Psoriasis: Towards a novel therapeutic approach

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Psoriasis is a frequent skin inflammatory disorder affecting 3% of the population. Psoriasis is characterized by hyperproliferation and defect of epidermal differentiation, leading to the scaly appearance of the skin.

Psoriatic skin also presents an increase in blood vessels, leading to the redness of the skin lesions and is associated with immune infiltration.

The cross talk between immune cells, blood vessels and keratinocytes have been previously shown to be crucial for psoriasis development. However, the respective role of each of these populations in the psoriasis initiation has been a matter of debate. Vascular endothelial growth factor A (VEGFA) is the principal factor responsible for the formation of new blood vessels.

Despite the well-known role of VEGFA in promoting psoriasis, it remains unclear whether VEGFA acts only on blood vessels, which in turn mediate recruitment of inflammatory cells and defect of epidermis differentiation, or whether VEGFA also acts directly on the skin epidermis to orchestrate psoriasis development.

In a study published in *Science Advances*, researchers lead by Pr. Cédric Blanpain, MD/Ph.D., WELBIO investigator and Professor at the Université libre de Bruxelles, Belgium, now provide evidence that targeting VEGFA signaling in the epidermis prevents psoriasis development.

To address this key question, Benhadou and colleagues used a mouse model overexpressing VEGFA, which induces a psoriatic like disease recapitulating the hallmarks of human psoriasis. By combining VEGFA overexpression and the genetic deletion of VEGFA receptor (VEGFR1) and co-receptor (Nrp1) in the skin epidermis, the authors demonstrate that the deletion of Nrp1 or Flt1 prevents psoriasis development. "It was very surprising to find that inhibiting VEGFA signaling only in the epidermis was sufficient to completely prevent psoriasis development including immune cell infiltration and increase in blood vessel formation mediated by VEGFA overexpression," comments Dr. Farida Benhadou, the first author of this study.

To assess whether inhibiting Nrp1/VEGFA interaction can be of therapeutic relevance for the treatment of psoriasis, Benhadou and colleagues administrated a therapeutic anti-Nrp1 antibody that blocks the interaction between VEGFA and Nrp1 to mice presenting psoriasis. Administration of Nrp1 blocking antibodies induced a rapid disappearance of psoriatic lesions. "These data demonstrate the therapeutic benefit of blocking VEGFA/Nrp1 interaction in the treatment of psoriatic disease, which may be safer for the treatment of psoriasis as compared to other therapeutic modalities that can be associated with serious side effects" comments Cédric Blanpain, the senior author of this study.

Altogether this new study demonstrates the essential role of Flt1 and Nrp1 expression in the skin epidermis to mediate psoriasis development. The results of this study have important implications for the understanding of mechanisms leading to psoriasis, one of the most frequent inflammatory diseases, and for the treatment of patients with psoriasis.

More information: Farida Benhadou et al, Epidermal autonomous VEGFA/Flt1/Nrp1 functions mediate psoriasis-like disease, *Science Advances* (2020). DOI: 10.1126/sciadv.aax5849

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