Cancer uses stem cells as a shield to escape drug attacks

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Cancer cell to stem cells: the drugs are coming. Credit: delgrossodotcom, CC BY-NC-SA

Chemotherapy is one of the most important treatments for all types of cancer. It involves the use of drugs that kill abnormally multiplying cells. The therapy uses one or more drugs in combination and has been practised since the 1950s, along with surgery and radiation therapy.

But chemotherapy does not always work. Doctors observe that even if the treatment is initially successful, patients often suffer a relapse. Sometimes this happens even after multiple sessions of chemotherapy. It seems some cancer cells manage to escape and hide within the body, allowing the disease to eventually return.

A dance of proteins

A recent study published in the journal *Cancer Cell* throws light on how cancer cells manage to dodge chemotherapy. Deng-Li Hong, professor of pathophysiology at Jiao Tong University School of Medicine, and his colleagues discovered that some cancer cells kidnap the patient's own stem cells.

With the onset of acute lymphoblastic leukaemia, Deng-Li and his associates found that some cancer cells hide in the bone marrow, where blood stem cells are located. Inside the bone marrow, their aim is to find some way to become resistant to cancer drugs, which they manage by the interaction of a series of proteins.

First, cancer cells give off signalling proteins called cytokines, which attract certain kinds of stem cells known as mesenchymal stem cells. After luring them, cancer cells form a nest within the stem cells and coax them to grow.

Cancer cells are aiming to harvest a special protein, called furin, from those mesenchymal stem cells. Furin has the unique ability to activate other proteins by chewing away useless parts of a protein, fine-tuning its structure and switching it on. Cancer cells use furin from the hostage stem cells to activate the master protein GDF15. GDF15 then activates the cancer cell's defense system, making it resistant to chemotherapy.

Without defence

While the experiments were mostly performed in mice, Deng-Li found that the hostage situation also occurs in humans. Leukaemia patients who did not respond well to chemotherapy possess cancer cells surrounded by hostage cells. These cancer cells have already switched on GDF15 production, causing resistance to chemotherapy.

This doesn't mean giving up on chemotherapy just yet. Some leukaemia patients respond well to chemotherapy and they don't show any trace of the hostage situation.

Better understanding of how cancer cells resist drugs may help us find new weapons. If cancer cells depend on GDF15 to escape drugs, maybe drugs that also inhibit GDF15 could be added to the mix of drugs given in chemotherapy.

"This work gives us a handle on treatment regimes for patients of ALL," Deng-Li said. "We could possibly use agents that prevent the hostage situation during the early stages of chemotherapy."

GDF15 has been found to play a role in other types of cancers, such as pancreatic cancer and multiple myeloma. It could be part of the reason why chemotherapy doesn't always work in these cancers as well.

Source: The Conversation