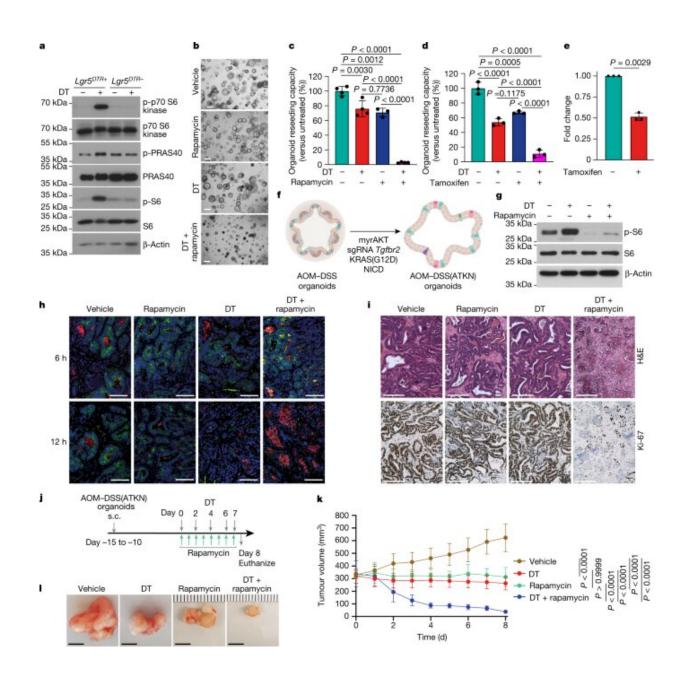


Colon cancer: Dying cancer cells give neighboring tumor cells instructions on how to survive

November 17 2022, by Markus Bernards





Dying tumor cells induce mTOR survival signaling in a paracrine manner. Credit: *Nature* (2022). DOI: 10.1038/s41586-022-05426-1

Colorectal carcinoma is the second most common cause of cancer death in Germany. Although cancer research in recent years has been able to significantly improve early diagnosis and therapy, the resistance of advanced colorectal tumors to common chemotherapies still constitutes a major problem and contributes substantially to the high mortality rate of patients with such tumors.

When chemotherapeutic agents cause <u>colon cancer cells</u> to die, they release ATP (<u>adenosine triphosphate</u>) molecules, the cell's energy currency, as a messenger substance. Researchers led by Professor Florian Greten at Georg-Speyer-Haus have now corroborated this in experiments. This ATP binds to certain receptors (P2X4 purinoreceptors) on the surface of surrounding <u>tumor cells</u>. This activates an important survival signaling pathway in these neighboring cells, which protects them from <u>cell death</u> and makes the tumor resistant to therapy.

The cells killed off by the chemotherapy "warn" their neighboring cells, as it were, and at the same time provide them with a survival strategy. However, if the communication between the dying tumor cells and their neighbors is interrupted—as the scientists were able to show in preclinical models—this raises the efficiency of the chemotherapy many times over, and tumors that were initially resistant respond very well to it.

Dr. Mark Schmitt, first author of the study, explains, "Our research



results demonstrate that—despite years of successful research—unknown mechanisms are still being discovered which show us how perfidiously tumor cells evade therapy. Our results now offer a new and promising starting point for substantially improving the response rate of advanced colorectal carcinomas to common chemotherapeutic agents by means of combination therapy."

Professor Florian Greten, director of Georg-Speyer-Haus and spokesperson for the LOEWE Centre Frankfurt Cancer Institute explains, "We were surprised to see that tumor cells have developed communication mechanisms to the point that even the dying ones play an active role in ensuring their neighbors' survival when under therapeutic 'attack'."

"We hope very much that by interrupting the communication between the cells we can achieve this tremendous increase in the effect of standard therapy in patients as well." The team now wants to work with colleagues at the Frankfurt Cancer Institute to test this new therapeutic concept in patients.

The research was published in *Nature*.

More information: Mark Schmitt et al, Colon tumour cell death causes mTOR dependence by paracrine P2X4 stimulation, *Nature* (2022). DOI: 10.1038/s41586-022-05426-1

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