

The communication pathway that controls cell growth and survival

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Cancer cell with the insulin-control mechanism removed. Credit: University of Sydney

Researchers have identified a cell communication pathway that controls cell growth and survival, and the finding could eventually help to develop



treatments for diseases such as cancer and diabetes.

Effective communication, crucial to human relationships, is also essential for the destruction of cancer cells within the body.

In the body's cells, communication involves the transmission of molecular or <u>chemical signals</u>. Just as a faulty antenna results in a garbled TV image, if these molecular signals are distorted, information is lost, and the outcomes can be catastrophic.

Researchers from the Charles Perkins Centre, University of Sydney and Monash University's Biomedicine Discovery Institute have recently identified a cell communication pathway that controls <u>cell growth</u> and survival. The finding could eventually help to develop treatments for diseases such as cancer and diabetes.

Central to the discovery was a powerful combination of cell biology (conducted by Ph.D. students Alison Kearney and Dr. Dougall Norris under the supervision of Dr. James Burchfield and Professor David James, University of Sydney) and mathematical modeling (conducted by Milad Ghomlaghi under the supervision of Dr. Lan Nguyen, Monash University).

"We were able to see the molecules involved in communication, and therefore, see when and where they are needed in the cell, and what happens when things go wrong," Dr. Burchfield said.

Dr. Nguyen described the discovery as a "powerful regulator of the insulin signaling network".

Mathematical modeling researchers used this information to predict how the molecules interact.



These predictions were then tested with further microscopic experiments. When repeated over and over, an understanding of this highly complex system was gleaned.

The findings were published in the journal *eLife* today.

Insulin moderation signal found

Insulin is a potent signal for growth that increases in the body following a meal to promote the storage of sugar in muscle and fat cells. If the insulin signal is inadequate, diseases like diabetes can develop. Conversely, if the signal cannot be adequately switched off, cancer can develop. Understanding where these signaling process can go wrong is therefore crucial for understanding disease development and designing new treatments





Researchers have discovered a crucial mechanism that regulates cell growth and survival. In this image a cancer cell (blue) reacts to removal of this mechanism. This causes critical changes in cell behaviour (yellow). Maths equations central to this work are superimposed across the image. Credit: University of Sydney

"We have discovered a new part of cell <u>communication</u> that is responsible for preventing the insulin signal from overactivating," Dr. Burchfield said.

"The mechanism can be compared to a thermostat in a heater or oven that prevents things from getting too hot. If <u>cells</u> were to lose this mechanism, the growth signal is no longer controlled, and tumors could



develop."

"There is still a lot we can learn about this sensitive signal system: some <u>anti-cancer drugs</u> may even impair the cell mechanism, ironically leading to increased tumor growth and drug resistance. Identifying these mechanisms and understanding how they work will aid the development of better cancer therapies."

Further studies will explore this mechanism in relation to <u>cancer</u> drug resistance, and how this can be leveraged to improve treatment regimes.

More information: Alison L Kearney et al, Akt phosphorylates insulin receptor substrate to limit PI3K-mediated PIP3 synthesis, *eLife* (2021). DOI: 10.7554/eLife.66942

Provided by University of Sydney

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