Scientists discover rogue messengers that hinder body's immune response to cancer

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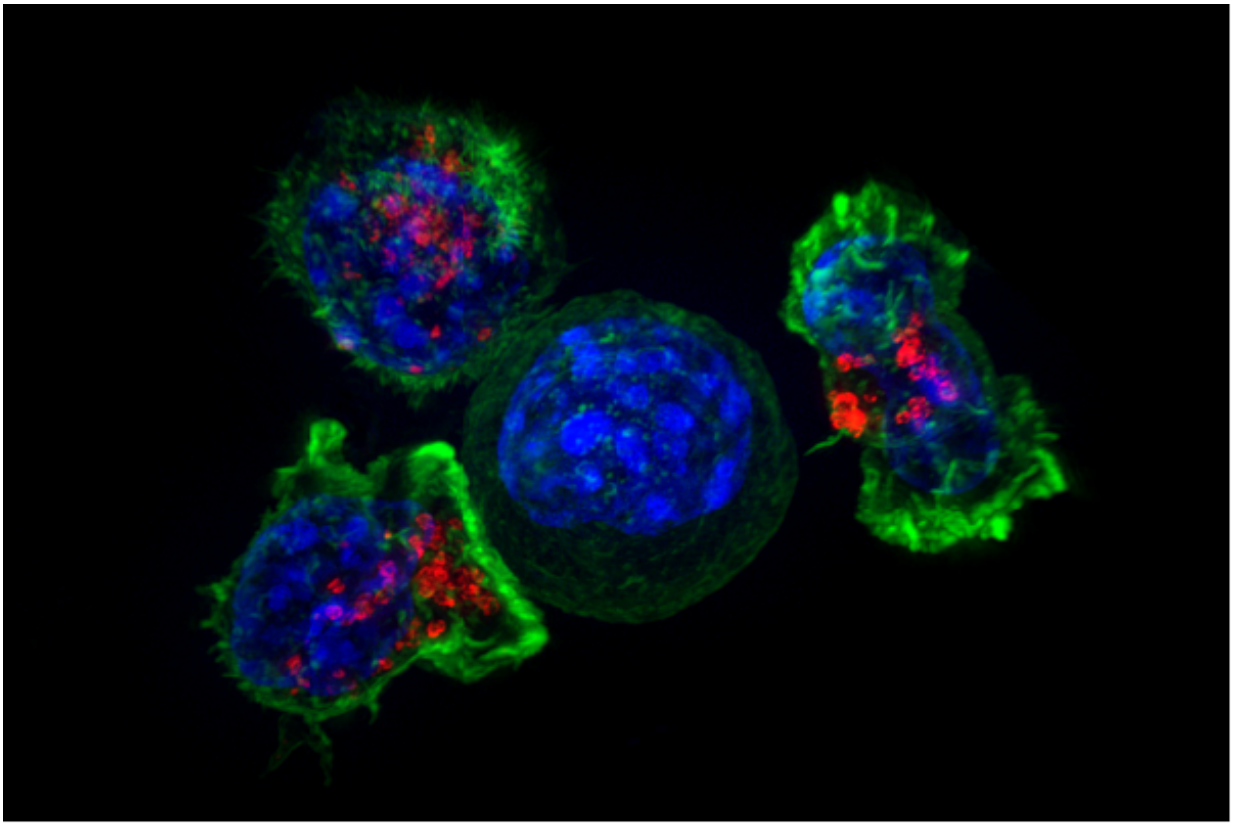

Killer T cells surround a cancer cell. Credit: NIH

Researchers from Trinity College Dublin have made a discovery around treatment-resistant breast cancer that may turn the phrase, 'don't shoot the messenger', on its head. The scientists have found that cell to cell

messengers released by cancer cells which are not responding to treatment, can negatively affect the body's immune system response against the cancer. They have also discovered a possible way for doctors to identify those patients most at risk of treatment resistance which allows them to choose the best possible treatment for each patient.

Essentially, the messengers were found to be bearers not of bad news, but of immunosuppressive agents which inhibit the body's immune system from fighting against the cancer. Making a bad situation worse, when the messengers were received by other cancer cells, they made those cells also release immunosuppressive agents, thereby multiplying the effect.

But how do you find out which patients have these rogue messengers and are therefore more likely to be resistant to treatment? The research which was published in the journal *Oncoimmunology*, showed that the messengers, called extracellular vesicles or EVs, can be detected in patients' blood and therefore, this could possibly be used by doctors to predict whether cancers will respond to treatment before it is given.

The researchers, led by Professor Lorraine O'Driscoll at the School of Pharmacy & Pharmaceutical Sciences at Trinity, studied the HER2-overexpressing type of breast cancer. This type of cancer can be treated with novel targeted therapies, one of the best known being trastuzumab (Herceptin). For some patients, however, such targeted treatment is not effective. This is because some tumours that initially respond to treatment cease to do so after some time (i.e. acquire resistance), while others never respond (i.e. are innately resistant).

Having found out the activity of the rogue messengers, the researchers looked for these EVs containing immunosuppressive material in breast cancer patients' blood. The blood, taken before treatment, of patients who then did not respond well to treatment carried EVs loaded with

much more immunosuppressive material than the blood of patients who went on to respond well. This suggests that testing EVs in blood could help doctors distinguish between patients that will respond and those who will not benefit.

Speaking about the potential next steps from this discovery, lead author of the study, Professor in Pharmacology at Trinity, Lorraine O'Driscoll said: "This study sets the proof-of-principle basis for the development of a predictive tool for doctors, which would be able to tell from a blood sample whether the patient would respond to targeted treatment before it is given. This would help ensure that only those patients that would benefit from this type of treatment would be given it, while non-responders would not receive unnecessary treatment, and associated side-effects and would instead be given a different, likely more effective treatment to begin with."

Professor O'Driscoll continued: "The study also suggests that patients that do not respond to this treatment would very likely benefit from therapies that enhance the immune response against the tumour, as lack of response to treatment appears to be related to immune system suppression."

More information: Vanesa G. Martinez et al, Resistance to HER2-targeted anti-cancer drugs is associated with immune evasion in cancer cells and their derived extracellular vesicles, *OncoImmunology* (2017). DOI: 10.1080/2162402X.2017.1362530

Provided by Trinity College Dublin