ASP NEWS

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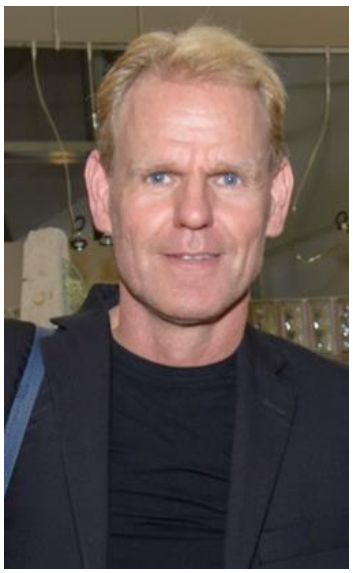
President's Note



This fall, as ASP president whose tenure started during our conference in Tampa, May 21-26, it is my pleasure to extend my warm greetings to all of you. First, I would like to thank you for the overwhelmingly positive feedback provided during and after the vibrant meeting in Tampa, which I thought perfectly reflected the scientific excellence, personal engagement, and great potential for future growth that are so characteristic of our society. As stated before, my tenure as ASP president focuses on developing ASP into a more visible society that better serves the needs of an increasingly interconnected global research community and more actively engages with a growing body of members at all career stages united by a passion for photon-directed research, drawing strength and inspiration from ASP's rich past while embracing a dynamic and 'photoexcited' future.

For the year 2017, I am happy to report that we are now preparing an attractive portfolio of high quality ASP events including:

• 1st ASP Presidential Symposium, San Diego, CA, April 6-7, 2017. Online Registration and abstract submission for this exciting event will open November 7, 2016, and specific information on program and format will become available on the ASP website later in October.

• 2nd ASP Virtual Poster Symposium for associate members, held in early summer 2017.

• ASP-ESP joint session to be held during the 7th Congress of the European Society for Photobiology (ESP), Pisa, Italy, September 4-8, 2017.

• 55th Anniversary celebration of Photochemistry and Photobiology, our society's own premier journal, to be held in fall 2017. As you know, Photochemistry and Photobiology has been published since 1962, and it is no overstatement that our journal has been instrumental in publishing breakthrough research that defined our field reaching far beyond our discipline.

On a different note, please check out the new feature 'Visit the Frontiers of Photobiology' on our webpage where you can access Nobel lectures of distinguished researchers in our discipline.

I hope that this is just the beginning of a whole set of activities that will move our society towards a more dynamic and 'photoexcited' future. Stay tuned. Good things are going to happen.

With warm regards,

GEORG

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Meet a Photobiologist

-Tayyaba Hasan, past ASP president

Q1: Why did you become a scientist?

Just curiosity. Actually, as a child, when I was about eight or nine years old, I had my first chemistry set for a soap making experiment. I had thought about becoming a medical doctor and attended lectures at the medical school; however, I realized at that time I wanted to explore more and gain additional in-depth experience in one or more areas of science and technology. That's what really brought me to chemistry originally, and for a long time I was totally a physical scientist learning chemistry, physical chemistry, statistical mechanics, quantum mechanics, and physical organic chemistry. At the point, after completing my Ph.D., I became interested in biochemistry, and made a major transition to biology and medicine, and that's when I came to Boston thinking I would bring my chemistry to the medical world. Of course, in reality, they both merged really well into the program that we have now.

Q2: How did you get involved in photobiology and photodynamic therapy?

My involvement in photobiology and photodynamic therapy came from chemistry and photochemistry, and that was looking at the mechanisms of tetracyclines antibiotic action. The underlying questions were 'what leads to resistance' and 'can we overcome resistance to tetracyclines'. To understand how exactly tetracyclines work, at that time we leveraged a reasonably new photoaffinity labeling approach. This technique uses photochemistry to label the high affinity sites in a drug, and for tetracyclines one of the targets is the S7 protein of a ribosome of the E. coli bacteria. Out of that came this whole mechanism that kept two ribosomal units of a bacteria from working together to synthesize proteins, which contributed to the killing of the bacteria. In a very broad sense, that was the mechanism, but what also came from that were some insights to the resistance in tetracyclines. So it was really a good transition to learning photochemistry and microbiology and seeing the bacteria in action. I used chemistry to understand biology essentially. That was my postdoctoral work at the University of Pennsylvania, where I studied tetracycline mechanisms for three years. When I moved to Boston, at that point I had wanted to really go into industry, and I already had a job offer. However, I decided to interview for a position at Wellman Center for Photomedicine of Massachusetts General Hospital (MGH), and it was going to be just a temporary one-year position because I liked the idea of working at a hospital in a translational research environment. At Wellman Center, I continued studying the

tetracyclines, but this time with mammalian cells. One of the properties of tetracyclines was that they gave skin phototoxicity, so I started to try to understand that. At that time, there was also a lot of buzz about trying targeted delivery of light activatable molecules through antibodies to cancer cells, and that sort of captured my interest because, again, it was chemistry that could help biology. So eventually I got into photodynamic therapy through photo-immunotherapy, a concept first articulated in a publication by Julia Levy.

Q3: You have published more than 200 scientific articles – do you have a favorite?

Well, that's really a hard question. I think some of my favorites are very basic studies that we did which were earlier in my career, such as looking at the ribosome tetracyclines interactions, molecular mechanisms in base-catalyzed reactions using kinetic isotope effects, a deactivation of cellular mitochondria by photosensitization. Since I've been at the MGH I got in a big way into biology and medicine. Some of my favorite papers are, again, looking at the tetracyclines in the mammalian cells, cancer cells, and also what happens when you shine light on it and how it kills cells. We were really contemplating using tetracyclines as a photochemistry mediated therapy for cancer and a diagnostic agent, so we actually showed beautiful apoptotic processes without recognizing it was apoptosis and wonderful localization of tetracyclines into mitochondria. At that time confocal microscopy was fairly new, and we actually were one of the first labs that received a free confocal system from Leica as a demo instrument, for about two years, which we used to publish several papers in PNAS and Cancer Research. Another paper that I really liked was targeted ovarian cancer patient tissue with photo-immunoconjugates, which took us to the next step. More recently, through the work of many people, we have the targeted nanoconstructs, and we've come to understand the mechanism of cancer biology and cancer development much better. This has led us to new strategies where, again, we can use chemistry and nanotechnology to design these new mechanism-based approaches. Now, we're moving into new and even more exciting work of taking cancer evolution into account for treatment design. It's difficult to name favorite papers, but these are some of the areas of favorite papers. Actually, there's one more publication I must mention, when we were dealing with the treatment of AMD. The first one we did was very basic, where we saw if we could target and destroy the LDL receptor in vitro with BPD photosensitizer and light. This project moved well and become the new basis for destroying neovasculature, which lead toward the successful treatment of AMD.

Q4: What is your philosophy for establishing and running a thriving research lab?

I've made a lot of mistakes and learned a lot on how to run a good lab. I think I do have a fantastic lab now. One of the lessons learned is to hire the best people you can and then create an environment where they can thrive. So the thriving of your lab members and your team members is really your own success. There's also a lot of sacrifice of the ego. You sort of serve the people, the team, and you get your ego out of it and you get out of the way except to keep them challenged and facilitated the teams progress. I insist on cooperation, and what I can't tolerate is a lack of collaborative spirit. Perhaps it's because of what we do, which is a very mixed bag of multidisciplinary work. Also you should create a sort of fun environment in the lab. Work should not be boring; it should be a fun, socially and professionally, and intellectual challenge. And finally, my philosophy is no one should be working for me. They should be working for themselves with me as a coach, and that's really the most important thing.

Q5: Can you tell us about something from your work that is exciting to you right now?

Right now there's a lot that's going on that's exciting. Some of it is because of our own work, and part of it is because of the development of new optical and nanotechnology and the understanding of

photochemistry. This has given us a really unique opportunity to exploit the mechanisms at both cancer biology and therapeutics levels in order to have a real impact, both transnationally and in basic science.

Q6: What, in your view, are the key challenges for translation of PDT into clinical practice?

PDT had a huge impact when the treatment for age-related macular degeneration (AMD) came out. It launched a lot of companies, and it put it there out front. At that time, residents would talk about photodynamic therapy in the medical school. Unfortunately, what I think PDT lost to a great extent was, in part, due to a lack of vision from a major industry. And that is one of the challenges. The other challenge is that PDT is a tough battle in the medical world because it's multidisciplinary, and the question is who would own it. There have been some mistakes made in PDT and it competes with some very established therapies, which are not necessarily successful. In fact, most cancer treatments aren't very successful, but they are well established, easier to apply, and there are people trained in it. We're going in with a new treatment which is not as established as it should be. However, it has something very special to offer and could actually be quite inexpensive. It needs a champion; it needs a clinical champion; it needs an academic champion. I think that combination came together in 2000 when Visudyne was approved as front-line therapy for AMD, and it's what needs to happen again.

Q7: As a founding Director of the Office for Research Career Development at Massachusetts General Hospital, how do you advise scientist to approach their careers.

For a scientist to approach their careers, it really depends on personalities, and I think you need to grant yourself the luxury of going with the personality you have to some extent. There are some people who really need a trajectory: what am I going to do this year to get where I want to be in five years, while others don't really need that level of detail. I happen to fall into that second category where I don't really need to know what I am going to do five years from now; what I need to know is what am I doing now and how to be the best at it that I can be. Whatever you do, it doesn't really matter what philosophy you adhere to; you need to do it the best you can. That makes it enjoyable! And what I've found, and what I tell young scientists, is not to worry too much about where you're going to be five years from now, but worry about what you need to do in the next year. Having that long-term goal is okay, but if you don't clear that first year successfully, making it to year five is going to be really tough, so do the best in year one. Also remember that in the end, there will be a lot of circumstances beyond your control that determine where you end up and what you do. I think people often waste their time being too anxious about a distinct future, while they could have spent it less anxiously and productively. A very fine balance between having a long-term goal, a mid term-goal, and a short-term goal is crucial. So my advice is: do the best that you can under the given circumstances, and in some cases, let the circumstances take their course. That allows you to capture opportunities you did not anticipate.

-We caught up with Tayyaba in Boston

We need YOU!

Please submit content (science highlights, suggested links, personal stories, etc) to ASP News. Email: jflovell@buffalo.edu or Huang.Huang-Chiao@mgh.harvard.edu

Honeybee Circadian Rhythms Are Affected More by Social Interactions than by Sunlight

Circadian rhythms are internal clocks that determine many of an organism's daily rhythms, for example sleep-wake, feeding, urinary output and hormone production. Aligned with the environment by external forces such as sunlight and ambient temperature, circadian rhythms are important for animal health and survival. Disturbances of the circadian clock are associated with a variety of diseases in humans and animals, including cancer, mental illnesses and metabolic disorders, such as diabetes and obesity.

The dominant role of light in adjusting the circadian rhythm to the local environment has consistently been emphasized in studies on individually-isolated animals in laboratories. Interactions with others of the same species, while very important for animal survival and fitness in nature, are not considered important external stimuli that affect the animal circadian clock.

Now, a study conducted by researchers from the Hebrew University of Jerusalem and published in the journal Nature Communications challenges this view.

The researchers performed a set of large scale experiments in which they manipulated social interactions and light exposure for more than 1,000 honeybees in cages, or in freely foraging colonies housed in observation hives, allowing research in an ecologically relevant context. Every experiment was repeated two to four times, each with bees from a different source colony (which were genetically different).

"We show for the first time that social time cues stably adjust the clock, even in animals experiencing conflicting light exposure and social cycles," said Prof. Guy Bloch from the Department of Ecology, Evolution & Behavior at The Hebrew University's Alexander Silberman Institute of Life Sciences, who led the study.

The researchers collected a massive data set which demonstrated that in honeybees, social interactions can override potent light exposure as external cues that influence the biological clock.

The data showed that resetting the circadian rhythm by manipulating the social environment had a robust and stable effect for several days even for 2-day-old bees, which are typically active around the clock with no overt circadian rhythms. Remarkably, young bees that experienced conflicting light and social cycles showed a phase that was more similar to the social cycle. When removed from the hive and monitored individually in constant laboratory conditions, they maintained the phase of the social cycle, meaning this potent social factor does not depend on physical contact with other bees in the colony.

"This study provides the strongest available evidence for the power of social entrainment, and emphasizes the importance of studying circadian rhythms in a species-specific, ecologically-relevant context," said Prof. Bloch.

Social insects are ecologically important and offer attractive model systems for studies on the interplay between social behavior and circadian rhythms. The best evidence for the influence of social activity on the internal clock is found in dark cavity-dwelling social animals, such as bees and bats. These species may be especially responsive to social influence, because individuals may not experience ambient conditions directly, but rather rely on information received from group mates that forage outside their domicile.

This study adds to recent research showing the circadian rhythms in complex natural environments may profoundly differ from those in controlled laboratory conditions. "Studies in the real world will

provide a better understanding of the function and regulation of biological clocks," said Prof. Bloch.

The study also indicates that social signals may be important time-givers for the clocks of other animals, including mammals, and could contribute to the research on sleep and behavioral disorders, as well as for the understanding of the complex life of bee societies.

Link: Fuchikawa, et al. Potent social synchronization can override photic entrainment of circadian rhythms. Nat Commun doi:10.1038/ ncomms11662 (2016).

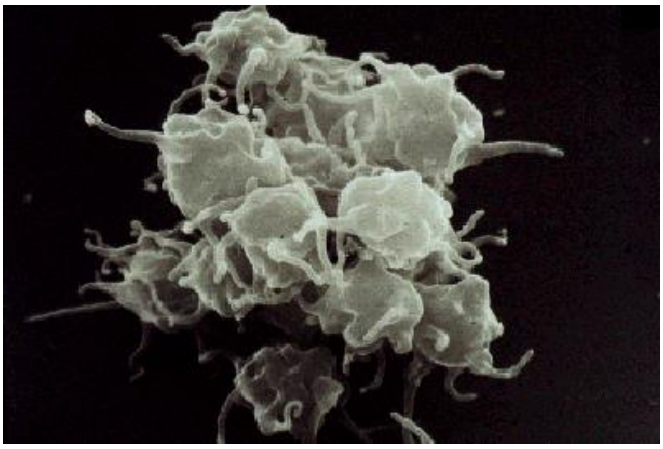
-source: Hebrew University

Low-Level Laser Therapy May Improve Treatment of Dangerous Bleeding Disorder

A low-intensity type of laser treatment may offer a non-invasive, drug-free treatment for thrombocytopenia – a potentially life-threatening shortage of the blood cells called platelets that are essential to blood clotting. In their paper appearing in Science Translational Medicine, a research team from the Wellman Center for Photomedicine at Massachusetts General Hospital (MGH) reports that low-level laser therapy increased the generation of platelets from precursor cells called megakaryocytes (MKs) and had the same effect in several mouse models of the condition. They also identified the probable mechanism underlying this effect.

"Our study reveals for the first time that low-level laser therapy enhances platelet production in animals with thrombocytopenia, but not in normal controls," says Mei X. Wu, PhD, of the Wellman Center at MGH, the senior author of the study. "This result suggests that a safe, drug-free method that does not depend on donated blood products can be developed for treating or preventing thrombocytopenia."

Among the conditions that can lead to thrombocytopenia are certain types of leukemia, an autoimmune disorder that attacks platelets, and side-effects of certain drugs, including some used for chemotherapy. The most established treatment is platelet transfusion, which since it risks complications including infection, allergic reaction and immunosuppression is limited to the most severe cases. Dosage levels of the FDA-approved drugs that increase platelet levels must be precisely controlled to avoid excessive platelet production that raises the risk of dangerous blood clots.



Low-level lasers (LLL) – sometimes called cold lasers – emit low-powered laser light that does not heat its target tissue. LLL has been used to improve wound healing, relieve pain, and treat conditions including stroke and neurodegenerative disorders. It is known to protect the function of mitochondria – cellular structures that provide cells with energy – and several conditions associated with impaired platelet production are characterized by abnormalities in mitochondria of the bone marrow cells that give rise to platelets.

The body responds to low platelet levels by rapid differentiation of MKs from hematopoietic stem cells and an exponential increase in the number of the cells. MKs expand in size, along with with many rounds of DNA replication without cellular division, which results in giant cells containing multiple copies of each chromosome – a condition called polyploidy – instead of the two copies found in most cells. Each of these giant, polyploid MKs generates many long, branched, small tubular structures called proplatelets that eventually fragment into thousands of platelets.

The MGH/Wellman team conducted a number of experiments to investigate whether LLL's ability to protect mitochondrial function could mitigate several forms of thrombocytopenia. Their results showed the following:

- LLL treatment of MKs increased their size, accelerated the formation of proplatelets and

doubled the production of platelets. Infusion of LLL-treated MKs into mice led to greater platelet production than did infusion of MKs treated with normal light.

- One of the keys to determining the number of platelets generated from MKs was mitochondrial production of the energy molecule ATP.
- LLL treatment greatly increased mitochondrial generation in polyploid MKs, but the increase was only slight in less mature MKs with only two copies of each chromosome.
- Whole-body LLL treatment of mice with radiation-induced thrombocytopenia induced the rapid maturation of MKs and restored platelet levels in a light-dose-dependent fashion. Platelets from LLL-treated mice had normal structure and function. LLL treatment of normal mice did not raise levels of either MKs or platelets.
- LLL treatment also restored platelet levels in mice with the autoimmune form of thrombocytopenia or with thrombocytopenia caused by chemotherapy treatment.
- In cultured human MKs. LLL treatment at dosage levels similar to that used in mice increased ATP production and platelet generation.

Wu notes that LLL's lack of an effect in animals without thrombocytopenia indicates it would probably avoid the potential complications of current drug treatments, which act by increasing the production of MKs from their progenitors in the bone marrow. "Directly stimulating the differentiation of MKs the way all current drugs do risks clotting if platelet levels rise too high. LLL appears to enhance MKs' inherent ability to produce platelets most effectively in response to low platelet levels in the circulation, a response that stops when platelet levels are normalized. The fact that treatment only has an effect in polyploid cells, which are very rare, implies that it would not increase production of mitochondrial in cancer cells or other cells. In fact, while LLL has been employed in research and in clinical treatment for decades, this is the first study reporting that it can promote mitochondrial biogenesis.".

-source: massgeneral.org

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Blue Stoplight to Prevent Runaway Photosynthesis

Through photosynthesis, solar energy is converted into biological energy. It is often thought that photosynthesis becomes stronger as light becomes stronger, but actually photosynthesis may run out of control if subjected to an overabundance of light, causing reactive oxygen species which break the photosynthetic apparatus. To avoid this, when exposed to intense light plants have a mechanism called "qE quenching" to prevent runaway photosynthesis by converting the excess energy to heat and discarding it.

An international team including researchers in France and Japan, using the green alga Chlamydomonas as a model, found a switch that triggers the suppression mechanism to prevent runaway photosynthesis. The switch is a blue light photoreceptor protein called phototropin. The research is published in Nature.

Professor Jun Minagawa of the National Institute for Basic Biology in Japan said "Too much direct sunlight is a painful thing for humans, and it is painful even for plants. Being in an environment where direct sunlight pours down all year round is a big burden for plants. We now know that within plants information regarding the active state of photosynthesis, combined with the sensing of blue light, fit together to activate the photosynthesis suppressing 'qE quenching' system." Drs. Dimitris Petroutsos and Giovanni Finazzi of the French National Center for Scientific Research (CNRS) have said "We looked at what have so far been considered to be completely separate phenomena, the perception of blue light by phototropin, photosynthesis by chlorophyll, and light protection by qE quenching, and to find that these three systems are connected at the molecular level has made us very happy."

This blue stoplight photosynthesis inhibiting system is believed to be shared among algae, moss, and other plants. It is expected to be useful in the optimization of applications such as biofuel production.

-source: National Institute for Basic Biology

Upcoming Photobiology Events

October 24-28, 2016
Photodynamic Therapy and Photodiagnosis
Nancy, France
http://www.pdt2016.com/

November 6-8, 2016
World Association for Laser Therapy Meeting
Sao Paulo State, Brazil
http://www.eventus.com.br/walt2016/

January 2-5, 2017
Inter-American Photochemical Society
26th Winter I-APS Conference
Sarasota, Florida
http://www.i-aps.org/pdf/IAPS-2017_flyer.pdf

March 2, 2017
26th Annual Meeting of the Photomedicine Society
Orlando, Florida
http://www.photomedicine.org/currentmeeting.php

April 5-9, 2017
American Society for Laser Medicine and Surgery
37th Annual Conference
San Diego, California
https://www.aslms.org/annual-conference

April 6-7, 2017
2017 ASP Presidential Symposium
San Diego, California
http://photobiology.org/wp/

June 8-13, 2017
16th International Photodynamic Association World Congress
Coimbra, Portugal
http://www.ipa2017.qui.uc.pt