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Bacteria could contribute to development of wound-induced skin cancer

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Researchers at King's College London have identified a new mechanism by which skin damage triggers the formation of tumors, which could have important therapeutic implications for patients suffering with chronic ulcers or skin blistering diseases.

The study, published today in *Nature Communications*, highlights an innate sensing of bacteria by immune cells in the formation of skin tumors. This molecular process could tip the balance between normal wound repair and tumor formation in some patients, according to researchers.

Although an association between tissue damage, chronic inflammation and cancer is well established, little is known about the underlying cause. Epidermolysis Bullosa (EB), for instance, is one of several rare inherited skin conditions associated with chronic wounding and increased risk of tumors.

However, this study - funded primarily by the Medical Research Council (MRC) and the Wellcome Trust - is the first to demonstrate that bacteria present on the skin can contribute to the development of skin tumors.

Researchers found that when mice with chronic skin inflammation are wounded they develop tumors at the wound site, with cells of the immune system required for this process to take place. They discovered that the underlying signaling mechanism involves a bacterial protein, flagellin, which is recognized by a receptor (Toll-like receptor 5) on the

surface of the immune cells.

Although the direct relevance to human tumors is yet to be tested, researchers have shown that a protein called HMGB1 - found to be highly expressed in mice with chronic skin inflammation - is increased in human patients with Epidermolysis Bullosa (EB). The study found a reduction in HMGB1 levels in mice when the TLR-5 receptor was removed from immune cells. This raises the possibility of future treatments aimed at reducing levels of the flagellin bacterial protein on the skin surface, or targeting the TLR-5 receptor.

Professor Fiona Watt, lead author and Director of the Centre for Stem Cells and Regenerative Medicine at King's College London, said: 'These findings have broad implications for various types of cancers and in particular for the treatment of tumors that arise in patients suffering from chronic ulcers or skin blistering diseases.

'In the context of chronic skin inflammation, the activity of a particular receptor in white blood cells, TLR-5, could tip the balance between normal wound repair and tumor formation.'

Professor Watt added: 'Our findings raise the possibility that the use of specific antibiotics targeting bacteria in wound-induced malignancies might present an interesting clinical avenue.'

Provided by King's College London