Targeted cancer treatment: Cause of skin infections identified

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Targeted, successful cancer treatments are very often accompanied by unpleasant side effects. Especially in anti-EGFR treatments the skin is often so badly affected by inflammations that patients consider breaking off the highly effective treatment. Researchers at the Comprehensive Cancer Center Vienna (CCC), an establishment belonging to the MedUni Vienna and the Vienna General Hospital, have now managed to break down the mechanisms significantly involved in the uncontrolled inflammatory process.

The growth of cells is triggered by messengers that dock with special

proteins on the surface of the cells, so-called EGF receptors (Epidermal Growth Factor Receptor: EGFR). There are increased numbers of receptors on the surface of nearly all tumour cells and they lead to uncontrolled cell growth.

In targeted treatment the EGFRs are switched off, thus hindering the tumour's growth. EGFRs do however control many processes in the skin and therefore play an important role in maintaining a healthy balance in this organ. If the receptors are in short supply then so are the messengers as well and acne-like rashes are the consequence. These are often so distressing to the sufferers that breaking off the treatment necessarily becomes a serious consideration.

Inflammatory mechanism broken down

A team of researchers around Maria Sibilia, the head of the Institute for Cancer Research at the MedUni Vienna and member of the CCC, has now been able to prove in an in vivo study that, once the EGFRs are switched off, inflammatory messengers such as CCL2 and CCL5 appear in increased numbers whilst important adhesion molecules and antimicrobial peptides in the skin's epidermis are produced in reduced numbers.

This causes damage to the skin barrier such that pathogens can penetrate more easily and thus contribute to increased skin inflammation. The results show that macrophages and mast cells play a significant role in the uncontrolled inflammatory reactions. Says Sibilia: "We were very surprised to find that T- and B-cells, which are such a significant component of the immune defence and thus are always at hand in the combating of pathogens, do not play a significant part in the combating of this inflammatory process."

Also taking part in this study was a team under Bernhard Homey,

Director of the Düsseldorf University Skin Clinic. It was also able to demonstrate the same results in clinical investigations on human skin. Says Sibilia: "Now that we know about this mechanism, treatments in the form of ointments or creams could be developed in future, which would strengthen the skin's barrier functions and thus alleviate these side effects."

More information: Lichtenberger et al. Epidermal EGFR controls cutaneous host defense and prevents inflammation, *Sci Transl Med*. 2013 Aug 21.

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