Fly antimicrobial defence system doubles as tumour-killer

July 30 2019, by Emily Packer

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An antimicrobial agent called Defensin kills tumour cells and shrinks tumour size in fruit flies, with help from a pathway that flags the cells for destruction.

These findings, published in *eLife*, provide the first evidence in live animals that antimicrobial peptides (AMPs), which help protect against infection, also defend against cancer. If confirmed in further studies in animals and humans, the discovery could one day lead to new cancer treatment strategies.

Previous studies have shown that AMPs kill cancer cells grown in the laboratory, but the findings had not been confirmed in living creatures.

"We used the fruit fly Drosophila melanogaster to investigate whether the machinery that is best known for its role in the recognition and elimination of harmful microbes is also capable of recognising malignant cells in a living organism and eliminating them in a similar manner," says lead author Jean-Philppe Parvy, a postdoctoral fellow at Cancer Research UK's Beatson Institute in Glasgow.

Their experiments showed that tumour-prone fruit flies produce more Defensin than their normal counterparts. Defensin interacts with dying tumour cells in the animals. Shutting down Defensin in the tumour-prone animals leads to tumour growth, suggesting that Defensin is actively killing the cells while sparing normal cells.

Next, Parvy and his colleagues showed that Defensin recognises tumour cells in the same way it recognises harmful microbes. The fly version of a protein called Tumour Necrosis Factor helps flag the tumour cells for destruction and makes the cells more sensitive to Defensin's attack. It does this by bringing a protein called phosphatidylserine to the surface of the tumour cells. Defensin then binds to phosphatidylserine-rich areas on the tumour cells and kills them.

"Our results reveal an anti-tumour role for Defensin in flies and provides insights on the molecular mechanisms that make tumours sensitive to the killing action of AMPs," Parvy explains.

Further research is now needed to see if these same mechanisms are at work in mammals and humans.

"Our work may have a significant translational potential for cancer research in mammalian models as it raises the possibility that human AMPs could have anti-tumour effects similar to those of Defensin in flies," says senior author Julia Cordero, Senior Research Fellow at the Institute of Cancer Sciences, University of Glasgow, UK. "If future work confirms this, natural AMPs or chemically designed analogues might be used in anti-cancer therapeutics."

More information: Jean-Philippe Parvy et al, The antimicrobial peptide defensin cooperates with tumour necrosis factor to drive tumour cell death in Drosophila, *eLife* (2019). DOI: 10.7554/eLife.45061

Provided by eLife