Cancer cell vulnerability points to potential treatment path for aggressive disease

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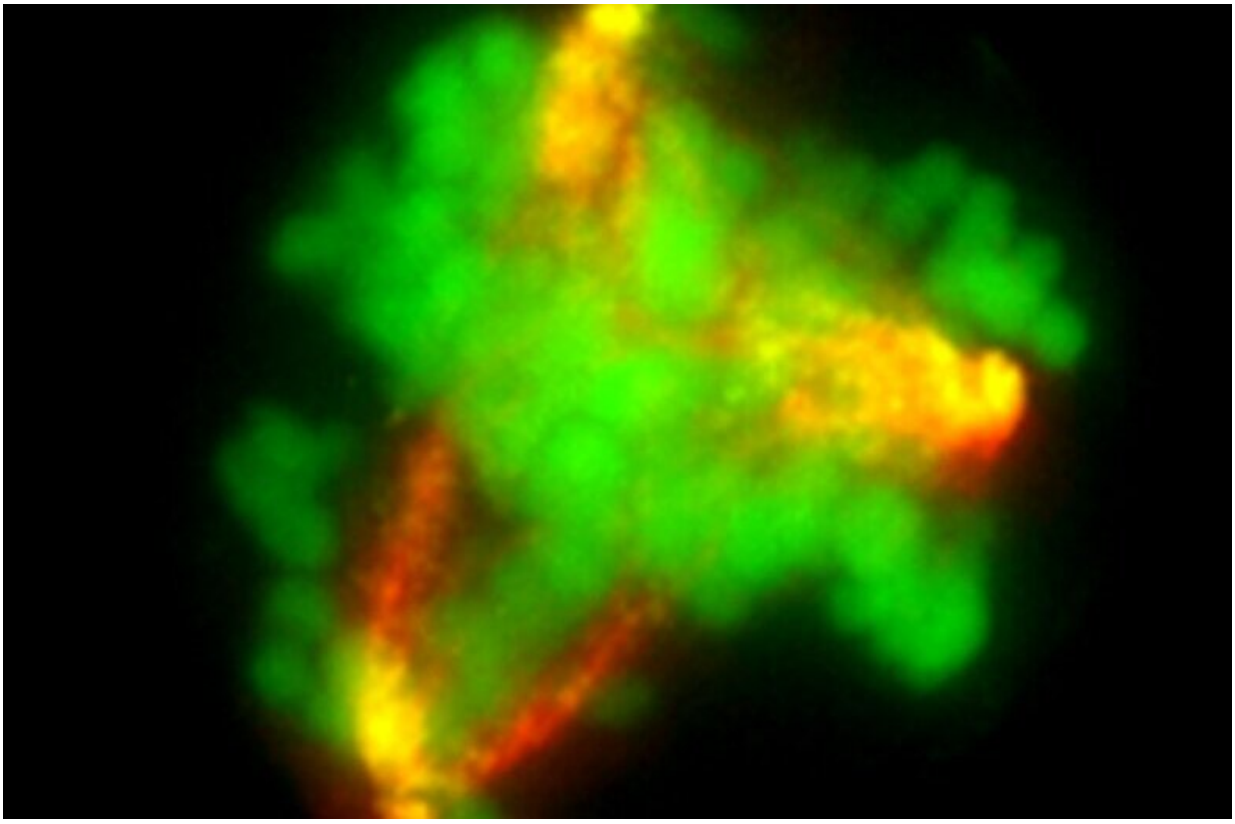

Image of a triple negative breast cancer cell undergoing abnormal division after inhibition of KIF18A (red = microtubules; green = chromosomes; yellow = spindle poles). Credit: Cindy Fonseca, M.S., Stumpff Lab, UVM Larner College of Medicine

Unravelling the unique characteristics of cancer cells and finding less-

harmful ways to stop their growth have long been a focus for cancer researchers worldwide. New findings, reported in *Nature Communications*, describe the discovery of a unique dependence of cancer cells on a particular protein, which could lead to desperately needed treatment for hard-to-treat cancers.

The publication caps off a series of groundbreaking studies appearing in *Nature* journals over the last month by members of a powerful international research collaboration.

Lead author and University of Vermont (UVM) Cancer Center researcher Jason Stumpff, Ph.D., has spent over two decades studying how cells divide and how mistakes in this process contribute to diseases, such as cancer. His recent work has enhanced understanding of the role of a protein called KIF18A in driving cell division. In these new studies, Stumpff's lab demonstrates that cancer cells, with the type of abnormalities seen in aggressive tumors, are more dependent on KIF18A for growth than normal cells. This vulnerability in the cancer cells could be a potential target for interrupting cancer cell growth, as the researchers demonstrated in triple negative breast cancer and colorectal cancer cells.

These findings mark a milestone step in a long research journey that began with support from an American Cancer Society Institutional Research Grant pilot award through the University of Vermont Cancer Center, and then led to Susan G. Komen and National Institutes of Health (NIH) funding. Stumpff, an associate professor of molecular physiology and biophysics at UVM's Larner College of Medicine, decided to publish his team's findings early, through an open access preprint. This led to an international collaboration with teams at the University of Tel Aviv, Israel, and Boston University School of Medicine. Each team was investigating genes required for growth by tumor cells containing abnormal numbers of chromosomes (the thread-

like structures that carry a cell's genetic information) to identify novel therapeutic targets.

Stumpff is an expert in the mechanical control of cell division and the aspects of this process that contribute to the development of conditions like cancer. His colleagues at the University of Tel Aviv were studying aneuploidy—which occurs when one or more chromosomes are added or deleted after cell division—and partners at Boston University were focused on whole genome duplication, where a complete duplicate set of chromosomes is found in a daughter cell after division.

The role of KIF18A proved important in each team's work and contributed to a clearer, larger picture of its role and importance in interrupting the growth of abnormal tumor cells. Critical to the groups' series of discoveries was the early sharing of knowledge and unpublished data, as well as collective troubleshooting of questions and verifying findings. Their efforts yielded strong results—three publications across *Nature* and *Nature Communications* reporting breakthrough findings that could contribute to more targeted and less harmful drug treatments for some cancers.

A confluence of openly sharing data, engaging clinical experts and cancer patients, and harnessing a collaborative approach were key components of the success of this research, notes Stumpff.

"The collective impact of this research collaboration exemplifies the importance of sharing data and enhancing rigor of scientific studies to move fundamental science discovery effectively toward important progress in the fight against cancer," says Stumpff. "This work has the potential to improve approaches for patient treatment in the future—and we are excited to keep it moving."

More information: *Nature Communications* (2021). DOI:

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