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Anti-cancer lymphatic drugs show potential

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Researchers at the University of Auckland are using zebrafish embryos to investigate potential medicines that will inhibit the spread of some cancers via the lymphatic system.

The latest experiment used the zebrafish embryos to screen thousands of compounds to identify four potential anti-cancer drugs. The results were recently published in the journal, *Molecular Cancer Therapeutics*.

"All four compounds had an impact, but one stood out as a particularly good option and that was then tested in a mammalian model," says lead researcher Dr Jonathan Astin. "It was successful in both zebrafish embryo and mammalian models. These could be used as potential anti-cancer therapeutics."

Some cancer tumours use the lymphatic system and lymph nodes to spread and multiply. For instance, many solid cancers metastasise or spread the disease this way, says Professor Phil Crosier who is leading this work with zebrafish. "We are working on drugs that will block that spread within the lymphatic system.

"This work explores lymphatics and the molecular basis of lymphatic system development", he says. "We were doing a large scale screen for compounds that inhibit the development of the lymphatic system."

"For those diagnosed with solid cancer tumours the compounds have the potential to prevent the disease from spreading into the lymphatic system and might be given alongside chemotherapy," says Professor Crosier.

"Four drugs were used in zebrafish and then taken and tried in mammalian models/mice. All four drugs blocked mouse lymphatic development, but one blocked disease spread in the lymphatic system," he says. "We found some compounds that work and established good proof of principle in the use of zebrafish."

These drugs were also evaluated in mammalian cancer systems in collaboration with researchers at the Auckland Cancer Society Research Centre.

"These big numbers allow us to weed out a lot of false positives and negatives using the zebrafish models," says Dr Astin. "Then we can take the rest into mammalian models with their in vivo efficacy already proven."

"Repurposing drugs in this way, using those that are already FDA approved, means we can take drug development further, faster" says Professor Crosier. "The successful drug taken to mouse model was a natural product found in plants such as broccoli, capers and tea."

"Using the zebrafish model before mammalian translation provides a much improved screening technique with this system."

All of the drugs that worked in zebrafish had an anti-lymphatic function in mice and can be investigated further for their potential in other uses, for example in corneal transplants.

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