PSORIASIS

Anti-VEGF antibody therapy for psoriasis?

Angiogenesis has a key role in the pathogenesis of psoriasis, a disease that is characterized by epidermal hyperplasia, enlarged blood and lymphatic vessels, and inflammatory infiltrates, but as yet research into antiangiogenic therapies for this chronic inflammatory condition has been limited. A study by Erwin Wagner and colleagues, published in the *Proceedings of the National Academy of Sciences*, now highlights the therapeutic potential of antibodies to vascular endothelial growth factor (VEGF) in a mouse model of psoriasis.

“Our results suggest that anti-VEGF antibodies, possibly in conjunction with other drugs, could be used to treat not only cancer patients, but also people suffering from psoriasis and other inflammatory skin diseases,” explains Wagner. The researchers tested the anti-VEGF antibody G6-31 in a mouse model of psoriasis; the mice lack expression of the AP-1 transcription factors JunB and c-Jun in the epidermis, which leads to the development of psoriasis-like symptoms in the skin (hyperkeratosis, parakeratosis, increased subepidermal vascularization, inflammatory infiltrates, and increased levels of cytokines and chemokines).

Mice showing the first symptoms of a psoriasis-like phenotype were injected

with anti-VEGF antibodies ($n=12$) or an IgG isotype control ($n=8$) every 48 hours for 8 days. By days 23–24, skin inflammation was almost completely resolved in the ears of five mice treated with anti-VEGF antibodies, was moderately improved in six, and only one mouse did not respond; by contrast, the ears of all mice treated with control IgG showed prominent inflammatory scaly skin lesions. Anti-VEGF antibody treatment also resulted in improvement of psoriasis-like symptoms in the paws, tails and toes of treated mice.

Further analyses showed that anti-VEGF antibody treatment led to normalization of epidermal architecture in the treated mice. In addition, in comparison with mice receiving the control IgG, the number of blood vessels, the size of blood and lymphatic vessels, and the numbers of infiltrating leukocytes and lymphocytes in the dermis were considerably reduced in mice treated with anti-VEGF antibodies.

“We have shown for the first time that blocking VEGF could be an effective treatment for psoriasis in this mouse model,” concludes Wagner. “We will continue to investigate how molecules produced by keratinocytes, and involved in the activation of the immune system,

Increased number of blood vessels in inflamed skin in a mouse model of psoriasis. Image courtesy of H. B. Schonthaler and S. K. Wculek.

can lead to psoriasis. Regarding the anti-VEGF approach, it is important for us to investigate whether topical application of the antibody to the affected psoriatic skin lesions is beneficial.”

Jenny Buckland

Original article Schonthaler, H. B. *et al.* Systemic anti-VEGF treatment strongly reduces skin inflammation in a mouse model of psoriasis. *Proc. Natl Acad. Sci. USA* 106 21264–21269 (2009) | **Further reading** Zenz, R. *et al.* Psoriasis-like skin disease and arthritis caused by inducible epidermal deletion of Jun proteins. *Nature* 437, 369–375 (2005)