Clinical Dermatology
UCD CHARLES INSTITUTE SEMINAR SERIES

UCD School of Medicine
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Charles Institute of Dermatology

Handling the pressure in wound-healing

*Attendees at UCD's Charles Institute Seminar Series recently heard the final presentation in the first series from **Dr Claire Higgins** of Imperial College London, who discussed efforts to re-engineer residual skin of amputees to prevent pressure sores*

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 Dr Claire Higgins, Senior Lecturer in Tissue Engineering and Regenerative Medicine in the Department of Bioengineering at Imperial College London. Dr Higgins also runs a research group focused on the skin and hair follicles, as well as wound repair and regeneration.

Dr Higgins explained to the attendees how the skin of amputees' residual limb must bear loads that it was not naturally designed to tolerate and as a result, superficial skin injuries are a common barrier to rehabilitation. One area of the body that routinely tolerates high loading is the sole of the foot, Dr Higgins explained, and it is important to understand why plantar skin performs better under load compared to non-plantar skin.

Dr Claire Higgins

Dr Higgins and her team are investigating why plantar skin can thrive under loading that would rapidly lead to degeneration of skin on other sites on the human body, such as residual limbs. Her team uses macro- and micro-scale experimental methods in an effort to resolve these questions, and show that plantar skin distorts substantially less, both in response to compression and shear loading.

She explained that computational models have revealed that both the geometry and material properties of plantar skin contribute to its ability to bear load, with geometry protecting skin against tears, while material properties protect against ulceration. This data, she explained, enhances and furthers understanding of the aetiology of superficial pressure ulcers and helps to explain why they are uncommon on plantar skin sites. This study has inspired Dr Higgins and her team to strive to re-engineer skin of the residual limb of amputees into plantar skin to resist superficial pressure sores.

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Necrosis

Dr Higgins told the seminar that it is the mechanism of injury that determines what type of pressure ulcer a patient gets. "There might be a high amount of pressure, resulting in distortion or deformation of the muscle, which would result in tissue necrosis, resulting in a deep tissue [grade 4] injury, which might only manifest at the skin surface after the necrosis is well developed," Dr Higgins told the seminar. "So these injuries do not necessarily start at grade 1 and move on to grade 4 [in a linear way]."

Pressure sores on stumps are a common and significant problem for amputees and Dr Higgins explained that the highest pressures are not in the muscle around the bone, but rather the highest amounts of shear strain are seen in the skin. "In bed-bound individuals, bed sores or pressure ulcers tend to be deep-tissue injuries and we hypothesise that the ulcers we are seeing in amputees are perhaps more superficial, perhaps grade 1 or grade 2 injuries, caused by an increase in shear forces, such as the prosthetic rubbing on the amputee's stump," she told the seminar.

"This is a huge problem for amputees — 75 per cent of them suffer from dermatoses on the stumps, and one-third of these dermatoses are pressure ulcers or pressure sores." While huge advances have been made in the design and functionality of prostheses, treatment itself has not progressed as quickly, she added.

Dr Higgins provided an overview of her studies and laboratory work which, among many other findings, showed that when plantar skin is subjected to shear stress, it deformed by approximately 40 per cent, while non-plantar skin deformed by almost 100 per cent. "Plantar skin is more tolerant to load, both in compressive and shear conditions, and it seems to resist deformation under loading," said Dr Higgins. "We know that the morphology is different… one of the well-known markers of plantar skin is keratin 9, which is very prevalent throughout the suprabasal layers of the epidermis and it's not present in non-plantar skin. Keratin 9 is a cytoskeletal protein, so we would theorise that it actually contributes to the structural integrity of keratinocytes in plantar skin and potentially contributes to their capacity for load tolerance."

The dermis in plantar skin also contains more collagen and the collagen fibres are thicker and have a higher SHG signal, indicating that it is "poised for loading", Dr Higgins pointed out.

Key point

"A key point to take home is that in non-plantar skin, we see a sharp drop in terms of tissue stiffness between the epidermis and dermis," said Dr Higgins. "In plantar skin, we do not see a sharp drop, but a gradual decrease. This is important, because the epidermis and dermis are obviously adjacent to each other, with the epidermal junction between them. They are two different tissues — there is an

Prof Desmond Tobin

epithelial tissue and a connective tissue — but in plantar skin, there is a gradual decrease in stiffness, whereas in non-plantar skin, we have what could be described as two very mismatched stiffnesses. This is relevant as mismatched stiffnesses in two adjacent materials increase the likelihood of failure."

No research groups have yet examined how reprogramming keratinocytes to a plantar identity affects other markers in addition to keratin 9 and whether it affects the composition of the skin and robustness of the cells. This is now an area of specific research that is of particular interest to Dr Higgins and her colleagues, she said.

Dr Higgins summarised: "Pressure ulcers can be either deep-tissue or superficial injuries, but pressure alone does not confer ulceration. Plantar skin is under high loads, but ulcerates very infrequently and so we propose that the morphological and mechanical characteristics of plantar skin actually protect epidermal cells and fibroblasts in the skin from compression forces," she explained. "Specifically, it's the composition of plantar skin that protects it against high shear strain and pressure ulcers, and it is the thickness of plantar skin that protects it against Von Mises stress, and therefore blisters and tears.

"We propose that the re-engineering of stump skin to a planter identity could be achieved by using plantar skin fibroblasts as an advanced therapeutic medicinal product - as a cell therapy, to try to make the skin on a stump more load-tolerant."

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