Study reveals metformin's role in slowing colorectal cancer cell growth

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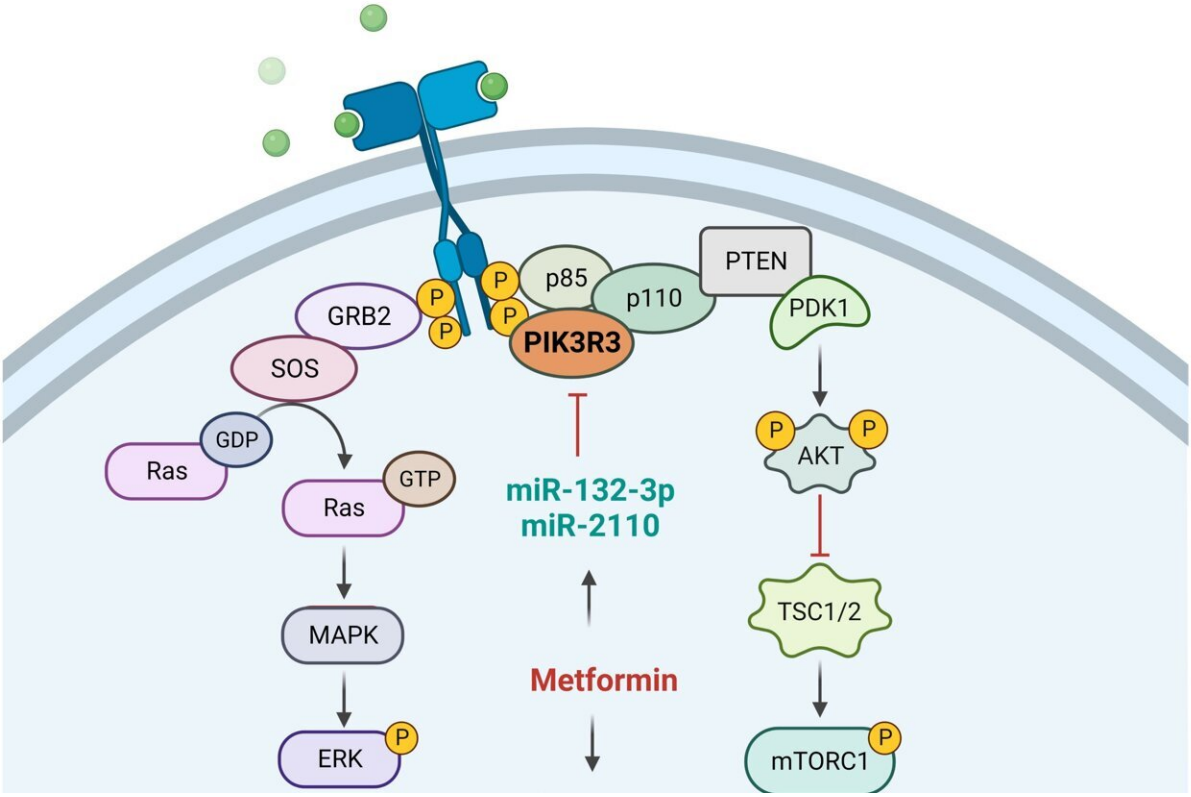

Credit: *Cancers* (2024). DOI: 10.3390/cancers16112055

Flinders University researchers have analyzed how an antidiabetic treatment could help control the growth of tumors, potentially paving the way for the design of better cancer treatments.

The new study investigated what happens when metformin, a type 2 diabetes medication, is used to treat colorectal cancer cells, in the process demonstrating that it could be exploited to develop new cancer therapies. The work is published in the journal *Cancers*.

Previous epidemiology studies show that taking metformin helps protect diabetes patients from developing some forms of cancer including bowel (colorectal) cancer.

The Flinders researchers sought to understand how taking metformin medication impacts cancer cells and how this could help with future cancer treatments.

"Using the latest techniques, we analyzed how metformin helps to stop colorectal cancer cells from growing and multiplying by controlling certain 'pathways' inside the cells that help to regulate growth and division," says lead author Dr. Ayla Orang from Flinders University's College of Medicine and Public Health.

"Importantly, our work has pinpointed that metformin uses small pieces of RNA (called microRNAs) to act as a 'circuit breaker' and turn off certain genes that are involved in cell growth and division, so it is possible that our findings could eventually be used to develop a new targeted cancer therapy.

"In particular, we found that metformin increases the levels of certain microRNAs, like miR-2110 and miR-132-3p, which then target specific genes and slow down the growth and progression of tumors. With this information we may be able to develop RNA-based therapies—new treatments for cancer that target RNA molecules (like microRNAs)," she says.

The research, titled "Restricting Colorectal Cancer Cell Metabolism with

Metformin: An Integrated Transcriptomics Study," used advanced techniques to study microRNAs, and the entire set of genes being expressed in the colon cancer cells, to help understand how metformin affects the cells.

Metformin increased the levels of certain microRNAs (miR-2110 and miR-132-3p) that target a specific gene (PIK3R3).

This process helps to slow down the growth of cancer cells and stop them from multiplying too quickly. Another gene (STMN1) was also targeted by different microRNAs, which led to slower cell growth and a delayed cell cycle.

Senior authors of the study Associate Professor Michael Michael and Professor Janni Petersen say the results are a step forward in our understanding of the way metformin disrupts cancer cell growth and how it could be used to fight cancer.

"Our research provides new insights into the molecular mechanisms of how metformin works, and how we might be able to target genes responsible for turning normal cells cancerous," says Associate Professor Michael.

"This is important because it shows the potential of metformin as a preventive agent for reducing the growth of cancer in the bowel, and the emergence of RNA therapeutics as a promising new avenue for exploring the clinical efficacy of these findings. We need to further investigate the potential therapeutic benefits of targeting specific miRNAs or pathways using RNA-based therapies for the treatment of cancer.

"Having used metformin to unravel metabolism in cancer cells, the next stage of research is focusing on specific cell pathways, which should

lead to animal studies and then human clinical trials."

More information: Ayla Orang et al, Restricting Colorectal Cancer Cell Metabolism with Metformin: An Integrated Transcriptomics Study, *Cancers* (2024). DOI: 10.3390/cancers16112055

Provided by Flinders University