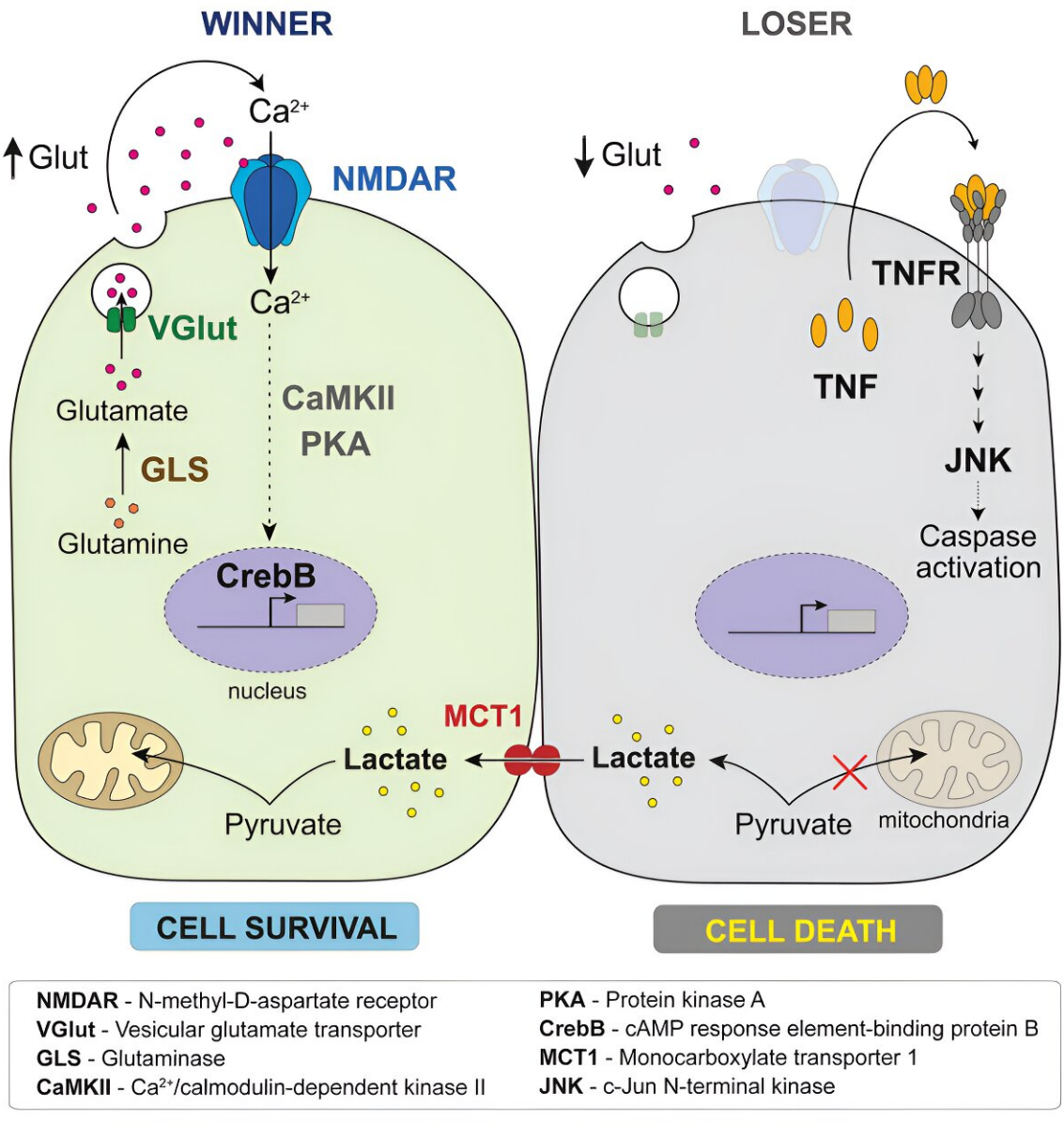
Cancer cells pretend to be 'super fit' to outsmart normal cells and invade the body

July 24 2024



Credit: *Developmental Cell* (2024). DOI: 10.1016/j.devcel.2024.06.022

Scientists have discovered that some cancer cells pretend to be "super fit" to fool normal healthy cells into giving them their nutrients, allowing them to expand and spread around the body.

A team from The Institute of Cancer Research, London, found that "cheating" cancer cells develop the ability to hijack the body's natural cell competition process, which ensures that substandard cells do not accumulate but instead are killed and removed.

The researchers, based in the Breast Cancer Now Toby Robins Research Center at The Institute of Cancer Research (ICR), hope that having a better understanding of how the cell competition mechanism is exploited by cancer cells will lead to new ways of treating the disease.

Normally, this evolutionary principle of "survival of the fittest" is a crucial quality control mechanism for maintaining tissue health and function. However, defects in cell competition can result in the retention of damaged or dangerous cells, potentially triggering the formation of tumors.

'Winners' and 'losers'

Until now, the way in which fitness disparities are measured across groups of cells and how it is determined which cells become winners and survive and which ones become losers and are killed off, has not been fully understood.

In this study, published in the journal *Developmental Cell*, the ICR team discovered that differing levels of extracellular glutamate, a crucial

building block and messenger molecule in the body, regulates competition between cells. They found that cells with a lower secretion of glutamate are earmarked as losers when surrounded by normal healthy cells.

When this happens, the loser cell starts to donate its nutrients to its fitter neighbors. In doing this, it actively contributes to the growth of the winner cells and consequently dies in an altruistic fashion.

Importantly, they also found that the process can be exploited by cancer cells, which cheat the system by pretending to be super-fit and increasing their glutamate production. This allows them to expand and spread at the expense of surrounding normal cells.

Understanding chemotherapy resistance

Furthermore, when cell competition takes place between cancer cells, it can lead to some cancer cells developing resistance to chemotherapy or other targeted therapies. These resistant cells survive and multiply, making treatment less effective.

This new research, which shows another way that cancer can hijack healthy cells and tissue within its surrounding environment, reinforces the importance of research to unravel and disrupt cancer ecosystems, a key part of the ICR's research strategy.

Lead study author Professor Pascal Meier, Professor of Cell Death and Immunity at The Institute of Cancer Research, London, said, "While cell competition generally serves as a quality control mechanism, this process can be highjacked by cheating cancer cells, which can pretend to be 'super-fit' by secreting higher levels of extracellular glutamate.

"This causes the normal healthy cells surrounding the cancer cells to be

deemed to be less fit and they start to donate their nutrients to their cancer neighbors. This effectively makes the cancer cells super fit and allows them to expand and spread at the expense of surrounding normal tissue.

"In addition, competitive interactions between cancer cells can also contribute to the cancer developing resistance to drug treatment.

"By better understanding cell competition and how cancer hijacks it, we hope to ultimately design new therapeutic approaches to treat cancer and stop it becoming resistant to treatment so people can live well for longer, even with advanced disease."

Professor Kristian Helin, chief executive of the Institute of Cancer Research, London, said, "Treating cancer successfully is more difficult once it has spread. The results of this research further our understanding of the biology of cancer and how cancer cells can outcompete normal cells and spread around the body.

"Discovery science like this reveals the nature of cancer cells, which is vital to the identification of new therapeutic targets that could form the basis of future cancer treatments."

Ben Atkinson, head of research communications at Breast Cancer Now, said, "While more research is needed to see how these findings could help develop new treatments for people with breast cancer, this exciting study deepens our understanding of cell competition and its role in cancer spread and survival.

"In the U.K., one woman is diagnosed with breast cancer every 10 minutes and, sadly, about 11,500 people die from the disease each year. Research like this could pave the way for kinder and more effective treatments which are urgently needed."

More information: Carmo Castilho Soares et al, Autocrine glutamate signaling drives cell competition in Drosophila, *Developmental Cell* (2024). DOI: 10.1016/j.devcel.2024.06.022