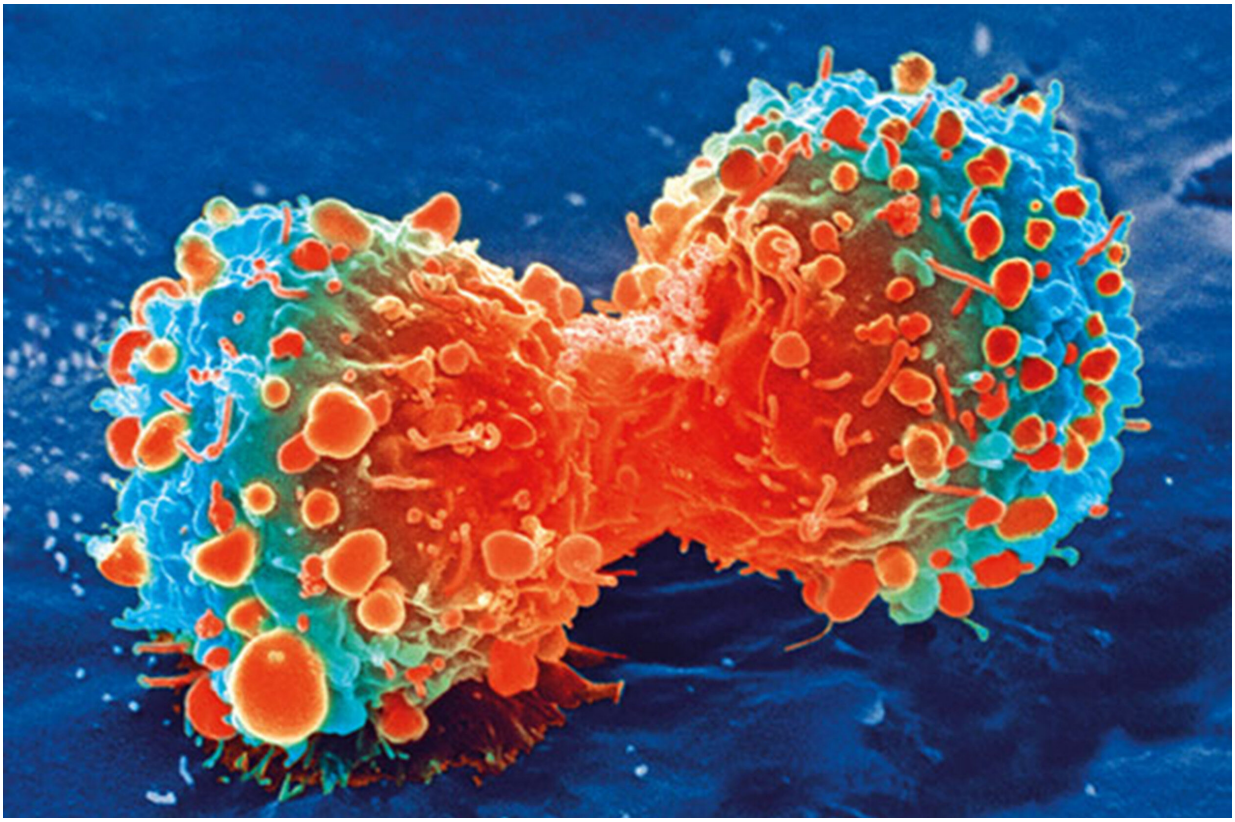
New insights into the development and therapy of cancer

April 2 2019



Cancer cell during cell division. Credit: National Institutes of Health

Oncologists at the University and University Hospital in Tübingen have discovered a new protein variant that plays an important role in the development and therapy response of cancer. For physicians, this

discovery opens up the opportunity for new options in the diagnosis and therapy of cancer. The results of the study were published on Tuesday, April 2nd in the journal *EBioMedicine*, the Open Access journal published by *The Lancet*.

The research team led by Dr. Kerstin Kampa-Schittenhelm discovered the protein variant ASPP2kappa in the cells of leukemia patients. They were able to show that as soon as this particular form of protein occurs, the cancer grows faster and is more difficult to treat with drugs. In the meantime, the researchers have also been able to detect this protein variant in other hematologic and solid tumors. The scientists were mainly funded by the Wilhelm Sander Foundation for Cancer Research.

The special feature of the newly discovered protein variant, which concerns a central gene in the signaling pathway of programmed cell death, is the dynamic character of its development: ASPP2kappa is not detectable in healthy cells or is only detectable to a limited extent – and occurs as a reaction to cell damage, such as that caused by radioactive or ultraviolet radiation, harmful environmental influences, or contact with toxins. The Tübingen researchers assume that the previously unknown protein variant is produced because the DNA in the affected cells is read incorrectly. This is followed by the formation of a protein that lacks important components.

Under normal circumstances, the cell would induce controlled cell death in the event of external damage. However, the defective protein variant apparently slows down this process and protects the cell from destruction. This protective mechanism is only advantageous at first sight as the damaged cells become a long-term problem for the organism – Cell damage accumulates and can eventually lead to degeneration of the cell, forming a tumor.

Widely accepted assumptions that gene mutations are causative for

degeneration of cells are complemented by this finding. "In the present case we were able to show that the corresponding DNA of the cell has no flaws," says Kampa-Schittenhelm. Obviously, even a protein that is incorrectly formed by external factors can lead to malignant degeneration of cells.

Better understanding of tumor development

These findings are of far-reaching importance for understanding the development of tumors but also offer starting points for improving the diagnosis and treatment of cancer. The Tübingen researchers are now working on ways of turning these new findings into improved therapeutic options. "Our results suggest that it may be useful in the future to check whether cancer patients have ASPP2kappa in their cells or not before starting therapy," says Kampa-Schittenhelm. In addition, an increase in the protein concentration during the treatment may indicate whether the treatment is successful: "If the protein multiplies, our findings suggest that the patient is less responsive to the respective therapy." Accordingly, there is the opportunity to better adapt therapies to individual needs in the future.

Further clinical studies are now needed with defined tumor entities and patient cohorts to validate the results of the study. In addition, the Tübingen researchers hope to develop drugs that will prevent the formation of the newly discovered protein. "It will certainly take several more years before the findings of the current study can be used in clinical everyday life," concludes Kampa-Schittenhelm.

More information: Marcus Matthias Schittenhelm et al. Alternative splicing of the tumor suppressor ASPP2 results in a stress-inducible, oncogenic isoform prevalent in acute leukemia, *EBioMedicine* (2019). DOI: 10.1016/j.ebiom.2019.03.028

Provided by Universitaet Tübingen