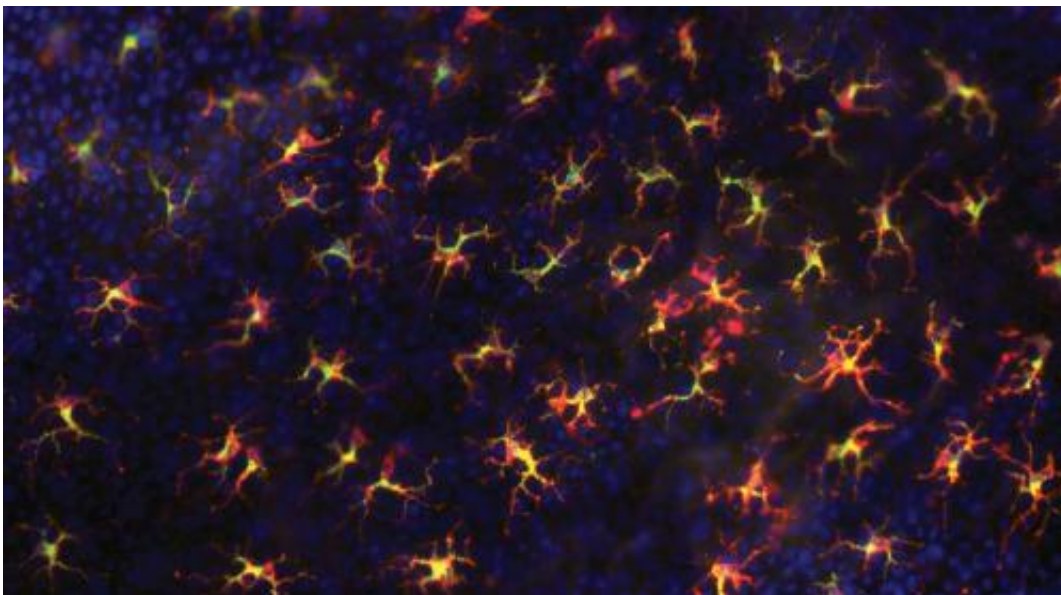


Messenger substance and signalling molecule influence the development of the skin's immune cells

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Flash mob in the skin. A signalling molecule has been discovered on immune cells of the epidermis.

A signalling molecule known as Axl has been discovered on immune cells of the epidermis. This recently published finding provides new insight into the development of important skin immune cells known as Langerhans cells. These cells fight off invading microorganisms and play a crucial role in our health. As the research project, funded by the Austrian Science Fund FWF, also discovered, the natural production of

the signalling molecule Axl is highly dependent on the messenger substance TGF-beta 1. Together, these findings provide a better understanding of how immune cells develop and offer new approaches for the treatment of autoimmune diseases.

Some infections can really "get under your skin". Fortunately, however, this is not always the case, as the skin provides very effective protection against infections – a function for which we have to thank a type of [skin cells](#), known as the Langerhans cells (LCs). These cells are found in the outermost layer of the skin, the epidermis, and on mucous membranes, and provide a first line of defence against invading viruses, bacteria and [fungi](#). A team of researchers at the Medical University of Vienna is currently examining how [immune cells](#) develop from haemopoietic or blood-forming [stem cells](#), and recently made some very important discoveries in the process.

Signal effect

A team headed by Prof. Herbert Strobl from the Institute of Immunology has not only demonstrated that a signalling molecule known as Axl occurs on the surface of LCs, but also how this process is controlled by the messenger substance or cytokine [transforming growth factor beta 1](#) (TGF-beta 1). Commenting on the significance of this study, Prof. Strobl explains that: "A large number of benign microbes are found on the skin, which are important for [human health](#). The ability to distinguish 'good' from 'bad' is therefore of critical importance for the LCs – and Axl plays an important role in this process."

Axl is, in fact, a receptor belonging to the family of TAM receptor tyrosine kinases. These messenger molecules have a crucial function in the prevention of undesired inflammatory responses – and are thereby also preventing the immune system from reacting to benign [microbes](#). Finding an explanation for when and how Axl is formed is therefore

very important for understanding the development of LCs from stem cells.

The group headed by Prof. Strobl, who recently started at the Institute of Pathophysiology and Immunology at the Medical University of Graz, has now succeeded in showing that precursor LCs form the signalling molecule Axl just a few hours after coming into contact with TGF-beta 1. In comparison to the duration of other cell differentiation processes, an astonishingly short time period. In addition, the researchers established that Axl is only produced in cells that go on to differentiate into LCs – and not in precursors that develop into other cell types, for example granulocytes, monocytes or lymphocytes. The scientists also succeeded in determining that Axl is the only receptor of the TAM family synthesised under these conditions.

These findings rapidly indicated to Thomas Bauer, first author of the study, that the effect of TGF-beta 1 on Axl production is vital for LC differentiation from precursor cells: A detail that is further substantiated by the fact that the continuous presence of TGF-beta 1 is essential throughout the differentiation process to guarantee Axl synthesis.

A systematic approach

These findings have now been published in the prestigious Journal of Experimental Medicine. This study, which is impressive from both a qualitative and quantitative perspective, was made possible by a well-established test system, as Prof. Strobl explains: "Thanks to an in vitro cell culture procedure for LC differentiation from isolated blood stem cells, we can analyse the effects of different [molecules](#) during LC differentiation in detail. This is exactly what we did with TGF-beta 1."

The importance of the findings of this FWF project extends far beyond the fundamental insights they provide into the development of skin

immune cells. Axl's ability to distinguish between "good" and "bad" also enables it to prevent [autoimmune diseases](#). Which is why these findings just may contribute to the treatment of these diseases in the future.

More information: Bauer, T. et al. Identification of Axl as a downstream effector of TGF-Beta1 during Langerhans cell differentiation and epidermal homeostasis. *J. Exp. Med.* 2012 Vol. 209 No. 11 2033-2047. [DOI 10.1084/jem.20120493](https://doi.org/10.1084/jem.20120493)

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