



PRESS RELEASE

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A “Mirror” Amino Acid Against Certain Tumors

Researchers from UNIGE and Marburg show that D-cysteine, the “mirror” form of cysteine, selectively targets certain cancer cells.

Most anticancer treatments also damage healthy cells, causing sometimes severe side effects. To limit these adverse effects, scientists are striving to develop therapies that can target only cancer cells. An international team, led by the Universities of Geneva (UNIGE) and Marburg, has discovered that a “mirror” form of cysteine, a sulfur-containing amino acid, strongly slows the growth of certain tumors while sparing healthy cells. Imported preferentially into certain cancer cells, this amino acid blocks vital processes such as respiration and DNA synthesis. In mice, this mechanism markedly slows the growth of aggressive breast tumors, paving the way for a simple, targeted, and innovative therapy. These findings are published in *Nature Metabolism*.

Amino acids are small basic molecules used to build proteins, much like beads strung into a necklace. There are 20 that make up the proteins of all living organisms. They exist in two forms: L (levorotatory) and D (dextrorotatory). These two forms are non-superimposable mirror images, like our left and right hands. They share the same chemical composition but have a different spatial geometry. Our bodies use almost exclusively the L-forms, particularly to make proteins. The D-forms, on the other hand, are very rarely used.

A cancer-cell-specific transporter

The team led by Jean-Claude Martinou, Honorary Professor in the Department of Molecular and Cellular Biology at the UNIGE Faculty of Science, investigated the role of different amino acids in cancer cell growth. They discovered that the D-form of the amino acid cysteine (D-Cys), which contains a sulfur atom, significantly reduces the proliferation of certain cancer cells in the lab, while having no effect on healthy cells.

“This difference between cancer cells and healthy cells is easily explained: D-Cys is imported into cells via a specific transporter that is present only on the surface of certain cancer cells,” explains Joséphine Zangari, a PhD student in Professor Martinou’s laboratory and first author of the study. “In fact, we observed that if we express this transporter on the surface of healthy cells, those cells stop proliferating in the presence of D-Cys.”

Thanks to a collaboration with the team of Professor Roland Lill at the University of Marburg, the scientists uncovered how D-Cys exerts its toxicity: “It blocks an essential enzyme called NFS1, located in the



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mitochondria – the cell’s ‘powerhouses’. This enzyme plays a key role in producing iron-sulfur clusters, small structures that are indispensable for many processes such as cellular respiration, DNA and RNA production, and maintaining genetic integrity,” explains Roland Lill. By inhibiting NFS1, D-Cys therefore shuts down a cascade of vital processes in cancer cells: respiration decreases, DNA is damaged, and the cell cycle halts.

Slowed tumor growth in mice

To evaluate the therapeutic potential of this approach, the researchers administered D-Cys to mice with highly aggressive, hard-to-treat mammary cancer. The results were encouraging: tumor growth slowed markedly, without major side effects in the animals. “This is a very positive signal – we now know it’s possible to exploit this specificity to target certain cancer cells,” says Jean-Claude Martinou. “However, we still need to determine whether D-Cys could be administered at effective doses in humans without causing harm.”

If this proves to be the case, D-cysteine could offer a simple, innovative, and selective therapy for cancers that overexpress the relevant transporter. It could also play a role in preventing metastasis, a critical step in the progression of the disease.

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