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Prostate cancer: Newly-developed inhibitor shows massive potential

More than 65,000 men fall ill with prostate cancer each year in Germany. Twelve thousand of them develop a treatment-resistant form which eventually ends in death. Now, a team of researchers from the Medical Faculty at the University of Freiburg has developed an active substance that might in future represent a new treatment option. This substance, known as KMI169, targets an enzyme that plays an important role in the development of prostate cancer. The inhibitor displayed massive potential in among others cancer cells that were resistant to conventional treatments. Researchers from the Department of Urology at the Freiburg University Medical Center as well as the Institut für Pharmazeutische Wissenschaften at the University of Freiburg published their study in Nature Communications on 2 January 2024.

"We've had our eye on the enzyme KMT9 as a possible target in prostate cancer for a long time. The development of this specific inhibitor is now a decisive step in combating prostate cancer far more effectively," explains study head Professor Roland Schüle, Academic Director of the Department of Urology at the Freiburg University Medical Center and member of the Cluster of Exzellence CIBSS - Centre for Integrative Biological Signalling Studies and Dr. Eric Metzger, group leader in Schüle's department. The substance's potential use against treatment-resistant forms of cancer makes it especially valuable. "This treatment-resistance means that the classic antihormonal treatment often fails within a few months and the disease then progresses rapidly. The inhibitor we've developed offers us a highly innovative therapeutic approach here," says Schüle.

New approach also relevant to bladder cancer

Using cell cultures, the groups headed by Schüle and co-author Professor Manfred Jung, head of the Chemical Epigeneticsgroup of the Institut für Pharmazeutische Wissenschaften and member of the Cluster of Exzellence CIBSS - Centre for Integrative Biological Signalling Studies, have shown that the enzyme KMT9, known as a methyltransferase, is a critical factor in the development and progress of certain types of cancer such as prostate or bladder cancer. "The inhibitor fits snugly like a key in its lock and blocks the functioning of KMT9 and therefore also the growth of both prostate and bladder cancer cells," says Jung. The development of KMI169 was guided by crystal structure analysis of KMT9 and numerous other studies. "We modified the compound many times to increase its potency, selectivity and medicinal properties."

Publication:

Wang, S., Klein, S.O., Urban, S. et al. Structure-guided design of a selective inhibitor of the methyltransferase KMT9 with cellular activity. Nat Commun 15, 43 (2024). DOI: doi.org/10.1038/s41467-023-44243-6.

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Further information

- University of Freiburg
- CIBSS Centre for Integrative Biological Signalling Studies