Surprise discovery made in cancer research

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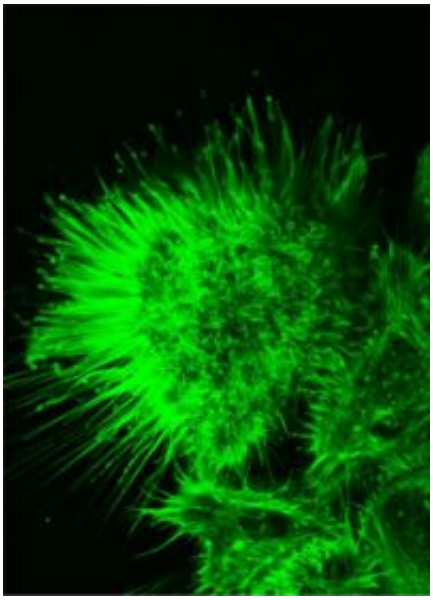

Reducing the expression of some inhibitors of apoptosis (IAPs) led to changes in cell shape and migration. Credit: Krishnaraj Rajalingam

One of the defining characteristics of cancer cells is that they systematically prevent programmed cell death (apoptosis), with which the body guards itself against the proliferation of defective cells. In order to do this, they express so-called apoptosis inhibitors (IAPs) among other proteins.

Many of the cancer drugs currently undergoing clinical trials target IAPs, since if the levels of IAPs are reduced, tumour cells will be destroyed by the body's own self-protecting mechanism or by the chemotherapeutic

drugs. However, as a research group from the Goethe University in Frankfurt, working with scientists at the Universities of Würzburg and Philadelphia have recently discovered, IAPs also have another life: they control cell migration.

Where IAP production is suppressed, there is a significant increase in C-RAF kinase, a crucial member of a signal cascade, which, among other functions, controls cell migration. This also means that when IAP levels are reduced, metastasis may be promoted unexpectedly in the absence of cell death. According to the researchers, drugs to target IAPs should therefore only be used with caution in future.

Dr. Krishnaraj Rajalingam, leader of the Emmy-Noether Group at the Institute for Biochemistry at Frankfurt's Goethe University, claims that these findings have been a great surprise. As he puts it: "Up until now, IAPs were well known for their role in apoptosis suppression, but we now realise that they can also influence other processes like cell migration". The classical mitogenic cascade (MAPK) is triggered by RAS proteins, which are activated by mutations in nearly 20 % of all human tumours. In this signalling cascade, the RAS-protein is immediately followed by the C-RAF kinase, which – as the researchers report in the current issue of 'Nature Cell Biology' – binds strongly to an apoptosis inhibitor (XIAP).

"If we reduce the expression of some IAPs by RNA interference technique, C-RAF kinase increases in both the healthy and the cancerous human cells. As a consequence, the cells alter their form and start to move faster." Co-author Prof. Ulf R. Rapp from the University of Würzburg, who discovered C-RAF kinase 25 years ago, claims that these findings will have a significant influence on cancer therapy.

Prof. Werner-Müller Esterl, Director of Frankfurt's Institute for Biochemistry II and the President-elect of the Goethe University, is

delighted by the success of his young colleague, who took up his post at the university only a few months ago. "These are very exciting results and with such an early success, our new Emmy Noether Group has proved that the University's programme of supporting young independent scientific investigators has once again paid off."

Source: Goethe University Frankfurt, Germany