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A potential milestone in cancer therapy

Researchers from the University of Bern, Inselspital, University Hospital Bern, and the University of Connecticut have made a significant breakthrough in the fight against cancer. They identified a previously unknown weak point of prostate cancer cells. This could also lead to entirely new therapeutic approaches for other types of cancer.

Prostate cancer is the most common non-skin cancer in men worldwide. According to international estimates about one in six men will get prostate cancer during their lifetime and worldwide, over 375'000 patients will die from it each year. Tumor resistance to current therapies plays an essential role in this and new approaches are therefore urgently needed. Now an international research team from the University of Bern, Inselspital Bern and the University of Connecticut (USA) has identified a previously unknown weak spot in prostate cancer cells. This weak spot is possibly also present in other cancer cells. The study was led by Mark Rubin from the Department for Biomedical Research (DBMR) and Center for Precision Medicine (BCPM) at the University of Bern and Inselspital Bern, and Rahul Kanadia from the Department of Physiology and Neurobiology and the Institute for Systems Genomics at the University of Connecticut. The research results have now been published in the journal *Molecular Cell*.

Previously unknown driver of prostate cancer identified

"We took a closer look at a certain molecular machine called the *spliceosome*", explains Anke Augspach, lead author of the study and researcher from the Department for BioMedical Research (DBMR). "It plays an important role in the translation of genes into proteins. In this process, the spliceosome separates parts of the gene that are not needed for the production of the protein and fuses the other parts."

While almost all genes undergo this process in the so-called *major* spliceosome, the *minor* spliceosome is used in less than one percent of genes. "Nevertheless, the minor spliceosome is enormously important because it particularly processes genes that play a crucial role in cell growth. And it is this cell growth that gets out of control in cancer – but the precise mechanism behind this remained unclear", explains Rahul Kanadia, study co-author from the Physiology and Neurobiology Department and the Institute for Systems Genomics at the University of Connecticut.

In their investigations, the team found various indications for the central role of the minor spliceosome in cancer. "We were able to show that a specific component of the minor spliceosome is significantly increased in advanced prostate cancer", explains study co-author Mark Rubin of the Department for BioMedical Research (DBMR) and Bern Center for Precision Medicine (BCPM). This led the researchers to suspect that cancer cells activate the minor spliceosome through this

component and thus stimulate uncontrolled cell growth.

An entirely new approach to cancer therapies

The researchers were able to confirm their assumption with the help of laboratory test models such as 2D cell cultures and organoids – miniature organs that are grown in the laboratory based on patient samples. They were also able to show that inhibiting the specific component led to a greater reduction in the growth of prostate cancer than current standard therapies. “Accordingly, blocking this process should hold therapeutic potential.”, Mark Rubin says. “This is the target that that we were hunting”. Rahul Kanadia adds that "The blocking leads to a decrease in cancer growth without affecting the growth and survival of normal cells." "This discovery is a game changer in developing more effective and targeted combination therapies for cancers such as prostate cancer and other types of cancer. We want to work on this in the coming years – and have already applied for the corresponding patent", Rubin concludes.

Research supported with 1 million dollars

The research results come from a project supported by the US Prostate Cancer Foundation (PCF) with the Igor Tulchinsky-Leerom Segal-PCF Challenge Award 2022. The foundation funds interdisciplinary projects that pursue promising approaches to combat recurrent or advanced prostate cancer. The award is endowed with 1 million dollars. “We commend the research team on their achievement and proudly support their work to bring us closer to our mission to eliminate death and suffering from prostate cancer”, says Howard R. Soule, Executive Vice President and Chief Science Officer of the PCF.

Publication details:

Minor intron splicing is critical for survival of lethal prostate cancer, Anke Augspach et al., Molecular Cell, 8 June 2023, [doi:10.1016/j.molcel.2023.05.017](https://doi.org/10.1016/j.molcel.2023.05.017)

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Department for BioMedical Research (DBMR)

The Department for BioMedical Research (DBMR) of the Faculty of Medicine at the University of Bern, led by Prof. Dr. med. Mark A. Rubin was established in 1994 by the University of Bern and Inselspital, Bern University Hospital. The DBMR comprises 13 research programs with approximately 100 participating individual labs and several independent research labs whose research spans all biomedical fields. To bridge the gap between bench and bedside, the DBMR promotes an integrative perspective to clinical research with a strong emphasis on the development of translational approaches, the use of omics and other cutting-edge technologies, as well as extensive interaction and collaboration between laboratory-based and patient-oriented clinical research. The DBMR is also committed to fostering the careers of young academics.

[Further information](#)

Bern Center for Precision Medicine (BCPM)

The Bern Center for Precision Medicine (BCPM) was founded in 2019 on the initiative and with the support of the Canton, the University of Bern, and Inselspital, Bern University Hospital. The BCPM is active in research, networking, and training. The center is dedicated to promoting approaches in precision medicine by supporting research and the development of medical diagnoses and therapeutic methods. It offers an interdisciplinary network for researchers and clinicians from various fields and faculties and unites more than 70 members. The BCPM will provide the best education for the next generation of caretakers and researchers through graduate schools. As a result, it is securing the long-term benefits that precision medicine brings to healthcare.

[Further information](#)

Physiology and Neurobiology (PNB) Department, University of Connecticut

The PNB is an interdisciplinary department with a vibrant research program and broad research portfolio including various model organisms and research questions. The department houses researchers from diverse cultural and educational background who are investigating neurobiology, reproductive biology, development, RNA processing, and human disease models, as well as research on STEM education. We integrate research into undergraduate education to increase participation of new generation into research and other biomedical fields.

[Further information](#)