

Aggressive cancer cells halted

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Zebrafish-human communication shows that cancer cells lacking a signaling protein are less able to develop aggressive metastatic properties. This discovery has been made by Claudia Tulotta. PhD defence 14 June.

Cancer cells create favourable circumstances for themselves in the human body. They do this by manipulating the body's direct environment, like immune cells, so that they do not attack but rather assist cancer cells. Scientists want to know how this interaction between cancer and immune cells works. This knowledge may provide possible starting points for halting the development of cancer.

Tulotta studied this interaction not in the [human body](#), but in zebrafish embryos. Zebrafish has been increasingly used as a model to study cancer biology and similarities between zebrafish and human immune system are present. Tulotta injected fluorescent human cancer cells into the blood circulation of transparent two-day-old zebrafish embryos, with fluorescent blood vessels and [immune cells](#). This made it possible for her to track the development and spread of the cancer cells in the living organism, while simultaneously interacting with surrounding zebrafish cells.

She studied two specific proteins. One – CXCR4 – is a product of cancer cells that is found on the surface of the cell. It plays an important role in the movement of cancer cells in response to another [protein](#), CXCL12. This second protein can be found in both zebrafish and humans. It is produced by organs where tumor metastases are formed.

Tulotta: 'I have shown that cancer cells that produce a lot of CXCR4 behave more aggressively than cells with less CXCR4, in the [zebrafish model](#). Aggressive cells leave the bloodstream and penetrate local tissues, where they can multiply. You can see this as an early step in the formation of metastases.

Tulotta applied two different methods to block the

function of CXCR4. First, a pharmacological method: using a recently discovered inhibitor that prevents the protein from doing its work. The second method was genetic: CXCR4 gene function was impaired resulting in no protein production. Using both approaches, the aggressive behavior of cancer cells was halted.

Tulotta also carried out tests on zebrafish embryos that do not produce the CXCL12 protein. The [cancer cells](#) introduced as part of the experiment did not demonstrate aggressive behaviour in these fish. 'This finding suggests that human and zebrafish cells communicate with each other, making the zebrafish embryo model suitable to study [human](#) tumor behavior and interaction with the surrounding microenvironment.'

Tulotta believes there are opportunities for testing new CXCR4 inhibitors as a possible cancer treatment. The research may also be applied to drug development for other forms of cancer. Inhibiting CXCR4 was also shown to prevent metastasis initiation of Ewing sarcoma, a very rare form of bone cancer, in zebrafish.

Provided by Leiden University

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