Fight against cancer gets help from salmonella bacteria

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Scientists have uncovered a novel mechanism by which Salmonella bacteria infect humans and say the discovery could potentially be exploited to kill cancerous cells.

In an article published in the journal *Science*, researchers from the University of Glasgow and the University of Massachusetts Medical School, describe how Salmonella uses caspase-3, an enzyme produced by the infected host cell, to deliberately increase inflammation at the site of infection.

Normally, caspase-3 plays an important role in the body by removing damaged or malfunctioning cells from the system through a process known as 'Programmed Cell Death'. It is this process of cell death that is often defective in cancer cells.

The researchers, Dr. Dónal Wall from the University of Glasgow and Dr. Srikanth Chittur and Professor Beth McCormick from the University of Massachusetts Medical School, demonstrate that the Salmonella bacterial protein SipA is responsible for inducing caspase-3 activation within the host cell.

Dr. Wall, a lecturer in microbiology in the Institute of Infection, Immunity & Inflammation, said: "The novelty of this research is that we show how the bacteria are undermining the host cell and getting it to process the bacterial toxins into smaller functional units.

“The bacteria deliver large toxins into the cell and then use the host enzyme, caspase-3, to divide these proteins. These toxins can then go to different parts of the cell to carry out their individual functions.

“It is very efficient: the bacteria deliver one toxin and, with the inadvertent help of the host, this one toxin can become many when inside the cell.”

Caspase-3 only cuts specific sequences within proteins known as caspase-3 cleavage sites. Notably, caspase-3 cleavage sites are found in several Salmonella proteins, however these appear to be restricted to proteins that play a role in bacterial entry or proteins that are used to overpower the host cell, indicating this may be a general strategy employed by the bacteria to aid with processing bacterial toxins.

Dr Wall added: “Although this work is important for the field of host-pathogen interactions it also highlights a process that could be exploited in cancer therapeutics to activate Programmed Cell Death in cells in which the early stages of this process are defective.”

Altered and attenuated forms of Salmonella have already been used by other scientists to target certain types of cancer cells in the lab but this latest research, supported by research funding body Tenovus Scotland, has the potential to make such treatments more effective.

More information: The paper Salmonella Pathogenesis and Processing of Secreted Effectors by Caspase-3 is available online at *Science*.

Provided by University of Glasgow