

Enzyme inhibitor slows tumor growth

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Dr Christian Kosan is examining proteins after separation in an electrophoresis. His team has discovered a novel therapeutic approach for treating malignant tumours of the lymphatic system. Credit: Jens Meyer/Uni Jena

Together with researchers from University Hospital Mainz, the University of Regensburg and the IRCM in Montreal (Canada), a research team from Friedrich Schiller University Jena has discovered a novel therapeutic approach for treating malignant tumors of the lymphatic system.

The team led by Dr. Christian Kosan from Jena University's Institute of Biochemistry and Biophysics shows that treating certain B-cell lymphomas with the enzyme inhibitor Marbostat 100 leads to significantly slowed growth of the tumor cells. The researchers present their results in the journal *Oncogene*

B-cell lymphomas are tumors of specific immune cells (B-lymphocytes). These cells, which belong to the [white blood cells](#), normally produce antibodies and are essential for the body to ensure an effective immune defense. A specific gene called MYC is often involved when B lymphocytes turn into tumor cells, says Christian Kosan. "This gene initially stimulates the cells to grow faster and to divide, which can lead to further mutations and thus ultimately to tumor formation."

Transcription factor Myc plays key role in tumorigenesis

The protein Myc encoded by MYC is a transcription factor. "It binds to the DNA of a cell and thereby regulates the expression of its target genes," explains Kosan, who has been studying Myc and its functions for some time. A large number of human genes are directly or indirectly regulated by Myc.

In tumors, such as aggressive B-cell lymphomas, the amount of the Myc protein is greatly increased. "Our goal was therefore to specifically block the function of Myc and to reduce the accelerated division of the tumor cells," says Kosan.

As the Myc protein is relatively small and offers few specific docking sites on its surface for other molecules, it is difficult to target. Therefore, the researchers used a roundabout route: they did not target Myc directly, but instead an enzyme that interacts with Myc and regulates its function.

In the current publication, the team led by Christian Kosan was able to show that the specific inhibition of this enzyme (histone deacetylase 6) leads to a significant decrease in Myc concentration in the tumor cells. The researchers treated human B-cell [lymphoma](#) cell lines with the enzyme inhibitor Marbostat 100 and found that four out of five tumor cell lines died.

"We were also able to show that, depending on the concentration and treatment period of the enzyme inhibitor, the Myc protein is degraded in the tumor cells," says Kosan. What is more, in experiments with mice that develop B-cell lymphomas due to a particular mutation and normally die as a result, treatment with Marbostat 100 led to a significantly higher life expectancy. Of 15 animals with tumors, 14 survived for the entire study period.

Combination therapy for treating aggressive tumors

Christian Kosan and his colleagues now want to transfer the newly gained knowledge to other tumor types. "We already know that Myc plays a role not only in B-cell lymphomas, but also in many other types of cancer," says Kosan.

The researchers therefore want to investigate whether the use of Marbostat 100 could also be suitable for treating other tumor cells. The long-term goal is to develop a combinatorial therapy for treating aggressive types of cancer. B-cell lymphomas have been treated with aggressive chemotherapeutic drugs so far, but these usually have equally strong side effects.

"We want to try to slow down tumor growth with therapeutics such as the enzyme inhibitor Marbostat 100, so that the chemotherapeutics can be administered in lower doses or over a shorter period of time and thus fewer side effects can be expected," says Kosan.

More information: René Winkler et al, Targeting the MYC interaction network in B-cell lymphoma via histone deacetylase 6 inhibition, *Oncogene* (2022). [DOI: 10.1038/s41388-022-02450-3](https://doi.org/10.1038/s41388-022-02450-3)

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