Forcing cancer to digest itself

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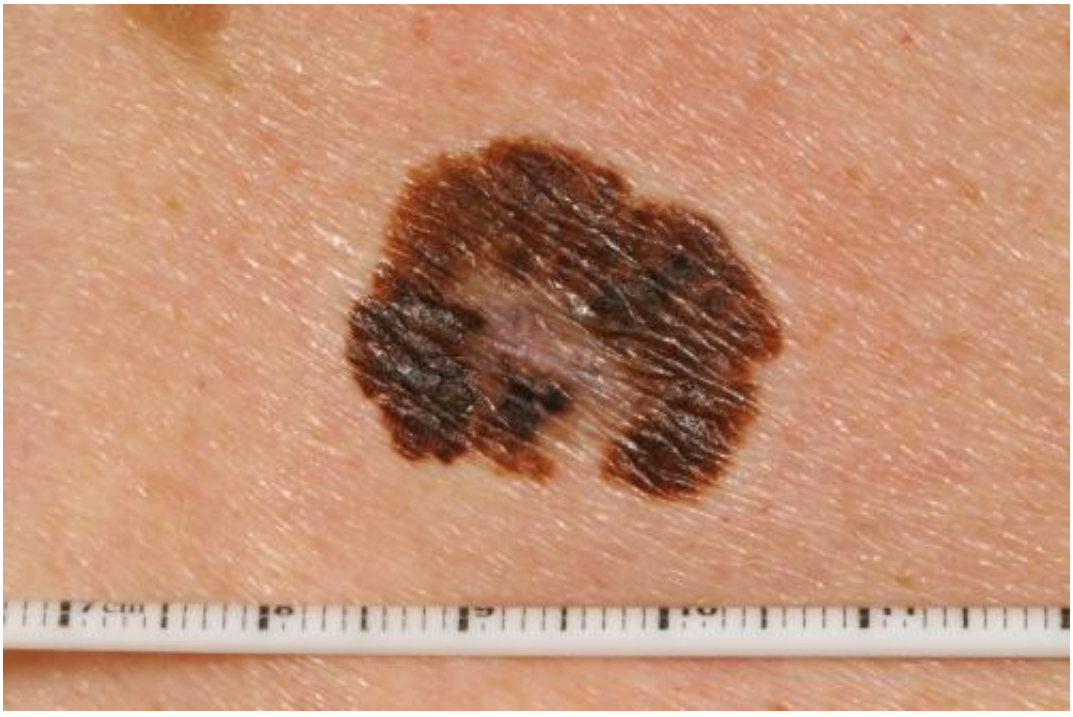


Melanoma. Credit: Hans-Uwe Simon, Institute of Pharmacology, University of Bern

When tumour cells no longer degrade themselves, cancer may develop. Using black skin cancer as an example, Bern Researchers have now shown that a protein plays an important role in the process of degradation of tumour cells. By reactivating this degradation therapeutically, you can virtually force tumours to digest themselves.

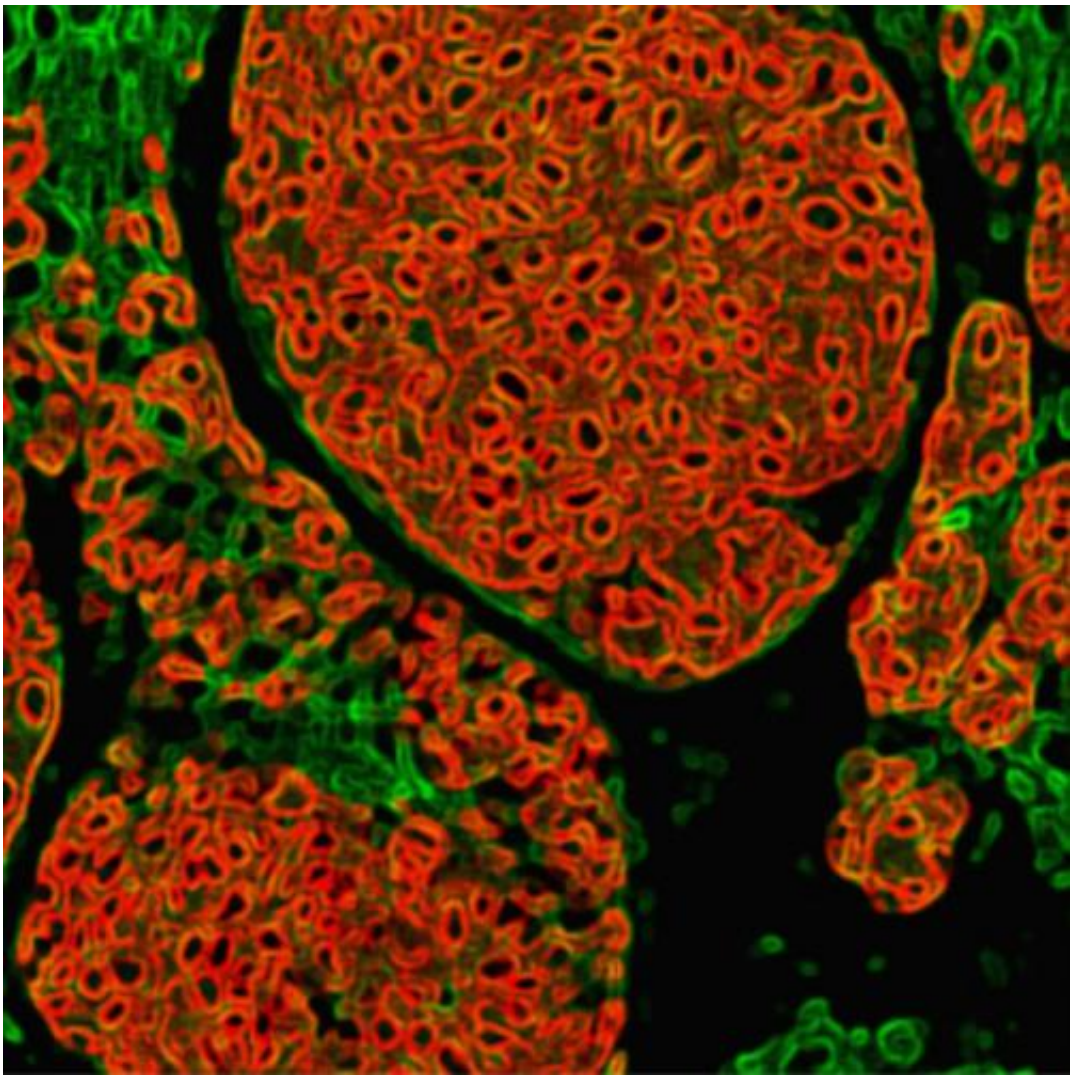
Cells are able to degrade damaged molecules as well as entire areas of

cells by self-digestion and use the resulting degradation products to gain energy and to produce new molecules or parts of cells. This process of self-digestion is called autophagy and can be considered a renovation of the cell.

Energy production through autophagy plays an important role for cells when they are lacking nutrients, oxygen or growth factors. A team of researchers of the University of Bern under the direction of Hans-Uwe Simon of the Institute of Pharmacology has now found out that a reduced self-digestion of tumour cells may contribute to the development of a melanoma. The discoveries demonstrate new therapy approaches for the treatment of black skin cancer. The study is being published today in *Science Translational Medicine*.

Nipping the tumour "in the bud"

The researchers examined the importance of autophagy for the formation of tumours. They particularly studied a central autophagy-regulating protein (ATG5) in a group of nearly 200 patients with melanoma. They found out that changes in the chromosomes - so-called epigenetic changes - resulted in the presence of an insufficient quantity of ATG5 in the tumour cells and thus in a restriction of their self-digestion.



Immunofluorescence analysis of a melanoma-containing skin tissue (tumor nests in red). Credit: Hans-Uwe Simon, Institute of Pharmacology, University of Bern

In addition, the group with Hans-Uwe Simon was able to show experimentally that the formation of tumours can be prevented through a therapeutic normalisation of self-digestion. This reveals a new approach for the future therapy of melanomas and perhaps also other types of cancer at an early stage: "In the future, ATG5 might not only play a role in the diagnosis of melanomas; we also hope for new therapies in order to force tumours at an early stage to digest themselves," Simon explains.

More information: Liu, H. et al. Down-Regulation of Autophagy-Related Protein 5 (ATG5) Contributes to the Pathogenesis of Early-Stage Cutaneous Melanoma, *Science Translational Medicine*, 11 September 2013. DOI: 10.1126/scitranslmed.3005864