MedicalXpress

Researchers identify mechanism that causes particularly aggressive types of cancer to develop

February 16 2016

Fast metastasis and resistance to treatment are characteristic of aggressive types of cancer such as pancreatic cancer and certain kinds of breast cancer. They are also the main causes of cancer-related death, as there is currently no specific treatment available that is able to stop tumours spreading throughout the whole body. Researchers at Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU) have recently made a discovery that could change this. They have discovered a mechanism that promotes metastasis and causes tumours to become resistant to treatment. Based on these findings they have identified a gene set that suggests a particularly bad prognosis in case of breast cancer. The researchers' findings have recently been published in the journal *Nature Communications*.

Two key characteristics must be activated in tumour cells in order for them to metastasise: the ability to spread throughout the body and the ability to form new tumours - metastases - in other remote parts of the body. In addition, such tumour cells must be especially resilient - a characteristic that also makes them more resistant to treatment.

The team of FAU researchers led by Prof. Dr. Thomas Brabletz from the Chair of Experimental Medicine I has now proven that these characteristics are activated when two fundamental embryonic signalling pathways, the EMT pathway and the HIPPO pathway, interact. When the key molecules of the two pathways, ZEB1 and YAP, interact with one

another directly they activate a range of genes that are required for aggressive tumour growth. The team was able to identify a set of eight genes from among this range that, when activated, is associated with particularly aggressive tumour growth in case of breast cancer. They now aim to use these findings to identify biological markers for aggressive tumours - known as prognostic markers - to confirm the clinical relevance of the mechanism that they have discovered.

As the fatal potential of the two key molecules ZEB1 and YAP is only activated when they are combined, the team also aims to search for inhibitors that can block this interaction, with the long-term goal to develop new treatment concepts for aggressive types of cancer.

More information: Waltraut Lehmann et al. ZEB1 turns into a transcriptional activator by interacting with YAP1 in aggressive cancer types, *Nature Communications* (2016). DOI: 10.1038/ncomms10498

Provided by University of Erlangen-Nuremberg