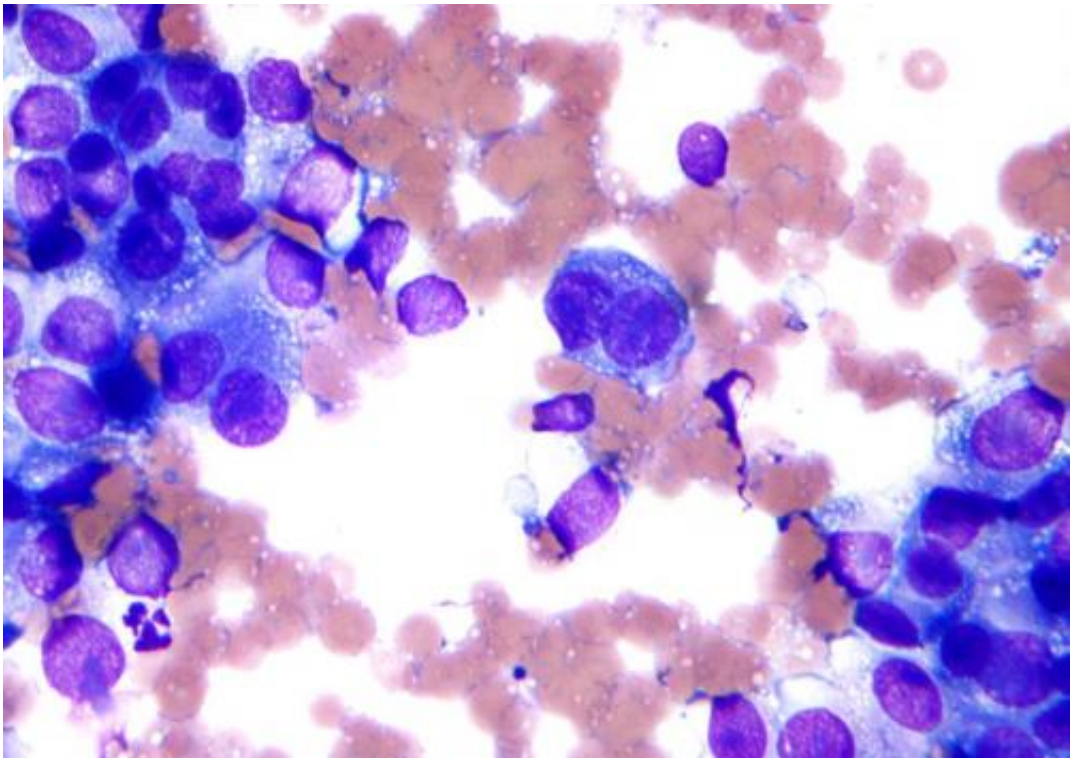
Researchers discover why photodynamic therapy for skin cancer can cause pain

June 23 2016



Micrograph of malignant melanoma. Cytology specimen. Field stain. Credit: Nephron/Wikipedia

Severe paleness and photosensitivity are two symptoms of a rare group of hereditary diseases that affect haem, a substance in the blood. While these metabolic disorders - known as the porphyrias - are extremely rare, a similar effect is often deliberately triggered by dermatologists in localised areas during the treatment of pre-cancerous skin lesions and

skin cancers. This treatment is called photodynamic therapy and involves using a special cream which stimulates haem production in the diseased cells. This produces several photosensitive molecules known as porphyrins. When the skin is exposed to light, these molecules form highly aggressive free oxygen radicals. The diseased skin cells are not able to defend themselves against these free radicals as effectively as healthy cells, causing them to die. Although this form of treatment is very effective, it can also be severely painful and cause inflammation - discouraging patients from undergoing the therapy again if it is needed in other locations. What causes the pain and inflammation was previously a mystery to researchers.

Painful blue light

An international group of researchers at FAU's Institute of Physiology and Pathophysiology has now managed to find the answer. The team carried out a study with volunteers whose skin was exposed to a dark blue laser pointer. The light from this type of pointer has exactly the right wave length to stimulate a haem precursor that is present in all cells, including nerve endings, to produce free radicals. When the laser pointer was directed at bare skin, participants began to feel a slight pinprick-like pain after around 30 seconds. However, when the cream used in photodynamic therapy was applied to the skin beforehand, the pain became much stronger, and none of the participants was able to withstand it for longer than 40 seconds. When skin is treated with the cream, even the red light - which has a longer wave length - that is used for the therapy as it penetrates the skin further can cause severe burning pain.

The FAU researchers' study showed that the aggressive free oxygen radicals were active not only in the diseased skin cells but also in certain nerve endings that recognise early signs of damage. In the nerve cells the free radicals activate the ion channel TRPA1 which triggers pain or

itching. When the skin is treated with the cream, exposure to light triggers a second ion channel, TRPV1, increasing the pain. TRPV1 is known as the capsaicin receptor and is also what triggers the burning sensation caused by chillis. Both TRPA1 and TRPV1 are activated by the free oxygen radicals and stimulate the nerve endings, causing pain and inflammation as these nerves also release inflammatory substances called neuropeptides.

'Medications that block both ion channels have already been tested in the treatment of other types of pain, such as the pain experienced in diabetic neuropathy or arthritis,' explains FAU researcher Prof. Dr. Peter Reeh. 'Based on the findings of this study, these should have two benefits in this case, as they would reduce both pain and inflammation.'

More information: A. Babes et al, Photosensitization in Porphyrias and Photodynamic Therapy Involves TRPA1 and TRPV1, *Journal of Neuroscience* (2016). DOI: 10.1523/JNEUROSCI.4268-15.2016

Provided by University of Erlangen-Nuremberg