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Tracking cancer's signaling pathways

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Malignant melanoma is one of the most common and dangerous types of cancer. Researchers at Friedrich-Alexander Universität Erlangen-Nürnberg (FAU) investigated how and why brown pigmented moles turn into malignant melanoma using innovative robot technology. The insights gained can simplify methods of diagnosis in the future; furthermore, they suggest that certain cosmetic products and creams should be avoided.

Until now, researchers only knew which genetic mutations were responsible for triggering the transformation of benign pigmented moles into malignant tumours. But little was known about what happens to proteins and signalling pathways when a malignant melanoma develops. The research group led by Prof. Dr. Andreas Baur at FAU's Translational Research Center (TRC) have now discovered that the ADAM10 signalling pathway is activated during the transformation. This pathway is a protein chain that passes the signal from one protein to the next, similar to chasing LED lights. This protein chain is normally inactive in healthy skin and is only activated in an immune response. It is known for its role in psoriasis, rosacea (a type of facial rash) and inflammation, i.e. when the immune system is activated but is also key in the development of malignant melanoma.

FAU researchers were able to demonstrate the significance of the ADAM10 signalling pathway with regard to the development of melanoma using a new kind of robot. The robot makes it possible to investigate development processes in skin samples at a cellular level. It uses anti-bodies marked with fluorochrome to stain tissue cell proteins.

A camera takes a photo of the tissue samples. The fluorochrome is then bleached to destroy it, rendering the anti-body invisible. The robot applies another anti-body and the process is repeated. This method produces a sequence of different images of the same tissue sample that can be superimposed to reveal which proteins are active in which cells and where. Prior to the new technology, only one to four markers could be stained; the robot can now stain more than 100 proteins.

The insights gained will enable a better diagnosis of malignant melanoma in the future. 'This is especially important in borderline cases where it is difficult to make a clear decision whether a tumour is benign or malignant', says Baur. In the long term, the findings will enable a simplified, automated diagnosis of malignant melanoma using staining robots. Additionally, the research suggests that cosmetic products and sun screen containing aluminium should be avoided, as aluminium ions can non-specifically activate the ADAM10 signalling pathway that leads to melanoma.

The research results were published as a feature article in a special cancer edition of *Science Signaling* 10 in March 2017: "Multiepitope tissue analysis reveals SPPL3-mediated ADAM10 activation as a key step in the transformation of melanocytes".

More information: Christian Ostalecki et al, Multiepitope tissue analysis reveals SPPL3-mediated ADAM10 activation as a key step in the transformation of melanocytes, *Science Signaling* (2017). DOI: 10.1126/scisignal.aai8288

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