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Understanding 'immune SOS signal' may lead to new psoriasis therapies

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Scientists at Trinity College Dublin have made an important breakthrough in understanding how an 'immune SOS signal', the protein Interleukin-36, serves an important role in switching on the immune system. The discovery may pave the way for the development of new therapies for treating psoriasis.

The Trinity research group, led by Smurfit Professor of Medical Genetics, Professor Seamus Martin, has just published the findings in the internationally renowned peer-reviewed journal, *Cell Reports*.

Interleukin-36 functions akin to an intruder alarm in the body, especially in the skin, switching on when injury and infection damages our tissues, and mobilizing all of the forces of the immune system to repair the damage. This process is called inflammation and causes the swelling and redness that we are all familiar with when we sprain our ankles or bump our heads.

Inflammation is generally a good thing as it is how the body heals wounds and shuts down infection. The problem is that some people, those with psoriasis, for example, switch on this alarm protein too readily and experience skin inflammation almost continuously. So, the question has been: How does interleukin-36 get switched on to send out the SOS signal?

Now, Professor Martin and recent Trinity PhD graduate, Dr Conor Henry, have discovered the molecules that convert Interleukin-36 from

its harmless form to its destructive one, by removing a small piece of Interleukin-36, rather like pulling the pin out of a grenade.

These molecules, called proteases, are overactive in the skin of people that suffer from psoriasis, which suggests an entirely new way of treating this condition.

Indeed, scientists from the Martin laboratory have also discovered and patented inhibitors of the Interleukin-36 activating proteases, and hope to develop their strategy further in partnership with a Pharma or Skincare company.

Commenting on the findings, Professor Martin said: "This discovery is very exciting and we really hope to develop this approach into a new way of treating psoriasis."

"We are very grateful for the support of Science Foundation Ireland, who funded this research. This work represents an excellent example of how basic research leads to fundamental breakthroughs in our understanding of how diseases arise. Without such knowledge, it would be very difficult to develop new therapies."

The work was carried out in Trinity's Department of Genetics by a team led by Professor Martin, which included Trinity PhD students Conor Henry and Graeme Sullivan. The Trinity team is internationally recognised for its work in the areas of cell death and inflammation.

Provided by Trinity College Dublin