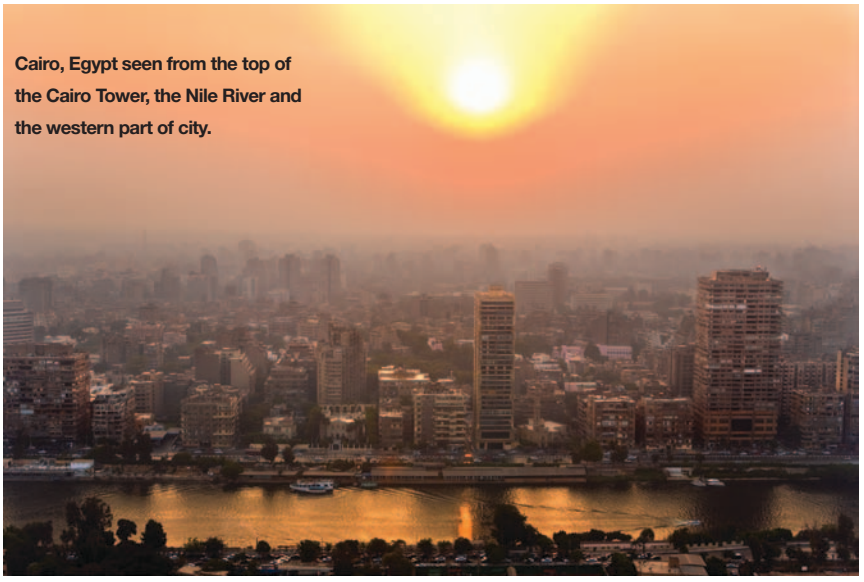
AUSTRALIAN STUDY CONFIRMS THAT SUNSCREENS SAVE LIVES

The view from Egypt, land of the sun, is dim. The killing of protesters is senseless. Here I am, in Cairo, in the middle of the so-called Arab Spring, writing about skin cancer while dodging demonstrations that are turning deadly! It is difficult to make sense of the tragedy unfolding and connect it to sun damage until you realize that actually far more people die each year from skin cancer than they do from violent demonstrations and protests. In fact, melanomas and carcinomas have been claiming more lives annually than many wars and civil disobedience occurring around the world today.

I was planning to devote a considerable part of my column this month to the lively discussions that occurred during this year's Florida Sunscreen Symposium, but a milestone study by Australian researchers was published that warrants our special focus and attention.



Cairo, Egypt seen from the top of the Cairo Tower, the Nile River and the western part of city.

A Landmark Study

In a study by Dr. Elke Hacker and her associates at the Queensland University of Technology, published in *Pigment Cell & Melanoma Research Journal*, "The Effect of MC1R Variants and Sunscreen on the Response of Human Melanocytes In Vivo to Ultraviolet Radiation and Implications for Melanoma."[1]

This landmark study discovered that properly applied sunscreen can prevent skin cancer and protect the "superhero" gene p53, a gene that works to repair sun-damaged skin and prevent skin cancer. Dr. Hacker and her associates found that sunscreen provides 100% protection against all three forms of skin cancer, namely basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and the deadly malignant melanoma (MM).

Lifesavers

Melanoma, the most lethal form of skin cancer, arises from melanocytes, and it is postulated that the proliferative response of melanocytes following sun exposure may play an important role in melanoma development. This study confirms the role of UV radiation in initiating melanocytic proliferation, implicates MC1R genotype as a key mediator in this process, and demonstrates the effectiveness of sunscreen in preventing these molecular responses. This study reinforces the 2011 clinical trials by Green et al[2] which reported that the proper application of sunscreen is very likely to significantly decrease the risk of UV radiation-induced melanoma risk.

Dr. Hacker's group conducted clinical trials on 57 Caucasian participants, who were grouped according to their MC1R genotype, and compared the molecular and cellular response of human melanocytes and keratinocytes in-vivo to solar simulated UV radiation. They found, on average, the density of epidermal melanocytes 14 days after exposure to 2 MED (Minimal Erythemal Dose) of UV radiation was two-fold higher than the baseline (unirradiated) skin. More importantly, they found that sunscreen applied to the skin before exposure to 2 MED solar-simulated ultraviolet radiation, completely blocked the effects of DNA damage, p53 induction, and cellular proliferation in both melanocytes and keratinocytes!

Their experiments using human volunteers yielded three principal findings:

1. They confirmed that melanocytes increase in number following exposure to solar simulated UV radiation. They double after 14 days of exposure!

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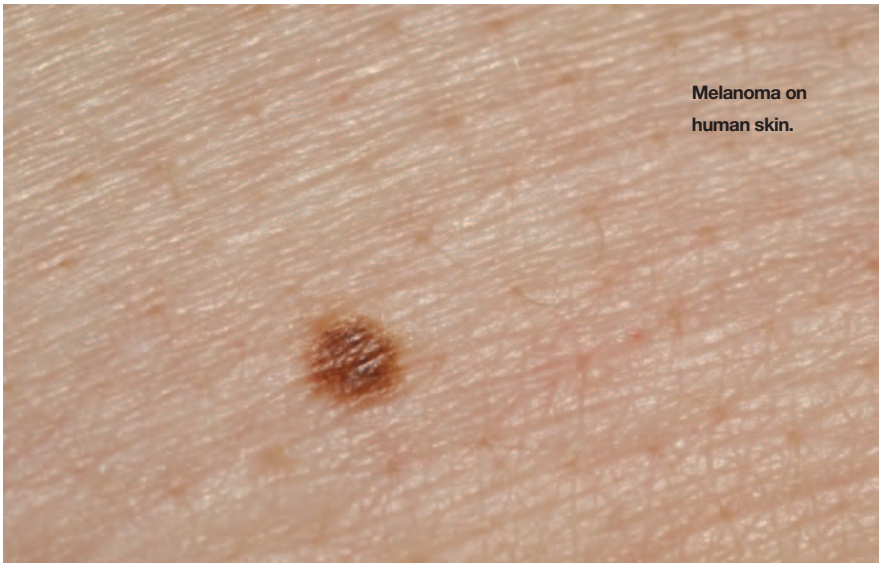

Melanoma on human skin.

2. They suggested that the melanocytic proliferative responses differ according to MC1R genotype.

3. They demonstrated that sunscreen completely blocks the molecular and proliferative effects of solar-simulated UV radiation on keratinocytes and melanocytes in-vivo.

This study utilized a solar simulated Model 601 (Solar Light Co., Philadelphia, PA) fitted with 300 Watt Xenon arc lamp with UV filters to administer the UV radiation dose. The MED of each participant was determined in accordance with the Australian Standard 2604: 1998. The treatment regimen dose of 2 MED, ranging from 44 to 130 mJ/cm^2 was applied via a fiber optic cable to the sun exposed sites.

Uncertainty Remains

Surprisingly, in reading the full, published article, I could not find any information or reference to the actual sunscreen product that was used in the study that yielded such dramatic results. After directly contacting Dr. Hacker in Australia, she promptly responded, "The commercially available broad spectrum sunscreen was 30+ SPF. Ultrastructural characterization of this sunscreen was performed using transmission electron micro graphs and X-Ray diffraction. The formulation contained Titanium Dioxide and Zinc Oxide with tubular/spindle particles up to 100 nm in length and larger rectangle shapes up to 200 nm."

No specific mention of the brand name was provided.

The study did acknowledge the fact that there remains considerable uncertainty as to the wavelengths and precise mechanisms through which sunlight causes melanoma in humans. They concluded that further exploration of the interactions between sunlight, genotype, and phenotype in melanoma development is the aim of their continuing research.

Both the Green et al study and this landmark study by Dr. Hacker et al suggest the importance of sunscreens in protecting individuals from all three forms of skin cancer. More importantly, both studies demonstrate that an SPF 30+ is sufficient for protection if applied properly and combined with other methods for protection such as avoiding the sun during peak hours and the use of proper clothing and umbrellas.

Well-Attended Symposium

The scientific community is steadily at work on these issues. The Florida Sunscreen Symposium attracted more than 400 participants, a record number for this bi-annual gathering, and featured podium presentations and poster presentations with an exhibition hall that had booths from over 60 suppliers and testing companies.

Mark Chandler of ACT Solutions and Julian Hewitt, JPH Suncare, presented an SCC Continuing Education Course entitled "Maximizing the Efficacy and Appeal of Your Suncare Formulations." This well-attended seminar was highly praised by the participants.

The symposium—perhaps the best to date—was extremely well attended and had moments of lively debate. The first day session, moderated by Tom Meyer from Merck Consumer Care, featured two timely presentations on the social media and other technical presentations on emulsifiers, photo stabilization, water resistancy, electron and proton transfer in sunscreens, zinc oxide, sunburns, testing, reducing photo generated radical species and formulating sunscreens for the 21st century. The second day was moderated by Dr. Michele Hines and featured three presentations on skin cancer prevention, the future of sunscreens and testing methods.

For more coverage of the Sunscreen Symposium, see p. 80 in this issue.

A Lively Roundtable

The roundtable discussion that was moderated by Dennis Lott allowed for two hours of presentations and lively debates. The panel consisted of Dr. Bob Sayre, John Staton and Joe Stanfield along with Dennis Lott who all spoke on testing protocols. It also included Dr. Nava Dayan and I speaking on IR and HEV (high energy visible) radiation. Stanfield addressed the pros for high SPF products and I countered with the cons of formulating high SPF products.

The panel included Dr. Reynold Tan from the FDA who very effectively fielded most of the questions posed by the audience and panel members. This is the second time in a row that Dr. Tan attended the panel discussion and he was accompanied this time by Dr. Lydia Velazquez, from FDA's Division of Nonprescription Regulation Development. They both attended a poolside gathering after the seminar and continued to field questions from the participants and the expert panelist—a very welcome development from the FDA!

Other topics discussed included the petition to the FDA by Dr. Sayre to withdraw

salicylates and benzophenones from the approved list of Category I Sunscreens. It was concluded that the data supplied by Dr. Sayre, which was based on one subject, was not adequate to warrant the withdrawal of six ingredients from the already dwindling list of 17 approved ingredients. Further studies by other researchers were recommended to assess the validity and reliability of those findings. Finally, I addressed the TEA applications and the role that the PASS (Public Access to Safe Sunscreens) coalition plays by lobbying the Congress and the FDA to take further action on our sunscreen actives.

PASS Plays

Some of the interesting developments with the PASS coalition included the House Appropriations Committee report for fiscal year 2014 requiring the FDA to eliminate the backlog of pending applications for sunscreen ingredients and calling on the agency to work with stakeholders to develop an improved review and approval process. It also called upon the FDA to take final action by June 1, 2014.

In my last column, I had reported that the FDA responded to Representative Dingell (D-MI) announcing that they would take action on pending sunscreen ingredients by introducing a proposed rule in the Unified Agenda at the end of the current fiscal year! As you may all know, the FDA made similar claims in 2009, 2010, 2011 and 2012, and has postponed the rule by a year each time. Specifications for draft legislation were sent to FDA for its review.

The legislation reforms the Time and Extent Application (TEA) process, and establishes a transparent and predictable review process of OTC sunscreen products. In particular, it calls for the Nonprescription Drug Advisory Committee (NDAC) to review pending and new applications, and to provide a recommendation to the Division of Nonprescription Regulation Development in the Center (DNRD) regarding an application's safety and effectiveness. The proposal keeps the existing eligibility criteria.

If it is determined that a product is "generally recognized as safe and effective and not misbranded," the nonprescription sunscreen ingredient becomes eligible for marketing within the US. To ensure accountability and oversight of the program, the FDA will be required to submit a report to Congress regarding the progress of the program and will contain specified items to Congress within 12 months of enactment, on March 1, 2015, and every two years thereafter.

Waiting on FDA

We expect the FDA to provide its views on the legislative proposal shortly. Based on the agency's feedback, the Coalition will determine subsequent courses of action. The recent developments in the House of Representatives provide a positive sign for the PASS Coalition. It highlights a potential pathway for sunscreen legislation in the future.

The Public Access to Safe Sunscreens (PASS) Coalition has also submitted comments to the Centers for Disease Control and Prevention (CDC) in response to a request for public comments regarding the prevention of skin cancer through the reduction of UV exposure in the US. The CDC's request for comment can be accessed in the Federal Register. In its comments, PASS requests the CDC to "urge the FDA to clear the 10-year backlog in new sunscreen applications and create a predictable, transparent and timely review process for pre-market approval of new sunscreen ingredients." The Centers for Disease Control and Prevention should lend its weight to help lean on the FDA and advance the agency's evaluation of sunscreen actives.

Recently, Health News Daily and *The Tan Sheet*[3] published an article regarding the Coalition's recent comments submitted to the CDC concerning strategies to reduce skin cancer. It states that consumers would be better equipped against harmful UV radiation if they had access to next-generation sunscreen actives that are currently mired in the FDA's time and extent application process. The Personal Care Products Council (PCPC) also submitted comments that emphasized the importance of sunscreen and identified sunscreen as the key to lowering the public's UV exposure and reducing incidences of skin cancer. The PCPC suggests that the data and information it has provided to the FDA on the safety and efficacy of sunscreens—over the 25 years the organization has been actively engaged in sunscreen-related rulemakings—has helped shape the agency's position in the 2011 final sunscreen rule on labeling and testing. That rule, "for the first time permitted companies to communicate the skin cancer prevention benefits that sunscreen provide when used as part of an overall sun safe regimen."

A Quiet Summer

Other than the intensive activities by the PASS Coalition outlined above, the summer has been particularly slow for announcements with the exception of the one made by Badger, a sunscreen manufacturer, that voluntarily recalled 30,000 of its SPF 30+ products due to microbial contamination.[4]

The Australian study demonstrating that sunscreens are extremely effective in combating skin cancer is the most hopeful news we have heard in some time. With recent developments and ongoing discussion, we can verify that work is being done to address these serious issues. As skin cancer claims another life, we ponder the senselessness of sun damage casualties. And while pointless death surrounds us, we hope for action and a Spring-like reawakening.●

References:

1. Hacker, E. et al (2013), The Effect of MC1R Variants and Sunscreen on the Response of Human Melanocytes In Vivo to Ultraviolet Radiation and Implications for Melanoma. Pigment Cell & Melanoma Research.doi: 10.1111/ pcmr.12157

2. Green, A.C. et al (2011), Reduced Melanoma After Regular Sunscreen Use: Randomized Trial Follow- Up. J.Clin.Oncol., 29, 257-263.

3."FDA Strengthens Sunscreen Testing and Label Requirements",(2011), The Tan Sheet, June 20,

4. Http://www.medicaldaily.com/ baby- sunscreen- recall- company- ws- badgers 10/10/2013