



Press Release

To Prevent Cancer in Butterfly Disease Patients

Researchers have revealed how a rare genetic skin condition causes aggressive skin tumours

Fragile skin that blisters easily: 90 percent of the patients that suffer from the skin condition recessive dystrophic epidermolysis bullosa (RDEB) develop rapidly progressing cutaneous squamous cell carcinomas, a type of skin cancer, by the age of 55. 80 percent of these patients will die due to metastasis within five years after the cancer has been first detected. Researchers from the University of Freiburg and the University's Medical Center have discovered how the two diseases are connected and which molecular mechanisms underlie the aggressive behaviour of squamous cell carcinomas in RDEB patients. Furthermore, the dermatologists and biologists found new potential targets for the development of drugs. Dr. **Venugopal Rao Mittapalli**, Prof. Dr. **Leena Bruckner-Tuderman**, Dr. **Dimitra Kiritsi** and Dr. **Alexander Nyström** from the Medical Center – University of Freiburg conducted the study in cooperation with Juniorprofessor Dr. **Winfried Römer** and Dr. **Josef Madl** from the University of Freiburg and BIOS Centre for Biological Signalling Studies. The team published the research findings in the journal "Cancer Research".

Epidermolysis Bullosa, also known as butterfly disease, is a genetic skin condition. The skin of patients with this disease is as fragile as the wings of a butterfly. It blisters easily in response to minor injury or friction such as rubbing or scratching. Furthermore, the patients develop chronic wounds that are not healing and their fingers and toes fuse, for example. The condition is caused by a mutation of the gene *COL7A1*, which contains the

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Freiburg, 10.03.2016



■ blueprint for the protein collagen VII. This protein helps to bind the epidermis and the dermis, two layers of the skin, together. In RDEB patient, collagen VII is completely absent and, therefore, the skin becomes fragile.

So far, little was known about the molecular mechanisms connecting squamous cell carcinomas and RDEB. The Freiburg research team discovered that the cancer progresses rapidly in RDEB patients, because the repeated mechanical injury alters the dermis. The amount of proteins called pro-fibrotic growth factors increases, thereby increasing stiffness of the dermis. This environment helps the tumour cells to spread.

The researchers have also identified mechanisms that could be potential drug targets. For example, molecules that inhibit the growth factor TGF β reduce the stiffness and the spread of the RDEB cancer cells. “The new knowledge we have gained facilitates the design of prophylactic and therapeutic measures for delaying tumour progression and extending cancer-free periods in RDEB,” says Venugopal Rao Mittapalli, the first author of the study.

Leena Bruckner-Tuderman is Director of the Department of Dermatology of the Medical Center – University of Freiburg. Dimitra Kiritsi, Venugopal Rao Mittapalli und Alexander Nyström are researchers in Bruckner-Tuderman’s group. Winfried Römer is juniorprofessor for Synthetic Biology of Signalling Processes at the Cluster of Excellence BIOSS Centre for Biological Signalling Studies and the Institute of Biology II of the University of Freiburg. Josef Madl is postdoctoral scientist in Römer’s research group.

Original publication:

Mittapalli VR, Madl J, Löffek S, Kiritsi D, Kern JS, Römer W, Nyström A, Bruckner-Tuderman L. (2016). Injury-Driven Stiffening of the Dermis Expedites Skin Carcinoma Progression. In: *Cancer Res.* 76(4):940-51. doi: 10.1158/0008-5472.CAN-15-1348.

Caption:

Cells of a cutaneous squamous cell carcinoma (green) that invade the skin.
Image by: Dr. Venugopal Rao Mittapalli

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