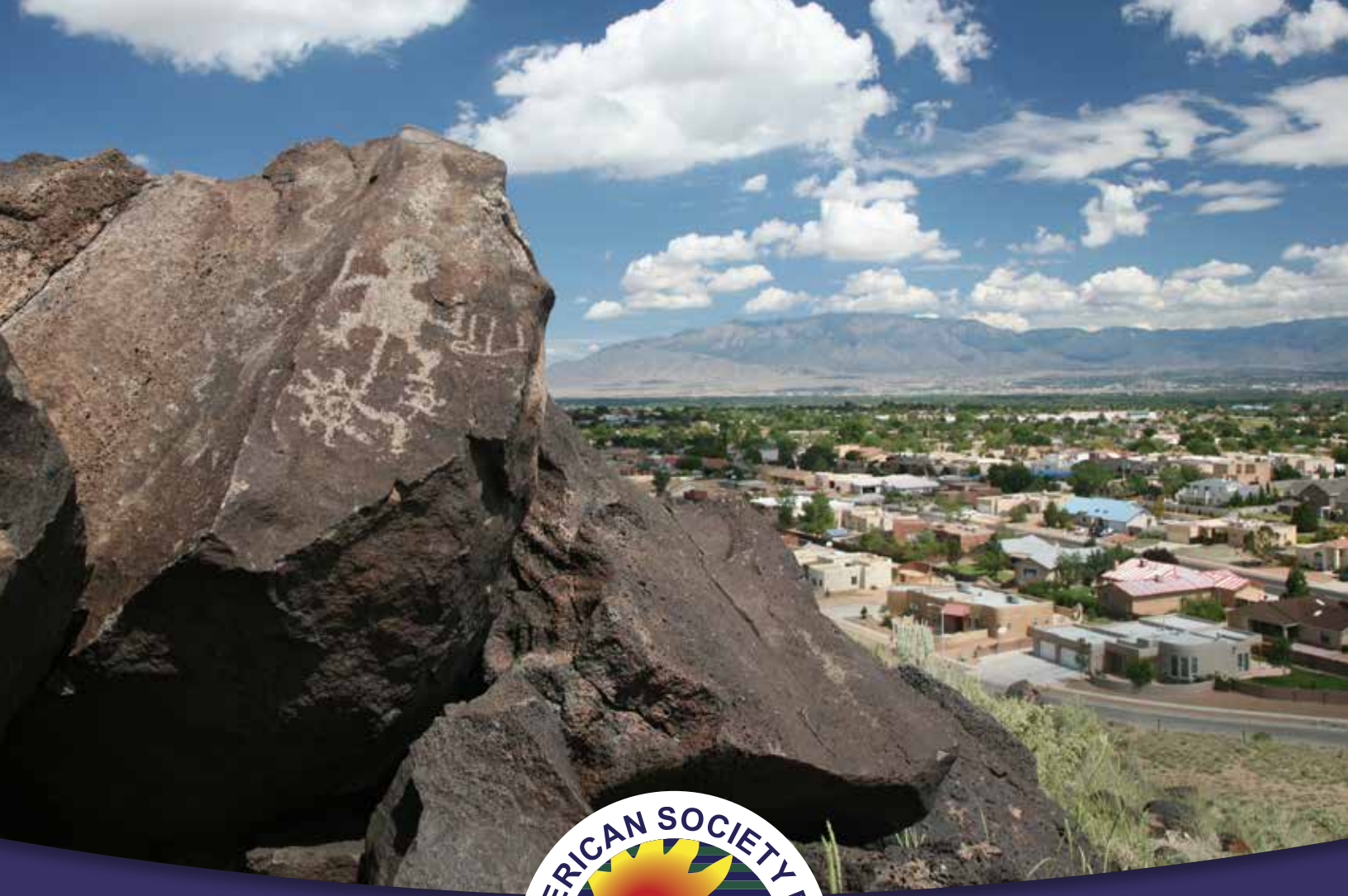


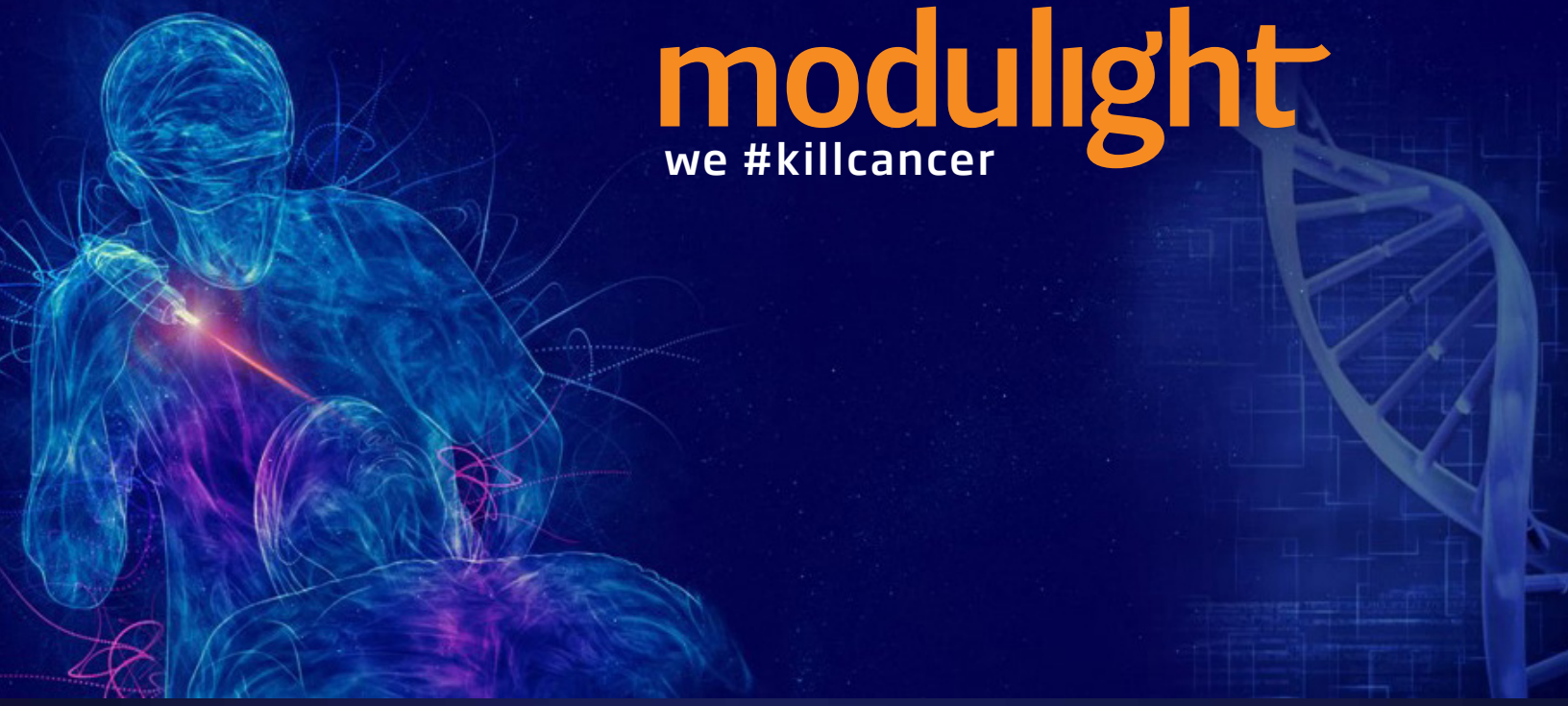
2022 Biennial Meeting
American Society for Photobiology

Albuquerque, New Mexico · September 25–28, 2022
Hotel Albuquerque at Old Town

PROGRAM AND ABSTRACTS

modulight

we #killcancer



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Social Media Channels

Please share your pictures and impressions taken during the meeting. Use **#photobio2022** when posting about the event!

ASPhotobiology

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WELCOME

TO THE 2022 AMERICAN SOCIETY FOR PHOTOBIOLOGY BIENNIAL MEETING

Dear conference participants, attendees, and ASP members and friends,

Welcome to the 41st scientific meeting of the American Society for Photobiology! You will be taking part in an absolutely vibrant conference covering many aspects of contemporary photochemistry and photobiology with attendees from many parts of the world. The meeting is being held at the Hotel Albuquerque in New Mexico.

The scientific program includes a wide range of scientific sessions and special symposia, as well as a poster session. We have a great lineup of keynote speakers including Yu-Ying He, David Lawrence, V. Ramamurthy, Martin Schnermann, David Sliney, and Xiaojing Yang. A Lifetime Achievement Award Lecture will be delivered by James Cleaver.

The program is also featuring the following symposia: 'Impact of circadian rhythm and aging on UV DNA damage responses and photocarcinogenesis', 'Photochemistry of photoreceptors and photosynthetic systems', 'Natural products in prevention of photodamage and photocarcinogenesis, 'Protein photo-oxidation: Mechanisms and biological consequences', 'Solar photons and the skin exposome', 'Recent advances on UV-mediated molecular signaling in cancer', 'UV Damage and Repair in Chromatin', 'Photochemistry and photobiology of melanin pigments', 'Photochemistry and photophysics in materials', 'PDT in imaging and cancer therapy', 'UV-induced responses and skin cancer', 'ALA-PDT in cancer therapy', 'Photosensitized reactions in biomolecules and carcinogenic cells', 'Photophysics: In vivo singlet oxygen detection and dosimetry', 'PDT and combinations to overcome resistance in cancer', 'Photodynamic treatments and mechanisms', 'Photobiological Studies to Advance Germicidal UV-C for Infection Control', 'Nanotechnology in PDT', and 'From predictions to practice: Approaches to PDT delivery'.

We are excited to announce the 'Past Presidents' Bridge-to-the-Future Symposium' chaired by Frank Gasparro and Albert Girotti. There will also be a presentation from the president of our sister society, the European Society for Photobiology (Amparo Faustino), as well as an ASP-ESP Joint Symposium 'New paradigms in photobiology' chaired by Thierry Douki. Finally, the Associate Members have an event planned which features lectures on grant writing by Theresa Busch and Shiyong Wu.

We look forward to seeing you in Albuquerque!

Shiyong Wu, President, Ohio University, ASP President
Alexander Greer, Brooklyn College, ASP Past-President
Yu-Ying He, University of Chicago

ASSOCIATE MEMBER ACTIVITIES

Dear Associate Members,

The associate council of the American Society for Photobiology (ASP) is very excited to host the following networking and mentoring events for students and postdoctoral fellows (Associate Members) at the upcoming ASP meeting from September 25th to September 28th at Albuquerque, NM. The goal of our events is to provide associate members with resources to further their knowledge on career paths in academia and industry, to foster a sense of community, and to support advancements in communicating Photobiology and Photochemistry. We encourage all associate members to participate and take advantage of these FREE events at the ASP meeting:

Grant Writing Workshop and Mentoring Luncheon
Wednesday, September 28th, 12:00 PM – 1:30 PM, Fireplace Room

Moderator: Caradee Wright
Associate Member Co-Chairs: Houston Cole and Shakeela Jabeen

- Theresa Busch – "Grant Writing: Hints and Hindrance"
- Shiyong Wu – "Are You Ready for Applying for a Small Business Grant?"

Students will also have the opportunity to interact with early career scientists as well as experienced principle investigators from both academia and industry and gain insights on career development, research interests, and much more. Associate Member elections will also occur at this event.

Please be advised that all of the above events are FREE to all ASSOCIATE MEMBER attendees REGISTERED for the 2022 ASP meeting. Also remember to share your pictures and impressions taken during the meeting. Use **#photobio2022** when posting about the event. Looking forward to meeting you in Albuquerque!

Best Regards,
Verónica Bahamondes Lorca, Houston Cole, and Shakeela Jabeen
Associate Councilors, ASP 2022

THE 2022 MEETING ORGANIZATION

ASP EXPRESSES ITS WARM APPRECIATION TO THE FOLLOWING INDIVIDUALS FOR THEIR OUTSTANDING CONTRIBUTIONS TO THE ORGANIZATION OF THE SCIENTIFIC PROGRAM

Chairs

Alexander Greer, Shiyong Wu, Yu-Ying He

Session Organization

Mauricio Baptista
Theresa Busch
Hao Chang
Carlos Crespo
Mike Davies
Thierry Douki
Shobhan Gaddameedhi
Frank Gasparro
Albert Girotti
Steffen Hackbarth
Tayyaba Hasan
Yu-Ying He
Joe Huang
Ajith Karunarathne
Masaoki Kawasumi
Lisa Kelly
Michael G. Kemp
Dae Joon Kim
Jon Lovell
Srivalleesha Mallidi
Edward Maytin
Ryan McCulla
Girgis Obaid
Tadeusz Sarna
Christian Schöneich
Gal Shafirstein
Andrés Thomas
David Welch
Georg Wondrak
Shiyong Wu
John Wyrick
Jin Xie
Xiaojing Yang

ASP OFFICERS AND COUNCILORS

Officers

Shiyong Wu, President
Sherri McFarland, President-Elect
Alexander Greer, Past-President
Theresa M. Busch, Treasurer
Ryan McCulla, Secretary
Brett Burk, Executive Secretary

Councilors

Mauricio Baptista
Shobhan Gaddameedhi
Huang Chiao (Joe) Huang
Masaoki Kawasumi
Dae Joon Kim
Jonathan Lovell
Girgis Obaid
José Robinson-Duggon
Andres Thomas
Caradee Wright
Xiaojing Yang
Youngjae You

Associate Councilors

Verónica Bahamondes Lorca
Houston Cole
Shakeela Jabeen

THE AMERICAN SOCIETY FOR PHOTOBIOLOGY THANKS THE FOLLOWING

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2022 AWARDS

ASP Research Award

2022 – Andrés Thomas

ASP New Investigator Award

2022 – Masaoki Kawasumi

ASP Light Path Award

2022 – Yu-Ying He

ASP Lifetime Achievement Award

2022 – James Cleaver

ASP Photon Award

2022 – Georg Wondrak

Editor's Student Research Award

2022 – Houston Cole

Photocite-A Award

2022 – Imran Ali et al.

Thermodynamics, and Modeling of Amido Black Dye Photodegradation in Water Using Co/TiO_2 Nanoparticles. *Photochem. Photobiol.* 2018, *94*:935-941. Citations: 100

Photocite-B Award

2022 – Michael R. Hamblin

Mechanisms and Mitochondrial Redox Signaling in Photobiomodulation. *Photochem. Photobiol.* 2018, *94*:199-212. Citations: 189

Frederick Urbach Memorial Student Travel Award

2022 –

Veronica Bahamondes Lorca

Chanda Bhandari

Sharayu Chandratre

Natalia Gutierrez

Brittany Rickard

Nimit Shah

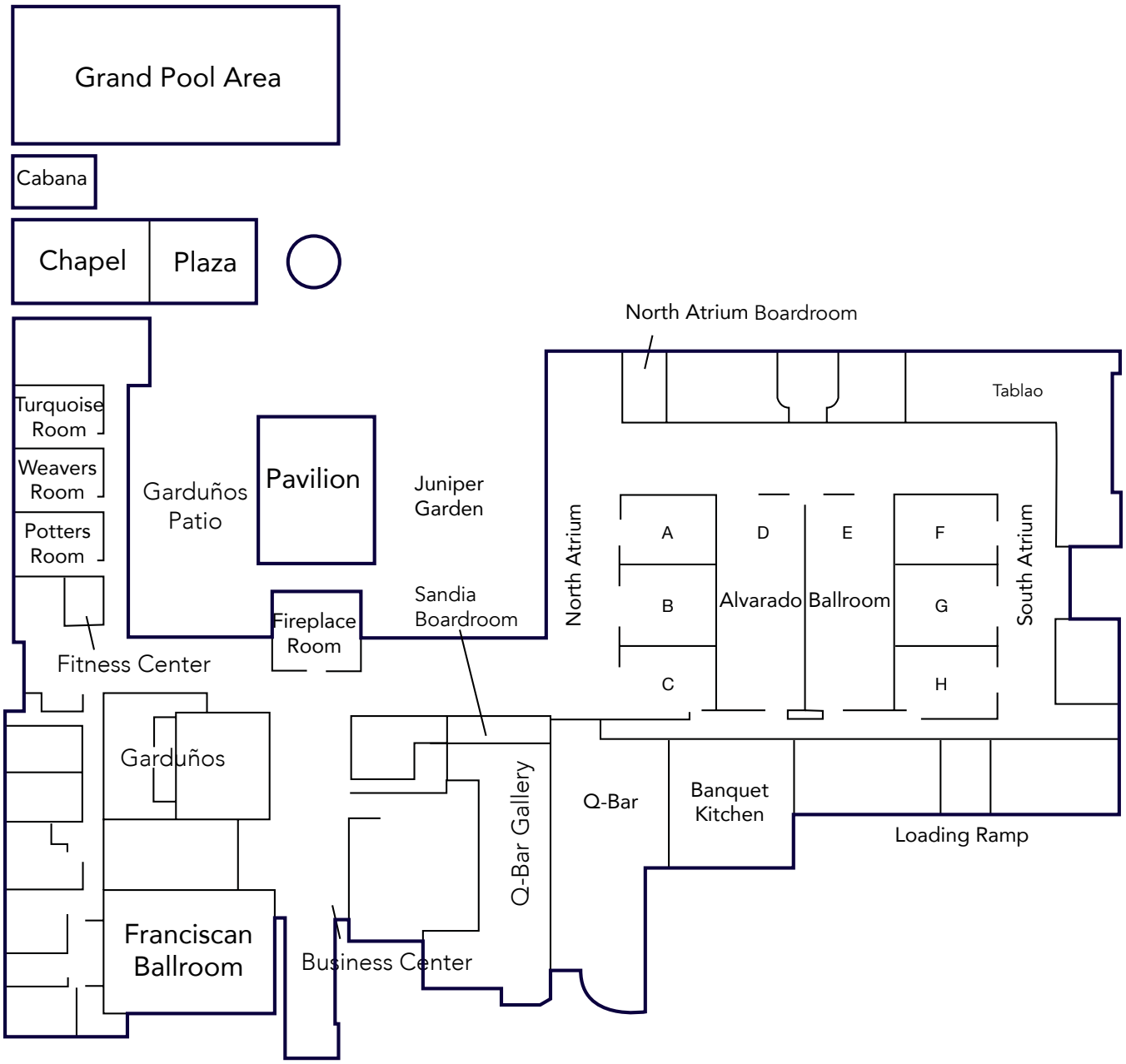
Dennis Sourvanos

Marvin Xavierselvan

Yuxi Zhou

FLOOR PLAN

Hotel Albuquerque at Old Town



GENERAL INFO

Registration Desk Hours

Location: North Atrium

Day	Time	Location
Sunday, September 25	4:00 PM – 6:30 PM	North Atrium
Monday, September 26	7:30 AM – 3:00 PM	North Atrium
Tuesday, September 27	8:00 AM – 3:00 PM	North Atrium
Wednesday, September 28	8:00 AM – 12:00 PM	North Atrium

Morning Refreshments

Coffee, hot tea, and breakfast items will be available near the registration desk each morning 30 minutes before presentations begin.

Monday, Tuesday, and Wednesday
7:30 AM – 8:30 AM

Coffee Breaks

Coffee Breaks will be available each day.

Monday, Tuesday, and Wednesday
10:00 AM and 2:00 PM

Social Media Channels

Please share your pictures and impressions taken during the meeting. Use #photobio2022 when posting about the event!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Poster Session

Sunday, September 25
5:30 PM – 6:15 PM
North Atrium

Opening Reception

Sunday, September 25
6:15 PM – 7:15 PM
Pavillion

Explore Albuquerque!

Visit Albuquerque will be available during Sunday evening's Welcome Reception to answer all of your questions about our host city. Whether you're looking for the best pizza in town or fresh seafood, this is where you'll find the answers. They can also recommend museums, local tours, outdoor adventures, and local shopping areas.

If you aren't able to connect with the Visit Albuquerque on Sunday night, no worries! City maps and visitor's guides will be available at the registration check-in desk.

ABBREVIATED SCHEDULE

Sunday, September 25

TIME	EVENT	CHAIR(s)	ROOM
4:00 PM – 5:30 PM	Opening Remarks, Welcome and Lifetime Achievement Award Lecture	Alexander Greer, Shiyong Wu	Alvarado D
5:30 PM – 6:15 PM	Poster Session		North Atrium
6:15 PM – 7:15 PM	Opening Reception	Alexander Greer, Shiyong Wu	Pavillion

Monday, September 26

TIME	EVENT	CHAIR(s)	ROOM
8:00 AM – 10:30 AM	Impact of circadian rhythm and aging on UV DNA damage responses and photocarcinogenesis.	Shobhan Gaddameedhi, Michael G. Kemp	Alvarado A
8:30 AM – 10:30 AM	Past Presidents' Bridge-to-the-Future Symposium	Frank Gasparro, Albert Girotti	Alvarado D
8:00 AM – 12:00 PM	ASP-ESP Joint Symposium: New paradigms in photobiology	Thierry Douki	VIRTUAL ONLY
8:00 AM – 10:30 AM	Photochemistry of photoreceptors and photosynthetic systems	Xiaojing Yang	Alvarado C
11:00 AM – 2:00 PM 11:00 AM 12:00 PM 1:00 PM	Keynote Lectures • Light-Triggered Drug Release from Cell-Conveyed Phototherapeutics *David Lawrence* • Harnessing Cyanine Chemistry for Imaging and Drug Delivery *Martin Schnermann* • UV radiation, DNA damage, and RNA modifications *Yu-Ying He*		Alvarado D
12:00 PM – 1:00 PM	ESP Presidential Lecture	Amparo Faustino	VIRTUAL ONLY
2:00 PM – 4:15 PM	Natural Products in Prevention of Photodamage and Photocarcinogenesis	Shiyong Wu, Hao Chang	Alvarado A
2:00 PM – 3:40 PM	Protein Photo-oxidation: Mechanisms and Biological Consequences	Mike Davies, Christian Schöneich	VIRTUAL ONLY
2:30 PM – 5:20 PM	Solar photons and the skin exposome	Georg Wondrak, Mauricio Baptista	Alvardo D
2:00 PM – 4:05 PM	Recent advances on UV-mediated molecular signaling in cancer	Dae Joon Kim, Yu-Ying He	Alvarado C
7:00 PM – 9:00 PM	ASP Editor's Dinner		Fireplace Room

ABBREVIATED SCHEDULE

Tuesday, September 27

TIME	EVENT	CHAIR(s)	ROOM
8:00 AM – 9:25 AM	UV Damage and Repair in Chromatin	John Wyrick	Alvarado D
8:00 AM – 11:00 AM	Photochemistry and Photobiology of Melanin Pigments	Tadeusz Sarna	VIRTUAL ONLY
8:00 AM – 12:20 PM	Photochemistry and photophysics in materials	Lisa Kelly, Ryan McCulla	Alvarado C
10:00 AM – 12:15 PM	PDT in imaging and cancer therapy	Tayyaba Hasan, Girgis Obaid	Alvarado A
10:00 AM – 12:30 PM	UV-induced responses and skin cancer	Masaoki Kawasumi	Alvarado D
1:15 PM – 4:15 PM	ALA-PDT in cancer therapy	Edward Maytin	Alvarado D
1:00 PM – 3:30 PM	Photosensitized Reactions in Biomolecules and Carcinogenic Cells	Carlos Crespo, Andrés Thomas	Alvarado C
2:00 PM – 3:50 PM	Photophysics: In vivo singlet oxygen detection and dosimetry	Steffen Hackbarth, Gal Shafirstein	Alvardo A
5:00 PM – 6:00 PM	ASP Business Meeting and Awards Ceremony *(open to conference participants)*		Alvarado D

Wednesday, September 28

TIME	EVENT	CHAIR(s)	ROOM
8:00 AM – 10:05 AM	PDT and Combinations to Overcome Resistance in Cancer	Joe Huang	Alvardo D
8:00 AM – 10:30 AM	Photodynamic Treatments and Mechanisms	Ajith Karunarathne	Alvardo A
10:15 AM – 12:20 PM	Photobiological Studies to Advance Germicidal UV-C for Infection Control	David Welch	Alvarado D
10:30 AM – 12:20 PM	Nanotechnology in PDT	Jon Lovell, Jin Xie	Alvardo A
12:00 PM – 1:30 PM	Grant Writing Workshop and Mentoring Luncheon	Houston Cole, Shakeela Jabeen	Fireplace Room
12:30 PM – 3:30 PM 12:30 PM 1:30 PM 2:30 PM	Keynote Lectures • Controlling Photochemical Processes with Confinement *V. Ramamurthy* • How do Bilin-based Photoreceptors Sense Light *Xiaojing Yang* • A History of Photobiology *David Sliney*		Alvardo D
1:30 PM – 3:35 PM	From Predictions to Practice: Approaches to PDT Delivery	Theresa Busch, Srivalleesha Mallidi	Alvardo A
5:00 PM – 6:00 PM	Executive Council Meeting		Fireplace Room
6:00 PM – 8:00 PM	Council Meeting		Fireplace Room

TECHNICAL PROGRAM

PRESENTER'S NAME IS ASTERISKED (*) IF OTHER THAN FIRST AUTHOR.

Sunday, September 25, 2022

Session 1. Lifetime Achievement Award Lecture

4:00 PM – 5:30 PM Alvarado D

1.1 4:00 PM – 4:15 PM
Opening Remarks

1.2 4:15 PM – 4:30 PM
Welcome to Albuquerque Visitor Information

1.3 4:30 PM – 5:30 PM
Two photosensitive diseases but only one gets cancer
James Cleaver

Poster Session

5:30 PM – 6:15 PM North Atrium

Opening Reception

6:15 PM – 7:15 PM Pavillion

Monday, September 26, 2022

Session 2. Impact of circadian rhythm and aging on UV DNA damage responses and photocarcinogenesis.

8:00 AM – 10:30 AM Alvarado A Co-Chairs: Shobhan Gaddameedhi, Michael G. Kemp

2.1 8:00 AM – 8:10 AM
Introduction
Shobhan Gaddameedhi

2.2 8:10 AM – 8:35 AM
The impact of solar UV-B exposure on circadian rhythms in SKH-1 hairless mice
Shobhan Gaddameedhi

2.3 8:35 AM – 9:00 AM
Circadian clock-modulating compounds impact cellular responses to UV radiation
Michael Kemp

2.4 9:00 AM – 9:25 AM
Predicting circadian time from single cell RNA-seq data
Bogi Andersen

2.5 9:25 AM – 9:50 AM
Circadain mechanism of metabolic adaptation to diet
Roman Kondratov

2.6 9:50 AM – 10:15 AM
Genomic characterization of the interplay between UV induced DNA damages and transcription
Sheera Adar

2.7 10:15 AM – 10:30 AM
Q&A

Session 3. Past Presidents' Bridge-to-the-Future Symposium

8:30 AM – 10:30 AM Alvarado D Co-chairs: Frank Gasparro, Albert Girotti

3.1 Past Presidents' Bridge-to-the-Future Symposium
Frank Gasparro
Albert Girotti
Kendric Smith
David Kessel
Alexander Greer

Session 4. ASP-ESP Joint Symposium: New paradigms in photobiology

8:00 AM – 12:00 PM VIRTUAL ONLY Chair: Thierry Douki

4.1 8:00 AM – 8:25 AM
DNA repair products as biomarkers of the genotoxicity of UV radiation
Thierry Douki

4.2 8:25 AM – 8:50 AM
Selective UV spectra for the induction of regulatory T-cells
Akimichi Morita

4.3 8:50 AM – 9:15 AM
RNA – target and mediator of cellular responses to ultraviolet radiation
Thomas Rünger

4.4 9:15 AM – 9:40 AM
Influence of chronic UV irradiation and the dermis on DNA repair of UV-induced DNA damage
Patrick Rochette

4.5 9:40 AM – 12:00 PM
Panel Discussion

Session 5. Photochemistry of photoreceptors and photosynthetic systems

8:00 AM – 10:30 AM Alvarado C Chair: Xiaojing Yang

5.1 8:00 AM – 8:30 AM
Primary dynamics of twisting in phytochrome and proton-coupled electron transfer in BLUF
Dongping Zhong

5.2 8:30 AM – 9:00 AM
Insight into the control of photoisomerization by the protein environment
Igor Schapiro

5.3 9:00 AM – 9:30 AM
Non-Heterogeneous vs Heterogeneous Ultrafast Photoisomerization Dynamics in Knotless Phytochromes
Chavdar Slavov

5.4 9:30 AM – 10:00 AM
Unscrambling mixtures of photoinduced intermediates of bacteriorhodopsin
Zhong Ren

5.5 10:00 AM – 10:30 AM
The Effects of Thiophene Chain Length on Energy Levels of [Ru(bpy)2(IP-nT)]2+ and [Ru(dmbpy)2(IP-nT)]2+: A Comprehensive Study using CV and CDPV
Abbas Vali

Session 7. Keynote Lectures

11:00 AM – 2:00 PM Alvarado D

7.1 11:00 AM – 12:00 PM
Light-Triggered Drug Release from Cell-Conveyed Phototherapeutics
David Lawrence

7.2 12:00 PM – 1:00 PM
Harnessing Cyanine Chemistry for Imaging and Drug Delivery
Martin Schnermann

7.3 1:00 PM – 2:00 PM
UV radiation, DNA damage, and RNA modifications
Yu-Ying He

Session 8. ESP Presidential Lecture

12:00 PM – 1:00 PM VIRTUAL ONLY

8.1 ESP Presidential Lecture
Amparo Faustino

Session 9. Natural Products in Prevention of Photodamage and Photocarcinogenesis

2:00 PM – 4:15 PM Alvarado A Co-chairs: Shiyong Wu, Hao Chang

9.1 2:00 PM – 2:10 PM
Introduction
Shiyong Wu

9.2 2:10 PM – 2:35 PM
Role of CTHRC1 in Non-Melanoma Skin Cancers
Hao Chang

9.3 2:35 PM – 3:00 PM
One-electron Oxidation of Biomolecules: Antioxidant Action of Resveratrol
Carolina Lorente

9.4 3:00 PM – 3:25 PM
The role of Carnosol in reducing ultraviolet B-Light-induced skin cancer development and progression
Veronica Bahamondes Lorca

9.5 3:25 PM – 3:50 PM
Validation of vitamin D3 action spectra
Peter Philipsen

9.6 3:50 PM – 4:15 PM
Nicotinamide and phytochemicals phloroglucinol and syringic acid delay UVR-induced squamous cell carcinoma onset in hairless mice
Celina Pihl

Session 10. Protein Photo-oxidation: Mechanisms and Biological Consequences

2:00 PM – 3:40 PM VIRTUAL ONLY Co-chairs: Mike Davies, Christian Schöneich

10.1 2:00 PM – 2:25 PM
Reaction of cysteine residues with oxidized tyrosine residues contributes to cross-linking of photo-oxidized proteins
Mike Davies

10.2 2:25 PM – 2:50 PM
A site-specific oxidation and fragmentation mechanism of a monoclonal antibody induced by visible light
Christian Schöneich

10.3 2:50 PM – 3:15 PM
Chemical, structural and functional modifications of proteins phototriggered by an endogenous photosensitizer
Laura Dantola

10.4 3:15 PM – 3:40 PM
Selective degradation of amyloids in vivo by chemical catalyst-promoted photooxygenation
Motomu Kanai

Session 11. Solar photons and the skin exposome

2:30 PM – 5:20 PM Alvardo D Co-chairs: Georg Wondrak, Mauricio Baptista

11.1 2:30 PM – 2:55 PM
A novel component of the skin exposome: Chlorination stress modulates the cutaneous response to solar UV exposure
Georg Wondrak

11.2 2:55 PM – 3:20 PM
Photochemical and Photobiological characterization of Methylglyoxal as a UVA-photosensitizer
Mauricio Baptista

11.3 3:20 PM – 3:55 PM
Arsenic potentiation of ultraviolet radiation damage in keratinocytes.
Laurie Hudson

11.4 3:55 PM – 4:20 PM
Type I interferons augment repair of photo damage and prevent cutaneous immune suppression
Nabiha Yusuf

11.5 4:20 PM – 4:45 PM
Mitigating long UVA-1 and Visible Light effects in skin with antioxidants
Eduardo Ruvolo

11.6 4:55 PM – 5:20 PM
Arsenic alters distinct mutational patterns of UVR exposure
Rachel Speer

Session 12. Recent advances on UV-mediated molecular signaling in cancer

2:00 PM – 4:05 PM Alvarado C Co-chairs: Dae Joon Kim, Yu-Ying He

12.1 2:00 PM – 2:25 PM
Emerging role of protein tyrosine phosphatase in skin photocarcinogenesis
Dae Joon Kim

12.2 2:25 PM – 2:50 PM
RNA methylation facilitates the repair of UV-induced DNA damage and suppresses photocarcinogenesis
Yu-Ying He

12.3 2:50 PM – 3:15 PM
Loss of CELF2 promotes skin tumorigenesis and increases drug resistance
Liang Liu

12.4 3:15 PM – 3:40 PM
Pro-NP mediated delivery of antioxidant enzymes protects from ultraviolet radiation induced DNA damage and skin carcinogenesis
Laura Hansen

12.5 3:40 PM – 4:05 PM
Enhanced skin tumor development in CHOP knockout mice after UVB exposure: role of compromised DNA damage recognition and enhanced proliferation
Sanjay Anand

ASP Editor's Dinner
7:00 PM – 9:00 PM Fireplace Room

Tuesday, September 27, 2022

Session 13. UV Damage and Repair in Chromatin
8:00 AM – 9:25 AM Alvarado D Chair: John Wyrick

13.1 8:00 AM – 8:10 AM
Introduction
John Wyrick

13.2 8:10 AM – 8:35 AM
Role of arsenic in affecting UV damage formation and DNA repair
Peng Mao

13.3 8:35 AM – 9:00 AM
DNA damage recognition by the XPC/Rad4 nucleotide excision repair protein complex
Jung Hyun Min

13.4 9:00 AM – 9:25 AM
Set2 Histone Methyltransferase Regulates Transcription Coupled-Nucleotide Excision Repair in Yeast
Kathiresan Selvam

Session 14. Photochemistry and Photobiology of Melanin Pigments

8:00 AM – 11:00 AM VIRTUAL ONLY Chair: Tadeusz Sarna

14.1 8:00 AM – 8:10 AM
Introduction
Tadeusz Sarna

14.2 8:10 AM – 8:35 AM
Deconstructing melanin using ultrafast laser spectroscopy
Bern Kohler

14.3 8:35 AM – 9:00 AM
Understanding melanin with theory and computations
Luis Blancafort

14.4 9:00 AM – 9:25 AM
The effect of oxidative modification of eumelanin on its photoreactivity and antioxidant properties
Michal Sarna

14.5 9:25 AM – 9:50 AM
A Bottom-Up, Synthetic Approach to the Melanin Challenge
Jean-Philip Lumb

14.6 9:50 AM – 10:15 AM
Catecholic materials show an independent response to orthogonal redox and optical stimuli
Gregory Payne

14.7 10:15 AM – 11:00 AM
Panel Discussion

Session 15. Photochemistry and photophysics in materials

8:00 AM – 12:20 PM Alvarado C Co-chairs: Lisa Kelly, Ryan McCulla

15.1 8:00 AM – 8:05 AM
Introduction
Lisa Kelly

15.2 8:05 AM – 8:10 AM
Introduction
Ryan McCulla

15.3 8:10 AM – 8:35 AM
Strategies to Achieve Photoactivation Using Visible Light
Arthur Winter

15.4 8:35 AM – 9:00 AM
Porphyrin Nanoemulsion for Antimicrobial Photodynamic Therapy: effective photosensitizer delivery to inactivate biofilm-related infections
Juan Chen

15.5 9:00 AM – 9:25 AM
Potentiation of photodynamic therapy by metal-coordination compounds as Photosensitizer
Roberto Santana da Silva

15.6 9:25 AM – 9:50 AM
Thiol induced photo-switching/stability of cyanine dyes
Gonzalo Cosa

9:50 AM – 10:15 AM
Break

15.7 10:15 AM – 10:40 AM
Next-generation light-triggered metallodrugs for cancer therapy
Sherri McFarland

15.8 10:40 AM – 11:05 AM
Exploration of a new class of photochromic molecules
Javier Read de Alaniz

15.9 11:05 AM – 11:30 AM
4-Amino-1,8-naphthalimides as potential photo-induced protein crosslinkers
Ryan Grant

15.10 11:30 AM – 11:55 AM
Liquid metal nanoparticles for photo theranostics
Marvin Xavierselvan

15.11 11:55 AM – 12:20 PM
Controlling Biology with Light and Ru(II) Complexes
Phoebe Glazer

Session 16. PDT in imaging and cancer therapy

10:00 AM – 12:15 PM Alvarado A Co-chairs: Tayyaba Hasan, Girgis Obaid

16.1 10:00 AM – 10:10 AM
Introduction
Tayyaba Hasan

16.2 10:10 AM – 10:35 AM
Strides Towards Photodynamic Image-Guided Surgery in Head and Neck Cancer
Girgis Obaid

16.3 10:35 AM – 11:00 AM
Unravelling the pivotal role of atropisomerism for cellular internalization and for the efficacy of photodynamic therapy
Luis Arnaut

16.4 11:00 AM – 11:25 AM
Tumor Ablation with Photodynamic Liposomal Irinotecan Sucrosulfate
Sanjana Ghosh

16.5 11:25 AM – 11:50 AM
Synthesis, Characterization, and Photobiological Evaluation of a New Class of Highly Active Metal Photosensitizers
Houston Cole

16.6 11:50 AM – 12:15 PM
TLD1433-mediated intraoperative photodynamic therapy with an optical surface applicator
Sarah Chamberlain

Session 17. UV-induced responses and skin cancer

10:00 AM – 12:30 PM Alvarado D Chair: Masaoki Kawasumi

17.1 10:00 AM – 10:25 AM
Estimation of UV-associated cutaneous squamous cell carcinoma incidence attributable to arsenic in U.S. water supplies
Masaoki Kawasumi

17.2 10:25 AM – 10:50 AM
PARP1 in nucleotide excision repair of UV-damaged DNA in mammalian cells
Girish Shah

17.3 10:50 AM – 11:15 AM
The keratinocytic PD-L1 response after acute and chronic UV in mouse and human epidermis: A target for topical intervention?
Sally Dickinson

17.4 11:15 AM – 11:40 AM
Loss of C/EBPβ enhances the type 1 IFN system to sensitizes keratinocytes to UVB-induced cell death
Jonathan Hall

17.5 11:40 AM – 12:05 PM
Post-labeling assay for the detection of photo-induced non-adjacent anti cyclobutane pyrimidine dimers that form in G-Quadruplex forming sequences
Natalia E. Gutierrez Bayona

17.6 12:05 PM – 12:30 PM
Detection of thymine dimers in urine after UVR exposure of volunteers by a new UPLC-MS/MS based method
Peter Philipsen

Session 18. ALA-PDT in cancer therapy

1:15 PM – 4:15 PM Alvarado D Chair: Edward Maytin

18.1 1:15 PM – 1:40 PM
Enhancement of Photodynamic Therapy for Basal Cell Carcinoma using Oral Vitamin D Pretreatment: Interim Results from a Prospective Clinical Trial
Ed Maytin

18.2 1:40 PM – 2:05 PM
5-Fluorouracil in combination with painless photodynamic therapy for actinic keratosis: Immune-modulatory effects in a murine model
Sanjay Anand

18.3 2:05 PM – 2:30 PM
It's a gift to be simple: Sandpaper curettage improves PDT outcomes for actinic keratoses
Lauren Heusinkveld

18.4 2:30 PM – 2:55 PM
Systemic versus topical 5-aminolevulinic acid administration for photodynamic therapy of murine mammary tumors after surgical resection
Gwendolyn Cramer

18.5 2:55 PM – 3:20 PM
Therapeutic enhancement of 5-aminolevulinic acid-mediated protoporphyrin IX fluorescence and photodynamic therapy with kinase inhibitor lapatinib
Sharayu Chandratre

18.6 3:20 PM – 3:45 PM
Mitochondria targeted prodrugs improve the PDT efficacy to treat non-muscle invasive bladder cancer (NMIBC)
Kazi Md Mahabubur Rahman

18.7 3:45 PM – 4:15 PM
Discussion

Session 19. Photosensitized Reactions in Biomolecules and Carcinogenic Cells

1:00 PM – 3:30 PM Alvarado C Co-chairs: Carlos Crespo, Andrés Thomas

19.1 1:00 PM – 1:25 PM
Development of All-Organic Photosensitizers for the Treatment of Cancer Cells Independent of the Oxygenation Status
Carlos Crespo

19.2 1:25 PM – 1:50 PM
Alkylation of hydrophilic type I photosensitizers is a simple synthetic tool to obtain efficient photosensitizers of biomembranes
Andrés Thomas

19.3 1:50 PM – 2:15 PM
Maurício da Silva Baptista

19.4 2:15 PM – 2:40 PM
Photochemical processes triggered by DNA damages
Virginie Lhiaubet

19.5 2:40 PM – 3:05 PM
Dormant singlet oxygen sensitizers for photodynamic inactivation and mechanistic studies
Gonzalo Cosa

19.6 3:05 PM – 3:30 PM
Bi-photonic ionization of nucleobases to mimic type I photosensitization reactions on both isolated and cellular DNA
Jean Cadet

Session 20. Photophysics: In vivo singlet oxygen detection and dosimetry

2:00 PM – 3:50 PM Alvardo A Co-chairs: Steffen Hackbarth, Gal Shafirstein

20.1 2:00 PM – 2:10 PM
Introduction
Gal Shafirstein

20.1 2:10 PM – 2:35 PM
Time-resolved Singlet Oxygen and Photosensitizer Phosphorescence Detection in vivo
Steffen Hackbarth

20.2 2:35 PM – 3:00 PM
Treatment plan development for intraoperative photodynamic therapy with our optical surface applicator
Sarah Chamberlain

20.3 3:00 PM – 3:25 PM
ROS explicit dosimetry of Photofrin-mediated Pleural PDT
Timothy Zhu

20.4 3:25 PM – 3:50 PM
Single photon detectors for biological applications
Val Zwiller

ASP Business Meeting and Awards Ceremony

5:00 PM – 6:00 PM Alvarado D

Wednesday, September 28, 2022

Session 21. PDT and Combinations to Overcome Resistance in Cancer

8:00 AM – 10:05 AM Alvardo D Chair: Joe Huang

21.1 8:00 AM – 8:25 AM
Comparison of photodynamic priming efficacy, with BPD or ALA-PpIX, to overcome PFAS-Induced Platinum Resistance in Ovarian Cancer
Brittany Rickard

21.2 8:25 AM – 8:50 AM
Photodynamic priming improves drug transport across the blood-brain tumor barrier
Joe Huang

21.3 8:50 AM – 9:15 AM
Inhibition of ABCG2 transporter by lapatinib enhances 5-aminolevulinic acid-mediated protoporphyrin IX fluorescence and photodynamic therapy response in human glioma cell lines
Bin Chen

21.4 9:15 AM – 9:40 AM
Engineering approaches to improve intraperitoneal photoimmunotherapy delivery and efficacy
Aaron Sorrin

21.5 9:40 AM – 10:05 AM
Combination photodynamic therapy with immunotherapy for immunogenic cancers
Janusz Dabrowski

Session 22. Photodynamic Treatments and Mechanisms

8:00 AM – 10:30 AM Alvardo A Chair: Ajith Karunarathne

22.1 8:00 AM – 8:25 AM
Experimental and theoretical studies on the mechanism of “dark” cyclobutane pyrimidine dimer formation and the possible role of tryptophan.
John-Stephen Taylor

22.2 8:25 AM – 8:50 AM
Nitric Oxide and Aggressiveness of Tumor Cells after Photodynamic Treatment
Witold Korytowski

22.3 8:50 AM – 9:15 AM
Origin of the red-shifted absorption maximum in channelrhodopsin Chrimson
Jonathan Church

22.4 9:15 AM – 9:40 AM
Photobiomodulation (PBM) to Reduce Pain After Dental Surgery. A Systematic Review and Quantitative Meta-Analysis of Prescribed Dose
Dennis Sourvanos

22.5 9:40 AM – 10:05 AM
Engineering Opsins for Subcellular Optogenetics
Ajith Karunarathne

22.6 10:05 AM – 10:30 AM
John Payton

Session 23. Photobiological Studies to Advance Germicidal UV-C for Infection Control

10:15 AM – 12:20 PM Alvarado D Chair: David Welch

23.1 10:15 AM – 10:40 AM
Examination of the wavelength dependency of DNA photodamage in a 3-D human skin model using UVC wavelengths
David Welch

23.2 10:40 AM – 11:05 AM
No Evidence of Induced Skin Cancer or Other Skin Abnormalities After Long Term (66 Week) Chronic Exposure to 222-nm Far-UVC Radiation
Manuela Buonanno

23.3 11:05 AM – 11:30 AM
Safety evaluation of Far-UVC irradiation to epithelial basal cells in corneal limbus
Sachiko Kaidzu

23.4 11:30 AM – 11:55 AM
Genesis of the Action Spectrum for Photocarcinogenesis – Estimating the Hazard of Germicidal UV
Don Forbes

23.5 11:55 AM – 12:20 PM
Sound GUV safety science does not guarantee public acceptance
Kate McPhaul

Session 24. Nanotechnology in PDT

10:30 AM – 12:20 PM Alvardo A Co-chairs: Jon Lovell, Jin Xie

24.1 10:30 AM – 10:40 AM
Introduction
Jon Lovell

24.2 10:40 AM – 11:05 AM
Radiodynamic Therapy with CsI(Na) Nanoparticles
Jin Xie

24.3 11:05 AM – 11:30 AM
Emerging Applications for Porphyrin-phospholipid Liposomes
Jonathan Lovell

24.4 11:30 AM – 11:55 AM
Targeted photo-activatable multi-agent liposomes for image-guided photodynamic therapy of peritoneal metastases
Joe Huang

24.5 11:55 AM – 12:20 PM
Nano-optogenetic immunotherapy
Gang Han

Grant Writing Workshop and Mentoring Luncheon

12:00 PM – 1:30 PM Fireplace Room Co-chairs: Houston Cole, Shakeela Jabeen

Session 25. Keynote Lectures

12:30 PM – 2:30 PM Alvardo D

25.1 12:30 PM – 1:30 PM
Controlling Photochemical Processes with Confinement
V. Ramamurthy

25.2 1:30 PM – 2:30 PM
How do Bilin-based Photoreceptors Sense Light
Xiaojing Yang

25.3 2:30 PM – 3:30 PM
A History of Photobiology
David Sliney

Session 26. From Predictions to Practice: Approaches to PDT Delivery

1:30 PM – 3:35 PM Alvardo A Co-chairs: Theresa Busch, Srivalleesha Mallidi

26.1 1:30 PM – 1:55 PM
Photodynamic therapy of hypoxic head and neck tumors with oxygenated photoacoustic nanodroplets
Srivalleesha Mallidi

26.2 1:55 PM – 2:20 PM
Development of low-cost technologies for delivery of PDT in resource-limited settings
Jonathan Celli

26.3 2:45 PM – 3:10 PM
Photostability studies on therapeutic monoclonal antibodies: the case of Ipilimumab
Giorgia Miolo

26.4 3:10 PM – 3:35 PM
Surgery-induced immunosuppression limits photodynamic therapy efficacy for mesothelioma
Theresa Busch

POSTERS

P.1 Transcriptional regulation of IKK alpha expression post-UVB irradiation
Yuxi Zhou

P.2 Inactivation of periodontal biofilm with singlet oxygen delivered as a gas from a superhydrophobic photosensitizer
Caroline Coradi Tonon

P.3 Photodynamic Priming improves the diagnostic accuracy and delivery of Cet-IRDye800 CW for image guided surgery in head and neck tumors
Chanda Bhandari

P.4 Function-driven membrane engineering of photodynamic liposomes in orthotopic head and neck tumors
Nimit Shah

P.5 Photochemical targeting of PFAS-induced platinum resistance in ovarian cancer
Brittany Rickard

P.6 Photoactive metallodrugs for applications in cancer therapy
Alisher Talgatov

P.7 Development of a Skin Explant Model for Studying UV-induced DNA damage
Hailey Payne

P.8 Ultraviolet Light Induced DNA Damage Reduced In Primary Fibroblast Cell Lines With Constitutive Nitric Oxide Synthase Knockout
Christina Athans

P.9 Influences of Cholesterol Depletion on Cellular Responses to Solar Ultraviolet (sUV) Radiation
Evelyn Potter

P.10 Biomimetic photooxidation to reach a tremetone-like natural product: Solvent and total singlet oxygen quenching studies
Shakeela Jabeen

P.11 Singlet Oxygen's Potential Role as a Non-oxidative Facilitator of Disulfide S–S Bond Rotation
Oliver Turque

P.12 Effect of Incident Wavelength on Singlet Oxygen Generation: Comparative Analysis of Photosensitizer in Solution and Immobilized on Superhydrophobic Surface
Hasanuwan Ihalagedara

P.13 Transition State-to-Intermediate Continuum: Mechanistic Distinction Between a Dry vs Wet Perepoxide in the Singlet Oxygen 'Ene' Reaction
Belaid Malek

Posters

P.14 Synthesis, Characterization, and Photocleavage of Bis-decyl Pteroic Acid: A Folate Derivative with Affinity to Biomembranes
José Luis Fonseca

P.15 Development of Novel Metal-based Photosensitizers for Photodynamic Therapy
Wesley McDonald

P.16 Exploring the Mechanistic Possibilities for Light-responsive Metallodrugs for Cancer Therapy
Gurleen Kaur

P.17 Metallodrug photosensitizers that exert anticancer effects in extreme hypoxia
Ge Shi

ABSTRACTS

Genomic characterization of the interplay between UV induced DNA damages and transcription.

Sheera Adar

May Merav, Elnatan Bitensky, Elisheva E. Heilbrun, Hadar Golan-Berman, Avital Parnas, and Sheera Adar

Department of Microbiology and Molecular Genetics, Institute for Medical Research Israel Canada, Faculty of Medicine, The Hebrew University of Jerusalem, Jerusalem, Israel

UV induced DNA Damages distort the DNA helix, block DNA and RNA polymerases and compromise cell function and survival. There is a complex relationship between helix distorting damages and transcription. These damages block RNA polymerases, and at the same time induce a transcriptional stress response. In parallel, active transcription enhances the ability to recognize and repair damages and reduces the mutation rates in transcribed DNA, resulting in asymmetric nucleotide composition and an asymmetry in damageable sites. To study the intertwined relationship between DNA damage and transcription, we utilized.

Damage-seq and XR-seq to map DNA damages and DNA repair at single nucleotide resolution, in parallel to RNA-seq to map transcription, across the human genome. Our analysis of UV and other helix-distorting damages such as those induced by cisplatin and smoking reveal that damage distributions are dictated primarily by sequence composition. In turn, we observe that nucleotide composition and gene architecture are major determinants of the transcriptional response to damage. These and other findings frame the transcriptional response to damage first as a direct mechanism for damage detection, and second, as a hard wired response in cis. Comparison of the transcriptional response to multiple damage types in multiple cell lines uncovered common genes with relatively higher expression in response to damage, implicating them in a general bulky DNA damage response. These include genes we've recently identified as primed in a cisplatin-resistant cancer model. These genes could serve as novel cancer risk or prognostic markers for therapy.

5-Fluorouracil in combination with painless photodynamic therapy for actinic keratosis: Immune-modulatory effects in a murine model

Sanjay Anand

Sanjay Anand[1,2,3], Lauren Heusinkveld[3], Lefatshe Lefatshe[1] and Edward V Maytin[1,2,3]

[1]Department of Biomedical Engineering, [2] Dermatology and Plastic Surgery Institute, [3]Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, OH

Painless photodynamic therapy (pPDT), compared to conventional PDT (cPDT) to treat actinic keratoses (AK) involves application of a photosensitizer (PS) followed by immediate exposure to light, instead of prolonged incubation with PS. Relative to cPDT, pPDT causes little-to-no pain, yet results in effective lesion clearance by exerting long-term immune responses. Here, we show that pretreatment of murine AK lesions with 5-fluorouracil (5FU), a common chemotherapeutic drug with immune-modulatory effects, causes enhancement of PDT-related immune responses in 5FU-treated lesions. A murine model of AK was generated by exposing SKH-1 mice to UVB (3 times a week) for 15-20 weeks. Lesions were treated topically with 5FU or with vehicle for three days prior to application of topical ALA followed immediately by light (Blu-U) exposure. AK lesions were harvested for a time-course analyses of intra-tumoral immune responses after PDT. Our preliminary immunofluorescence data showed increased recruitment of Ly6G+ neutrophils and F4/80+ macrophages, the cells of innate immunity, which peaked at 72 hours and 1-week post pPDT, respectively, in 5-FU treated lesions. Subsequently, an adaptive immune response with enhanced infiltration of CD3+ activated T cells throughout the time course, and of CD8+ cytotoxic T cells at ~1-2 weeks after pPDT, was observed in 5FU treated lesions. Additionally, 5FU pretreatment significantly reduced the presence of cells expressing the immune checkpoint marker PD1, at ~72 hours post pPDT, promoting an anti-tumor immune response by inducing inflammatory, cytotoxic T cell activity. Our preliminary data suggest that a combination of these two popular cancer therapies (5-FU and pPDT), each individually known to exert long-term anti-tumor immune responses in addition to their primary effects on cancer cells, may synergize to provide an immuno-modulatory effect for better management of non-melanoma skin cancer and pre-cancer in the dermatology clinic.

Enhanced skin tumor development in CHOP knockout mice after UVB exposure: role of compromised DNA damage recognition and enhanced proliferation

Sanjay Anand

Sanjay Anand[1,2,3], Vai Pathak[4], Lauren Heusinkveld[3] and Edward V Maytin[1,2,3]

[1]Department of Biomedical Engineering, [2]Dermatology and Plastic Surgery Institute, [3]Cleveland Clinic Lerner College of Medicine, [4]Department of Quantitative Health Sciences, Cleveland Clinic, Cleveland, OH

The CCAAT/Enhancer Binding Proteins (C/EBPs) are a family of leucine zipper transcription factors originally discovered as regulators of metabolism, cell cycle, development and differentiation. Involvement of C/EBPs has been described in several diseases including diabetes and cancer. In this study, we report the involvement of one of the newest C/EBP family members, CHOP (C/EBP Homologous Protein, also known as C/EBPζ, gadd153 or ddit3) in UV-induced skin carcinogenesis. CHOP knockout (CKO) mice, along with wild type (WT) mice, were exposed to UVB at progressively increasing doses up to 180 mJ/cm2, 3 times weekly for 20 weeks. At week 25, the number and size of tumors were significantly higher (~3-fold) in CKO mice than in WT controls. To elucidate the short-term events following UVB exposure that eventually result in this tumor phenotype, mice were exposed to UVB (100 mJ/cm2) and skin was harvested at different times for transcriptomic, immunofluorescence and western blot analyses. CKO epidermis showed delayed DNA repair evidenced by higher levels of CPD and 6-4PP positive nuclei at 72 h and 24 h after UVB exposure, respectively. Transcriptomic analysis revealed a downregulation of XPC-RAD23B-CETN2 complex, supported by western analyses showing reduced levels of XPC and DDB2 in CKO skin after UVB exposure, indicating a defect in DNA damage recognition. In parallel, a significant increase in keratinocyte proliferation (Ki67, PCNA, greater epidermal thickness) in response to UVB was observed in CKO epidermis relative to WT skin. These observations suggest that compromised DNA damage repair and enhanced proliferation in the epidermis after UVB exposure may contribute to the increased tumor response in CKO mice. Our results suggest that in addition to its well-established roles in ER stress and apoptosis, CHOP may also play an important role in skin carcinogenesis that involves regulation of DNA damage recognition and cell proliferation/growth arrest pathways.

Predicting circadian time from single cell RNA-seq data

Bogi Andersen

Bogi Andersen[1,2], Junyan Duan[1,2], Michelle Ngo[2], Babak Shahbaba[2,3], John Lowengrub[2,4]

[1] Departments of Medicine and Biological Chemistry, School of Medicine, University of California, Irvine, [2] Mathematical, Computational, and Systems Biology Program, University of California, Irvine, [3] Departments of Statistics and Computer Science, University of California, Irvine, [4] Department of Mathematics, University of California, Irvine

We have previously used gene expression profiling to define the diurnal genome in whole adult mouse skin. As this data mostly reflects the gene expression in epidermal cells, we have now used single cell RNA-sequencing to determine the diurnal genome in dermal cells, fibroblasts and immune cells. We have also developed a computational method, tauFisher, which can be trained on diurnal time course data for circadian time prediction in single time gene expression datasets, including from single cell RNA seq. tauFischer can also be used to characterize cell-cell heterogeneity in clock phase in single cell RNA seq data. We find that dermal fibroblasts have a more robust and synchronized clock gene expression than dermal immune cells. We also find that a higher proportion of dermal fibroblast genes are diurnal compared to immune cells. These data, also allow us to predict cell-cell interaction pathways that exhibit diurnal activity. We will review diurnal biological pathways in dermal fibroblasts and immune cells, which can be predicted from the single cell diurnal genomes.

Unravelling the pivotal role of atropisomerism for cellular internalization and for the efficacy of photodynamic therapy

Luis Arnaut

Luis Arnaut, L.C. Gomes-da-Silva, C. Donoho

University of Coimbra

The atropisomers of redaporfin (a fluorinated sulfonamide bacteriochlorin photosensitizer in clinical trials) are separable and display orders of magnitude differences in photodynamic efficacy. For example, a light dose of 0.2 J.cm–2 at 740 nm kills 50% of U-2 OS cells in vitro incubated with 0.2 μM of the α4 atropisomer (all meso-phenyl sulfonamide substituents on the same side of the macrocycle) but incubation with 2.5 μM of the αβαβ atropisomer (substituents on alternate sides of the macrocycle) has negligeable phototoxicity with the same light dose. The photodynamic efficacies of the atropisomers are directly related to their differential cellular uptake. The rotation along two single C–C bond between separable atropisomers increases cell uptake by a factor of 40x. Redaporfin atropisomer uptake is passive and only marginally affected by ATP depletion, plasma proteins or formulation in micelles. The α4 atropisomer is the most amphipathic atropisomer with a conformation that optimizes hydrogen bonding with polar head groups of membrane phospholipids. Consequently, α4 binds to the phospholipids on the surface of the membrane, flips into the membrane to adopt the orientation of a surfactant and eventually diffuses to the interior of the cell (bind-flip mechanism). We observed increased α4 internalization by cells of the tumor microenvironment in vivo and correlated this to the response of photodynamic therapy (PDT) when tumor illumination is performed 24 h after α4 administration. These results reveal unexpected biological consequences of atropisomerism in PDT.

The role of Carnosol in reducing ultraviolet B-Light-induced skin cancer development and progression

Veronica Bahamondes Lorca

Verónica A. Bahamondes Lorca[1,2,3], Shiyong Wu[1,2], and Lingying Tong[1,2]*

[1] Edison Biotechnology Institute, Ohio University, [2] Department of Chemistry and Biochemistry, Ohio University, [3] Departamento de Tecnología Médica, Facultad de Medicina, Universidad de Chile

Carnosol is a natural compound extracted from rosemary and sage, which many studies had demonstrated to have anti-inflammatory, antioxidant, and anti-cancer properties. Here, we evaluated the therapeutic potential and elucidated possible mechanism of action of carnosol in chemoprevention of ultraviolet B-light (UVB) induced non-melanoma skin cancer formation. Our data indicated that carnosol could partially reduce the inducibility of reactive oxygen species (ROS) production and thus reduce DNA damage post UVB. It could also reduce UVB-induced formation of cyclobutane pyrimidine dimers (CDP) in keratinocytes and mice' epidermis possibly through its known ability in absorbing at wavelength that overlap UVB radiation. In addition, carnosol could inhibit the UVB-induced activation of NF-κB and reduce UVB-induced transformation of keratinocytes. Taken together, the results indicate a role of carnosol as a potential chemo-preventive agent upon UVB radiation.

Photochemical and Photobiological characterization of Methylglyoxal as a UVA-photosensitizer

Mauricio Baptista

Mauricio S. Baptista, Universidade de São Paul

Lohanna de Faria Lopes[1], Jana Jandova[2], Jessica Perer[2], Rebecca Justiniano[2], Maurício S. Baptista[1], and Georg T. Wondrak[2]

[1]Biochemistry Department, Institute of Chemistry, University of São Paulo, São Paulo, Brazil [2]Department of Pharmacology and Toxicology, RK Coit College of Pharmacy, and UA Cancer Center, University of Arizona, Tucson, Arizona

Skin chromophores are a major source of cutaneous reactive oxygen species (ROS), and the molecular identity of the numerous endogenous chromophores acting as UVA-photosensitizers in human skin may allow the development of better sun care strategies. Methylglyoxal (MG), a glycolytic byproduct bearing a UV-active α-dicarbonyl-chromophore, is generated under metabolic conditions of increased glycolytic flux (such as diabetes-associated hyperglycemia and oncogene-driven aerobic glycolysis in cancer cells) and has been associated with formation of posttranslational protein adducts detectable in human tissue attracting much interest in diabetes, cancer, and aging research. Here, for the first time, we undertook a photophysical and photochemical characterization of MG that includes Stokes shift, phosphorescence lifetime, and quantum yield of singlet oxygen (1O2) formation. Furthermore, we demonstrate that MG acts as a UVA photosensitizer targeting cultured human HaCaT keratinocytes with induction of photooxidative stress and caspase-dependent cell death. Transcriptomic analysis indicated that the photosensitized oxidation induced by MG elicits a gene expression response (not observable upon isolated exposure to MG or UVA), characterized by upregulation of proteotoxic (CRYAB, HSPA6) and oxidative (HMOX1) stress responses. We show that MG acts as a typical UVA photosensitizer that could explain the skin photosensitivity of patients facing glycolytic dysregulation, such as in diabetes and cancer.

Understanding melanin with theory and computations

Luis Blancafort

Jun Wang[1], Daniel Bosch[2], Anju Manickoth[2], Marco Bortoli[2], Lluís Blancafort[2] [1] Jiangsu Key Laboratory for cheistry of Low-Dimensional Materials, Jiangsu Engineering Laboratory for Environment Functional Materials, Huaiyin

Normal University, Huaian, Jiangsu Province, P.R. China

[2] Institut de Química Computacional i Catàlisi and Departament de Química, Universitat de Girona, Girona, Spain

Melanin is the photoprotecting biomaterial in animal organisms, and is also a promising smart biomaterial due to a manifold of properties including a broad absorption spectrum, radiationless deactivation of electronic excitation, or redox agility. Eumelanin, the main variant, is composed of oligomers of 5,6-dihydroxyindole (DHI) and 5,6- dihydroxyindole carboxylic acid (DHICA). However, a full understanding of its biological function and exploitation of its properties in a material science context have note yet been achieved because of its atomic-level structure is unknown.

In this talk we will present our work aiming at elucidating the structure and function of eumelanin components, including characterization of a comprehensive virtual library of DHI dimers, study of the photophysics and compro-portionation of elemental components, and an outlook on the use of machine learning in a melanin context.

No Evidence of Induced Skin Cancer or Other Skin Abnormalities After Long Term (66 Week) Chronic Exposure to 222-nm Far-UVC Radiation

Manuela Buonanno

Manuela Buonanno[1], David Welch[1], Norman J. Kleiman[2], Peter C. Arden[2], Christine L. Kuryla[2], Brian Ponnaiya[1], Xuefeng Wu[1], and David J. Brenner[1]

[1] Center for Radiological Research, Columbia University Irving Medical Center, New York, NY, [2] Department of Environmental Health Sciences, Mailman School of Public Health, Columbia University Irving Medical Center, New York, NY

Far-UVC radiation, typically defined as 200-235 nm, has similar or greater anti-microbial efficacy compared to conventional 254-nm germicidal radiation. In addition, biophysical considerations of the interaction of far-UVC with tissue, as well as multiple short-term safety studies in animal models and humans, suggest that far-UVC exposure may be safe for skin and eye tissue. Nevertheless, the potential for skin cancer after chronic long-term exposure to far-UVC has not been studied. Here, we assessed far-UVC induced carcinogenic skin changes and other pathological dermal abnormalities in 96 SKH-1 hairless mice of both sexes that were exposed to average daily dorsal skin doses of 396 mJ/cm2, 126 mJ/cm2 or 56 mJ/cm2 of 222 nm far-UVC radiation for 66 weeks, 5 days per week, 8 hours per day, as well as similarly treated unexposed controls. No evidence for increased skin cancer, abnormal skin growths, or incidental skin pathology findings were observed in the far-UVC exposed mice. In addition, there were no significant changes in morbidity or mortality. The findings from this study support the long-term safety of long-term chronic exposure to far UVC radiation, and therefore its potential suitability as a practical anti-microbial approach to reduce airborne viral and bacterial loads in occupied indoor settings.

Surgery-induced immunosuppression limits photodynamic therapy efficacy for mesothelioma

Theresa Busch

Lung-sparing radical pleurectomy with intraoperative photodynamic therapy (PDT) promisingly extends survival for patients with malignant pleural mesothelioma (MPM). Nevertheless, most patients treated with this multimodal approach go on to develop local tumor recurrence, so it is crucial to determine potential mechanisms that prompt treatment failure and develop mitigation strategies. Surgery is known to induce inflammation, and we have seen in our preclinical models of murine MPM given simulated surgery (tumor injury without cytoreduction) followed by Photofrin-PDT that the surgical procedure diminishes the curative potential of PDT. To further explore the mechanisms by which surgically induced inflammation might diminish PDT efficacy, we have used these murine MPM tumor injury/PDT models to determine key leukocyte players in the development of local tumor response and establishment of long-term systemic tumor control. Using flow cytometry-based immunophenotyping and functional studies focusing on myeloid-derived suppressor cells and T cells, we have found distinct patterns of innate and adaptive inflammatory cells in tumors, tumor draining lymph nodes, and spleens of MPM tumor bearing animals. Overall, these studies suggest that surgically mediated modulation of immune cell trafficking and functionality prior to PDT leads to a systemic suppression of PDT-induced anti-tumor immune response. Targeted inhibition of these molecular or cellular signals of surgically induced inflammation may reestablish PDT efficacy in the intraoperative setting.

Bi-photonic ionization of nucleobases to mimic type I photosensitization reactions on both isolated and cellular DNA

Jean Cadet

[1]Jean Cadet, [2]Dimitar Angelov and [1]J. Richard Wagner

[1]Département de Médecine Nucléaire et Radiobiologie, Université de Sherbrooke, Sherbrooke, Québec, Canada, [2]Ecole Normale Supérieure de Lyon, CNRS, Laboratoire de Biologie et Modélisation de la Cellule (LMMC), Université de Lyon, Lyon, France

Photooxidation of cellular DNA is an ultra-minor UVB radiation-mediated process that is enhanced at the expense of the still predominant cyclobutane pyrimidine dimer formation by UVA irradiation. This is rationalized by the singlet oxygen oxidation of guanine base according to type II photosensitization mechanism. Several exogenous photosensitizers including riboflavin and methylene blue (MB) are able to operate, at least partly for MB, by one-electron oxidation of nucleobases, with guanine being the preferential substrate. A convenient way to mimic the latter type I photosensitized reaction is to expose isolated and cellular DNA to high intensity 266-nm nanosecond laser pulses. As shown by detailed mechanistic studies, bi-photonic ionization of the bases generates radical cations that are converted into stable degradation products after efficient charge transfer along the double stranded DNA chain leading to preferential trapping of the positive hole by guanine. This explains why 8-oxo-7,8-dihydroguanine is the predominant oxidation product in both isolated and cellular DNA through hydration of the guanine radical cation and subsequent one-electron oxidation of resulting 8-hydroxy-7,8-dihydroguanyl radical. It is likely that competitive one-electron reduction of the latter intermediate gives rise to 2,6-diamino-4-hydroxy-5-formamidopyrimidine that however remains to be identified. In addition the formation of several base oxidation products including 8-oxo-7,8-dihydroadenine, cis and trans 5,6-dihydroxy-5,6-dihydrothymine, 5-hydroxymethyluracil, 5-formyluracil and 5-hydroxycytosine that are produced in much lower yields have been measured by accurate HPLC-MS/MS analysis. The formation of the latter products is rationalized in terms of hydration/deprotonation of other purine and pyrimidine radical cations in agreement with mechanistic model studies. Evidence was also provided for the formation of intrastrand cross-links as the result of nucleophilic addition of thymine through N3 to proximal guanine radical cation. The generation of DNA-protein and inter-strand cross-links, only observed so far in model systems, may also be considered as hallmarks of one-electron oxidation of the guanine moiety.

Development of low-cost technologies for delivery of PDT in resource-limited settings

Jonathan Celli

Jonathan P. Celli[1] and Tayyaba Hasan[2]

[1] Department of Physics, University of Massachusetts Boston, Boston, MA, [2] Wellman Center for Photomedicine, Massachusetts General Hospital, Boston, MA

The lack of medical infrastructure for timely diagnosis and treatment of cancer in low and middle income countries (LMICs) is a major factor driving stark disparities in cancer outcomes globally. Photodynamic therapy (PDT) emerges as a candidate treatment modality which is well-suited to adaptation for use in resource-limited clinics, provided that key design criteria including portability, ease-of-use, operability on battery power and availability of a low-cost photosensitizer, can be met. Motivated specifically by the public health crisis of oral cancer in India, we have developed technology to enable use of PDT with aminolevulinic acid (ALA)-induced protoporphyrin IX (PpIX) for treatment of early stage oral lesions. Our team designed and tested a portable, battery-powered, fiber-coupled 635nm LED light source with a system of interchangeable 3D printed applicators for ergonomic light delivery to lesions of varying size and position in the oral cavity. The system uses an embedded microcontroller and Bluetooth to interface with a smartphone while an attachment for imaging PpIX fluorescence is used for treatment guidance and monitoring. Clinical evaluation led by collaborators in India has shown excellent outcomes, with complete tumor response in 73% of oral cancer patients following a single PDT treatment. Here we discuss challenges and opportunities moving forward for broader implementation of low-cost technology for oral cancer imaging and PDT in India and potential for adaptation to other conditions globally.

TLD1433-mediated intraoperative photodynamic therapy with an optical surface applicator

Sarah Chamberlain

Sarah Chamberlain [1], Sherri McFarland [2], David Bellnier [1], and Gal Shafirstein [1]

[1] Photodynamic Therapy Center, Roswell Park Comprehensive Cancer Center, NY, [2] Department of Chemistry and Biochemistry, University of Texas: Arlington, TX

The ruthenium (Ru)-based photosensitizer TLD1433 has been shown to be safe in a phase 1b II clinical trial for treating non-muscle invasive bladder cancer and is being tested for efficacy in a phase II study. We propose TLD1433 can be used for safe and effective IO-PDT of abdominal serosal surface disease. We have previously demonstrated that our optical surface applicator can deliver effective TLD1433-mediated PDT in-vitro. Here, we report the safety of TLD1433 delivery to the abdomen of BALB/c mice. Next, we report the safety of TLD1433-mediated IO-PDT with our miniature OSA light delivery through treatment of human lung adenocarcinoma (A549) luciferase-expressing tumor in the abdomen of RNU rats.

Mice underwent laparotomy for TLD1433 delivery via instillation. TLD1433 was delivered to the abdominal cavity at 50 mg/kg body weight for 1 hour, followed by washing to remove excess TLD1433 not up taken by the tumor, then closure of the surgical site. Rats bearing A549-luciferase expressing tumors underwent laparotomy for TLD1433 and IO-PDT light delivery. TLD1433 was delivered at 14 mg/kg to the abdomen of the RNU rats for 1 hr. Light was delivered by a miniature OSA containing two 1-cm cylindrical diffuser fibers. The output power for the 1-cm diffuser fibers within the miniature OSA was determined by simulating the light our miniature OSA using the FullMonte software. Followed IO-PDT, rats were observed for 24 hours, then normal and tumor tissue were collected for histology.

Mice recovered with no observable toxicity from TLD1433 delivery to the abdomen. Rats recovered from surgery with no adverse events. Histology revealed hydropic degeneration and tumor lysis in tumors treated with TLD1433-mediated IO-PDT. These results demonstrate the first application of TLD1433-mediated IO PDT in a preclinical model with abdominal serosal surface disease.

Treatment plan development for intraoperative photodynamic therapy with our optical surface applicator

Sarah Chamberlain

Sarah Chamberlain [1], David Bellnier [1], Alan Hutson [2], and Gal Shafirstein [1]

[1] Photodynamic Therapy Center, Roswell Park Comprehensive Cancer Center, NY [2] Biostatistics and Bioinformatics, Roswell Park Comprehensive Cancer Center, NY

Intraoperative photodynamic therapy (IO-PDT) of non-small cell lung cancer (NSCLC) has been shown to improve overall survival in patients. Our group has developed a novel optical surface applicator (OSA) for improved control of light delivery during IO-PDT. Previously, we reported that Monte Carlo light simulations with our OSA geometry has the potential to develop a platform for treatment planning for IO-PDT. We hypothesize that we can accurately simulate propagation of green and red laser light through our OSA. Here we present the results of testing the validity of our simulations in optical tissue-mimicking phantoms.

Our 8-channel light dosimetry system was used to measure the irradiance in optical tissue-mimicking phantoms illuminated with OSA emitting either 665-nm or 532-nm wavelength light. The OSA was placed at the top of the phantoms and measurements were taken at a prescription depth of 5 mm. This experimental configuration was reproduced in a computer model using Paraview and the FullMonte software with up to 1.1 million elements in the tetrahedral mesh. Light propagation was simulated with 10 million photon packets. The Bland Altman test was used to compare between the computer simulations and the light dosimetry measurements.

The Bland Altman calculated concordance correlation coefficients were above 0.9 indicating an acceptable agreement between the light simulations and dosimetry measurements. These results suggest that we can accurately simulate laser light propagation from the OSA with Paraview and FullMonte software and that can be used to develop treatment planning for IO-PDT with OSA.

Therapeutic enhancement of 5-aminolevulinic acid-mediated protoporphyrin IX fluorescence and photodynamic therapy with kinase inhibitor lapatinib

Sharayu Chandratre

Sharayu C[1], Matthew M[1], Richard H[1], Daniel M[2], Kenneth M[2], Bin C[1]

[1] Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy, Saint Joseph's University, Philadelphia, PA, [2] Department of Biological Sciences, Misher College of Arts and Sciences, Saint Joseph's University, Philadelphia, PA

Glioblastoma is a CNS malignancy with poor disease prognoses. The median patient survival is only 12-14 months with the standard treatment regimen composed of maximum surgical resection, chemotherapy and radiation therapy. 5-aminolevulinic acid (ALA) has been approved as an intraoperative probe to facilitate the maximum resection of glioblastoma. As a prodrug, ALA is endogenously converted to protoporphyrin IX (PpIX) with red fluorescence by the heme biosynthesis pathway. The preferential accumulation of PpIX in tumors enables neurosurgeons to perform fluorescence-guided resection (FGR) of glioblastoma with high surgical precision and good outcomes. Because PpIX is also a photosensitizer, there is a growing interest in killing remaining glioblastoma cells after surgery with photodynamic therapy (PDT),

a cytotoxic modality through the generation of reactive oxygen species following light activation. The use of ALA for FGR and PDT is limited by low PpIX fluorescence and PpIX fluorescence heterogeneity, the reason for which is not fully understood. Once generated in cells, PpIX can be converted to heme or transported out of the cell through the ABCG2 efflux transporter. We have recently found that ABCG2 inhibition by a tyrosine kinase inhibitor lapatinib significantly decreases PpIX efflux in certain cancer cell lines. Here we show that lapatinib increases PpIX fluorescence and sensitizes tumor cells to ALA-PDT in a panel of glioma cell lines. Our study also probes into the mode of cell death initiated by this combination treatment. Overall, this study highlights that targeting ABCG2 with lapatinib is a novel and effective approach for enhancing PpIX fluorescence and PDT response in glioblastoma.

Role of CTHRC1 in Non-Melanoma Skin Cancers

Hao Chang

Hao Chang, University of Wisconsin-Madison

Chandra K. Singh[1], Gagan Chhabra[1], Minakshi Nihal[1], Nihal Ahmad[1,2], Hao Chang[1,2]

[1]Department of Dermatology, University of Wisconsin-Madison, Madison, WI, [2]William S. Middleton Memorial Veterans Hospital, Madison, WI

Non-melanoma skin cancers (NMSCs) are the most diagnosed cancers in the USA, and exposure to solar ultraviolet (UV) radiation is the major contributing factor. The two most common NMSCs are basal cell carcinoma (BCC) and squamous cell carcinoma (SCC). While BCC can be surgically removed and rarely spreads, SCC frequently metastasizes (lesions >2 cm in diameter have a recurrence and metastasis rate of 15% and 30%, respectively). SCC risk also increases in immunocompromised patients. Thus, it is important to develop mechanism-based approaches for SCC management. Collagen triple helix repeat containing 1 (CTHRC1), a protein initially reported to be involved in vascular remodeling and bone formation, has been found aberrantly expressed in various cancers and promotes cancer cell proliferation. Recent studies also suggest an association of CTHRC1 with epithelial-mesenchymal-transition (EMT) and metastasis by modulating key cancer pathways. Thus, it is critical to elucidate how complex molecular mechanisms of CTHRC1 affect SCC development and progression. We have found that CTHRC1 is overexpressed in several human SCC cell lines and patient tissues. Knockdown of CTHRC1 significantly inhibits cell proliferation of SCC cells. Also, CTHRC1 knockdown downregulates the expression of several EMT genes, suggesting a potential role of CTHRC1 in EMT regulation in SCC. Interestingly, CTHRC1 expression is significantly upregulated in tumor tissues from the SKH-1 mice exposed to UVB, and dietary grape powder treatment causes a decreasing trend in the CTHRC1 mRNA level. This suggests that the protective effect of dietary grape against UVB-induced skin carcinogenesis might be partially due to the inhibition of CTHRC1. We have generated novel Cthrc1 transgenic and knockout mouse lines for dissecting the function and mechanisms of Cthrc1 in vivo. Overall, our ongoing study suggests that CTHRC1 might promote SCC development and progression and could potentially serve as a target for SCC management. "" Oral (preferred) Non Student I consent

Inhibition of ABCG2 transporter by lapatinib enhances 5-aminolevulinic acid-mediated protoporphyrin IX fluorescence and photodynamic therapy response in human glioma cell lines

Bin Chen

Bin Chen, University of the Sciences

Matthew Mansi, Richard Howley, Sharayu Chandratre, Bin Chen

Department of Pharmaceutical Sciences, Philadelphia College of Pharmacy, University of the Sciences, Philadelphia, PA

5-Aminolevulinic acid (ALA) is an intraoperative molecular probe approved for fluorescence-guided resection (FGR) of high-grade gliomas to achieve maximal safe tumor resection. Although ALA has no fluorescence on its own, it is metabolized in the heme biosynthesis pathway to produce protoporphyrin IX (PpIX) with red fluorescence for tumor detection and photosensitizing activity for photodynamic therapy (PDT). The preferential tumor accumulation of PpIX following ALA administration enables the use of ALA as a prodrug for PpIX FGR and PDT of gliomas. Since intracellular PpIX in tumor cells after ALA treatment is influenced by biological processes including PpIX bioconversion catalyzed by ferrochelatase (FECH) and PpIX efflux by ATP-binding cassette subfamily G member 2 (ABCG2), we determined the activity of FECH and ABCG2 in a panel of human glioma cell lines and correlated with intracellular and extracellular PpIX levels and PDT response. We found that glioma cell lines with ABCG2 activity exhibited the trend of low intracellular PpIX, high extracellular PpIX and low PDT response, whereas no particular correlation was seen with FECH activity. Inhibition of PpIX efflux with ABCG2 inhibitors was more effective in enhancing ALA-PpIX fluorescence and PDT response than blocking PpIX bioconversion with iron chelator deferoxamine. We also showed that a clinically used kinase inhibitor lapatinib could be repurposed for therapeutic enhancement of ALA due to its potent ABCG2 inhibitory activity. Our study reveals ABCG2 as an important biological determinant of PpIX fluorescence in glioma cells and suggests ABCG2 inhibition with lapatinib as a promising therapeutic enhancement approach."" I would like ASP to pull my presentation after the conclusion of the meeting on April 12, 2022 I do not consent

Porphyrin Nanoemulsion for Antimicrobial Photodynamic Therapy: effective photosensitizer delivery to inactivate biofilm-related infections

Juan Chen

Juan Chen[1], Hilde Harb Buzzá[2], Fernanda Alves[2], Vanderlei S. Bagnato[2], Cristina Kurachi[2], Gang Zheng[1]

[1] Princess Margaret Cancer Centre, University Health Network, Toronto, Ontario, Canada [2] Sao Carlos Institute of Physics, University of Sao Paulo, Brazil

The management of biofilm-related infections is a challenge in healthcare since the microorganisms in this community are protected by an extracellular matrix that hinders the antimicrobial agent action. Antimicrobial photodynamic therapy (aPDT) is a powerful tool and has demonstrated a broad-spectrum antimicrobial activity. We recently developed a NewPS nanoplatform, a simple, versatile and safe surfactant-free nanoemulsion with a porphyrin salt shell in stabilizing a food-grade oil core and have demonstrated its

intrinsic multimodality for imaging and effective PDT. The NewPS system has excellent colloidal stability, is amenable to different porphyrin salts and oils, and is capable of co-loading with chemotherapeutics and antibiotics. We investigate here the use of NewPS for aPDT against microorganisms in planktonic, biofilm and in vivo model of infected wound. A high NewPS-bacteria cell interaction was achieved since 10 nM and 30 J/cm² was able to kill S. pneumoniae suspension, and 500 nM reduced ~6 logs of S. aureus. In the S. aureus biofilm, enhanced efficacy of NewPS-aPDT was achieved when a higher NewPS concentration (100 μM) was applied with longer periods of incubation, in either one or two aPDT sessions at the light dose of 60 J/cm2. The best single-aPDT resulted in 5.6 logs of reduction and double-aPDT reduced ~6 logs. The confocal images revealed a homogeneous NewPS distribution within all biofilm regions at the 6-hour incubation time, resulting in a high number of dead cells after aPDT. When translating to an in vivo aPDT on an infected wound mouse model,

NewPS proved to be non-toxic, enabled great wound healing process, and resulted in more than 6 logs reduction and faster tissue healing in comparison to the other groups. In conclusion, the NewPS-mediated aPDT enables a safe and highly effective treatment for biofilm-related infections.

Origin of the red-shifted absorption maximum in channelrhodopsin Chrimson

Jonathan Church

Jonathan Church, Tal Dogon and Igor Schapiro

Fritz Haber Center for Molecular Dynamics Research Institute of Chemistry, The Hebrew University of Jerusalem, Jerusalem, Israel

Rhodopsins belong to a class of photoreceptor proteins which are strong candidates for biotechnological applications such as optogenetics. These proteins obtain their light sensitivity from a covalently bound retinal chromophore, which initiates the biological function of the protein through photoisomerization. One challenge hindering rhodopsins from widespread application is that their absorption maxima often overlap with other biological molecules. One area of research has focused on how to rationally design these proteins to absorb in the optical transparency window of the body. This optical window has maximum tissue penetration and ranges from red light (^{650} nm) to the infrared (^{1350} nm).

In this contribution we focus on red-light sensitive channelrhodopsin Chrimson (λ_{max} = 590 nm), that naturally absorbs close to this window. Furthermore, a single mutation (S169A) has been found to further red-shift the absorption maximum to 605 nm. The current hypothesis is the spectral tuning in Chrimson is due to the binding pocket having one negatively charged counterion near the Schiff base at physiological pH. However, there is still debate as to which counterion contains the proton, E165 or D295. In addition, there is a third counterion located near the protonated Schiff base, E132, which may play a role in the spectral tuning of this protein. The present study uses classical molecular dynamics in tandem with QM/MM sampling to determine how changing the protonation states of these counterions impacts the absorption maximum. The resulting absorption maxima and structural changes are also compared to experiment to determine the correct protonation of the protein.

Two photosensitive diseases but only one gets cancer

James Cleaver

Synthesis, Characterization, and Photobiological Evaluation of a New Class of Highly Active Metal Photosensitizers

Houston Cole

Photodynamic therapy (PDT) is a promising approach to cancer treatment that remains underutilized rous tissue. PDT uses a non-toxic prodrug, or photosensitizer (PS), to, in the presence of light and oxygen, cause localized cell death. Photofrin, an organic porphyrin-based PS, is currently the only FDA-approved PS for cancer therapy. We believe that PDT could become a more accessible alternative or adjuvant therapy with the development of next-generation PSs. Metal-based PSs are of particular interest due to their tunable photophysical and physicochemical properties. Ruthenium and osmium polypyridyl PSs serve as examples, with our own TLD1433 recently entering Phase II clinical trials for the treatment of bladder cancer. This presentation will show how the rational molecular design of PSs can lead to significant improvements in PS activity for PDT.

Thiol induced photo-switching/stability of cyanine dyes

Gonzalo Cosa

Gonzalo Cosa

Department of Chemistry, McGill University, Otto Maass Chemistry Building, Sherbrooke Street West, Montreal, QC, Canada

From the inception of single molecule fluorescence studies cyanine dyes, specifically Cy3 and Cy5, have been key to cementing the field by enabling different methodologies. Notably, photostabilization but also photoswitching of these dyes relay on photochemical reactions in the presence of thiol compounds. This dual behavior for the cyanine dyes under otherwise identical conditions has been an enigma for years. Here we provide a unified mechanistic framework highlighting the principles that dictate the photoswitching susceptibility of cyanine dyes in the presence of thiols and their close relationship to the mechanism governing the photostabilizing properties thiols confer to these dyes. This understanding provides a roadmap for the design of fluorophores, photoswitching agents, and triplet quenchers with desired characteristics, and a set of guidelines toward a better photochemical control over currently used dye/thiol pairs, including photoswitching rates and enhanced photon budgets.

Dormant singlet oxygen sensitizers for photodynamic inactivation and mechanistic studies

Gonzalo Cosa

In order to minimize undesired side effects, including damage to healthy tissue during Photodynamic therapy (PDT) treatment, photosensitization of $^1O_2$ is controlled via the specific targeting of the photosensitizer to ailing over healthy tissue and through the precise delivery of the exciting light. Recently the chemical activation of an otherwise dormant photosensitizer specifically in the targeted tissue has emerged as an effective new level of control. The method exploits differences in the proteome or metabolome of an ailing tissue over the healthy tissue.

Here I will describe the design of new dormant sensitizers that activate under oxidative stress or in the presence of cellular nucleophiles. These compounds are based on two-segment photosensitizer-trap molecules where the photosensitizer segment consists of a Br-substituted BODIPY dye. For activation via oxidative stress the trap segment consists of the chromanol ring of α-tocopherol, the most potent naturally occurring lipid soluble antioxidant. Photoinduced electron transfer to either the singlet or triplet excited state of the BODIPY core leads to deactivation of the dye. Following ROS scavenging, the probe becomes active. In turn, for activation by cellular nucleophiles, the compound incorporates a reactive acrolein warhead. The acrolein moiety serves as an intramolecular switch, deactivating the BODIPY dye in its singlet and triplet excited states via internal conversion. Reaction with cysteine residues restores the photosensitizing properties. Time-resolved absorption, fluorescence, and $^1O_2$ phosphorescence studies together with fluorescence and $^1O_2$ phosphorescence emission quantum yields and DFT studies support these mechanisms.

The usefulness to selectively activate the production of singlet oxygen will be described both in therapeutic applications and mechanistic studies involving photodynamic inactivation of Gram negative E.coli strains and in HeLa cell studies.

Systemic versus topical 5-aminolevulinic acid administration for photodynamic therapy of murine mammary tumors after surgical resection

Gwendolyn Cramer

Shirron Carter[1], Joann Miller[1], Gwendolyn Cramer[1], Min Yuan[1], Stacy Guzman[3], Mary E.

Putt[2], Keith A. Cengel[1], Gary M. Freedman[1], and Theresa M. Busch[1]

[1]Department of Radiation Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [2]Department of Biostatistics, Epidemiology & Informatics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA, [3]Department of Biochemistry and Biophysics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, PA

Strategies for treatment de-escalation are needed for managing ductal carcinoma in situ (DCIS) and early-stage breast cancers. As an adjuvant to lumpectomy, photodynamic therapy (PDT) may be an effective option with a tolerable side effect profile. We examined 5-aminolevulinic acid (ALA) based PDT in combination with resection of murine mammary tumors (TUBO), where ALA was delivered orally 5 hours prior or topically 10 minutes prior to 632 nm illumination at 135 J/cm2. Both oral-ALA-PDT (oALA-PDT) and topical-ALA-PDT (tALA-PDT) to the mammary fat pad after complete resection (CR) of TUBO tumors produced long-term tumor control significantly better than CR alone. CR/oALA-PDT caused more vasculature damage, a larger influx of neutrophils, and more tissue inflammation than CR/tALA-PDT. While levels of ALA-induced protoporphyrin IX were about 10-fold higher in CR/oALA-PDT compared to CR/tALA-PDT, tumor control was similar with 90-day complete response rates of 21% and 32% respectively. Overall, these data support continued investigation of ALA-PDT as an adjuvant for lumpectomy in breast cancer treatment.

Development of All-Organic Photosensitizers for the Treatment of Cancer Cells Independent of the Oxygenation Status

Carlos Crespo

Carlos E. Crespo-Hernández

Department of Chemistry, Case Western Reserve University, Cleveland, Ohio

Photodynamic therapy (PDT) is a clinically approved, noninvasive therapy for cancer treatment that relies on the administration of a photosensitizer (PS) and light to the affected area. PDT is more attractive than conventional therapies such as radiotherapy and chemotherapy because it is minimally invasive, has exceptional spatiotemporal selectivity, diminished side effects, and is overall simplistic among other important considerations. Notwithstanding the significant benefits over traditional therapies, PDT has yet to reach its full potential primarily because optimal PSs, applicable to a wide range of cancers and biological tissues, are difficult to develop. There is a clinical need for diverse alternatives offering improved target cell selectivity and the efficiency of more than one sensitization mechanism. An approach developed in our group that is swiftly gaining increased attention is to replace the oxygen atom with a sulfur atom in carbonyl groups of existing organic molecules to redshift their absorption spectra and increase their triplet yields and the generation of singlet oxygen and other reactive oxygen species. These PSs are inexpensive to make and offer good biocompatibility, biodegradability, minimal dark cytotoxicity, and structural stability. In this presentation, I will demonstrate how fundamental physicochemical investigations can be used to develop all-organic PSs exhibiting tunable absorption spectra from the ultraviolet-A (UVA) to the near-infrared and nearly 100% greater photoreactivity than the carbonyl counterparts. When applied in vitro with a low dose of light, these PSs substantially decrease the proliferation of cancer cells, some independent of the oxygenation status (i.e., under both normoxic and hypoxic conditions).

Combination photodynamic therapy with immunotherapy for immunogenic cancers

Janusz Dabrowski

[1]Faculty of Chemistry, Jagiellonian University, Krakow, Poland

The most important features of cancer that limit the effectiveness of current treatments include: i) ability to stimulate angiogenesis; ii) ability to infiltrate surrounding tissues and create distant metastases; iii) ability to escape from the control of the immune system, which under normal conditions prevents tumor progression. The negative immune checkpoints inhibition has become an attractive strategy for cancer treatment. The most common way is the blockade of binding between the programmed death [1] receptor (PD-[1]) and its ligand PD

L1. However, in order to achieve total therapeutic success, it is crucial to apply a strategy operating in a multiple directions, through various biological mechanisms aimed at complete destruction of the tumor. Here, we present the design of combining anticancer modality based on photodynamic therapy (PDT) with checkpoint blockade immunotherapy. We developed novel PD-1/PD-L1-targeting molecules and present their therapeutic potential in combination with bacteriochlorin-based PDT. We also compare the results with those obtained with anti-PD-1/PD-L1 mAbs. After comprehensive in vitro screening, we performed PDT augmented by systemic PD-1/PD-L1 inhibition in vivo. Using the multitarget approach it was possible to evaluate whether modulation of inflammatory response induced by PDT affect the tumor microenvironment and determine the susceptibility to systemic PD-1/PD-L1 inhibition including effects on primary tumor control as well as prevention of metastasis in a preclinical model. In summary, our data provide evidence for the role of PDT for local immune modulation, and that the combination with PD-1/PD-L1 checkpoints inhibitors is a promising strategy in the therapy of more resistant tumors.

Chemical, structural and functional modifications of proteins phototriggered by an endogenous photosensitizer

Laura Dantola

Lara O. Reid,[1] Virginie Lhiaubet-Vallet,[2] Vanesa Herlax,[3] Carolina Lorente,[1] Andrés H. Thomas,[1] M. Laura Dántola[1]

[1] 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, Argentin, [2] Instituto de Tecnología Química, Universitat Politècnica de València - Consejo Superior de Investigaciones Científicas, Valencia, Spain, [3]Instituto de Investigaciones Bioquímicas La Plata (INIBIOLP), CCT-La Plata, CONICET, UNLP, Facultad de Ciencias Médicas, La Plata, Argentina

Electromagnetic radiation is able to modify the chemical structure of many biomolecules. Most of the solar UV energy incident on Earth surface corresponds to UV-A radiation, which is not absorbed significantly by the components of the biological systems, but acts indirectly through photosensitized reactions. These reactions are key players both on beneficial and harmful processes triggered by UV and visible light. Epidemiological evidence has shown that exposure of humans to artificial UV-A radiation, is a major risk factor for melanoma induction. On the other hand, photosensitization can be used to treat different types of cancer by photodynamic therapy and is also important due to several applications in disinfection and photodynamic inactivation of microorganisms.

Pterins, a family of heterocyclic compounds, are widespread in living systems and participate in important biological functions. In pathological conditions, such as vitiligo, oxidized pterins accumulate in the white skin patches of patients suffering this depigmentation disorder. These molecules present a profuse and amazing photochemistry and are endogenous photosensitizer that act via type I (electron transfer) or type II (singlet oxygen), or a combination of both mechanism.

Proteins are one of the preferential targets of the photosensitized damaging effects of

UV radiation on biological system. In general, it is accepted that the photosensitization of proteins occurs mainly through the reactions of singlet oxygen with different amino acid residues. Nevertheless, it has been demonstrated that pterins photosensitize peptides, proteins and their components mainly through a type I mechanism. In the context of our investigations on the photosensitizing properties of pterins, an overview of the photosensitization damage of different kind of proteins by pterin derivatives will be presented, focusing the attention on the chemical modifications of tyrosine and tryptophan residues and its effect on protein structure and function.

Reaction of cysteine residues with oxidized tyrosine residues contributes to cross-linking of photo-oxidized proteins

Mike Davies

Michael Davies, University of Copenhagen

Chiara Rossi, Laura Doblas, Eduardo Fuentes-Lemus and Michael J. Davies

Department of Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark

Photo-oxidation of proteins is commonplace due to widespread exposure to UV radiation, or visible light in the presence of a chromophore. A major consequence is protein cross-linking and aggregation, but the nature of the crosslinks formed is poorly defined. Previous work has focused on di-tyrosine formed from two tyrosine radicals, but recent data indicate that this may only be a minor species. Here, we investigated the occurrence of secondary reactions between oxidized protein side-chains and Cys residues. Caseins, the major proteins in milk, were subjected to photooxidation using visible light, a sensitizer (riboflavin/vitamin B2, an endogenous sensitizer in milk, or rose Bengal) and O2, then incubated with glutathione or thiol-containing proteins (kappa-casein, beta-lactoglobulin), with analysis by SDS-PAGE, immunoblotting and LC-MS. Photo-oxidized (but not parent) caseins react efficiently with Cys-containing species, via Michael addition to quinones formed from Tyr residues to give glutathionylated or protein-protein adducts. Thus, oxidized α-casein react with native κ-casein to give high molecular mass aggregates. This adduct formation was prevented by alkylation of the Cys residue. The cross-link site and the residues involved have been confirmed by liquid chromatography-mass spectrometry (LC-MS) proteomic analysis. Further studies indicate that Cys residues also react with oxidized disulfide bonds via the intermediacy of thiosulfinate species generated by reaction of the disulfide bond with singlet oxygen. These reactions result in both glutathionylation of proteins (when GSH is the attacking species) and the formation of new inter-protein disulfide bonds when the Cys residue is present on a second protein. Together these data provide strong evidence for reactions of Cys residues with photo-oxidized amino acids as major contributors to protein crosslinking and aggregation generated by photo-oxidation.""

The keratinocytic PD-L1 response after acute and chronic UV in mouse and human epidermis: A target for topical intervention?

Sally Dickinson

Sally E. Dickinson[1,2]*, Prajakta Vaishampayan[2], Viktoria Kirschnerova[2], Maria Khawam[2], Sara M. Centuori[2,3], Kathylynn Saboda[2], Valerie S. Calvert[4], Emanuel F. Petricoin III[4] and Clara Curiel-Lewandrowski[2,5]

[1]Department of Pharmacology, University of Arizona, Tucson, AZ, [2]University of Arizona Cancer Center, Tucson, AZ, [3]Department of Medicine, University of Arizona, Tucson, AZ, [4]Center for Applied Proteomics and Molecular Medicine, George Mason University, Manassas, VA, [5]College of Medicine, Division of Dermatology, University of Arizona, Tucson, AZ

Overexpression of PD-L1 (CD274) on tumor cells may represent a hallmark of immune evasion, and high expression levels of this protein has been documented in several tumors including cutaneous squamous cell carcinoma (cSCC). While PD-L1/PD-1 activity in the skin has been primarily described in inflammatory models, our goal was to examine PD-L1 expression in human keratinocytes exposed to UV irradiation. We assessed PD L1 expression in human sun-protected (SP) and sun-damaged (SD) skin, actinic keratosis (AK), and cSCC using IHC and protein microarray. Both methods found low baseline levels of PD-L1 in SP and SD skin and significantly increased expression in cSCC. Next, we examined PD-L1 expression in acute models of UV exposure. In human SP skin exposed to 2-3 MED of UV (n = 20), epidermal PD-L1 was induced in 70% of subjects after 24 h ($p = 0.0001$). SKH-1 mice exposed to acute UV also showed significant epidermal PD-L1 induction at 16, 24 and 48 h. A time- and dose-dependent induction of PD-L1 was confirmed in cultured human keratinocytes after UV, which was markedly reduced in the presence of MEK/ERK, JNK or STAT3 inhibitors. Notably, topical treatment of mouse skin or cultured human keratinocytes with a pharmacological small-molecule inhibitor of PD-L1, BMS-202, significantly reduced UV-induced PD-L1 stimulation at the RNA and protein levels. These findings suggest that UV induces the upregulation of PD

L1 through established, pharmacologically targetable stress-signaling pathways in keratinocytes. Topical inhibition of this immune checkpoint ligand in the epidermis may therefore represent a novel target for early intervention in UV-induced skin cancer.

DNA repair products as biomarkers of the genotoxicity of UV radiation

Thierry Douki

Thierry Douki[1], Noémie Reynaud[1], Laura Belz[1], David Béal[1], Daniel Bacqueville[2], Hélène Duplan[2], Emmanuel Questel[3], Gwendal Josse[3]

[1] Univ. Grenoble Alpes, CEA, CNRS, IRIG, SyMMES, Grenoble, France, [2] Service de Pharmacologie et Pharmacocinétique cutanée, Centre R&D Pierre Fabre, Toulouse, France, [3] Centre de Recherche sur la Peau, Pierre Fabre Dermo Cosmétique, Toulouse, France

Many analytical tools have been developed for their quantification in DNA of the pyrimidine dimers induced by UV radiation. In the present work, we investigated whether photoproducts could be quantified by a non-invasive approach in urine or in the culture medium of in vitro models. We developed an assay for the pyrimidine dimers removed from DNA by nucleotide excision repair in 30-bases long or shorter oligonucleotides. A solid phase extraction method was optimized for the isolation of the repair products from urine or culture medium. These DNA fragments were enzymatically hydrolyzed like DNA in order to release individual photoproducts. For the final detection, we improved our previous HPLC-mass spectrometry method by including on-line SPE and ultra-high performance liquid chromatography. Relevant internal standards were used to insure the quantitative aspect of the measurements. The technique was first applied to the validation of the biological relevance of the underlying hypothesis of the excretion of the photoproducts from cells. Experiments on cultured HaCat cells showed that, after formation in nuclear DNA, photoproducts are excised by repair, transferred into the cytoplasm and finally extracted into the culture medium. Similar work on human skin explants showed that a more complex and dense tissue does not prevent the release of repair products. Last, a small human investigation showed that pyrimidine dimers could be readily detected in urine following classical recreational exposure to sunlight.

New challenges of photobiology

Amparo Faustino

M. Amparo. F. Faustino

[1]Department of Chemistry and LAQV-REQUIMTE, University of Aveiro, Aveiro, Portugal, [2]European Society for Photobiology

The interaction of light and matter has been recognized since ancient times as a valuable tool for human health and well-being. However, only throughout the 20th century several biological processes were understood, opening new opportunities for different applications. In this communication will be discussed the contribution of photobiology in the development of new scientific areas and potential challenges for the 21st century, particularly in Europe.

Genesis of the Action Spectrum for Photocarcinogenesis – Estimating the Hazard of Germicidal UV

Don Forbes

The recent/ongoing COVID pandemic has elevated the interest and concern in and about germicidal UV (GUV) to help reduce the potential spread of the virus in working environments. Original animal studies in the 1970s and 80s helped to define the hazard of photocarcinogenesis from solar UV-B and UV-A, now published as a CIE Standard non-melanoma skin cancer action spectrum. It is noteworthy that only one study was considered in estimating the relative hazard from UV-C in this model. An additional published study from the early 1970s, utilizing a germicidal lamp and the available dose-response model, added further evidence that the hazard from GUV is indeed very low relative to other parts of the UV spectrum. More recent studies using newly developed sources of filtered 222nm GUV also show little potential for damage from skin or eye exposures, thus lending to the utility of shortwave GUV for environmental control. Regarding long-term safety, estimates will benefit from additional studies on cellular markers for damage in human skin, or skin models, since depending on lifetime studies to establish an action spectrum (for example for human photocarcinogenesis or induced life-shortening) is, by definition, impractical.

The impact of solar UV-B exposure on circadian rhythms in SKH-1 hairless mice

Shobhan Gaddameedhi

Adam J. Greer[1], Sean Cone[1], Bala S.C. Koritala[2,3], Shobhan Gaddameedhi[1,4]

Department of Biological Sciences, North Carolina State University, Raleigh, NC, [2]Division of Pediatric Otolaryngology-Head and Neck Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [3]Division of Otolaryngology-Head and Neck Surgery, University of Cincinnati, Cincinnati, OH, [4]Center for Human Health and the Environment, North Carolina State University, Raleigh, NC

Background: The International Agency for Research on Cancer has recognized circadian clock disruption through nightshift work as a probable human carcinogen and risk factor for the development of skin cancers. However, the precise physiological relationship between tumor-inducing stimuli—such as solar ultraviolet-B (UV-B) radiation—and their respective impacts on circadian rhythmicity is unclear.

Objectives: We continuously recorded locomotor activity of hairless SKH-1 mice over the course of at least 25 weeks to evaluate changes in rhythmic behavior following long-term exposure to rotating light-dark cycles in the presence or absence of UV-B radiation. Results were further contrasted with a genetic clock disruption model (mPer1/mPer2).

Methods: We used 3-week old SKH-1 mice of each sex (192 total) in a program varied by genotype, light schedule, and exposure to UV-B radiation. Mice were classified as either DS (wildtype-dayshift), RS (wildtype-rotatingshift), or mPer1/mPer2 (Period1/2 mutant-dayshift), with treatment subcategories for either UV-B or No-UV-B. Dayshift protocol followed a standard and consistent 12-hr light/12-hr dark cycle, whereas Rotating shift experienced a weekly 12-hour delay. For applicable mice, a sub-erythemal UV-B dose of 353 J/m2 was administered three times a week for 27-weeks. Locomotor activity counts were recorded every 3 minutes via infrared motion sensor and subject to analysis by Lomb-Scargle periodogram and cosinor methods. Various physiological measurements were also taken for future evaluation, such as bodyweight, ear thickness, and photocarcinogenesis characteristics.

Results: In comparison with DS (24 hr), our results suggest a longer period of activity rhythms under RS (25.85 hr) and a shorter, though insignificant, period under the mPer1/mPer2 condition (23.98 hr). We also observed a substantial decrease in amplitude of activity rhythms for mPer1/mPer2 mice. This periodic relationship did not remarkably change for UV-B exposed groups or across sex. Our circadian analysis further suggests an anti-phasic relationship of 12.81-hr difference between DS and RS conditions, whereas mPer1/mPer2 exhibit a 6.24-hr phase advance relative to DS controls.

Conclusion: Solar UV-B exposure and sex had a negligible impact on the circadian rhythmicity of locomotor activity. RS and mPer1/mPer2 mice did not yield identical results, suggesting either a physiologically pertinent distinction in the mechanism of action or degree of severity of circadian disruption.

Tumor Ablation with Photodynamic Liposomal Irinotecan Sucrosulfate

Sanjana Ghosh

Sanjana Ghosh[1], Boyang Sun[2], Dushyant Jahagirdar[3], Dandan Luo[4], Joaquin Ortega[3], Robert M. Straubinger[5] and Jonathan F. Lovell[1]

[1] Department of Biomedical Engineering, University at Buffalo, State University of New York, Buffalo, New York, [2] Department of Chemical and Biological Engineering, University at Buffalo, State University of New York, Buffalo, New York, [3] Department of Anatomy and Cell Biology, McGill University, Montreal, Quebec, Canada, [4] CSL Behring LLC, King of Prussia, PA, [5] Department of Pharmaceutical Sciences, University at Buffalo, State University of New York, Buffalo, New York

Irinotecan (IRI) liposomes have been approved recently to treat advanced metastatic pancreatic cancer. Motivated by its recent approval, a similar PEGylated liposomal composition with Sucrosulfate was developed that includes a low mole fraction (1 mol. %) of porphyrin-phospholipid (PoP), a photosensitizer that gets stably incorporated into liposomes that enables light-triggered IRI release upon irradiation. IRI-loaded PoP liposomes loaded by entrapping agent ammonium sucrosulfate (ASOS) were more stable in serum compared to liposomes loaded by conventional ammonium sulfate. IRI-PoP liposomes with no irradiation released less than 5% IRI during 8 hours of incubation in bovine serum at 37 °C but released over 90% of the drug within minutes of exposure to red light (665 nm) irradiation. Single treatment with 15 mg/kg IRI-PoP liposomes and 250 J/cm2 light treatment led to tumor eradication in mice bearing either MIA PaCa-2 tumors or low-passage patient-derived tumor xenografts that recapitulate characteristics of the clinical disease whereas similar monotherapies of IRI or photodynamic therapy were found ineffective in reducing tumor growth. Direct in situ imaging of irinotecan on laser-treated tumors showed augmented tumoral drug uptake. Biodistribution analysis of the irinotecan prodrug (IRI), active metabolite (SN-38), and major metabolite (SN-38G) showed that tumoral aggregation of all IRI-derived molecular species were notably enhanced by laser treatment. Furthermore, a single treatment with 18 mg/kg IRI-PoP liposomes and light treatment with 250 J/cm2 along with 5 mg/kg of immune-checkpoint blockades (ICBs) anti PD-1 and anti CTLA-4 for three times at an interval of three days showed faster tumor shrinkage in immunocompetent mice bearing KPC tumors.

Controlling Biology with Light and Ru(II) Complexes

Phoebe Glazer

New tools are needed that will provide spatial and temporal control over biology for both basic research purposes and for application as potential therapies. Coordination chemistry provides the optimal platform for the generation of libraries of compounds, where their photochemistry, biological interactions, and downstream biological effects can be rationally optimized through utilization of individual structural elements. In theory, both the metal center and the organic components of the coordination complex can be the "active" system. We will present our approach to the development of Ru(II) "prodrugs", where photons trigger the creation of either a reactive metal center or the unmasking of a biologically active organic ligand. These agents can serve as DNA damaging vectors, ionophores, enzyme inhibitors, and systems to regulate protein:protein interactions. We will share how these features are all combined to create red light activated cytochrome P450 1B1 (CYP1B1) inhibitors with unprecedented photocontrol for treatment resistant cancers.

4-Amino-1,8-naphthalimides as potential photo-induced protein crosslinkers

Ryan Grant

Ryan Grant[1], Lisa Kelly[1]

[1] University of Maryland, Baltimore County, Department of Chemistry and Biochemistry

1,8-Naphthalimides have been previously shown to have photochemical reactivity with protein-rich tissues, leading to linkages between separate tissue samples. The introduction of an amino moiety on the 4-position changes the photophysics of the compound by creating an internal charge transfer (ICT) state upon photoexcitation. This strong dipole moment increases the oxidation ability of the excited state. This can be utilized against certain amino acids to create radical species, and these radicals have the ability to create covalent linkages between protein units. Experiments are being conducted with a series of 4-amino-1,8-naphthalimides against various amino acids to determine their ability to create these covalent protein-protein linkages. 4-dimethylamino-1,8-naphthalimide shows a higher fluorescence quantum yield than 4-imidazolo-1,8-naphthalimide in aqueous and organic solvents, with the N-linked ethanoic acid substitution yielding a higher yield than the ethanol substitution. This correlates with preliminary results suggesting a stronger Stern-Volmer relationship with the N-linked ethanoic acid substitution as opposed to the ethanol substituted compound. Cyclic voltammetry and Stern-Volmer fluorescence quenching experiments in aqueous PBS buffer suggest that tyrosine and tryptophan are potential targets for photochemical crosslinking reactions, with tryptophan being a stronger fluorescence quencher.

Post-labeling assay for the detection of photo-induced non-adjacent anti cyclobutane pyrimidine dimers that form in G-Quadruplex forming sequences

Natalia E. Gutierrez Bayona

Natalia E. Gutierrez-Bayona, Savannah Scruggs, Hisn-Chieh Yang, Michael L. Gross, John-Stephen Taylor

DNA largely exists as a double stranded helix structure (B-DNA) in cells. Under certain circumstances, DNA can adopt non-B DNA forms that have been suggested to play various roles in vivo. One class of such structures are G-quadruplexes which are thought to play a role in stabilizing the ends of DNA in telomeres and to play regulatory roles in gene promoters. Unfortunately, it has been difficult to detect the presence of these structures in vivo due to their transient nature and lack of techniques that can unambiguously identify and locate them in living cells. We have previously shown that UV irradiation of G-quadruplex forming sequences in vitro leads to the formation of unique, non-adjacent cyclobutane pyrimidine dimers (CPDs) between loops with an anti-orientation, whereas in B-form DNA only cis orientation forms. This suggests that UV light could be used to irreversibly trap non-B DNA structures for subsequent detection in vivo, and that the identification of the anti-CPDs formed would provide unambiguous proof that non-B DNA structures exist in cells. To detect the formation of anti-CPDs we have developed a highly sensitive radioactive post-labeling assay that utilizes snake venom phosphodiesterase (SVP). SVP degrades cis-syn CPD containing DNA to trinucleotides but anti-CPD containing DNA to tetranucleotides of the form pY(pN)=pYpN. The products are then dephosphorylated with alkaline phosphatase, followed by 5'-phosphorylation with polynucleotide kinase and [γ 32P] ATP and analyzed by high resolution gel electrophoresis. The anti-CPD containing tetranucleotides can be further distinguished from other co-migrating products by photoreversal to dinucleotides. The application of this method to G-quadruplex forming sequences will be described.

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Time-resolved Singlet Oxygen and Photosensitizer Phosphorescence Detection in vivo

Steffen Hackbarth

Steffen Hackbarth[1], Vladimir Subr[2], Rayhanul Islam[3], Jun Fang[3]

[1] Photobiophysics, Institute of Physics, Humboldt-Universität zu Berlin, Berlin, Germany, [2] Institute of Macromolecular Chemistry, Czech Academy of Sciences,Prague, Czech Republic, [3] Laboratory of Microbiology and Oncology, Faculty of Pharmaceutical Sciences,Sojo University, Kumamoto, Japan

Optical imaging of singlet oxygen during PDT treatment was aspired for a longtime, but there was doubt, whether it was technically possible. Recently we could establish the detection of singlet oxygen phosphorescence in sarcoma mouse models in vivo. Modern NIR-PMTstogether with Time-Correlated Multi Photon Counting allow for direct supervision of photosensitizer activity, even from outside the animal. We place the tip of anoptical multimode fiber bundle directly above the skin for site-selective pulsed excitation and detection.

Our polymer-bound photosensitizers circulate for a long time in the bloodstream due to EPR effect. Extravasation occurs mainly in the tumor. However,outside of the blood vessels the oxygen supply is diffusion limited and may be exceeded by oxygen consumption due to chemical quenching of the vast majority of generated singlet oxygen. Whether or not this results in local anoxia depends on the local drug concentration and the illumination intensity.In our experiments,we used illumination intensities below such typically applied during PDT. Stillthe triplet decay times of the photosensitizers indicate anoxia everywhere butin direct vicinity of the blood stream.As a consequence, all the detected luminescence kinetics at around 1270 nm comprise mainly two components, singlet oxygen phosphorescence from photosensitizers in or near the bloodstream and slow decaying phosphorescence from the photosensitizer triplet in anoxic regions. The relative ratio of these two components is characteristic for tumors, necrotic areas therein and normal tissue.

It turns out that PDT-induced oxygen consumption is the major limiting factor of classical PDT. Better understanding of the supply-consumption equilibrium will help to optimize and develop new treatment strategies.Optical real-time supervision will play a major role therein. Furthermore, these results offer new options for tumor diagnostics at superior contrast.

Loss of C/EBPβ enhances the type 1 IFN system to sensitizes keratinocytes to UVB-induced cell death

Jonathan Hall

Emma E. Tobin[2], Sophia M. Gray[1], and Jonathan R. Hall[1,2,3]

[1] Department of Biological Sciences, NC State University, Raleigh, NC, [2] Toxicology Program, NC State University, Raleigh, NC, [3] Center for Human Health and the Environment, NC State University, Raleigh, NC

In addition to activation of canonical DNA damage responses including cell cycle checkpoints and DNA repair, recent studies indicate that DNA damage can also activate the innate immune response. The host innate immune response mediated by type 1 interferons (IFNs) and the subsequent up regulation of IFN-stimulated genes (ISGs) is widely recognized for its critical role in preventing infection of viruses and other pathogens. Recent studies suggest this same IFN system can also mediate diverse cellular and biological responses such as proliferation, apoptosis, senescence, and the DNA damage response. Epidermal keratinocytes play a critical role in the type 1 IFN response as the skin is the first line of defense to cutaneous microbes/viruses and environmental DNA damage. The conditional knockout in skin of CCAAT/enhancer-binding protein-β (C/EBPβ), a basic leucine zipper transcription factor, results in increased levels of apoptosis in response to UVB-induced DNA damage. UVB-treatment of C/EBPβ skin conditional knockout (CKOβ) mice increased p53 protein levels in the epidermis and enhanced p53-dependent apoptotic activity 3-fold compared with UVB treated control mice. RNAseq and pathway analysis of UVB-treated CKOβ epidermis unexpectedly revealed that type 1 IFN pathway was the most highly enriched pathway. Numerous pro-apoptotic interferon stimulated genes were upregulated including genes that regulate p53 and extrinsic apoptosis. We found that CKOβ mice/keratinocytes challenged with DNA damaging UVB radiation displayed increased levels of p53 protein, enhanced activation of caspase-8 and caspase-3, and increased cell death which was dependent on the interferon α/β receptor. Our results indicate that the loss of C/EBPβ enhances activation of a noncanonical UVB DNA damage response pathway involving the type 1 IFN system and activation of caspase-8 to induce keratinocyte cell death.

Nano-optogenetic immunotherapy

Gang Han

Gang Han[1]

[1]Biochemistry and Molecular Biotechnology, University of Massachusetts Chan Medical School, Worcester, MA

Chimeric antigen receptor (CAR) T cell-based immunotherapyhas shown curative potential in patients. However, owing to the lack of control over the location and duration of the anti-tumour immune response, CAR T cell therapy still faces safety challenges arising from cytokine release syndrome and on-target, off-tumour toxicity. Herein, we will discuss the design of light-switchable CAR (designated LiCAR) T cells that allow real-time phototunable activation of therapeutic T cells to precisely induce tumour cell killing. When coupled with imaging-guided, surgically removable upconversion nanoparticles that have enhanced near-infrared-to-blue upconversion luminescence as miniature deep-tissue photon transducers, LiCAR T cells enable both spatial and temporal control over T cell-mediated anti-tumour therapeutic activity in vivo with greatly mitigated side effects. Our nano-optogenetic immunomodulation platform not only provides a unique approach to interrogate celluar anti-tumour immunity, but also sets the stage for developing precision medicine to deliver personalized anticancer therapy.

Pro-NP mediated delivery of antioxidant enzymes protects from ultraviolet radiation induced DNA damage and skin carcinogenesis

Laura Hansen

Patrick Kuwong[1], Sarah Gwazdacs[1], Keven Nguyen[1], Chris Porter[2], Jordan Grewal[1], Jack Branby[1], Poonam Sharma[3], Jim Grunkemeyer[1], Matt Zimmerman[4], Gary Madsen[2], Laura A. Hansen[1]

[1] Department of Biomedical Sciences, Creighton University, Omaha, NE, [2] ProTransit Dermal Therapy, Omaha, NE, [3] Department of Pathology, Creighton University, Omaha, NE, [4] Department of Cellular and Integrative Physiology, University of Nebraska Medical Center, Omaha, NE

Ultraviolet radiation (UV), the primary cause of skin cancer, generates reactive oxygen species (ROS) that can damage the DNA and lead to mutations. Currently available sunscreens are inadequate at preventing UV-induced ROS-mediated DNA damage because they are often poor at blocking UVA, must be frequently reapplied and can increase ROS. Therefore, we reasoned that effective and sustained delivery of the antioxidant enzymes superoxide dismutase (SOD) and catalase (CAT) to the skin could reduce UV-induced ROS, DNA damage and skin cancer. Pro-NPTM, consisting of SOD and CAT encapsulated in Poly(lactic-co-glycolic acid) (PLGA) nanoparticles, was developed to allow for stable and sustained delivery of these ROS scavenging enzymes. We hypothesized that Pro-NP would safely deliver SOD and CAT to the viable layers of the epidermis, decrease UV-induced DNA damage and suppress skin cancer development. Daily topical application of Pro-NP decreased UV-induced ROS, DNA damage and DNA damage response pathway activation in male and female mice in a dose response manner. Pro-NP also delayed tumor development, reduced tumor multiplicity and delayed progression to SCC in female mice but had no effect on skin carcinogenesis in male mice. No toxicity was observed in Pro-NP treated mice of either gender in our long-term carcinogenesis experiments. Pro-NP also suppressed UV-induced ROS and DNA damage in pig skin. Taken together, these results suggest that Pro-NP may be useful clinically for protection from sun-induced skin damage and skin cancer.

UV radiation, DNA damage, and RNA modifications

Yu-Ying He

Department of Medicine, Section of Dermatology, University of Chicago, Chicago, IL

Excessive, high doses of ultraviolet B (UVB) UVB irradiation are known to cause DNA damage, which can lead to skin inflammation skin cancer, aging, and immunosuppression. UVB-induced DNA damage across the whole genome can be repaired by nucleotide excision repair (NER) to prevent mutations and tumorigenesis. NER is the major DNA repair mechanism that removes bulky DNA damage products caused by UVB radiation as well as other environmental carcinogens. Although biochemical and genetic analyses have identified the essential NER factors, including the xeroderma pigmentosum complementary group A-G (XPA-XPG), the molecular mechanism of regulating NER capacity and its role in skin cancer remains poorly understood. In addition to causing DNA damage and an increased mutation burden, UVB also causes the inflammatory damage response, which can contribute to tumorigenesis. In the past decades, tremendous progress from many investigators and our group has been made in elucidating the mechanism of skin cancer development, including the regulatory and functional role of DNA repair and inflammation in UVB damage response and skin tumorigenesis. Recently, we discovered a critical role for N^6-methyladenosine (m^6A) RNA methylation in UVB damage response and skin tumorigenesis. m^6A RNA methylation is the most abundant internal chemical modification

in eukaryotic messenger RNA (mRNA) as well as long non-coding RNA (lncRNA). m^{6}A RNA modification plays important roles in development and in diseases, including cancer. m^{6}A modification regulates RNA fate and functions such as mRNA stability, nuclear processing, and translation. Our findings add unique insights into the well-coordinated molecular machinery in UVB damage response.

RNA methylation facilitates the repair of UV-induced DNA damage and suppresses photocarcinogenesis

Yu-Ying He

Zizhao Yang[1], Seungwon Yang[1], Yan-Hong Cui[1], Jiangbo Wei[2], Palak Shah[1], Gayoung Park[1], Xiaolong Cui[2], Chuan He[2,3], Yu-Ying He[1]

[1]Department of Medicine, Section of Dermatology, University of Chicago, Chicago, IL, [2]Departments of Chemistry, Department of Biochemistry and Molecular Biology, Institute for Biophysical Dynamics, University of Chicago, Chicago, IL [3]Howard Hughes Medical Institute, University of Chicago, Chicago, IL

UV-induced DNA damage is repaired by nucleotide excision repair (NER) that corrects bulky helix-distorting DNA lesions across the whole genome and is essential for preventing mutagenesis and skin cancer. Here we show that METTL14 (methyltransferase-like 14), a critical component of the m6A RNA methyltransferase complex, promotes the repair of UV induced DNA damage through regulating m6A mRNA methylation-mediated translation of the NER factor DDB2 and suppresses UV-induced skin tumorigenesis. Ultraviolet irradiation down regulates METTL14 protein through NBR1-dependent selective autophagy. METTL14 knockdown decreases NER and DDB2 abundance. Conversely, overexpression of wild-type METTL14, but not its enzymatically inactive mutant, increases NER and DDB2 abundance. METTL14 knockdown decreases m6A methylation and translation of the DDB2 transcripts. Adding DDB2 reverses the DNA repair defect in METTL14 knockdown cells, indicating that METTL14 facilitates NER through regulating DDB2 m6A methylation and translation. Similarly, knockdown of YTHDF1, an m6A reader promoting translation of m6A modified transcripts, decreased DDB2 protein levels. Both METTL14 and YTHDF1 bind to the DDB2 transcript. In mice, skin-specific heterozygous METTL14 deletion increases UV-induced skin tumorigenesis. Furthermore, METTL14 as well as DDB2 is down-regulated in human and mouse skin tumors and by chronic UV irradiation in mouse skin, and METTL14 level is associated with the DDB2 level, suggesting a tumor-suppressive role of METTL14 in UV-associated skin tumorigenesis in association with DDB2 regulation. Taken together, these findings demonstrate that METTL14 is a target for selective autophagy and acts as a critical epitranscriptomic mechanism to regulate the repair of UV-induced DNA damage and suppresses photocarcinogenesis.

It's a gift to be simple: Sandpaper curettage improves PDT outcomes for actinic keratoses

Lauren Heusinkveld

Lauren E. Heusinkveld[1]; Taylor A. Bullock[2]; Christine B. Warren[1,2]; Edward V. Maytin[1,2]

Cleveland Clinic Lerner College of Medicine of Case Western Reserve University, Cleveland Clinic, Cleveland, OH, Department of Dermatology, Cleveland Clinic, Cleveland, OH

INTRODUCTION: Photodynamic therapy (PDT) is FDA-approved for actinic keratosis (AK) and is non-scarring, repeatable, and free of long-term side effects. Although PDT is moderately effective for AK, improvements in treatment efficacy are needed.

BACKGROUND: Known devices to remove hypertrophic stratum corneum on AK lesions (to promote ALA absorption and improve outcomes) include cold-steel curettes, needle rollers, and lasers. Curettage with fine sandpaper may be a gentler, less expensive, and effective alternative.

METHODS: A retrospective study was designed to compare AK clearance in patients receiving PDT with or without sandpaper curettage. Patients were selected from a large longitudinal database registry of patients with ten or more AKs on the face and/or scalp (ClinicalTrials.gov NCT03319251). Group 1 comprised patients who underwent PDT alone (20% ALA, 15 min; blue light 417 nm, 30 min). For patients in Group 2, all AK were pretreated with gentle sandpaper curettage, prior to ALA application and illumination as in Group 1. The two groups were compared using multivariate matching to normalize for age, sex, initial AK counts, and time to follow-up.

RESULTS: Sixty-six patients were selected for matching analysis (n=38, PDT only; n=28, PDT+curettage). Eighty-five percent of patients were male. Other demographics between the two groups (PDT vs PDT+curettage) were similar (mean±SD), including age (71.0±8.3 vs. 71.0±8.0 years), baseline AK count (53±39 vs. 44±32), and time to follow-up exam post-PDT (111±28 vs. 113±32 days), respectively. At follow-up, patients who received curettage showed an overall 55% improvement in scalp AK clearance compared to patients who did not receive curettage, adjusting for sex, age, time to follow-up, and baseline AK count ($p = 0.0322$, multivariable linear regression).

DISCUSSION: Sandpaper curettage before PDT treatment is easy, inexpensive, and significantly improves AK clearance rates. Further investigation is required to determine efficacy for sites other than the face and scalp.

Photodynamic priming improves drug transport across the blood-brain tumor barrier

Joe Huang

Huang-Chiao Huang, Ph.D.

Fischell Department of Bioengineering, University of Maryland, College Park, MD

Most primary brain tumors are managed by maximal safe resection followed by adjuvant chemoradiation to treat residual and potentially infiltrative tumor cells. However, these adjuvant approaches do not effectively treat the tumor-invaded brain regions due to an intact blood-brain barrier (BBB) that restricts drug penetration or a high risk of toxicity to nearby neural structures. The strength of the BBB in protecting brain tumors from exposure to circulating drugs is maintained by not only the intact endothelial tight junctions, but also a range of ATP-binding cassette (ABC) drug efflux transporters on endothelial and cancer cells. My research program is interested in using verteporfin-based photodynamic therapy (PDT) to open the BBB tight junctions and shut down ABC transporters without damaging normal tissues. This approach offers a more specific and less disruptive strategy to deliver drugs to recurrent or residual brain tumors effectively. Furthermore, we will discuss a surfactant-free approach to prepare novel amorphous verteporfin nanosuspensions. The verteporfin nanosuspensions can be activated upon cancer cell uptake, enabling PDT and fluorescence imaging of tumors in vivo. We demonstrate up to 10-fold increase in anti-cancer efficacy of the verteporfin nanosuspensions in glioblastoma cells and animal models, compared to the clinically used liposomal verteporfin formulation.

Targeted photo-activatable multi-agent liposomes for image-guided photodynamic therapy of peritoneal metastases

Joe Huang

Huang-Chiao Huang, Ph.D.

Fischell Department of Bioengineering, University of Maryland, College Park, MD

The prognosis for women with advanced stage and recurrent ovarian cancer has remained dismal for decades. The poor response rates

result in part from resistance to chemotherapy. Ovarian cancer often metastasizes via transcoelomic routes along currents of ascitic fluid in the peritoneal cavity. Targeted photodynamic therapy (PDT) has shown promise in selectively imaging and treating disseminated tumors in the peritoneal cavity, and it can resensitize cancer cells to chemotherapy. However, the high thresholds of intracellular photoimmunoconjugate required for cell death have hindered the effectiveness of PDT in physiologically relevant models. We have recently shown that successful conjugation of photoimmunoconjugates onto nanoliposomes can effectively enhance intratumoral photoimmunoconjugate delivery and improve PDT outcomes in mice. Our nanoplatform is designed to co-deliver biological agents, photosensitizers, and anticancer drugs that target the plasma membrane protein, cytoplasmic organelle, and nuclear DNA for enhanced treatment outcomes. Furthermore, fluorescence image guidance was used to inform drug delivery and PDT dosimetry in vivo. The knowledge gained in our study plays a transformative role in developing improved PDT tailored to the molecular profile of disseminated tumors in individual ovarian cancer patients.

Arsenic potentiation of ultraviolet radiation damage in keratinocytes.

Laurie Hudson

Laurie G. Hudson, Ke Jian Liu, Lindsay Volk, and Karen L Cooper

Department of Pharmaceutical Sciences, University of New Mexico Health Science Center, Albuquerque, NM

Arsenic is widely present in the environment, and in many parts of the world, arsenic is part of the skin exposome contributing to elevated risk of skin cancer. The impact of arsenic reaches beyond single agent carcinogenicity: arsenic inhibits DNA repair at low, non-cytotoxic concentrations and amplifies the mutagenic and carcinogenic impact of other DNA-damaging agents, such as ultraviolet radiation (UVR). This observation has led to definition of arsenic as a co-carcinogen. We find that trivalent arsenite binds selectively to zinc finger motifs and RING domain motifs containing three or more cysteine residues, including proteins critical for base excision repair, nucleotide excision repair and translesion synthesis. Site-directed mutations to reduce the number of cysteine residues ablate arsenite binding while retaining zinc binding to the zinc finger motif. Arsenic exposure leads to oxidation of zinc coordinating cysteine residues, zinc loss and decreased activity of target DNA repair proteins. Importantly, zinc content, DNA binding activity and DNA repair in arsenic-treated keratinocytes is largely restored in the presence of supplemental zinc. In addition, zinc supplementation protects against arsenic augmentation of solar-simulated UVR induced DNA damage and mutations in human keratinocytes and in mice in vivo. From these findings we can conclude that zinc offsets the impact of arsenic in models of co-carcinogenesis. The work suggests that zinc supplementation may provide a strategy to improve DNA repair capacity and reduce carcinogenesis in the estimated 220 million people exposed to high arsenic concentrations.

DNA damage recognition by the XPC/Rad4 nucleotide excision repair protein complex

Jung Hyun Min

Department of Chemistry and Biochemistry, Baylor University, Waco, Texas

Nucleotide excision repair (NER) repairs DNA lesions caused by diverse environmental agents such as UV, pollutants, cigarette smoke, etc. The lesions, if left unrepaired, block essential cellular functions and lead to cell death or diseases. To initiate NER, the XPC protein complex (Rad4 in yeast) initially locates diverse lesions scattered around the genomic DNA and recruits downstream factors to the damaged sites. The recognition efficiency of the lesions can, however, vary widely depending on the lesions, and certain lesions can evade detection by XPC and thus become resistant to NER. Our research aims to address how Rad4/XPC recognizes DNA lesions and how certain lesions evade Rad4/XPC by using multiple complementary approaches including X-ray crystallography, time-resolved fluorescence spectroscopy, chemical crosslinking and molecular dynamics (MD) simulations.

Recently, we observed that Rad4 can 'open' undamaged DNA containing a string of consecutive C/G's (CCC/GGG) when provided a long residence time by tethering, but not a sequence containing alternating CG/GC's (CGC/GCG). Fluorescence lifetime studies of DNA conformations showed that CCC/GGG exhibits local pre-melting that is absent in CGC/GCG. In MD simulations, CGC/GCG failed to engage Rad4 to promote 'opening' contrary to CCC/GGG, reminiscent of the differences observed between CPD and 6-4PP. These results illustrate how local sequences can also impact DNA recognition by Rad4/XPC and how certain DNA sites/lesions may resist being 'opened' even with Rad4 held at that site indefinitely. I will discuss the implications of these findings for understanding the varying NER efficiencies of DNA lesions and the functions of Rad4/XPC. I will also present our studies of using photoactive DNA as a surrogate lesion to study NER.

Safety evaluation of Far-UVC irradiation to epithelial basal cells in corneal limbus

Sachiko Kaidzu

Sachiko Kaidzu[1], Kazunobu Sugihara[1], Masahiro Sasaki[2], Aiko Nishiaki[2], Hiroyuki Ohashi[2], Tatsushi Igarashi[2] and Masaki Tanito[1]

[1]Department of Ophthalmology, Shimane University Faculty of Medicine, Izumo, Japan, [2]Ushio Inc., Tokyo, Japan

Basal cells in the corneal limbus play an important role in the turnover cycle because they are the source of all cells that consist of the corneal epithelium. We examined the penetration depth of ultraviolet (UV) light in the corneal limbus and considered the safety of Far-UV-C on stem cells in the basal area of the corneal limbus. Sprague-Dawley albino rats were irradiated with UVs with a peak wavelength at 207 nm, 222 nm, 235 nm, 254 nm or 311 nm under anesthesia. Corneas of pigs obtained from slaughterhouses were irradiated with UV-Cs with a peak wavelength at 222 or 254 nm. From the results, the penetration depth of UV in the rat corneal limbal epithelium was wavelength dependent, as was the central corneal epithelium: 311 nm UV-B and 254 nm UV-C reached to the basal cells of the epithelium, 235 nm reached to the middle area, but 207 and 222 nm UV-C reached only to the superficial layer of the epithelium. The corneal limbal epithelium of pigs was about twice as thick as the central corneal epithelium, therefore 254-nm UV-B did not reach to the basal area but did reach to a depth of 50-100 µm from the surface layer. On the other hand, 222 nm UV-C reached only the superficial layer of the corneal limbal epithelium as in rats. Given that 207 and 222 nm UV-Cs didn't reach until corneal epithelial stem cells, the turnover of the corneal epithelium can't be diminished by these far UV-Cs. Furthermore, it is unlikely to develop diseases such as conjunctival tumors and pterygium, which are assumed to be caused by chronic exposure of UVs to the eye.

Selective degradation of amyloids in vivo by chemical catalyst-promoted photooxygenation

Motomu Kanai

The University of Tokyo

Our long-term research goal is to develop a new paradigm of medicine, catalysis medicine, using small-molecule catalysts that can function in our body complementarily to enzymes. This research direction should in turn contribute to the greener in-flask synthesis of functional molecules with high structural complexity, such as drugs. Success requires powerful chemical catalysts that can target stable, multifunctional organic molecules, ranging from

small molecules to biomacromolecules, under mild conditions with synthetically/biologically valuable selectivity.

Along this line, we are studying amyloid-selective photooxygenation in vivo. We developed a small-molecule catalyst that can penetrate through blood-brain barrier after intravenous injection and selectively oxygenate Aβ under the irradiation of orange light from outside the mouse skull. Furthermore, photooxygenation promoted degradation and clearance of oxygenated-Aβ through lysosomal digestion. Our non-invasive method merging a chemical catalysis and biological protein degradation mechanism may facilitate the treatment of amyloid diseases, including Alzheimer's disease.

Engineering opsins for subcellular optogenetics

Ajith Karunarathne

Dhanushan Wijayaratna[1,2], Filippo Sacchetta[3], Laura Pedraza-González[3], Massimo Oluvucci[3,4]*, and Ajith Karunarathne[1,2]*

[1]Department of Chemistry, Saint Louis University, Saint Louis, MO, [2]Department of Chemistry and Biochemistry, The University of Toledo, Toledo, OH, [3]Department of Biotechnology, chemistry and pharmacy, University of Siena, Siena, Italy, [4]Department of Chemistry, Bowling Green State University, Bowling Green, OH

Opsins are retinal binding G proteins couple receptors that regulate various crucial biological processes such as vision and circadian clock regulation. We recruit spectral and signaling properties of opsins to control single cell and subcellular signaling and thereby regulate cell physiology and behaviors. For instance, we have engineered blue opsin to make it an ideal optogenetic tool to achieve precise spatial and temporal control of subcellular G protein signaling. Our engineered blue opsins revealed much-hidden information about subcellular signaling regulation that is otherwise difficult to unmask.

Melanopsin (Opn4) is the primary photoreceptor in intrinsically photosensitive ganglion cells (ipRGCs). MeOp is bi-stable and thus functions at low retinaldehyde concentration due to the recycling of the chromophore. Unlike mono-stable opsins such as rhodopsin, bi-stability allows MeOp to become functional under low retinal concentrations outside the retina. However, the 450 nm-centered absorption spectrum makes MeOp sensitive to the entire visible range, and thus its optogenetic utility is limited.

Here we show the reengineering of MeOp to improve it as a next-generation in-vivo GPCR optogenetic tool with red light resistance. Due to the unavailability of a clear X-ray structure for MeOp, an in-silico QM/MM homology model for MeOp was built using the available Squid Rhodopsin (SqRh) structure as the template. QM/MM models of Squid Rhodopsin (SqRh), Human Melanopsin (hMeOp), and Mouse Melanopsin (mMeOp)-Wild Type (WT) were constructed using the Automatic Rhodopsin Modeling (ARM) protocol. ARM was used to capture and reproduce the reported spectral properties of these opsins. Extensive characterization of the retinal-binding cavity of MeOp allowed us to identify promising blue-shift mutations. Here we show two mutant MeOps that are sufficiently blue-shifted and show resistance to activation by red light, however sensitive to yellow, green, and blue light. Furthermore, these MeOp mutants allow subcellular Gq/i/o activation with millisecond temporal control in living cells, making our engineered Opn4s ideal for single-cell and subcellular optogenetics.

Further characterization showed that our engineered MeOp mutants are not only blue-shifted but also bistable. Altogether, our data show the engineering feasibility of spectrally tuned opsin mutants for user-defined optogenetic applications.

Estimation of UV-associated cutaneous squamous cell carcinoma incidence attributable to arsenic in U.S. water supplies

Masaoki Kawasumi

Division of Dermatology, Department of Medicine, University of Washington, Seattle, WA

Cumulative exposure to ultraviolet (UV) radiation is the major risk factor for cutaneous squamous cell carcinoma (cSCC), the second most common cancer in the U.S. Arsenic enhances UV-induced cSCC development. Arsenic in water supplies potentially exposes millions of people to increased disease risk worldwide. Despite strengthened regulation by the U.S. Environmental Protection Agency (EPA) for public water supplies, arsenic at current levels in U.S. water supplies may increase the incidence of cSCC. However, no prior studies have quantified this arsenic-associated incidence. We analyzed three national-scale datasets: urinary arsenic from the National Health and Nutrition Examination Survey, public water supply data from the EPA Six-Year Review 3, and private well user data from Ayotte et al. (2017). These data were combined with published odds ratios for cSCC incidence in order to estimate arsenic-attributable cSCC incidence among U.S. non-Hispanic whites, a demographic with disproportionately high skin cancer incidence, at national and county levels. Based on urinary arsenic data representative of U.S. non-Hispanic whites, we estimate that 32,058 out of 2,548,845 cSCCs annually in the U.S. are attributable to arsenic in water supplies: 25,861 cSCCs among public water users and 6,196 among private well users. Separately, water supply data suggest that 10,159 and 4,414 cSCCs are attributable to arsenic in public water supplies and in private wells, respectively. Private well users have twofold greater risk of arsenic-attributable cSCC than public water supply users. In this first estimation of arsenic-attributable cSCC incidence, 1.3% of cSCC incidence in the U.S. is due to arsenic in current water supplies. Thousands of cSCCs may be prevented by further restricting arsenic in U.S. water supplies.

Circadian clock-modulating compounds impact cellular responses to UV radiation

Michael Kemp

Circadian clock-modulating compounds impact cellular responses to UV radiation

William Cvammen[1], Prashant Gaikwad[1], and Michael G. Kemp[1,2]

[1]Department of Pharmacology and Toxicology, Wright State University Boonshoft School of Medicine, Dayton, Ohio, [2]Dayton VA Medical Center, Dayton, Ohio

The cellular response to DNA damage induced by UV radiation has been demonstrated to be under the control of the circadian clock, and the recent discovery of small molecule compounds that target clock proteins now offers the possibility of pharmacologically manipulating the clock to alter UV DNA damage responses (DDR). To explore this hypothesis, we examined how the retinoic acid receptor-related orphan receptor (ROR) agonist nobiletin, the REV-ERBα antagonist SR8278, and the cryptochrome (CRY) inhibitor KS15 impact keratinocyte survival following exposure to UV light sources. Nobiletin was found to exhibit different effects on cell survival following exposure to UVB versus a solar simulating UV light (SSL) source due to the absorption of UVA light and the generation of reactive oxygen species. In contrast, the combination of SR8278 and KS15 exhibited pro-survival effects with both UV light sources. Furthermore, human skin explants treated topically with SR8278 and KS15 displayed altered expression of core clock genes as well as modestly increased expression of clock control genes known to be important in the DDR, including the nucleotide excision repair factor XPA and anti-mitotic kinase Wee1. Finally, we observed that these clock-modulating compounds promote the stability of the XPA protein by causing the reduced expression of the endopeptidase cathepsin L, which is

capable of cleaving XPA at its C-terminus. These results provide the first evidence that clock modulating compounds may lead to improved cell survival following exposure to UV radiation.

Emerging role of protein tyrosine phosphatase in skin photocarcinogenesis

Dae Joon Kim

Obed Asare[1], Lindsey Shim[1], Bilal B. Hafeez[1], and Dae Joon Kim[1]*

[1]Department of Immunology and Microbiology, School of Medicine, University of Texas Rio Grande Valley

T-cell protein tyrosine phosphatase (TC-PTP, encoded by PTPN2) is a nonreceptor PTP that is most highly expressed in hematopoietic tissues. TC-PTP modulates a variety of physiological functions including cell cycle progression, cell survival and proliferation, and hematopoiesis through tyrosine dephosphorylation of its target substrates, such as EGFR,

JAK1, JAK3, STAT1, and STAT3. Studies with whole or tissue-specific loss of TC-PTP function transgenic mice have shown that T-PTP has crucial roles in the regulation of the immune response, insulin signaling, and oncogenic signaling. We demonstrate that TC-PTP has a protective function during UVB-induced skin damage by utilizing skin specific TC-PTP-deficient and TC-PTP-overexpressing mice. Immortalized TC-PTP deficient keratinocytes from TC-PTP knockout mice showed increased cell survival against UVB-induced apoptosis by negatively regulating Flk-1/JNK signaling. Flk-1 phosphorylation was increased in TC-PTP-deficient cells after UVB exposure. Immunoprecipitation analysis using the TC-PTP substrate-trapping mutant TCPTP D182A revealed that TC-PTP directly dephosphorylate Flk-1 and their interaction was stimulated by UVB. Similar with these results, loss of TC-PTP leads to increased resistance to UVB-induced apoptosis in vivo epidermis, which is concomitant with increased Flk-1 phosphorylation following UVB in the epidermis of TC-PTP knockout mice. The generation of epidermal-specific TC-PTP-overexpressing mice further demonstrated that TC-PTP contributes to the attenuation of UVB-induced skin carcinogenesis through the regulation of p38 MAPK signaling pathway. Mice overexpressing TC-PTP in the epidermis developed significantly reduced numbers of tumors during UV skin carcinogenesis and presented a prolonged latency of tumor initiation. Examination of human papillomas and squamous cell carcinomas (SCCs) revealed that TC-PTP expression was significantly reduced and TC-PTP expression was inversely correlated with the increased grade of SCCs. Our findings demonstrate that TC-PTP is a potential therapeutic target for the prevention of human skin cancer given that it is a major negative regulator of oncogenic signaling in epidermis.

Deconstructing melanin using ultrafast laser spectroscopy

Bern Kohler

Understanding property emergence in melanins is of great interest not only for understanding their biological function but also for creating bioinspired, multi-functional materials that exploit melanin's intrinsic electronic and ionic conductivity, redox activity, ability to stabilize free radicals, and broadband optical absorption. These properties are highly attractive for applications in bioelectronics, catalysis, energy conversion and storage. Amorphous and nearly insoluble, the atomistic structures present in melanins have remained elusive and the subject of debate, impeding understanding of their structure-function relationships. To gain insight into the chromophores of melanin, femtosecond transient absorption experiments have been carried out on synthetic melanins like DOPA melanin. Transient spectral holes centered about the laser excitation wavelength are detected at room temperature, providing evidence of absorbing subunits with a broad distribution of transition energies. The observed bleach recovery dynamics provide valuable insights into couplings among melanin's chromophores. By combining femtosecond time-resolved infrared (TRIR) spectroscopy with the ability to select chromophore subensembles with a tunable UV-vis excitation pulse, a vibrational fingerprinting technique is demonstrated that correlates electronic and vibrational properties of melanin's chromophores. Finally, I will also discuss our bottom-up studies of the photophysics of protected indole quinones that mimic many of the hallmark properties of eumelanin.

Circadain mechanism of metabolic adaptation to diet

Roman Kondratov

Volha Mezhnina[1], Oghogh Ebeigbe[1], Nikkhil Velingkaar[1], Yana Sandlers[2] and Roman V Kondratov[1]

[1] Center for Gene Regulation in Health and Disease and BGES Department, Cleveland State University, Cleveland, OH, [2] Chemistry Department, Cleveland State University, Cleveland, OH

Dietary interventions became a popular way to improve health. Caloric restriction (CR) is a scientifically confirmed dietary intervention that improves metabolism and extends longevity across the taxa. CR interacts with the circadian clock, an internal time keeping system that generates 24-hour rhythms, known as circadian rhythms, in metabolism and physiology and synchronizes the organism with rhythmic environment. CR induced strong circadian rhythms in the expression of fatty acid oxidation and ketogenesis genes in the liver. As result, CR induced high amplitude circadian rhythms in intermediate metabolite of fatty acids catabolism: acyl-CoAs, acylcarnitines and beta-hydroxybutyrate (βOHB). The transcriptional factor PPARα is a master regulator of fatty acid metabolism. Circadian clock proteins interfered with PPARα transcriptional activity and PPARα transcriptional network became highly rhythmic in the CR liver. The data suggest that CR recruits the circadian clock to reprogram circadian rhythms in fatty acid metabolism.

Nitric Oxide and Aggressiveness of Tumor Cells after Photodynamic Treatment

Witold Korytowski

W. Korytowski[1,2], J. Bazak[1], AW. Girotti[2]

[1] Dept. of Biophysics, Jagiellonian University, Krakow, Poland, [2] Medical College of Wisconsin, Milwaukee

We have recently shown that human breast cancer cells (adenocarcinoma MDA-MB231), exploit endogenous nitric oxide (NO) to resist elimination by photodynamic therapy (PDT), cisplatin (CDDP) chemotherapy or combination of both. Inducible nitric oxide synthase (iNOS) was rapidly and persistently upregulated after the treatment challenge, and the resulting NO signaled not only for greater resistance but also growth, migration, and invasion/aggressiveness of not only cells surviving the therapeutic challenge, but also bystander cells, which escape PDT challenge. Ionizing radiation of specifically targeted cells in a given population is known to elicit pro-death or pro-survival responses in non-targeted bystander cells, but far less is known about such effects in non-ionizing PDT. We are testing the hypothesis that photodynamically or pharmacologically stressed breast adenocarcinoma cells can elicit adeNO-mediated pro-growth/migration aggressive responses not only in surviving target cells but also in non-stressed bystanders. Switching to a more aggressive phenotype during clinical therapeutic treatment would be an alarming prospect because it might lead to greater cancer metastatic spread. We will also report on our attempts to overcome/minimize such effects by using classical inhibitors of iNOS activity (e.g. 1400W) and recently introduced bromodomain and extraterminal domain (BET) transcriptional inhibitors (e.g. JQ1). (Supported by NCN grant 2017/27/B/NZ5/02620)."""

KEYNOTE – Light-Triggered Drug Release from Cell-Conveyed Phototherapeutics

David Lawrence

Photochemical processes triggered by DNA damages

Virginie Lhiaubet

Instituto Universitario Mixto de Tecnología Química (UPV-CSIC), Universitat Politècnica de València, Consejo Superior de Investigaciones Científicas, Avenida de los Naranjos, Valencia, Spain

The natural DNA bases are highly resistant to UV excitation as they dissipate more than 90% of their energy through efficient nonradiative channels leading to the ground state. Nonetheless, it is now well established in the literature that small structural changes might drastically modify the photochemical properties of DNA by lengthening the excited states lifetime and/or increasing intersystem crossing efficiency.

During this last decade, our group has focused its attention on studying DNA lesion photobehavior. The photochemistry of DNA damages is indeed of utmost importance as some of them are able to absorb in the UVA UVB region and behave as a potential intrinsic photosensitizer. Here, we will discuss the photophysical and photochemical properties of damages such as the (6-4) photoproducts, 5-formylpyrimidine derivatives, or etheno adducts3 to evaluate if they fulfil the basic requirements of a good DNA photosensitizer: (i) to absorb in the UVA UVB region, (ii) to populate efficiently their triplet excited state and (iii) to be able to interact with DNA components through a Type I or II process and/or a triplet-triplet energy transfer.

Loss of CELF2 promotes skin tumorigenesis and increases drug resistance

Liang Liu

The Hormel Institute, University of Minnesota

CELF2 belongs to the CELF RNA-binding protein family and regulates target mRNA stability, splicing, and translation. Pan-cancer TCGA analyses reveal a strong correlation between CELF2 expression with better prognosis in cancer patients. To investigate CELF2 antitumor activity in non-melanoma skin cancer development, we performed immunofluorescence studies and found significantly reduced CELF2 expression in human squamous cell carcinoma (SCC) tumors compared to adjacent normal skin. Consistent with the observation in clinical samples, we found loss of CELF2 expression during both UV- and DMBA-induced mouse skin tumors, suggesting that CELF2 loss might promote skin tumorigenesis. By using shRNA-mediated expression knockdown (KD), we demonstrated that CELF2 KD significantly increased SCC cell proliferation and anchorage-independent colony growth in vitro, and SCC tumor growth in xenograft mouse model. Intriguingly, while parental SCC cells were sensitive to UNC0642, an anticancer agent that inhibits genomic histone methylation, CELF2-KD SCC cells are more resistant to UNC0642-induced growth retardation, suggesting that CELF2 loss not only augments tumor growth but might also confer drug resistance. Through RNA-seq analysis, we found activation of KRT80 and GDF15, two tumor promoters, in CELF2-KD SCC cells. Taken together, we demonstrate for the first time that CELF2 loss promotes skin tumorigenesis and increases drug resistance, highlighting the anticancer function of CELF2 in skin cancer development and the potential of CELF2-regulated pathways in cancer treatment.

One-electron Oxidation of Biomolecules: Antioxidant Action of Resveratrol

Carolina Lorente

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, La Plata, Argentina

During the last years, the interest in Resveratrol (3,4´,5,-trihydroxystilbene, RSV) has increased due to the evidence found that it protects biomolecules and cells from oxidative damage. RSV is a natural polyphenolic compound naturally present in a variety of plant species, especially in fruits and flowers such as grapevines, nuts, lilly flowers, and it is synthesized in response to stress situations such as infections or UV radiation.

It was previously reported that biomolecules are degraded in aqueous solutions containing pterin (Ptr) exposed to UV-A radiation, by both type I (electron transfer reactions) and type II mechanisms (energy transfer to O2, to form 1O2). Concisely, Ptr absorbs UV-A radiation, yielding singlet and triplet excited states (1Ptr* y 3Ptr*, respectively). The species responsible of biomolecules oxidation is 3Ptr* and the mechanism depends on the experimental conditions. In aqueous acidic solutions Ptr-photosensitized degradation of biomolecules is mainly by type I mechanism.

In our laboratory we have obtained experimental evidence that clearly demonstrates the ability of RSV to protect a group of amino acids and nucleotides from one-electron oxidation. The mechanistic analysis indicates that after one-electron transfer to 3Ptr*, the biomolecules obtain an electron from RSV and thus prevent their oxidation. Therefore, in the presence of RSV during radiation exposure of aqueous acidic solution containing a given biomolecule and Ptr, the biomolecule is preserved, and RSV is oxidized, with RSV being a sacrificial antioxidant

Emerging Applications for Porphyrin-phospholipid Liposomes

Jonathan Lovell

Department of Biomedical Engineering, University at Buffalo

We have developed liposomes that are doped with a small amount of a photosensitizing lipid; porphyrin-phospholipid (PoP).[1] Long-circulating doxorubicin (Dox) in porphyrin–phospholipid (PoP) liposomes (LC-Dox-PoP) is similar to the FDA-approved liposomal doxorubicin form of Doxil, but incorporates a phospholipid-like photosensitizer (2 mole %) in the bilayer of Dox-loaded stealth liposomes.[2] A liposomal irinotecan formulation has been made in a similar manner based on the FDA-approved liposomal Onivyde.[3] Drugs loaded in PoP liposomes, as well as the PoP itself are stable and exhibit long circulation times in blood. However, red laser irradiation rapidly releases the entrapped drug from the carrier. When mouse or rat tumors are treated with these chemophototherapy agents, a single treatment is frequently sufficient to ablate established tumors at a relatively low chemotherapy dose of drug. Pharmacokinetic analysis shows that a major mechanism for the efficacy pertains to enhanced drug delivery following permeabilization of tumor blood vessels damaged by PDT. We will discuss our experience and outlook for this approach to chemophotherapy as a strong ablation modality with systemic drug delivery.

A Bottom-Up, Synthetic Approach to the Melanin Challenge

Jean-Philip Lumb

Xueqing Wang[1], Lilia Kinziabulatova[2], Marco Bortoli[3], Anju Manickoth[3], Marisa A. Barilla[2], Haiyan Huang[1], Lluís Blancafort[3], Bern Kohler[2], Jean-Philip Lumb[1]

[1]Department of Chemistry, McGill University, Montreal, Quebec, Canada, [2]Department of Chemistry and Biochemistry, The Ohio State University, Columbus, Ohio, [3]Institut de Química Computacional i Catàlisi, Facultat de Ciències, Universitat de Girona, Girona, Spain

Melanins are multifunctional, biological materials found in virtually every organism. They are best known as sunscreens that color the hair, skin, and eyes of mammals, but they also play myriad other roles, and often in parts of

the body that are not exposed to light. Despite their critical function in biology, the structures of melaninsremain poorly understood. Unlike the carefully controlled enzymatic processes that assemble DNA or polypeptides, melanins are produced by aerobic oxidations of aminophenols that afford dynamic mixtures of redox-active fragments that are largely insoluble. This talk will describe our efforts to address the challenge of understanding melanin's structure by using a bottom-up, synthetic approach. By dissecting melanin biosynthesis into 3-disctete phases of chain-growth, chain-oxidation and chain aggregation, we show that low-molecular weight, atomistically defined fragments can exhibit signature melanin-properties, including near-IR absorption, a persistent radical signal and ultra-fast, excited state decay. The talk will disclose the first synthesis of a sterically stabilized indole-5,6-quinone, and chart a path towards structure-property relationships that could help to design the next generation of melanin inspired materials.

Photodynamic therapy of hypoxic head and neck tumors with oxygenated photoacoustic nanodroplets

Srivalleesha Mallidi

Marvin Xavierselvan[1], Jason Cook[2], Jeanne Duong[1], Kimberly Homan[2], and Srivalleesha Mallidi[1,3]

[1]Department of Biomedical Engineering, Tufts University, Medford, Massachusetts, [2]Nanohybrids Inc., Austin, Texas, [3]Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts

One of the key factors limiting the efficacy of head and neck cancer (HNC) treatment is hypoxia. A condition stemming from the excessive oxygen demand than the supply, hypoxia renders HNC resistant to conventional radiation and chemotherapy. As photodynamic therapy (PDT) primarily depends on oxygen radicals to destroy cancer cells, its efficacy is affected due to the hypoxic regions in HNC. To combat hypoxia, we developed perfluorocarbon-based photoacoustic nanodroplets for the co-delivery of oxygen and photosensitizer (BPD) to enhance the impact of PDT on hypoxic HNC. With the aid of a photoacoustic (PA) absorber, indocyanine green, oxygen is spatiotemporally released into the tumor microenvironment. The nanodroplets generated significantly higher singlet oxygen under hypoxic conditions than in control. The delivery of oxygen in vivo was investigated in a murine model with subcutaneous FaDu xenografts via PA monitoring of tumor oxygen saturation. The oxygen saturation analysis confirmed a significant increase in tumor oxygenation post administration of nanodroplets. Further, the results of oxygen saturation analysis were validated with the histologic examination (vasculature and hypoxia marker, pimonidazole) performed on these tumors which revealed a significant reduction in hypoxic regions in nanodroplets treated groups. Additionally, HNC spheroid models were used to demonstrate the heterogeneity in the distribution of hypoxia in these tumors, and the effectiveness of the nanodroplets in penetrating the core of spheroids and reliving hypoxia was also evaluated. Finally, the nanodroplets accumulation in the tumor was monitored in real-time with PA imaging and in vivo PDT was performed. The nanodroplets had better efficacy and resulted in significantly higher necrosis and collagen degradation than the liposomal formulation of BPD. In summary, the photoacoustic nanodroplets offer a better option for the treatment of hypoxic HNC.

Role of arsenic in affecting UV damage formation and DNA repair

Peng Mao

Mingrui Duan[1], Rachel M. Speer[2], Ke Jian (Jim) Liu[2], and Peng Mao[1]

[1] Department of Internal Medicine, University of New Mexico Comprehensive Cancer Center, University of New Mexico, Albuquerque, NM, [2] Department of Pharmaceutical Sciences, College of Pharmacy, University of New Mexico, Albuquerque, NM

Arsenic in food and drinking water is a global health concern that affects over 200 million people worldwide. Epidemiological studies and experimental data have shown that chronic arsenic exposure, even at a low dose, significantly enhances skin cancer risk when combined with environmental ultraviolet (UV) radiation. However, the molecular mechanism underlying arsenic's co-carcinogen role in skin cancer is not fully understood. UV induces helix-distorting DNA damage such as cyclobutane pyrimidine dimers (CPDs), which can cause mutations and lead to skin carcinogenesis. The cellular repair mechanism against CPDs plays a critical role in preventing UV mutagenesis and skin cancers. To better understand how arsenic affects UV damage and its repair, we used a novel UV damage sequencing method, CPD-seq (cyclobutane pyrimidine dimer sequencing), and generated a genome-wide and single nucleotide-resolution UV damage map in human skin cells treated by both arsenic and UV. Our data revealed that arsenic exposure significantly affected CPD formation at the binding sites of a subset of zinc-finger transcription factors (ZF-TFs). The effect of arsenic is specific, because CPD formation at binding sites of non-zinc finger transcription factors or other ZF-TFs was not affected, suggesting that arsenic may target specific ZF-TFs to disrupt their interaction with DNA and change the UV susceptibility of their binding sites. Additionally, our data showed that repair of UV damage by nucleotide excision repair (NER) was significantly inhibited by arsenic across the genome. Intriguingly, transcription coupled NER (TC-NER), a subpathway of NER that specifically repairs damage in active genes, was inhibited more strongly than global genomic NER (GG-NER). Hence, these new data suggest that arsenic affects two key steps of UV mutagenesis, CPD formation and NER, to elevate the carcinogenesis potential of UV radiation.

Enhancement of Photodynamic Therapy for Basal Cell Carcinoma using Oral Vitamin D Pretreatment: Interim Results from a Prospective Clinical Trial

Ed Maytin

Edward V. Maytin[1,2,3,4,5], Lauren E. Heusinkveld[4], Jeffrey Negrey[3], Abigail Updyke[2], Sanjay Anand[2], Christine B. Warren[2,4], Nathalie Zeitouni [5] , and Tayyaba Hasan[6]

[1]Department of Dermatology, [2] Department of Biomedical Engineering, [3] Lerner Research Institute, [4]Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland OH; [5] US Dermatology Partners, Phoenix, AZ; [6]Wellman Center for Photomedicine, Massachusetts General Hospital, Boston MA

Photodynamic therapy using aminolevulinic acid and visible light (PDT) is approved in Europe to treat basal cell carcinoma (BCC), but is not approved in the USA due to uncertainties about efficacy. Pretreatment using Vitamin D3 (VD3; cholecalciferol) prior to PDT improves BCC responses in mice. A prospective, double-blind, crossover clinical trial [NCT03467789] was designed to test whether oral VD3 pretreatment enhances BCC responses to blue light PDT. Participants received 3 PDT treatments (20% ALA, 4 h; 417 nm, 30 min) 2 months apart. High-dose VD3 or placebo was administered prior to each of the first two PDT sessions. Lesions were recorded with a 3D digital camera to allow software-assisted tumor volume analysis. Treatment-resistant tumors were biopsied at the final visit. To date, 24 patients and 128 BCCs have been analyzed. Two-thirds (70%) of all lesions cleared completely after PDT. Of the 30% of tumors that failed to clear, all except one superficial BCC were either nodular, micronodular, adenoid, or infiltrative subtypes. To assess the ability of neoadjuvant VD3 to potentiate PDT efficacy, we evaluated all available lesions to determine their relative volume reduction after VD3+PDT and placebo+PDT. Tumors that fulfilled a prediction that shrinkage (% volume reduction) would be greater after VD3+PDT compared to placebo+PDT were scored as "Yes". In our

analysis, 15 patients scored "Yes" and 6 scored "No". This >2-fold difference provides preliminary evidence that neoadjuvant VD3 augments therapeutic responsiveness to PDT for many BCC tumors. PDT may be an effective treatment for BCC, especially superficial BCC. The combination of oral VD3 given prior to PDT represents a novel and safe approach toward making the treatment more efficacious.

Next-generation light-triggered metallodrugs for cancer therapy

Sherri McFarland

The University of Texas at Arlington

There has been an ongoing interest in the development of new photosensitizers (PSs) for photodynamic therapy (PDT), specifically to address some of the drawbacks associated with the pyrrole-based PSs that are most commonly employed. A related area of active investigation has been the design of PSs with novel mechanisms of action, including oxygen-independent photoprocesses (known as photochemotherapy, or PCT) or the capacity to switch to such modes in hypoxia. Transition metal complexes have emerged as attractive PSs for both PDT and PCT. One example is our own TLD1433, currently in a Phase II clinical trial for treating bladder 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 photodynamic reactions as well as oxygen independent pathways that form the basis of PCT, and can elicit the hallmarks of immunogenic cell death. The attractive features of Ru extend to other metals, and we therefore expect metallodrugs to play an important role in the future of light-triggered cancer therapy. In this presentation, we will discuss the design and development of metallodrug PSs that can potentially exploit both PDT and PCT effects that lead to the hallmarks of immunogenic cell death. The emphasis will be on the structural features and photophysical models that produce excited triplet states with characteristic reactivities.

Sound GUV safety science does not guarantee public acceptance

Kate McPhaul

Kathleen M. McPhaul[1], Donald K. Milton[1], Cynthia Baur[2]

[1]University of Maryland School of Public Health Institute of Environmental Health, [2]University of Maryland School of Public Health Center for Health Literacy

Public perception will ultimately determine the extent of GUV utilization for air disinfection in indoor public spaces. The polarization of attitudes towards masks and vaccines puzzled public health scientists during the COVID-19 pandemic, but much has been learned which can be applied to GUV. As an air disinfection strategy, GUV possesses predictable communication challenges. UVC, particularly Far UVC, is difficult to explain and not well-understood by the public. Furthermore, UV is associated with radiation, cancer and cataracts. Finally, federal sources of information are not yet supportive of GUV for air disinfection and do not provide easy to understand messages and graphics.

Learning about the information needs of diverse communities is critical but it is just as important to determine the range of characteristics of credible and trusted messengers and, finally, the features of effective messages. We are integrating public attitudes and communication (PAC) research into our GUV field studies using participatory research processes. These methods are known to build trust and two-way communication which will inform and benefit all the GUV projects.

A key component of the PAC research program will be focus groups in urban, suburban and rural communities with varying demographics. These groups will initially help us learn about preexisting knowledge and attitudes and subsequently be used to test messages and communication strategies. Our PAC research will support a planned field intervention study, pay specific attention to low income, Black, indigenous, people of color (BIPOC), rural and politically conservative communities and ultimately other groups such as stakeholders in education, childcare, and other industries.

The formative research phase including message development and testing has begun with two GUV installations at the UMD School of Public Health. Preliminary findings as well as a discussion of the stakeholders, overall design, and participatory research methods for the PAC will be presented.

Photostability studies on therapeutic monoclonal antibodies: the case of Ipilimumab

Giorgia Miolo

Giorgia Miolo, Patrizia Polverino de Laureto

Department of Pharmaceutical and Pharmacological Sciences, University of Padova, Padova, Italy

The photostability of the monoclonal antibody Ipilimumab, the active ingredient of Yervoy® for the treatment of different types of cancer, has been investigated. The non-diluted form of the initial pharmaceutical product and the diluted saline or glucose solutions (the infusions prepared and administered in the ward) were irradiated under two very different doses of artificial solar light. The mAb showed to be sensitive under the minimum dose tested (720 kJ/m2, corresponding to the exposure criteria for ICH confirmatory photostability studies) with formation of aggregates, particularly when diluted in commercial glucose solution, containing glucose degradation products able to react with the active principle under light exposure. The soluble aggregates (7.5%) were lower (1.5 and 3%) in the case of saline and lab-made glucose diluted samples, respectively. For the samples irradiated with much higher light doses (10460 kJ/m2, forced stressor) soluble aggregates reached 34% for the glucose diluted mAb but they were 12 and 20% in saline solution and in lab-made glucose, respectively. The insoluble aggregates were about 30% of the initial diluted irradiated sample, independently from the diluent used. However, the aggregation of Ipilimumab took place also by irradiating the non-diluted formulation, indicating that the ingredients did not protect the drug from photodegradation. Amino acid oxidation and deamidation were found but soluble Ipilimumab maintained its typical β-sheets structure, and the tertiary structure was nearly maintained compared to the dark.

As this study has demonstrated the susceptibility of Ipilimumab to light, specific solutions and excipients, as well as the use of safe light in manufacturing, handling, and storage of this drug could be indicated to avoid the detrimental effect of light on its efficacy.

A detailed understanding of Ipilimumab physicochemical properties and stability could assure the best storage and manipulation conditions for its safe and successful application in cancer therapy.

Selective UV spectra for the induction of regulatory T-cells

Akimichi Morita

Akimichi Morita[1]

[1]Department of Geriatric and Environmental Dermatology, Nagoya City University Graduate School of Medical Sciences, Nagoya, Japan

Phototherapy utilizes the beneficial effects of ultraviolet (UV) wavelengths to affect immunoregulatory functions. Dual-action operative mechanisms of UV phototherapy have been identified: apoptosis and immune suppression. NB-UVB depletes pathogenic T cells by inducing apoptosis and regulatory T cells. Other wavelengths are also utilized for phototherapy, i.e., 308-nm excimer light and 312-nm flat-typed NB-UVB. Excimer light (308 nm) therapy effectively targets the affected skin without unduly exposing other areas and increases the levels of T regulatory cells. Phototherapy improves impaired resting regulatory T cells and increases activated regulatory T cells in patients with psoriasis. In mouse, UVB increases regulatory T cells by clustering with dermal CD11b type Langerin- DCs to induce immunological self-tolerance. Furthermore, UVB expanded skin regulatory T cells are tissue regulatory T cells and express proenkephalin (PENK), an endogenous opioid precursor, and amphiregulin (AREG), the epidermal growth factor receptor ligand. UVB-expanded skin regulatory T cells play a key role in promoting wound healing in vivo.

More rational designs of phototherapy devices and irradiation protocols are under development. The long-term safety of biologic therapies, however, is not well established, and they are expensive. Phototherapy takes advantage of wavelengths found in natural sunlight, which, despite its well-known deleterious effects, such as premature skin aging and increased risk of cancer, also has beneficial effects on diseased skin. Sunlight exposure has been historically recommended to maintain health and to treat disorders, and natural sunlight comprises beneficial wavelengths, such as 311-nm NB-UVB. Several ongoing studies are investigating various wavelength-dependent effects on both skin disease and the underlying immunomechanisms. A light-emitting diode that emits UV will be a more desirable and feasible light source, particularly if it has a high enough intensity level for the treatment of skin diseases.

Strides Towards Photodynamic Image-Guided Surgery in Head and Neck Cancer

Girgis Obaid

Chanda Bhandari[1†], John Fakhry[1†], Menitte Eroy[1], Jane Junghwa Song[1], Kimberley Samkoe[2], Tayyaba Hasan[3,4], Kenneth Hoyt[1] and Girgis Obaid[1]*

[1]Department of Bioengineering, University of Texas at Dallas, Richardson, TX, [2]Thayer School of Engineering, Dartmouth College, Hanover, NH, [3]Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts, [4]Division of Health Sciences and Technology, Harvard University and Massachusetts Institute of Technology, Cambridge, Massachusetts

Sub-therapeutic photodynamic therapy, photodynamic priming (PDP), has been shown to sensitize tumors to combination agents and improve the tumor delivery of nanomedicines. This work demonstrates for the first time that PDP can be used to improve the tumor delivery and diagnostic accuracy of the clinical fluorescence image-guided surgery (IGS) probe Cetuximab

IRDye800CW (Cet-IRDye800). We demonstrate that PDP primes orthotopic FaDu human head and neck tumors in mice for Photodynamic Image-Guided Surgery (P-IGS) by increasing the delivery of the probe Cet-IRDye800 by up to 138.6%, and expedites its accumulation by 10.5-fold. Furthermore, fractional tumor coverage is improved by 49.5% at 1 h following Cet-IRDye800 administration. The diagnostic accuracy of tumor detection is improved by 264.2% with respect to the salivary glands at 1 h. As such, Photodynamic Image-Guided Surgery provides a time-to surgery benefit by reducing the time to plateau from 25.7 h to 2.5 h. We therefore propose that a pre-operative PDP regimen can expedite and augment the accuracy of IGS-mediated surgical debulking of head and neck tumors and reduce the time-to-IGS. Beyond this application, the role of PDP in the homogenous delivery of diagnostic, theranostic and therapeutic antibodies in solid tumors is of considerable significance to the wider community.

Catecholic materials show an independent response to orthogonal redox and optical stimuli

Gregory Payne

Institute for Bioscience and Biotechnology Research, University of Maryland College Park, MD

Catechol-based materials (e.g., melanin) are ubiquitous in nature and offer diverse functional properties that are incompletely understood. In many cases, such catecholic materials are reversibly redox-active and can be repeatedly switched between their oxidized and reduced states. Previous measurements with melanins and biomimetic catechol films (e.g., catechol chitosan films) have shown that the redox activities of these materials correlate to their anti/pro oxidant properties and to their radical scavenging properties. Also in many cases, such catecholic materials (e.g., catechol-chitosan films) are photothermally-active and can transduce near infrared (NIR) radiation into heat. When we simultaneously stimulated catechol-chitosan films with redox and NIR inputs, we observed the responses were reversible and largely independent. Fundamentally, these top-down measurements suggest that the flow of energy through catechol-based materials via the redox-based molecular modality and the electromagnetic-based optical modality can be independent.

Validation of vitamin D3 action spectra

Peter Philipsen

Peter A. Philipsen[1], Arjan van Dijk[2], Antony R. Young[3]

[1]Department of Dermatology, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark, [2]RIVM, Bilthoven, The Netherlands, [3]St. John's Institute of Dermatology, King's College London, United Kingdom

An action spectrum for previtamin-D3 published by the Commission Internationale d'Eclairage (CIE)(1) is widely used in risk/benefit assessments of solar ultraviolet radiation (UVR) exposure. The validity of this spectrum has been challenged, both by theoretical calculations and in-vitro studies.

We have developed an experimental data tool based on monitoring serum 25-hydroxyvitamin D3 increases in healthy humans after serial sub-erythemal UVR exposures with 5 different UVR broad-band spectra. The tool generated linear standard erythema dose (SED) –response curves that were different for each spectrum. A valid vitamin D3 action spectrum weighting the UVR doses would result in a common regression line for all UVR spectra.

We present the validation of candidate action spectra for vitamin D3: CIE previtamin-D3, wavelength shifted CIE previtamin-D3, Bolsee, Olds and the RIVM vitamin D3 action spectra(2). The latter with different skin absorption profiles: none (Quartz), inner forearm, outer forearm, lower back, and ball of thumb.

The CIE previtamin-D3 action spectrum did not result in a common regression line but was valid after adjusted by a blue shift of 5 nm. The RIVM profiles for inner forearm, lower back and outer forearm all resulted in a common regression

line, with inner forearm having the best model fit.

We conclude that the CIE previtamin-D3 action spectrum is not optimal for estimation of serum 25(OH)D3 increases after solar UVR exposures unless a 5 nm shift is performed. The RIVM action spectrum for inner forearm is the best candidate but further validation is needed.

Detection of thymine dimers in urine after UVR exposure of volunteers by a new UPLC-MS/MS based method

Peter Philipsen

Catharina M. Lerche[12], Peter A. Philipsen[1], Sigurd Hermansson[3], Jakob Heydenreich[1]and Hans Christian Wulf[1]

[1]Department of Dermatology, Copenhagen University Hospital Bispebjerg, Copenhagen, Denmark, [2]Department of Pharmacy, University of Copenhagen, Copenhagen, Denmark, [3]Waters Corporation, Solna, Sweden

Objectives: Solar ultraviolet radiation (UVR) is a carcinogen and results in DNA damage in the skin after irradiation. The most frequent UVR induced DNA damage is cyclobutane pyrimidine dimers (CPDs) which includesthymine dimers. When CPDs are formed the nucleotide excision repair system is activated and repaired CPDs are excreted in the urine. The aim of this study was to quantify thymine dimers in the urine using our developed mass spectrometry-based method on a group of UVR irradiated volunteers.

Methods: After years of method development, we successfully detected thymine dimers in the urine using "dilute and shoot" principle. Prior to analysis, sample preparation consisted of a simple dilution before injection to an ultra-high-pressure liquid chromatography (UPLC) coupled to a tandem mass spectrometer. Eight healthy volunteers were whole-body UVR irradiated with 1.5 or 2.0 standard erythema dose (SED) for 3 consecutively days. Morning urine was collected at baseline (day 1), before first irradiation, and the following 7 days, recording urine output duration and volume. Results: 216 samples were analyzed in at least triplicates, resulting in 9 undetectable values of which 8 was baseline samples and with a relative standard deviation of 14.5% (0.8-49.0%). The volunteers had the highest excretion of thymine dimers (mean 1178ng/24h) on day 6, 3 days after last exposure. All measurements day 2-7 were significantly higher than baseline ($p > 0.016$).

Conclusions: We succeeded to quantify thymine dimers in the urine after whole-body UVR exposure and rediscovered a maximal urine excretion 3 days after last exposure.

Nicotinamide and phytochemicals phloroglucinol and syringic acid delay UVR-induced squamous cell carcinoma onset in hairless mice

Celina Pihl

Celina Pihl[1,2], Flemming Andersen[3,4], Peter Bjerring[3], Merete Haedersdal[1,5], Catharina Margrethe Lerche[1,2]

[1] Department of Dermatology, Copenhagen University Hospital—Bispebjerg and Frederiksberg, Copenhagen, Denmark, [2] Department of Pharmacy, University of Copenhagen, Copenhagen, Denmark, [3] Department of Dermatology, Aalborg University Hospital, Aalborg, Denmark, [4] Private Hospital Molholm, Vejle, Denmark, [5] Department of Clinical Medicine, University of Copenhagen, Copenhagen, Denmark

Background/Aim: Ultraviolet radiation (UVR) is the primary risk factor for skin cancers such as squamous cell carcinomas (SCCs). Because of poor adherence to topical sun protection regimes, other prevention measures must be explored. Phytochemicals have demonstrated numerous protective effects and therefore presents a promising avenue for photoprevention. The aim of this study was to explore the protective effects of phytochemical compounds on UVR-induced carcinogenesis in hairless mice. Materials and Methods: 125 female C3.Cg-Hrhr/TifBom Tac mice were randomized into five groups. Through the drinking water, the mice either received 100 mg/kg of hesperidin methyl chalcone (HMC), phloroglucinol (PG), or syringic acid (SA), 600 mg/kg of nicotinamide (NAM), or no supplementation (UV control). Thrice weekly, the mice were irradiated with three standard erythema doses (SED) of UVR to induce and promote carcinogenesis. Results: Oral supplementation with NAM, PG, and SA significantly ($P<0.05$) delayed the onset of SCCs in hairless mice. In the NAM and SA groups, this effect was associated with an increase in pigmentation following six months of UVR ($P<0.05$). In the HMC group, no effect on carcinogenesis was observed compared to the control group, and none of the four experimental groups exhibited any change in erythema following UVR. Conclusion: We have demonstrated that oral supplementation of NAM, PG, and SA to hairless mice can protect against the development of SCCs following UVR.

Mitochondria targeted prodrugs improve the PDT efficacy to treat non-muscle invasive bladder cancer (NMIBC)

Kazi Md Mahabubur Rahman

Kazi Md Mahabubur Rahman[1], Youngjae You[1]

[1]School of Pharmacy and Pharmaceutical Sciences, University at Buffalo, Buffalo, NY

In the USA, bladder cancer (BC) is the 4th most common cancer in men and more than 70% patients get diagnosed with NMIBC. Treatment options after surgery include BCG, chemotherapy, and PD-1 checkpoint inhibitors. They all have mild to severe side effects and cannot completely prevent recurrences. Upon intravesical administration of hexaminolevulinate (HAL), cancer cells produce 9-16 times more protoporphyrin IX (PpIX, a potent photosensitizer produced in the mitochondria) than normal cells, the basis of FDA approved diagnosis of BC. HAL was also tried

in the NMIBC treatment but suffered low efficacy. We hypothesized that PpIX-photodynamic therapy (PDT) efficacy can be improved by combining prodrugs developed with a light activatable linker system and activating them preferentially in tumors using PpIX-PDT. A number of prodrugs, mitochondria-targeted and non-mitochondria-targeted with a range of molecular weight and lipophilicity, have been synthesized in order to overcome the diffusion limitations in the bladder, as well as to improve drug pharmacokinetics and efficacy. In-vitro and ex-vivo evaluations using cell monolayer and 3D spheroids revealed that mitochondria targeting not only increases uptake due to mitochondrial membrane potential but also helps retain most of the drugs in the mitochondria and helps to achieve higher efficacy. Formulation development further helped drug penetration deep inside (>500µm) the rat bladder wall to treat NMIBC. Primary in vivo evaluation confirmed the initial hypothesis of achieving greater efficacy from HAL-prodrugs combination compared to HAL only group. In vivo efficacy studies are currently being conducted with the selected prodrugs in orthotopic rat models of bladder cancer. In summary, the prodrugs we have developed can generate better efficacy than HAL alone, while sparing the normal bladder of chemotherapy-related side effects.

KEYNOTE – Controlling Photochemical Processes with Confinement

V. Ramamurthy

From time immemorial it is well known that curtailment of freedom often leads to changes in the behaviour of living beings. Similar restriction of freedom leads to selectivity in the chemical

behavior molecules embedded in biological systems. Extending these well-known concepts supramolecular chemists have established that even small molecules upon confinement in synthetic hosts exhibit behaviour distinctly different from the ones in an isotropic solution.

In this lecture the role a "Medium" in bringing about changes in the well-established behaviour of excited molecules would be illustrated with select examples. Results of steady state and ultrafast experiments will be presented that highlight how the confinement alters the excited state dynamics of anthracene, stilbenes and azobenzenes, the molecules that act as triggers in various biological systems and man-made devices. Another reaction to be discussed concerns with electron transfer (eT) that plays a fundamental role in a number of biological events including photosynthesis. Examples and ultrafast dynamics of donors, imprisoned within an organic capsule, transferring an electron to an acceptor across a molecular wall would be presented.

The main message of the talk is that molecules like humans behave differently when confined within synthetic cages.

Exploration of a new class of photochromic molecules

Javier Read de Alaniz

Photons have multiple enabling advantages to control chemical reactions, processes and stimuli-responsive materials. In this seminar, I will discuss our groups effort to design and develop a new class of negative photochromic molecules termed DASA, their incorporation into materials and subsequent effort to unlock their unique potential as multi-stage photoswitches.

Unscrambling mixtures of photoinduced intermediates of bacteriorhodopsin

Zhong Ren

Department of Chemistry, University of Illinois at Chicago, Chicago, IL

I recently took an independent second look at the serial crystallographic datasets collected from bacteriorhodopsin, the light driven proton pump. From the outset, my analysis assumes that each crystallographic dataset was derived from a mixture of several unknown intermediates induced by the excitation light. An analytical strategy of decomposition and deconvolution based on singular value decomposition (SVD) and the subsequent Ren rotation achieves a numerical resolution of concurrent chemical events from mixed observations. This method now resolves simultaneous signals mixed in the structural dynamics of bacteriorhodopsin. The unscrambled electron density maps of the intermediates are substantially clearer than the original maps of mixtures. Based on these pure intermediate structures from tens of femtoseconds to milliseconds, isomerization sampling of the retinal is directly observed in bacteriorhodopsin (Ren, PNAS Nexus 10.1093/pnasnexus/pgac103, 2021). The intermediate structures preceding and following the productive isomerization led me to reexamine the current working hypothesis of the unidirectional proton conductance (Ren, bioRxiv 10.1101/2021.10.04.463074, 2021).

Comparison of photodynamic priming efficacy, with BPD or ALA-PpIX, to overcome PFAS-Induced Platinum Resistance in Ovarian Cancer

Brittany Rickard

Per- and polyfluoroalkyl substances (PFAS) are endocrine-disrupting compounds that frequently pollute drinking water supplies worldwide. As such, certain PFAS are linked to adverse female reproductive outcomes, including increased ovarian cancer risk. Ovarian cancer is the most lethal gynecologic cancer with a mortality rate of ~65%. A major contributor to the high lethality is resistance to platinum-based chemotherapy, highlighting the need for an improved understanding of the sources of chemoresistance and the development of mechanism-based treatments. Since environmental exposures have been linked to therapy resistance in other cancers, the effect of PFAS on the response of ovarian cancer to chemotherapy was evaluated. Interestingly, two emerging PFAS, perfluoroheptanoic acid and perfluoropentanoic acid, induced platinum resistance in ovarian cancer cells. We hypothesized that the observed platinum resistance was due to PFAS-induced mitochondrial dysfunction. Studies have shown that PFAS induce adverse ovarian effects through disruption of mitochondrial respiration, and that platinum-resistant ovarian cancer cells demonstrate increased flexibility in using glycolysis and oxidative phosphorylation for energy production compared to platinum-sensitive cells. In the present study, changes in mitochondrial membrane potential were measured following PFAS exposure and after treatment with platinum-based chemotherapy. An increase in mitochondrial membrane potential was observed in ovarian cancer cells post-PFAS exposure and after treatment with carboplatin, suggesting improved cellular health. Since these data implicate mitochondria in PFAS-induced resistance, the ability of photodynamic priming (PDP), a light-based treatment modality that can target specific organelles, including mitochondria, was evaluated. PDP resensitizes platinum-resistant tumor cells to subsequent chemotherapy treatment by producing reactive molecular species, causing organelle damage, and modulating apoptotic regulatory proteins. PDP using a clinically approved photosensitizer (benzoporphyrin derivative) or pro-drug (5-aminolevulinic acid-induced protoporphyrin IX) was compared and performed on PFAS-exposed ovarian cancer cells prior to treatment with platinum therapy. Data showed that mitochondrial-targeted PDP successfully overcame PFAS-induced platinum resistance and induced photodamage to the mitochondrial membrane, indicated by decreased mitochondrial membrane potential. Taken together, these findings suggest PFAS contribute to platinum resistance in ovarian cancer by altering mitochondrial function. Targeting mitochondria using PDP may prove effective for the treatment of platinum-resistant ovarian cancer.

Influence of chronic UV irradiation and the dermis on DNA repair of UV-induced DNA damage

Patrick Rochette

Marie-Catherine Drigeard Desgarnier[1], Roxanne Bérubé[1], Marie Dorr[1], Sébastien Méthot[1], Sophie Amouret[1], Thierry Douki[2], Patrick J Rochette[1,3]

[1] CHU de Québec research center – Université Laval, Hôpital du Saint-Sacrement, Québec, Qc, Canada, [2] INAC/LCIB UMR-E[3] CEA-UJF/Commissariat à l'Énergie Atomique (CEA), Grenoble, France ,[3] Département d'Ophtalmologie et ORL - chirurgie cervico-faciale, Université Laval, Québec, Qc, Canada

Exposure to solar UVB leads to the formation of the highly mutagenic cyclobutane pyrimidine dimers (CPD), the DNA damage responsible for mutations found in skin cancers. Skin cells have mechanisms to prevent the conversion of CPD into mutations, including DNA repair and apoptosis. Many factors can influence CPD repair rate, including their sequence and localization, but also the fluence and regimen of UV exposure. Here we show that pre-stimulation of cells with chronic irradiation with chronic low-dose of UVB (CLUV) influences CPD repair. Indeed, CLUV treatment greatly enhance CPD repair and increases the level of NER recognition proteins, DDB2 and XPC, in fibroblasts. Surprisingly, the opposite has been found in HaCaT keratinocytes, i.e. an important decrease in CPD repair efficiency. In both cell types, CLUV irradiation leads to the accumulation of residual CPD that persist on DNA and are diluted via the semi-conservative replication, and they catalyze the incidence of sister chromatin exchange (SCE). About UV-induced apoptosis, we have shown that the incorporation of functional mitochondria in fibroblasts increases the sensitivity

to UV-induced apoptosis of fibroblasts and that this increase is dependent on the p53 status of mitochondria donor cells. Altogether, our results show that the study of the response to UV rays is influenced by different factors, and it is important to consider them in the study of photo-carcinogenesis.

RNA – target and mediator of cellular responses to ultraviolet radiation

Thomas Rünger

Department of Dermatology, Lahey Hospital and Medical Center, Beth Israel Lahey Health, and Tufts University School of Medicine

DNA is a critical chromophore that mediates many cellular responses to ultraviolet radiation (UVR). Photoexcitation of cellular nucleic acids also includes RNA. In fact, there is more RNA damage than DNA damage following UVR exposure. RNA damage results in translational arrest, RNA degradation, and decreased protein synthesis. However, because of the usually limited life span of RNA, RNA damage is usually not regarded to be as detrimental as DNA damage. We recently reported that UVR-induced oxidative RNA damage induces alternative RNA splicing. For the lamin A gene, this results in the transcription of a truncated pre-lamin A protein, called progerin. Progerin lacks degradation signals, accumulates in cells, and interferes with many cellular functions. Ultimately, it causes cellular senescence and with that plays a critical role in aging. This is one example how UVR-induced RNA damage causes not only a brief disturbance of cellular homeostasis, but exerts permanent effects.

Furthermore, RNAs are also critically involved in regulating cellular responses to UVR that far extend beyond messenger RNA coding for proteins. There are many types of non-coding RNA genes. E.g., there are about 60,000 genes for long non-coding RNAs (lncRNAs). The functions of the vast majority of these lncRNAs remain unknown, but they are thought to be involved in regulating expression of protein-coding genes. Using DNA microarrays following exposure of primary human fibroblasts to UVA and UVB, we found that the expression of thousands of lncRNAs is up- or down-regulated in a wavelengths-dependent manner. We were then able to identify the functions of three of these lncRNAs. Two UVB-altered lncRNAs regulate genes in the intrinsic and extrinsic pro-apoptotic pathways, and a UVA-induced lncRNA the expression of IL-8.

In summary, RNA is a prime chromophore for cellular responses to UVR and mediates many short- and long-term effects of UVR.

Mitigating long UVA-1 and Visible Light effects in skin with antioxidants

Eduardo Ruvolo

Beiersdorf Inc

Studies have demonstrated that visible light (VL) produces sustained pigmentation and combination with ultraviolet (UV) (VL+UVA1) is synergistic. Ex vivo studies using a topical antioxidant complex demonstrated efficacy in preventing formation of free radicals in skin. Studies have demonstrated that antioxidants blend can effectively mitigate the effects of long UVA-1 and visible light in skin, in simple blend solution or when incorporated in sunscreens.

The reduced intensity of the VL+UVA1-induced effects in some of the treatment sites with this product supports the hypothesis that the effects of VL+UVA1 can be mitigated by antioxidants. This clinical effects and biomarker protection cannot be generalized to all concentrations. The mechanism of action and variability in response between skin-types warrants further studies.

Potentiation of photodynamic therapy by metal-coordination compounds as Photosensitizer

Roberto Santana da Silva

Amanda Becceneri[1], Francisco Rinaldi[1], Matheus Torelli[1], Laisa Negri[2]and Roberto S. da Silva[1]*

[1]Faculdade de Ciências Farmacêuticas de Ribeirão Preto University of Sao Paulo, Ribeirão Preto, SP-Brazil, [2] Department of Dermatology, Harvard Medical School, Boston, MA

Light irradiation known as Photodynamic Therapy (PDT) has been used for several decades for cancer treatment, based on the combination of photosensitizer (PS), oxygen and visible light irradiation. We have found that combined effects of nitric oxide (NO), infrared (photobiomodulation - PBM) and visible light components are helpful to enhance PDT. The PBM modulates signaling pathways via ROS, ATP, Ca2+, while PDT generates reactive oxygen species. Besides, NO generation could be an important tool when combined with both kinds of light therapy. By using ruthenium-phthalocyanine or porphyrin as metal-based compounds, we found that PBM combined with PDT could be a beneficial cancer treatment option. The metal-based PS's are producers of reactive oxygen and nitrogen species (RONS). The UV-Vis spectra of ruthenium complexes displayed an intense band in the 660 nm region ($\varepsilon \approx 10(5)$ M-1cm-1). In vitro cytotoxicity experiments using several cancer cell lines showed that the developed RONS approach produces a strong synergistic toxic effect to tumoral cells compared to the ROS; additionally, PBM enhances the cytostatic efficacy allowing cell toxicities above 96 % after a single low irradiation dose. With only PDT the cell viability drops to 65 %. This may be due to NO and PBM causing increased cell metabolism, ATP and uptake of the ruthenium compounds. Western Blotting assays showed an increase of cleaved-PARP and cleaved-caspase-3 expression under light irradiation. The use of metal-based PS's and the combination of light therapy may be relevant to PDT in the future.

The effect of oxidative modification of eumelanin on its photoreactivity and antioxidant properties

Michal Sarna

Krystian Mokrzynski[1], Andrzej Zadlo[1], Grzegorz Szewczyk[1], Michal Sarna[1], Shosuke Ito[2], Kazumasa Wakamatsu[2], Tadeusz Sarna[1]

[1]Department of Biophysics, Faculty of Biochemistry, Biophysics and Biotechnology, Jagiellonian University, Krakow, Poland, [2]Institute for Melanin Chemistry, Fujita Health University, Toyoake, Aichi, Japan

Although melanin is believed to act as a natural photoprotective pigment, an animal study indicated that melanoma induction by UVA required the presence of melanin pigment (F. Noonan et al. Nature Commun. 2012). Therefore, photosensitizing abilities of melanin, demonstrated in several model systems, could be responsible for harmful effects in pigmented cells, at least under certain conditions. In this study, we analyzed photoreactivity and antioxidant capacity of DOPA-melanin – a synthetic model of eumelanin, subjected to oxidative degradation induced by UVA and short wavelength visible light, or hydrogen peroxide. It is postulated that oxidative degradation of melanin can occur in situ under extreme conditions. The degree of oxidative degradation of DOPA-melanin was determined by EPR and UV-vis spectroscopies, and by measuring characteristic markers of the melanin chemical state. The efficiency of the melanin before and after oxidative degradation to photogenerate singlet oxygen and superoxide anion was determined by time-resolved singlet oxygen phosphorescence and EPR-spin trapping, respectively. The effect of oxidative degradation of DOPA-melanin on its antioxidant capacity was assessed by measuring the melanin ability to reduce 2,2-diphenyl-1-picrylhydrazyl (DPPH). The analysis showed that while oxidatively degraded DOPA-melanin photogenerated superoxide anion with lower efficiency, such melanin photogenerated singlet oxygen with significantly higher yields when excited with UVA or short-wavelength visible light. On the other hand the oxidatively modified melanin exhibited lower antioxidant capacity and reduced efficiency to quench singlet oxygen. Chemical analysis of photodegraded

DOPA-melanin, indicated a substantial reduction in the melanin content of 5.6-dihydrooxyindole units. The obtained data suggest that partial oxidative degradation of eumelanin, particularly induced by aerobic photolysis, can increase phototoxic potential of the melanin by elevating its efficiency to photogenerate singlet oxygen and reducing the melanin antioxidant ability.

Insight into the control of photoisomerization by the protein environment

Igor Schapiro

Institute of Chemistry, The Hebrew University of Jerusalem, Israel

Photoinduced isomerization allows to convert light into molecular energy. Rhodopsins are proteins that carry a retinal chromophore which exploits this energy conversion mechanism.1 Retinal is covalently linked to the protein by a Schiff base bond. Two types of rhodopsin have evolved, which differ in the initial configuration of the retinal: type 1 or microbial rhodopsins with all-trans isomer of the chromophore and type 2 or vertebrate rhodopsins with 11-cis retinal. The all-trans starting configuration is converted to 13-cis, while the 11-cis chromophore converts to all-trans. 2 Recently, the discovery of the rhodopsin-bestrophin fusion protein has been reported. In this "bestrhodopsin" an unusual photoisomerization from all-trans to 11-cis is reported. 3 We have studied the origin of the bond selectivity in this photoisomerization by hybrid quantum mechanics/molecular mechanics simulations and revealed which amino acid sidechains control it.

Harnessing Cyanine Chemistry for Imaging and Drug Delivery

Martin Schnermann

In vivo imaging methods are poised to address problems across the spectrum of fundamental to applied biomedical science. Here we detail our efforts to use cyanine fluorophore chemistry to enable dynamic and multicolor imaging in living organism. Photoconversion reactions using NIR wavelengths have significant potential for advanced microscopy and cell-tracking applications but were unknown. Multicolor imaging studies had periodically noted the light-dependent conversion of cyanine probes to blue-shifted species. Through careful characterization studies, we uncovered the chemical basis of this phenomenon. The chemistry involves a previously unknown cyanine phototruncation reaction, wherein irradiation of hepta- and penta-methine cyanines leads to the formation of penta- and tri-methine products. The talk will describe efforts to examine the mechanism of the reaction, identified conditions to significantly optimize the yield, and apply it to microscopy and cell tracking applications. This talk will as describe our efforts to apply in vivo optical imaging to assess the role of antibody payloads on tumor targeting. By developing synthetic methods that enable the rapid synthesis of chemically varied heptamethine cyanines, we have assembled and quantitatively compared the targeting of a series of substituted variants. These efforts suggest that highly polar, and specifically zwitterionic, substituents dramatically improve the in vivo properties of mAb conjugates. To examine the role of ADC linkers, conventional always-ON probes are not suitable to study the site and extent of bond cleavage. To address this, we have created a new class of fluorogenic probes in the near-infrared (NIR) range that result from modification of heptamethine norcyanines with stimuli-responsive carbamate linkers. These norcyanine carbamates (CyBams) exhibit exceptional turn-ON ratios and can be activated by a range of enzymatic and chemical triggers. By optimizing the cellular uptake and retention of these probes, we have been able to create mAb-targeted variants that allow us to quantitatively study linker chemistry in animal models. Overall, our goal is to develop and ultimately apply an "imaging-first" workflow for the design and testing of well-tolerated targeted drug delivery agents.

A site-specific oxidation and fragmentation mechanism of a monoclonal antibody induced by visible light

Christian Schöneich

The production of safe and efficacious protein therapeutics requires a thorough understanding of chemical and physical mechanisms, which cause instability. During manufacturing, storage and administration, formulations of therapeutic proteins are subject to the exposure to UVA and visible light. It has been reported that visible light can lead to the degradation of therapeutic proteins. Here, we present evidence for a site-specific oxidation reaction of an IgG1, targeting the constant region, which leads to fragmentation. This mechanism is promoted by visible light, requires the presence of iron, and a largely intact protein structure. The efficiency of fragmentation depends on the nature of the excipients present in the formulation. Surprisingly, only relatively large concentrations of EDTA inhibit the iron-induced fragmentation, suggesting that the target site of the protein may have a significant affinity to iron. Mechanistic studies, supported by HPLC-MS/MS analysis, suggest a light-induced formation of a protein alkoxyl radical, which undergoes fragmentation to a variety of products.

Set2 Histone Methyltransferase Regulates Transcription Coupled-Nucleotide Excision Repair in Yeast

Kathiresan Selvam

Kathiresan Selvam[1], Dalton A Plummer[1], Peng Mao[3], John J Wyrick[1,2]

[1]School of Molecular Biosciences, and [2]Center for Reproductive Biology, Washington State University, Pullman, WA, [3]Department of Internal Medicine, Program in Cellular and Molecular Oncology, University of New Mexico Comprehensive Cancer Center, Albuquerque, NM

Nucleotide excision repair (NER) pathway is a conserved DNA repair pathway that removes helix-distorting DNA lesions, including ultraviolet (UV) light-induced cyclobutane pyrimidine dimers (CPDs). There are two sub-pathways of NER: global genomic-nucleotide excision repair (GG-NER) and transcription coupled-nucleotide excision repair (TC-NER) pathways. While GG-NER removes lesions anywhere in the genome, TC-NER is specific for the repair of lesions in the transcribed strand of active genes. Modulation of chromatin structure by post-translational modifications (PTMs) such as histone acetylation and methylation have been shown to promote GG-NER. Whether histone PTMs also regulate the repair of DNA lesions by the TC-NER pathway in transcribed DNA is unknown. Here, we found that histone H3 K36 methylation (H3K36me) by the Set2 histone methyltransferase in yeast regulates TC-NER. Mutations in Set2 or H3K36 result in UV sensitivity that is epistatic with Rad26, the primary TC-NER factor in yeast. We confirmed that both these mutants are defective in TC-NER by analyzing rate of repair of CPDs at single nucleotide- resolution using genome-wide CPD sequencing (CPD-seq) method. However, in the absence of GG NER (i.e., rad16Δ), mutations in Set2 or H3K36 increase resistance to UV. Using the CPD-seq data, we found that this increase is due to activation of new TC-NER pathway associated with activation of antisense cryptic transcription in these mutants, so that the non-transcribed strand (NTS) of yeast genes is repaired by cryptic TC-NER. These findings indicate that Set2 methylation establishes transcriptional asymmetry in repair by suppressing TC-NER of the NTS and promoting TC-NER of the TS.

PARP1 in nucleotide excision repair of UV-damaged DNA in mammalian cells

Girish Shah

Université Laval and CHU de Quebec Research Centre, Québec (QC) Canada

Poly(ADP-ribose) polymerase-1 (PARP1) is among the earliest responders to various types of DNA damage in mammalian cells. It has been shown to accumulate at the site of local UVC irradiation within seconds and gets activated by UV-damaged DNA to form polymers of ADP-ribose (PAR). It is also activated in response to UVB irradiation induced direct and indirect DNA damage. The PARP1 interacts with some of the key proteins at the site of UV-induced DNA damage and PAR chains covalently or non-covalently bind to (i.e., PARylate) various proteins in the vicinity of DNA damage to transiently modify their properties. Together PARP1 and PARylation facilitate participation of their partner proteins in a variety of responses to UV irradiation, ranging from chromatin remodeling to repair of UV-induced DNA lesions. We will discuss our results with human skin fibroblasts and mice with impaired PARP1 function that reveal different definitive functions of PARP1 with DDB2 and XPC in the global genomic sub-pathway of the nucleotide excision repair that removes a majority of the UV-induced DNA lesions from the genome. Our results indicate a potential for therapeutic targeting of PARP1 in UV-induced skin cancers.

Non-Heterogeneous vs Heterogeneous Ultrafast Photoisomerization Dynamics in Knotless Phytochromes

Chavdar Slavov

Tobias Fischer[2], Lisa Köhler[3], Wolfgang Gärtner[3], Chen Song[3], Josef Wachtveitl[2], Chavdar Slavov[1,2]

[1] Department of Chemistry, University of South Florida, [2] Institute of Physical and Theoretical Chemistry Goethe University Frankfurt, Germany [3] Institute for Analytical Chemistry, University of Leipzig, Germany

Phytochrome photoreceptors regulate a variety of biological processes. Their function is enabled by the Z ↔ E photoisomerization of a bilin chromophore embedded in the protein scaffold. The photosensory core module of phytochromes consists of GAF, PAS and PHY domains. However, knotless phytochromes lack the PAS domain and can even photoconvert with just the GAF domain, which makes them an ideal system to evaluate the effect of the PHY domain on the photoconversion.

We present the ultrafast forward (Pr → Pfr) and reverse (Pfr → Pr) [4] dynamics of the GAF domain (g1) and the GAF-PHY construct (g1g2) of the knotless phytochrome All2699 (Nostoc punctiforme). We discuss the effect of the PHY domain and its "tongue" region on the photoisomerization step leading to the primary photoproduct intermediates (Lumi-R, Lumi-F, and Meta-F), and address the controversial question concerning the role of heterogeneity on the ultrafast dynamics and extend our conclusions to other related phytochrome systems.

KEYNOTE – A History of Photobiology

David Sliney

The term, "photobiology" is reported in the Meriam Webster's Dictionary to have first been used in print 1923, at least by its current definition given by Webster's, as: "a branch of biology that deals with the effects on living organisms of radiant energy (such as light)." Clearly, the subject's history can be traced to the ancients, and certainly to the scientific studies in the 19th century. There are several excellent and detailed histories of photobiology, such as that by Thomas Coohill in 2000 and historical details by a founder of the ASP, Kendric Smith that are available on-line and it would be superfluous at this 50th Anniversary of the ASP, for me to repeat much of that detail. There are any number of historical perspectives that have been presented in the past – such as from the view of photochemistry, from plant photobiology, from photodermatology, from photomedicine, from vision science, from photobiomodulation, from studies of DNA and photocarcinogenesis to UV spectroradiometry and applications of germicidal UV. We represent an amalgamation of specialties and subspecialties, and the organizational concept of ASP (and later ESP) was to provide a platform to exchange ideas and common experimental techniques, since any one of these fields has its own conferences, journals and societies, but we have basic dosimetric concepts, such as exposure dose, reciprocity and action spectra to contend with. From my point-of-view of applied photobiology, I think it quite informative to examine some historical examples of where applied problems led to photobiological research, such as by Nils Finsen, or accidental observations, such as by K. W. Hauser led to fundamental photobiological research. The lesson that I learned was that very often behind the solution of practical problems, lurk the possibilities of basic scientific discoveries. So I advise those basic scientists here to listen when someone visits with a "practical, applied problem" to solve. It might prove interesting.

Engineering approaches to improve intraperitoneal photoimmunotherapy delivery and efficacy

Aaron Sorrin

Aaron Sorrin[1], Keri Zhou[1], Katherine May[1], Cindy Liu[1], Dana Roque[2,3] and Huang Chiao Huang[1,3]

[1]Fischell Department of Bioengineering, University of Maryland, College Park, MD, [2]Department of Obstetrics, Gynecology, and Reproductive Sciences, University of Maryland School of Medicine, Baltimore, MD, [3]University of Maryland Marlene and Stewart Greenebaum Comprehensive Cancer Center (UMGCCC), University of Maryland School of Medicine, Baltimore, MD

Locally disseminated metastases in the peritoneal cavity are hallmarks of advanced ovarian cancer. Despite current standard-of-care regimen (surgery and platinum-chemotherapy cocktail), recurrence rates for stages III-IV remain over 70% due to residual micrometastases implanted throughout the peritoneal cavity. To address this challenge, photodynamic therapy has been employed in clinical trials for peritoneally metastatic ovarian cancer. Photodynamic therapy leverages spatiotemporally controlled photochemical generation of reactive oxygen species, via light-activation of photosensitizers, to ablate cancer cells. However, clinical trials reveal that the off-target toxicities caused by non-targeted photosensitizers remain a barrier to clinical translation. A strategy to overcome this barrier is photoimmunotherapy, which leverages antibody-photosensitizer constructs (photoimmunoconjugates) for cancer cell targeting. This technology is rapidly gaining traction in the clinic with a recent approval in Japan and five ongoing clinical trials in the United States. While this approach improves photosensitizer selectivity for cancer cells, it sacrifices uptake, limiting intracellular accumulation. This study addresses this challenge by improving uptake through two mechanisms: 1) utilizing fluid shear stress (FSS) to mediate delivery, and 2) leveraging nanoengineering approaches to maximize photosensitizer payload. Photoimmunotherapy delivery using physiologically-relevant intraperitoneal flow rates (0-5 dynes/cm2) are investigated in this study using an in vitro laminar flow model with OVCAR-8 ovarian cancer cells. Photoimmunotherapy is achieved using a clinically-relevant construct composed of United States Food and Drug Administration-approved agents, cetuximab and benzoporphyrin derivative. Uptake studies reveal that FSS promotes photosensitizer delivery to ovarian cancer cells while modulating subcellular localization and cytotoxicity. We explore further improvements in FSS-mediated delivery using our published liposomal formulation decorated with photoimmunoconjugates.

Results from this work support that physiological FSS and nanoengineering approaches can be leveraged to stimulate photosensitizer-cell interactions and improve the resulting anti-cancer effect. This generates important implications for the clinical implementation of photoimmunotherapy for the treatment of locally disseminated cancers and beyond.

Photobiomodulation (PBM) to Reduce Pain After Dental Surgery. A Systematic Review and Quantitative Meta-Analysis of Prescribed Dose

Dennis Sourvanos

Dennis Sourvanos[1,2,3,*], Timothy C. Zhu[2,4], Bradley Lander[1], Hector Sarmiento[1,5], Joseph P. Fiorellini[1,2]

[1]Department of Periodontics, School of Dental Medicine, University of Pennsylvania, PA, [2]Center for Innovation and Precision Dentistry (CiPD), School of Dental Medicine, School of Engineering, University of Pennsylvania, PA, [3]Institute for Translational Medicine and Therapeutics (ITMAT), Perelman School of Medicine, University of Pennsylvania, PA, [4]Department of Radiation Oncology, Perelman Center for Advanced Medicine, University of Pennsylvania, PA, [5]Private Practice, New York City, New York

The adjunctive use of Photobiomodulation (PBM) in dental surgery has shown to reduce pain following a tooth extraction procedure. The underlying biological mechanisms of PBM are believed to promote extracellular growth factor upregulation through degranulating platelets. PBM dose delivery can predictably increase the rate of the biological cascade by dampening the inflammatory response, progressing the stages of fibrin clot formation, epithelialization, and woven bone reconfiguration. Although several PBM human clinical trials support this hypothesis, there are no validated protocols for pain reduction in the human dental surgical extraction model. A systematic review was performed according to the Cochrane Collaboration in line with PRISMA reporting criteria. Meta-analyses analyzed the prescribed therapeutic dose of PBM. A total of 608 publications were screened for eligibility, with 67 human studies identified for review. Wavelengths ranged from 550nm – 1064nm. Based on the 20 papers that met the inclusions/exclusion criteria, 13 papers reported irradiation parameters for having a statistically significant effect on pain reduction. None of the studies reported negative or adverse effects directly correlated to PBM therapy. The location and number of clinical points per therapeutic dose will vary based on the device, wavelength, and pathology. It is realized that the use of adjunctive PBM to dental extraction therapy can be prescribed with safety and efficacy.

Arsenic alters distinct mutational patterns of UVR exposure

Rachel Speer

Rachel M. Speer[1], Shuvro Nandi[2,4], Xixi Zhou[1], Yan Guo[5], Laurie G. Hudson[1], Ludmil B. Alexandrov[2,4], Ke Jian Liu[1]*

[1]Department of Pharmaceutical Sciences, College of Pharmacy, University of New Mexico, Albuquerque, New Mexico, [2]Department of Cellular and Molecular Medicine, UC San Diego, La Jolla, CA, [3]Department of Bioengineering, UC San Diego, La Jolla, CA, [4]Moores Cancer Center, UC San Diego, La Jolla, CA, [5]Department of Internal Medicine, Division of Molecular Medicine, University of New Mexico, Albuquerque, New Mexico

Arsenic exposure is a worldwide health concern. Of its many health effects, arsenic is a carcinogen of the lung, bladder, kidney, and skin. Although arsenic alone induces cancers, it is also a potent co-carcinogen. The EPA and WHO set drinking water limits for arsenic to 10 ppb, but this limit was does not fully consider arsenic as a co-carcinogen. Arsenic acts as a co carcinogen at concentrations below the current arsenic drinking water limit. Arsenic enhances UVR skin cancer, however, the mechanisms are not fully understood. One proposed mechanism of arsenic enhanced UVR skin cancers is inhibition of the nucleotide excision repair (NER) pathway, which is responsible for repairing cyclobutane-pyrimidine dimers (CPDs), a type of UVR induced DNA damage known to result in mutations found in UVR skin cancers. Mechanisms of carcinogenesis can be explored using mutational signatures analysis, a novel whole genome sequencing approach that associates mutation patterns with specific molecular mechanisms. The UVR mutational signature is well defined. However, how arsenic enhances UVR-induced mutations that ultimately promote cancer is unknown. To date, no studies have used mutational signatures to investigate co-carcinogenesis. In this study human skin cells exposed to arsenic and UVR were used to investigate arsenic-altered mutation patterns of UVR exposure. Arsenic alone did not induce mutations, but significantly increased UVR mutations. Arsenic also selectively altered the spectra of several known UVR mutational signatures indicating arsenic enhances specific UVR mutational processes. These findings show arsenic alters specific mutational processes of UVR carcinogenesis, but not all. These data can be used to target specific mechanisms of arsenic co-carcinogenesis and demonstrates mutational signatures analysis is a novel tool to investigate metal carcinogenesis.

Experimental and theoretical studies on the mechanism of "dark" cyclobutane pyrimidine dimer formation and the possible role of tryptophan.

John-Stephen Taylor

Yanjing Wang,[1] Elena M. Cacchillo,[1] Sarahi Vera,[1] Dariusz M. Niedzwiedzki,[2,3] John Stephen Taylor[1]

[1]Department of Chemistry, Washington University, St. Louis, MO, [2]Center for Solar Energy and Energy Storage, Washington University, St. Louis, MO, [3]Department of Energy, Environmental & Chemical Engineering, Washington University, St. Louis, MO

Cyclobutane pyrimidine dimers (CPDs) have been discovered to form by a "dark" pathway in melanocytes that have been subjected to prior UV irradiation. The formation of CPDs was proposed to arise from chemisensitization by dioxetanes produced from peroxynitrite oxidation of melanin and/or melanin precursors such as DHI and DHICA (dihydroxyindole and DHI carboxylic acid, respectively). The intermediate dioxetanes are proposed to decompose to triplet state compounds which sensitize CPD formation by triplet-triplet energy transfer. The decomposition products of 2,3-dioxetanes of 5- hydroxy and 5,6-dimethoxy indoles used as models for melanin precursors had triplet energies lower than norfloxacin (NFX) which has the lowest known triplet energy for sensitizing CPD formation and were shown to be incapable of photosensitizing CPD formation. Theoretical calculations suggest that the decomposition products of the 2,3- dioxetanes of melanin precursors DHI and DHICA will have similarly low triplet energies. Decomposition products of the 2,3-dioxetanes of indole derivatives lacking oxygen substituents had higher triplet energies than NFX and were capable of photosensitizing CPD formation, suggesting that peroxynitrite oxidation of tryptophan and derivatives could play a hitherto unrecognized role in the dark pathway to CPDs. To determine whether dioxetane formed at other positions of DHI and DHICA might be involved in the dark pathway, a theoretical investigation of the mechanism of dioxetane formation by peroxynitrite at all positions of DHI and DHICA as well as indole has been undertaken. The triplet state energies of the resulting decomposition products were also estimated by time dependent DFT calculations.

Alkylation of hydrophilic type I photosensitizers is a simple synthetic tool to obtain efficient photosensitizers of biomembranes

Andrés Thomas

Mariana Vignoni[1], María José Sosa[1], José Luis Fonseca[1], María Noel Urrutia[1], Gonzalo Cosa[2], Alexander Greer[3], Mauricio S. Baptista[4], Rosangela Itri[5], Andrés H. Thomas[1]

[1] Instituto de Investigaciones Fisicoquímicas Teóricas y Aplicadas, Universidad Nacional de La Plata, CONICET, La Plata, Argentina, [2] Quebec Center for Advanced Materials, McGill University, Montreal, Canada, [3] Brooklyn College, City University of New York, New York, [4] Instituto de Química, Universidade de São Paulo, São Paulo, Brazil, [5] Universidade de São Paulo, Institute of Physics, São Paulo, Brazil

Photosensitized oxidations that occur through type I mechanism are initiated by electron or hydrogen transfer from the substrate to the triplet excited state of the photosensitizer. All unsaturated lipids are well-known targets of oxidative damage, which can occur by photosensitized oxidation. In the case of vesicles dispersions, a hydrophilic photosensitizer will remain in the aqueous phase and the photosensitized oxidation of a target molecule in the membrane will be a dynamic process. On the other hand, if the photosensitizer is lipophilic, an association with a biomembrane is expected and, as the photosensitization is not limited by diffusion, the oxidation might be much faster. Pterins and flavins are natural hydrophilic compounds that efficiently photosensitize the oxidation of DNA, proteins and other biomolecules in aqueous solutions. These photosensitizers do not bind to phospholipid membranes. In the search of better compounds that retain the photosensitizing properties of pterins and flavins and, at the same time, are able to bind to biomembranes, a set of decyl derivatives were synthesized and studied. Pterin (Ptr) and riboflavin (Rf) were chosen as model compounds. Conjugation of a decyl chain to the photosensitizer moiety enables its facile intercalation in large unilamellar vesicles (LUVs). Upon UVA irradiation lipid oxidation, photosensitized by decylated Ptr and Rf, leads to the formation of hydroxyl derivatives, hydroperoxides and hydroxyhydroperoxides. These photoproducts undergo a fast conversion into short-chain secondary products most likely due to further photosensitized processes. These short-chain oxidized lipids are responsible for destabilizing the phospholipid bilayer and promoting membrane leakage. The efficiency of photodamage, assessed in terms of oxidized products formation rate and membrane permeabilization, is much higher for decylated derivatives than for the corresponding hydrophilic precursors, which indicates that the intercalation of the lipophilic photosensitizers to the membrane enhances the photosensitized reactions.

The Effects of Thiophene Chain Length on Energy Levels of [Ru(bpy)2(IP-nT)]2+ and [Ru(dmbpy)2(IP-nT)]2+: A Comprehensive Study using CV and CDPV

Abbas Vali

Abbas Vali, Houston Cole, Wesley McDonald, Elamparuthi Ramasamy, Colin G. Cameron and Sherri A. McFarland*

Department of Chemistry and Biochemistry, The University of Texas at Arlington, Texas

Light-based cancer therapies such as photodynamic therapy (PDT) and photochemotherapy (PCT) can take advantage of the orbital energy levels of metal complexes to drive the desired excited state photochemical processes. Derivatization of the complexes can tune these energy levels and thus the efficacy of processes. For example, replacing one bipyridine ligand in Ru(bpy)32+ with two strong π* acceptor CO groups lowers the HOMO and makes the Ru2+→Ru3+ oxidation more difficult. On the other hand, substitution with two Cl- shifts the HOMO to a higher energy and makes the Ru2+→Ru3+ oxidation easier. Knowledge of the absolute orbital energies is important to understanding the photochemistry involved in PDT and PCT, and electrochemistry is therefore a useful tool that complements spectroscopy.

Our lab has been evaluating Ru(II)-oligothiophene complexes for PDT and PCT, and reconciling photobiological performance with excited state energetics as they correlate to thiophene chain length. As part of this effort, we are undertaking a systematic study of the electrochemical parameters of these of Ru(II)-oligothiophene complexes.

This presentation focuses on two series of complexes that have yielded promising PDT results: [Ru(bpy)2(IP-nT)]2+ and [Ru(dmbpy)2(IP-nT)]2+, where bpy is 2,2'-bipyridine, dmbpy is 2,5'-dimethyl-2,2'-bipyridine, IP is imidazo[4,5-f][1,10]phenanthroline, and nT is the number of thiophenes (n=0 to 4). Two complementary electrochemical techniques, cyclic voltammetry (CV) and cyclic differential pulse voltammetry (CDPV), were deployed to evaluate the fundamental energetics of these two series.

Examination of the wavelength dependency of DNA photodamage in a 3-D human skin model using UVC wavelengths

David Welch

David Welch, Marilena Aquino de Muro, Manuela Buonanno, and David J Brenner

Center for Radiological Research, Columbia University Irving Medical Center, New York, NY

The effectiveness of ultraviolet C (UVC) radiation to reduce transmission of surface and airborne mediated diseases is well-established. However conventional germicidal UVC (~254 nm) cannot be used directly in occupied spaces because of the potential for damage to the skin and eye. A recent alternative to 254 nm conventional germicidal UVC is far-UVC (wavelength range from 200 to 235 nm, generally used at 222 nm) which, because its effective range in biological material is much smaller, is typically absorbed largely in the dead-cell stratum corneum of the skin, and thus has very limited ability to produce DNA damage in the skin epithelium. Similar considerations apply for the eye with regard to the tear layer and the surface cells of the cornea. By contrast because of the small size of viral and bacterial pathogens, far-UVC and conventional germicidal UVC have similar anti-microbial capabilities. Optimal use of far-UVC technology is hampered by limited knowledge of the precise wavelength dependence of UVC-induced skin and ocular damage, and thus we have constructed a monochromatic UVC exposure system suitable for assessing wavelength-dependent biological effects. We exposed a realistic 3-D human skin model to mono-wavelength UVC exposures of 100 mJ/cm^2 at wavelengths throughout the UVC region from 215 to 255 nm (full width half maximum of approximately 2.0 nm) in 5 nm steps. At each wavelength we measured yields of DNA-damaged keratinocytes, and their distribution within the layers of the epidermis. No increase in DNA damage was observed in the epidermis at wavelengths from 215 to 235 nm, but at higher wavelengths (240-255 nm) significant levels of DNA damage were observed. These measurements support the direct use of far-UVC light to safely reduce the risk of airborne disease transmission in occupied locations, and allow optimized far-UVC sources to be designed.

Strategies to Achieve Photoactivation Using Visible Light

Arthur Winter

Iowa State University

Photocages are light-sensitive chemical protecting groups that mask a substrate through

a covalent linkage that renders the substrate inert. Upon irradiation, light is absorbed by the photocage and the substrate is released, restoring the substrate's biological activity. These chemical tools are valuable in biological settings because they allow investigators to control when, where, and how much of a bioactive substrate is released using targeted pulses of focused light. A drawback of most known photocages is that they absorb ultraviolet light. Irradiation with UV light can be biologically problematic because UV light is phototoxic. This talk describes our work developing chemical protecting groups that can release bioactive molecules using visible light, particularly with light wavelengths in the biological window where light penetration into tissue is maximal to allow photorelease in living systems. Our work to develop a theoretical framework to understand photorelease reactions leads to the development of a family of BODIPY-derived photocages that release substrates with visible light.

A novel component of the skin exposome: Chlorination stress modulates the cutaneous response to solar UV exposure

Georg Wondrak

Department of Pharmacology and Toxicology, College of Pharmacy, UA Cancer Center, University of Arizona, Tucson, AZ

A multitude of extrinsic environmental factors (referred to in their entirety as the 'skin exposome') impact structure and function of skin and its corresponding cellular components. The complex (i.e. additive, antagonistic, or synergistic) interactions between multiple extrinsic (exposome) and intrinsic (biological) factors are important determinants of skin health outcomes. Recently, we have investigated the molecular consequences of solar ultraviolet (UV) radiation and HOCl combinations, a procedure mimicking co-exposure experienced for example by recreational swimmers exposed to both HOCl (pool disinfectant) and UV (solar radiation). First, we have profiled the HOCl-induced stress response in reconstructed human epidermis and SKH-1 hairless mouse skin (36). In AP-1 transgenic SKH-1 luciferase-reporter mice, topical HOCl suppressed UV-induced inflammatory signaling assessed by bioluminescent imaging and gene expression analysis documenting HOCl-antagonism of solar UV-induced AP-1 activation. Co-exposure studies (combining topical HOCl and UV) performed in SKH-1 hairless mouse skin revealed that the HOCl-induced cutaneous stress response blocks redox and inflammatory gene expression elicited by subsequent acute solar UV exposure. Remarkably, in the SKH-1 high-risk mouse model of UV-induced human keratinocytic skin cancer, relevant to actinic keratosis and subsequent malignant progression, topical HOCl blocked tumorigenic progression and inflammatory gene expression (Ptgs2, Il19, Tlr4), confirmed by immunohistochemical analysis including 3-chloro-tyrosine-epitopes. In contrast, it was observed that cutaneous exposure to the chloramine trichloroisocyanuric acid (TCIC), used worldwide as alternate freshwater chlorination agent, significantly enhances UV-induced inflammation (as profiled at the gene expression level in AP-1 reporter SKH-1 mice), suggesting a heretofore unrecognized potential to exacerbate UV induced functional and structural cutaneous changes. These observations deserve further molecular investigations in the context of chlorination-based freshwater disinfection with health implications for populations worldwide.

Liquid metal nanoparticles for photo theranostics

Marvin Xavierselvan

Marvin Xavierselvan[1], Sumeyra Gokalp[2], Sabrina S Hafiz[2], Michelle Foster[2]and Srivalleesha Mallidi[1]

[1]Department of Biomedical Engineering, Tufts University, Medford, MA, [2]Department of Chemistry, University of Massachusetts, Boston, MA

Liquid metal nanoparticles have been employed in various medical applications such as biosensors and bioelectrodes. Moreover, owing to their unique property of shape transformation/degradation to release drugs and high photothermal conversion efficiency, they are being investigated for the photo-treatment of cancer as well as contrast agents in medical imaging. Particularly, Eutectic Gallium Indium (EGaIn) nanoparticles are of high interest due to their low cytotoxicity and good biocompatibility. They can be easily synthesized by sonication, unlike other metal nanoparticles. EGaIn is a liquid metal at room temperature and when exposed to air, it oxidizes to form a thin (~0.7 nm) passivating oxide layer that can be functionalized with ligands and coated with drugs. In this study, we report the "green" synthesis of EGaIn nanoparticles by sonication without using harsh chemicals and functionalize the surface with hyaluronan for stability and as targeting moiety along with photosensitizer benzoporphyrin derivative (BPD) for photodynamic therapy. The resulting EGaIn-HA-BPD (EGaPs) nanoparticles were stable over a month and had good biocompatibility with low cytotoxicity. Furthermore, EGaPs have high optical absorption in the near-infrared region due to which they were utilized as contrast agents for photoacoustic imaging. To monitor the effect of EGaIn on BPD's photoactivity, we quantitatively compared the singlet oxygen generated by EGaPs with free BPD under physiological conditions. Finally, the photodynamic efficacy of EGaPs was investigated both in vitro and in vivo conditions to serve as multi-purpose nanoparticles for targeting, imaging, drug delivery, and photodynamic therapy.

Radiodynamic Therapy with CsI(Na) Nanoparticles

Jin Xie

Fangchao Jiang[1], Zhengwei Cao[1], Wei Yang[1], Shuyue Zhan[1], Jianwen Li[1], Jin Xie[1]

[1] Department of Chemistry, University of Georgia, Athens, GA

Radiodynamic therapy (RDT) holds the potential to overcome the shallow tissue penetration issue associated with conventional photodynamic therapy (PDT). To this end, complex and sometimes toxic scintillator-photosensitizer nanoconjugates are often used, posing barriers for large-scale manufacturing and regulatory approval. We explored a streamlined RDT strategy based on CsI(Na) nanoparticles and 5-aminolevulinic acid (5-ALA). 5-ALA is a clinically approved photosensitizer, converted to protoporphyrin IX (PpIX) in cancer cells' mitochondria. CsI(Na)@MgO nanoparticles produce strong ~410 nm X-ray luminescence, which matches the Soret band of PpIX. We hypothesize that the CsI(Na)-and-5-ALA combination can mediate RDT where mitochondria-targeted PDT synergizes with DNA-targeted irradiation for efficient cancer cell killing. Because scintillator nanoparticles and photosensitizer are administered separately, the approach forgoes issues such as self-quenching or uncontrolled release of photosensitizers. We tested the approach in vitro with multiple cell lines and found that the combination can efficiently elevate cellular reactive oxygen species (ROS), causing damages to the mitochondria, DNA, and lipids. These destructions culminate at reducing cell proliferation and clonogenicity. When tested in vivo, RDT with CsI(Na) nanoparticles and 5-ALA significantly improved tumor suppression and animal survival relative to radiation therapy (RT) alone. After treatment, the scintillator nanoparticles, made of low-toxic alkali and halide elements, were efficiently excreted, causing no detectable harm to the hosts.

KEYNOTE – How do Bilin-based Photoreceptors Sense Light

Xiaojing Yang

Phytochromes are bilin-based photoreceptors that regulate a wide range of light responses in plants, fungi, cyanobacteria, and bacteria such

as germination, flowering, phototaxis, shade avoidance, and chromatic acclimation. These photoreceptors are multi-domain, dimeric signaling proteins that integrate the light perception and the generation of a biological signal in the same molecule. At the molecular level, light signaling of a bilin-based photoreceptor starts with a photoisomerization event in the bilin chromophore embedded in the N-terminal sensor domains. These light-triggered local structural changes are then transmitted and amplified via the modular protein framework to generate a biological output either via auto-phosphorylation or protein-protein interactions mediated by the C-terminal effector domains. In my talk, I will present the landmark findings and recent developments in our pursuit of capturing light-induced structural dynamics at the atomic resolution in a few representative bacteriophytochromes using dynamic crystallography and cryoEM. Findings from these structural biology studies will provide a mechanistic framework for engineering light-activated proteins of desired signaling logic.

Type I interferons augment repair of photo damage and prevent cutaneous immune suppression

Nabiha Yusuf

Mohammad Asif Sherwani[1]Israr Ahmad[1], Chander Raman[1], Craig A Elmets[1,2,3], Nabiha Yusuf [1,2,3]

[1]Department of Dermatology, [2]O'Neal Comprehensive Cancer Center, University of Alabama at Birmingham, AL, [3]Veteran Affairs Medical Center, Birmingham, AL

Type I interferons (IFNs) are important enhancers of immune responses which are downregulated in human cancers, including skin cancer. Solar ultraviolet (UV) B radiation is a proven environmental carcinogen, and its exposure contributes to the high prevalence of skin cancer. The carcinogenic effects of UV light can be attributed to the formation of cyclobutane pyrimidine dimers (CPD) and errors in repair and replication of DNA. Treatment with a single dose of UVB (100 mJ/cm2) upregulated IFNα and IFNβ in the skin of C57BL/6 mice. They were predominantly produced by CD11b+ cells. Mice lacking the type I IFN receptor 1 (IFNAR1) had decreased repair of CPD following cutaneous exposure to a single dose of UVB (100 mJ/cm2). UVB induced expression of the DNA repair gene xeroderma pigmentosum A (XPA) in wild type (WT) mice. In contrast such treatment in IFNAR1 (IFNAR1-/-) mice downregulated XPA. A local UVB regimen consisting of UVB radiation (150 mJ/cm2) for 4 days followed by sensitization with the hapten 2,4, dinitrofluorobenzene (DNFB) resulted in significant suppression of immune responses in both WT and IFNAR1-/- mice. However, there were significantly higher CD4+CD25+Foxp3+ regulatory T-cells and CD11b+Gr1+ myeloid cells in draining lymph nodes of IFNAR1-/- mice in comparison to WT mice. Overall, our studies reveal a previously unknown action of type I IFNs in repair of photodamage and prevention of immune suppression. Strategies that enhance type I IFN production may be useful for prevention of pre-malignant skin lesions before they develop into skin cancer.

ROS explicit dosimetry of Photofrin-mediated Pleural PDT

Timothy Zhu

Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA

Explicit dosimetry of light fluence, photosensitizer concentration, and oxygen concentration can be used to quantify the reactive oxygen species explicit dosimetry (ROSED) during Photofrin-mediated pleural PDT. Preclinical studies show improved prediction of treatment outcome using [ROS]rx than light fluence rate alone, or PDT dose for Photofrin-mediated PDT. We demonstrate ROSED in a clinical setting, Photofrin-mediated pleural photodynamic therapy, by utilizing tumor blood flow information measured by diffuse correlation spectroscopy (DCS). A DCS contact probe was sutured to the pleural cavity wall after surgical resection of pleural mesothelioma tumor to monitor tissue blood flow (blood flow index) during intraoperative PDT treatment. Isotropic detectors were used to measure treatment light fluence and photosensitizer concentration. This study summarizes the current result of ROSED for a Phase II pleural PDT clinical trial. Large inter- and intra-patient heterogeneities in [ROS] rx were observed although an identical light dose of 60 J/cm2 was prescribed to all patients.

Primary dynamics of twisting in phytochrome and proton-coupled electron transfer in BLUF

Dongping Zhong

Phytochrome is a red photoreceptor with unique photophysical properties from the photoinduced isomerization of a linear tetrapyrrole chromophore. BLUF is a blue photoreceptor with a critical chemical reaction of photoinduced proton-coupled electron transfer between the flavin cofactor and nearby tyrosine. Here, we employ femtosecond-resolved fluorescence and transient-absorption methods and unambiguously showed the various dynamics from a few to hundreds of picoseconds. These studies were carefully designed with integration of the active-site fluctuations. The obtained dynamics reveal the new molecular mechanisms for initial essential dynamics of biological functions.

Single photon detectors for biological applications

Val Zwiller

KTH Royal Institute of Technology

Using high performance superconducting single photon detectors, we demonstrate the possibility to perform optical measurements on systems with biological relevance. Our ability to detect single photons in the near infrared enables oxygen singlet measurements as well as confocal microscopy at the single photon level to image living tissue deeper and with lower photodamage. We will report on the development of a scanning confocal microscope specifically developed for in-vivo measurements at the single photon level.

NOTES

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