

Cancer Cells Can Cooperate to Grow

When deprived of amino acids, cancer cells cooperated to extract and share them from their environment.

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Cancer cells, which can grow and divide rapidly, often compete with each other and with surrounding normal cells for nutrients, oxygen, and other substances. However, studies have suggested that cells in tumors may sometimes need to cooperate to survive. A better understanding of how cancer cells cooperate could provide new targets for treatments. But this aspect of tumor growth has not been studied in depth.

In a new study, funded in part by NIH, a team led by Dr. Carlos Carmona-Fontaine from New York University investigated a peculiar characteristic of cell growth called the Allee effect. In the Allee effect, the viability of a cell population drops below a certain cell density. This suggests the cells are somehow cooperating to survive. The study appeared on February 19, 2025, in [Nature](#).

To look at whether cancer cells exhibit an Allee effect, the researchers grew several types of cancer cells with various restricted nutrients. They found that depriving the cells of an amino acid that the cells need to grow appeared to create an Allee effect. Only higher-density cell populations survived under these conditions. This indicated that a cooperative survival strategy had kicked in.

The team then further explored how cancer cells might be cooperating to survive in low-amino acid environments. Chains of amino acids called oligopeptides can be broken down by cells into individual amino acids. The scientists found that cancer cells released substances into their immediate environment that broke nearby oligopeptides down. Because this occurred outside the cancer cells, any cell in the immediate vicinity could use the resulting free amino acids.

Further experiments found that a single enzyme called CNBP2 was needed to extract the amino acids from oligopeptides. When the researchers blocked CNBP2 activity in a variety of cancer cell types, the cells could no longer break down oligopeptides, and the populations died.

The team next tested whether blocking CNBP2 could slow or stop tumor growth in living animals. They implanted mice with a type of lung cancer cell known to be sensitive to amino acid deprivation and fed the mice a diet designed to reduce circulating levels of these nutrients. Mice injected with a drug called bestatin, which blocks CNBP2, had substantially smaller tumors than mice injected with an inactive control compound.

Even more dramatic results were seen when the team used techniques to delete the gene that produces CNDP2 from cancer cells. When fed the special diet, a significant number of the mice injected with these cells didn't develop observable tumors. These results suggest that inhibiting CNDP2 may be a promising therapeutic approach for cancer types sensitive to amino acid deprivation.

"Competition is still critical for tumor evolution and cancer progression, but our study suggests that cooperative interactions within tumors are also important," Carmona-Fontaine says. "Thinking about [these] mechanisms that tumor cells exploit can inform future therapies."

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