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> ONE MONTH, ONE PROTEIN <

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about water

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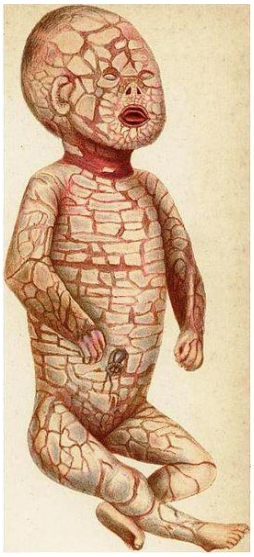
There is no life without water. However, living beings can only go through life with given amounts of water inside them. Which is why there has to be a system that sustains this balance, to prevent too much water from flowing in, or indeed pouring out. Too large a volume of water in an organism, or too small a one, brings about serious deficiencies, which can lead to an organism's death. So Nature devised a water barrier which it built around all its creations – a sort of seal that makes sure the volume of water we carry within us remains as stable as possible. When this barrier is deficient, though, individuals can suffer from skin disorders known as ichthyosis – or dry skin – to varying degrees: some mild, others lethal. Since the 1920s, it has been known that fatty acids have a role in mammalian skin hydration. Recently, researchers discovered how two lipooxygenases – epidermis-type lipoxygenase 3 and 12 – have a crucial role in the construction of the mammalian water barrier – and hence our aqueous well-being – thanks to their interactions with essential fatty acids.



Harlequin foetus, lithography, 1886

Source: wikipedia

Ichthyosis is more commonly known as 'dry skin', with which many of us are familiar. If we take a closer look at even a mild condition of ichthyosis, we can see that our skin is cracked and resembles the scales of fish. The word 'ichthyosis' stems from 'ichthys' which means'fish' in Ancient Greek. There can be very serious cases of congenital ichthyosis where babies – also known as 'Harlequin babies' – are born with a thickening of the skin's keratin layer and have developed massive, diamond-shaped scales. Such an affliction limits movements hugely, and the areas surrounding the cracked skin are an unfortunate haven for infections, which until about only 20 years ago were usually fatal.

The most vital components in our skin, with regards to water permeability, are fatty acids. As is frequently the case in the world of science, the importance of fatty acids to life became clear following research whose initial aim had nothing to do with theses molecules in the first place but rather with the nutritional importance of vitamin E in rats. That, however, is another story. Until the 1920s, the notion that fatty acids could be essential to life at all came as a surprise since they had never been considered to be particularly important in an organism's diet. It took the work of an American biochemist George Burr and his wife, Mildred, a technician, to make the observation that fatty acids were not only needed but actually essential to the dynamics of a mammal's physiology – in particular linoleic acid, which is why they coined the expression 'essential' fatty acid. In fact, for many years, linoleic acid was thought to be the only essential fatty acid. So much so,

that it was the only one which was added to infant formula right up until the mid-1990s, when the World Health Organization took the decision that infant formula should have a fatty acid distribution similar to human milk.

The link between linoleic acid and the two lipooxygenases – epidermis-type lipoxygenase 3 and 12, also known as ALOXE3 and 12R-LOX – had already been established in the early mid-1980s, but it has taken a further 30 years or so to understand the intimacy of their involvement in the construction of the epidermal water barrier. To cut a long story short, 12R-LOX followed by ALOXE3 oxygenate their substrate known as *O*-linoleoyl-ω-hydroxyceramide which, in turn, facilitates its hydrolysis and subsequently allows the bonding of the ω-hydroxyceramide moiety to proteins which are found on the surface of corneocytes. Corneocytes are cells which are located on the outermost part of the skin, and replaced by desquamation and then renewal by cells from lower epidermal layers. What 12R-LOX and ALOXE3 are ultimately involved in, is the sealing of the skin – perhaps comparable to the silicone you would apply to the lower part of your shower to prevent the water from inundating the bathroom floor.

Understanding the molecular intimacy of the molecules involved in this novel pathway, and how they interact, will help in the development of new therapies for people suffering from dry skin – in particular, those suffering from harsh forms of congenital ichthyosis. Designing substrates that mimic in great detail the substrates of both lipoxygenases – 12R-LOX and ALOXE3 – could form the basis of creams that could then be directly applied to a patient's skin, in the event of ichthyosis caused by a deficiency in either one of these enzymes. And, naturally, a greater knowledge of all the substrates and the enzymes involved in building the water barrier will gradually help in the design of therapies for all forms of congenital ichthyosis as well as less severe dryness of the skin. Something that does tend to increase with the passing of the years.

Cross-references to UniProt

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