

Understanding of cell enzyme flipped on its head

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Researchers from Manchester, working with scientists in California, have found that certain molecules long thought to promote cancer growth, in fact suppress tumours, suggesting that therapeutic approaches should aim to restore, rather than block, their activity.

The protein kinase C (PKC) family of molecules are enzymes that facilitate a range of cellular processes, including cell survival, proliferation, migration and death. In the 1980s it was found that PKCs were activated by [cancer](#)-causing phorbol esters, and led to the conclusion that PKCs themselves induced the development of tumours.

However, attempts to develop new treatments that prevent tumour cell growth by blocking the activity of PKCs have had little success. A recent study involving Manchester scientists, the findings of which have been published in the journal *Cell*, has explored the effect of [mutations](#) in PKC on [tumour growth](#).

Dr John Brognard, from the Cancer Research UK Manchester Institute at The University of Manchester - part of the Manchester Cancer Research Centre - said: "Despite phorbol esters being known to cause cancers, we've seen frustratingly little progress when targeting PKCs to stop tumour growth."

The Manchester group collaborated with a team from the University of California, San Diego, to analyse PKC mutations in human cancer cells. They found that most were 'loss of function' mutations, meaning that the

genetic changes stopped PKC from working.

When they corrected these mutations in bowel cancer cells, they saw a reduction in tumour growth, meaning that contrary to our previous understanding, PKC normally acts to block cancer.

"Clinical trials have so far been working on the incorrect assumption that PKC enzymes cause [cancer growth](#). This new insight from our studies has turned current thinking on its head. Looking ahead, instead of blocking PKC activity, new therapies should instead be targeting mechanisms to restore its activity," added Dr Brognard.

More information: Paper entitled "Cancer-Associated Protein Kinase C Mutations Reveal Kinase's Role as Tumor Suppressor" Antal CE et al. (2015) *Cell*. www.cell.com/cell/abstract/S0092-8674%2815%2900002-1

Provided by University of Manchester

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