

Shedding light on UVB radiation and wound-healing

Skin and hair biology specialist **Dr Julie Thornton** delivered a presentation to UCD's Charles Institute Seminar Series on the mechanisms of light-based therapy and vitamin D supplementation, among other topics

The Charles Institute, Ireland's national dermatology research and education centre, played host to a range of guest speakers who covered a variety of topics ranging from skin cancer to psoriasis, among others. The series, which was sponsored by RELIFE (part of the A.Menarini group), was designed to provide expert practical advice from a range of distinguished national and international experts in their respective fields and was chaired by Prof Desmond Tobin, Professor of Dermatological Science at UCD School of Medicine and Director of the Charles Institute of Dermatology.

The second talk in the series was delivered by Dr Julie Thornton, Director of the Centre for Skin Sciences and Senior Lecturer in Biomedical Sciences at the University of Bradford, UK, on the topic 'Can Sunshine Heal Your Wounds?' Dr Thornton's areas of specialty include wound-healing, skin and hair biology, ageing, steroid hormones, inflammation, photoreceptors and circadian regulation.

She began by presenting an outline of skin damage due to UVB over-exposure and provided an overview of the various skin phototypes, particularly in relation to their geographical locations, and how people in Northern Europe often do not get sufficient vitamin D via sunshine. "The majority of our vitamin D gets produced in the skin," explained Dr Thornton. "Vitamin D is actually a hormone, because it is produced in the body and we can't rely on getting sufficient vitamin D through dietary intake alone."

She explained how the cholesterol in the

hormone that has a role in cardiovascular protection, inflammation, and research has also shown that it plays a beneficial role in certain cancers. She presented an overview of research on vitamin D and the "three basic processes involved in wound-healing".

"When you first get a wound, there is clotting and inflammation, so the inflammatory cells will move to the site of the wound to destroy any invading micro-organisms," Dr Thornton explained. "The next step is a proliferative phase, so it's very important that the fibroblasts in the dermis synthesise new granulation tissue, and then the keratinocytes can migrate and reform the barrier. After that, you have the remodelling phase, where the fibroblasts underneath will remodel the granulation tissue to form a mature scar. Although these three phases are sequential, they also overlap," she said, adding that in some patients, wound-healing can become stuck in the first inflammatory phase, which can lead to the development of a chronic wound, emphasising that wound-healing is a complex process which can become impaired.

Dr Thornton also presented research to show that when three different concentrations of the active form of vitamin D are administered, this stimulates the migration of keratinocytes. "What surprised us is that in fibroblasts it had completely the opposite effect, inhibiting migration or movement," said Dr Thornton, indicating that vitamin D signalling is far more complicated than was previously thought.

visual opsin-3 receptor (found in skin) by blue light and the vitamin D receptor.

Dr Thornton concluded her presentation by stating: "Light from sunshine is actually very good for people, as long as they are sensible and don't get their skin burned and damaged," she said.

During a lively interactive Q&A session, Dr Thornton addressed the question of humans evolving in sunlight. This has resulted in a huge part of the human genome being filtered through the vitamin D receptors — potentially up to 6 per cent of the entire human genome has an interaction with vitamin D receptors, with huge implications for populations migrating from UV-intense areas of the world. Understanding the role of the large number of potential vitamin D metabolites has opened up a new area of science, which is currently being examined.

Cancer and vitamin D

Asked whether she thinks there is a relationship between vitamin D and cancer metastases, Dr Thornton said: "The relationship in skin cancer is mostly unexplored, but there is some evidence to suggest that vitamin D may be important in reducing cancer risk," she said, "but there is limited research on metastases specifically."

Prof Tobin referenced a recent conference where a leading dermatologist suggested that suberythemal doses of UV may be important for human health: "We should have enough sun exposure that keeps us just under the reddening transition, regardless of where you are on the range of phototypes," said Prof Tobin. "Even phototype 6 people will get burned if they exceed a certain level of photo-intensity. That [the conference] saw the first senior voice [Dr Peter Elias, US dermatologist] speaking up to raise the theory that sunlight at suberythemal dose has a very significant and positive effect on system-wide behaviour. There is some data on vitamin D levels in breast cancer and there is increasing work being done on vitamin D and melanoma... it's a hot topic in cancer research."

Addressing the question of the relationship between circadian rhythms and cell behaviour, Prof Tobin provided an explanation for the often poor congruence of data from laboratories around the world where experiments are being conducted at different times of the day without appreciating of the impact of the tissue's and cells' circadian clock. For example, there is fluctuation in gene expression at different times (eg, especially during the day versus night), which could be influencing research outcomes. "I would stress the benefits of standardising when during the day we conduct particular experiments to avoid variations in gene expression," he told the attendees. "We can't control competitors' or collaborators' labs, but there is increasing evidence that the variability in scientific data may be in part down to when people are actually doing their experiments."

Dr Thornton added: "It makes sense that the skin has that circadian rhythm, because the cells, when they are dividing, should not be exposed to UV light, so any



Dr Julie Thornton

risk of direct DNA damage from the sun is minimised," she said. "If that process is dysregulated, the circadian clock in the skin is disrupted and people may be at a higher risk of getting skin damage from UV rays in daytime sunshine."

Prof Tobin commented: "Any PhD students should also be aware that even when cells are removed from their host organ, they retain their own circadian clock in the laboratory, even though the cells don't have a central clock to 'entrain' them. That's a really important element that could explain some of the 'noise' we see when looking at results from our experiments."

Speaking with the *Medical Independent (MI)* after her address, Dr Thornton spoke about the need for general practitioners as well as dermatology specialists to have a firm grasp of dermatology, considering such consultations comprise a significant percentage of presentations. "That is hugely important — the system in England is different. I am not sure how it compares to Ireland, but there are actually fewer dermatology specialists [in England] — it is becoming more of an issue, particularly with the ageing population."

"It's really about catching these patients early because the longer impaired wound-healing goes on and wounds become infected, the more people become at risk of sepsis, and the more diabetic patients become at risk of an amputation, for example," she said.

Asked for her take-home message from the talk, Dr Thornton told *MI*: "I think in chronic diseases, it's important to look at vitamin D levels in blood tests, especially in older patients, because their vitamin D levels will be decreased. This is also true for people with chronic illnesses, because they can also have an impact. With all the warnings people receive about skin cancer, it's important to achieve a balance [regarding vitamin D intake] because, for example, people who normally get very little sun exposure go on holiday for two weeks and they get burned and damage their skin. That's a problem but if they get small, regular doses of sunshine, that's a healthy balance."

Relife has had no input into the content of the series or article.

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keratinocytes of the epidermis is broken down via the mechanism of action of UV produced by sunlight to generate a sterol called cholecalciferol, or vitamin D3. This is then circulated to the liver, where an enzyme called 25 hydroxylase then metabolises it to 25 hydroxy vitamin D3. "This is the major circulating form of vitamin D3, but it's not the active form," she explained. An enzyme called 1 alpha hydroxylase in the kidney then converts it to the active form of vitamin D. "The active form is the important one, because it binds with the receptor," said Dr Thornton.

Important hormone

Dr Thornton told the attendees that it is now known there are many non-classical actions of vitamin D and it is an important

Signalling

She added that more needs to be known about the relationship between vitamin D and vitamin A. "We need to explore the signalling between the keratinocytes and fibroblasts, because keratinocytes can make it [vitamin D] and the fibroblasts have such high levels of the receptor, that suggests that these are important target cells," said Dr Thornton. "So rather than an endocrine response, it may be a paracrine response."

She outlined research to show the effects of visible light on wound-healing, including specific wavelengths of blue and red light, pointing out that results varied according to study participants. Dr Thornton explained that preliminary findings from microarray-based research show a potential link between the activation of the