Worm 'cell death' discovery could lead to new drugs for deadly parasite

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Drs. Erinna Lee (left) and Doug Fairlie from the Walter and Eliza Hall Institute in Melbourne, Australia, are studying the cell death pathway in parasitic worms. Credit: Walter and Eliza Hall Institute

Researchers from the Walter and Eliza Hall Institute have for the first time identified a 'programmed cell death' pathway in parasitic worms that could one day lead to new treatments for one of the world's most serious and prevalent diseases.

Dr Erinna Lee and Dr Doug Fairlie from the institute's Structural Biology division study programmed cell death (also called apoptosis) in human cells. They have recently started studying the process in schistosomes, parasitic fluke worms responsible for the deadly disease schistosomiasis.

Dr Lee said that the group has shown that, unexpectedly, the cell death machinery that exists in fluke worms is remarkably similar to the cell death pathway in human cells. The finding was recently published in the journal Proceedings of the National Academy of Sciences.

"We found that schistosomes have a complex cell death mechanism that relied on a delicate balancing act of pro-survival and pro-death molecules, just like in humans," Dr Lee said. "Using the Australian Synchrotron, we also determined that the three-dimensional structure of a key schistosome cell death molecule was very similar to the protein which controls the process in humans. This structure is important because it will potentially guide future efforts to design drugs that target the schistosome cell death pathway."

More than 700 million people worldwide are at risk of schistosomiasis and 200 million people are currently infected, 85 per cent of whom live in Africa. Each year, an estimated 200,000 people die from the disease. The parasitic worm is carried by freshwater snails in contaminated water systems, and causes damage to the spleen, liver and other organs that can be fatal.

Dr Fairlie said that there is only one drug widely used for treating schistosomiasis, and concerns about the potential for drug resistance have increased the urgency for new drug targets and treatments. "Schistosomiasis ranks with malaria as a major source of human disease," Dr Fairlie said. "More than 2 billion people globally are at risk of parasitic worm infection, and we need to invest in the development of new drugs and vaccines, particularly as there are very few options currently available."

In the 1980s, scientists from the Institute and elsewhere discovered that defects in the cell death pathway were associated with cancer development. Dr Lee said the team are currently exploring the possibility

that so-called 'BH3 mimetic' compounds such as ABT-737, discovered by biotechnology company Abbott, could also have a niche application for the treatment of parasitic worm diseases such as schistosomiasis. BH3 mimetics target the cell death pathway in humans and are currently being trialled as anti-cancer agents.

"The Bcl-2-regulated cell death pathway is currently being investigated as a therapeutic target for the treatment of some cancers," Dr Lee said. "We have found that a BH3-mimetic compound called ABT-737 binds to at least one schistosome pro-survival protein, suggesting it is feasible that BH3-like molecules could also be developed for treating schistosomiasis, and potentially other parasitic worm infections."

While the discovery leads to exciting new possibilities for the treatment of parasitic worm diseases, Dr Fairlie said there is still a lot to be understood about the cell death process in fluke worms before this becomes a reality. "Though we have found that this cell death pathway exists in the parasite, we don't yet know how important it is for the survival of the worm, or what the effect of drugs targeting the pathway will be. But we are excited about the possibility of developing an entirely new treatment strategy for schistosomiasis, which is a significant disease burden in developing countries," he said.

Provided by Walter and Eliza Hall Institute