

# How inflammatory signalling molecules contribute to carcinogenesis

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Previously unknown molecular connection between an inflammatory signalling molecule and one of the main oncogenes identified. Credit: Medical University of Vienna

A team of MedUni Vienna researchers led by Johannes A. Schmid at the

Center for Physiology and Pharmacology, Institute of Vascular Biology and Thrombosis Research, has managed to identify a previously unknown molecular connection between an inflammatory signaling molecule and one of the main oncogenes. The study has been published in the leading journal *Molecular Cancer*.

Johannes A. Schmid's working group at the Center for Physiology and Pharmacology, Institute of Vascular Biology and Thrombosis Research, already has many years' experience in the molecular and cellular aspects of inflammatory processes and is investigating what role these processes play in the development of [cancer](#), as well as cardiovascular diseases. Based on structural similarities between key inflammatory enzymes, the so-called I-kappa B kinases (IKKs), and c-Myc, a protein that is present in elevated quantities in many forms of cancer, the researchers suspected that there might be a [direct interaction](#) between these [molecules](#). They could now confirm this interaction using a special microscopic technique.

"We were able to show that the inflammatory enzymes attach phosphates at a very specific site of the c-Myc protein, causing a slower degradation of the molecule, and a subsequent accumulation in the cells leading to a higher activity," explains Schmid. "Cells that contain a c-Myc variant that imitates this phosphorylation are characterized by a higher rate of cell division and greater resistance to chemotherapeutics."

Using CRISPR/Cas9 gene editing, the lead author of the study, Bernhard Moser, was able to eliminate both c-Myc and the inflammatory enzymes IKK-alpha and IKK-beta from prostate cancer [cells](#), thereby demonstrating, on a [genetic basis](#), that the interaction between IKK-alpha and c-Myc is crucial. Second author Bernhard Hochreiter was able to confirm the correlation between these two proteins in a prostate-cancer mouse model. Finally, bioinformatics analyses were performed, showing that this correlation can also be observed in different types of

human cancer.

Schmid summarizes as follows: "The important point about this study is that, we found a previously undiscovered molecular mechanism that links a central inflammatory signaling molecule with cancer development, thereby adding another specific aspect to previously identified links between inflammation and cancer. This finding indicates that drugs that inhibit this inflammatory [enzyme](#) could be used therapeutically in certain types of cancer."

**More information:** Bernhard Moser et al. The inflammatory kinase IKK $\alpha$  phosphorylates and stabilizes c-Myc and enhances its activity, *Molecular Cancer* (2021). [DOI: 10.1186/s12943-021-01308-8](https://doi.org/10.1186/s12943-021-01308-8)

Provided by Medical University of Vienna

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