Clinical Dermatology

UCD CHARLES INSTITUTE SEMINAR SERIES

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Clinical perspectives on skin ageing

*Attendees at UCD's Charles Institute Seminar Series recently heard a presentation from **Prof Rachel Watson** of the University of Manchester on the mechanisms of skin ageing and photodamage*

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 advice from a range of distinguished national and international experts in their respective fields and was chaired by Prof Desmond Tobin, Full Professor of Dermatological Science at UCD School of Medicine and Director of the Charles Institute of Dermatology. The seminars were broadcast to attendees with a special interest in dermatology in other locations, who accessed the talks remotely via an audio-visual link.

Attendees at the series recently heard a presentation from Prof Rachel Watson, Professor of Cutaneous Science and Head of the Division for Musculoskeletal and Dermatological Sciences within the School of Biological Sciences, Faculty of Biology, Medicine and Health at the University of Manchester, UK. Prof Watson addressed the current understanding of photoageing in her talk titled 'Ageing in the Dermis: Lessons Across Ethnicities'.

She began by providing examples of the differences between skin ageing and photoageing and said: "Skin is a fascinating organ to work with and to treat. We see the impact of the intrinsic ageing process and superimposed on that, particularly around the face, arms and décolletage, we see the impact of the environment on that rate of ageing.

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"We see different types of increased skin problems in the elderly, different infections, different diseases, a propensity towards slower wound-healing and on top of that, skin that looks visually old, which has a psychological impact on the individual, including on their social participation. In combination, these have an impact on an individual's quality of life and independence, as well as functional loss in the skin itself."

Testing

Prof Watson provided an overview of non-invasive biochemical testing and told the seminar that in the past 10 years, she and her colleagues have been researching the impact of how skin ageing affects how the organ behaves, using a non-invasive Cutometer. "It's a very gentle device — at the flick of a switch, it pulls the skin up into a small aperture in the probe under a constant pressure, producing a mechanical force that we can measure multiple times," she told the seminar. "We can then measure the skin's elasticity and other biomechanical functions of the skin over a huge range of different parameters."

As skin ages, not only does it become more deficient in collagen, but there is also a reduced capacity to create new collagen, Prof Watson told the seminar. "It is possible to quantify the degree of photoageing and look at the amount of procollagen in the tissue… and we can see a linearity," she said. "The less photodamaged the skin is, the more collagen content it seems to have. There seems to be a relationship between the severity of photodamage and the amount of collagen it contains, so there is a slow, rate-dependent loss of collagen."

One of the more prominent features of photodamaged or photoexposed skin is the appearance of solar elastosis, Prof Watson told the seminar. She presented some case studies to illustrate the effects of photodamage on different areas of the body and said: "In the forearm, this fine structure is generally degraded and we see an elastotic, dystrophic mass that stains very dark purple using the histological dye Weigert's resorcin fuchsin and this is typical of the solar elastosis that we see. If you dissolve away the rest of the matrix by using enzymes such as metalloproteinases, you see the dystrophic nature of elastin in skin following chronic photoageing."

If microfibrils are extracted from the superficial part of the skin and examined, they resemble "pearls on a string," said Prof Watson. "They are very regular and it doesn't really matter whether you extract a microfibril from a sea cucumber, a mouse or a human — they all have the same structure and you can measure the periodicity from each bead to its neighbour, and that is always around 56 nanometres. So they are a very preserved architectural piece of the extracellular matrix and are very regular in their structure.

"This means that we can start to manipulate them and experiment with them to try to understand why things change in disease and with photodamage."

Ageing

Regarding the skin's structural changes associated with ageing, Prof Watson told the seminar that a colleague has studied the surface topography of skin in order to better understand changes that occur in the epidermis with ageing. "What was shown was in younger buttock skin for example, there is quite a plump epidermis, with many rete ridges present," she said. "With an ageing buttock, there isn't really a great deal of difference in the thickness of the epidermis, but we do see a reduction in the number of rete ridges, although that reduction is not highly significant.

"However, we do see a diminution of the depth of those rete ridges; they do not go as deeply into the skin, as we would expect to see in younger skin."

Matrix metalloproteinases (MMPs) remove damaged microfibrils, explained Prof Watson, and there is now a model showing a direct pathway whereby photochemistry initiates degradation of microfibrils in the skin. Speaking about lightly-pigmented skin, Prof Watson explained: "This model also shows a cellular pathway, whereby we get a breakdown of collagen over a longer time period because of the action of extracellular matrix proteases," she told the seminar. "MMPs are really important for skin health — we need them for wound-healing and we need them to mediate any signs of damage. When we irradiate our microfibrils, it's the damaged microfibrils that are particularly susceptible to degradation subsequent to irradiation by MMPs.

"So if you artificially irradiate a microfibril and then exhibit it to an MMP, you see a protection of the normal structure and a remodelling or destruction of those that are not functionally normal. In subsequent irradiation, MMPs are there to 'mop-up' the damage and remove any damaged microfibrils."

Regarding darker-pigmented skin phenotypes, Prof Watson stated: "We decided to look at younger skin before examining ageing skin," she explained. "We saw that even in photoprotected skin, the anatomy of the skin is slightly different, dependent on the level of pigmentation, or at least aligning to that level of pigmentation, although we cannot say yet that there is a causal relationship."

In African skin, for example, there is a much stronger dermal-epidermal junction structure and the skin is far more inter-digitated, with longer and stronger rete ridges, explained Prof Watson. "Both lightly- and darker-pigmented skin have a large amount of elastin. When we biomechanically test the skin, regardless of the pigment, it behaves in a very similar way in photoprotected sites," she told the seminar. "If we look specifically at the elastin fibres, we see that lightly-pigmented skin, even in younger individuals, shows the beginnings of the signs of elastosis, we see a loss of microfibrils, and we see an effacement of the rete ridge structure. All of that is preserved in skin of colour," she said.

"When we biomechanically test the skin, this plays out, so we see a strong response in darkly-pigmented skin and a reduced biomechanical function in the photoaged skin sites of those with lightly-pigmented skin."

Prof Watson continued: "If we map-out the functionality between the elastic fibre abundance, the DEJ convolution and biomechanical function, what we see again is that when we start to remove one of these elements, that's when we start to see changes in how the skin behaves and again, that is around flattening of the DEJ and changes to the number of elastic fibres."

Prof Rachel Watson

Prof Watson summarised by telling the seminar: "In lightly-pigmented skin with chronic sun exposure, this leads to an accelerated ageing phenotype, so we see wrinkles and altered pigmentation, and changes in fragility, for example," she said. "We also see epidermal thinning and loss of rete ridges, as well as a loss of fibrillin-rich microfibrils, and this precedes the appearance of solar elastosis.

"In more pigmented skin, those signs of photoageing and photo damage do occur, but they happen much later in life," she continued. "We see the same epidermal thinning and the same loss of rete ridges and a loss of fibrillin-rich microfibrils, but no solar elastosis."

Basal keratinocytes

During a lively Q&A session following the presentation, Prof Tobin noted that Prof Watson had acknowledged the basal keratinocyte as having a role in the superficial ECM fibrillin role, and asked Prof Watson: "To what extent is targeting the basal keratinocyte therefore a potentially important consideration in perhaps prolonging function in skin, particularly visually?"

Prof Watson responded: "I think that is absolutely key. We talk about the functionality of tissue but I think the basal keratinocytes are not only producing cells for barrier function — they are also producing absolutely vital extracellular matrix molecules that help with the functionality of tissue. Whether that is an unappreciated role or whether there has just been a bias towards fibroblasts… We published that work 20 years ago showing that the keratinocytes are really the ones that are making the most of the fibrillin, but nobody has really picked up on that.

"So I think when looking at treatments, particularly if you work with industry, there doesn't seem to be a desire for a treatment that impacts fibroblasts — they want a treatment that impacts the keratinocytes, which then 'tell' the fibroblasts what they need to do," she continued. "I think basal keratinocytes have a fundamental role; you could say they are the 'conductors', orchestrating the rejuvenation response, so I think they are really very important indeed."

RELIFE has had no input into the content of this article or series of seminars