

Microparticles may be breast cancer's secret weapon to evade the immune system

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Video Abstract

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Abstract

Researchers from Australia have uncovered a unique way that drug-resistant breast cancer cells trick the immune system, potentially allowing them to spread through the body unchecked. The mechanism relies on cancer cells' shedding of microparticles, tiny sacs filled with protein and nucleic acids, from their membranes. It's been shown that these sacs bind with other cells to transfer drug resistance, but now it's clear that they also use the particles to shut down the immune system. To find out what causes this inhibition, the researchers focused on white blood cells known as macrophages. These cells are found throughout the body and mainly work to destroy pathogens and other harmful cells by engulfing them. But this key defense mechanism fails as breast cancer progresses. Because microparticles help cancer cells spread harmful traits to recipient cells, the researchers thought these particles might also play a role in immune evasion. To test this hypothesis, the group collected microparticles from drug-resistant and non-resistant breast cancer cell lines and non-cancerous cell lines and then mixed them with macrophages. Using in vitro assays, they found that macrophages exposed to microparticles from the drug-resistant cancer cells were less likely to travel towards chemoattractants, a type of chemical that would normally lure them in. Macrophages exposed to microparticles from non-cancerous cells or cancer cells that weren't drug resistant showed no such impairment. In a surprising role reversal, the drug-resistant cancer cells were able to engulf the macrophages. Exposing non-resistant cancer cells to microparticles from resistant cells allowed them, too, to destroy the macrophages, giving a clue into how cancer cells use multiple strategies to thrive. The microparticles also caused the macrophages to secrete pro-inflammatory molecules, which can potentially attract additional macrophages and other immune cells, creating a vicious cycle that helps cancer to spread. This directed progression of macrophage shut down, destruction, and subsequent immune cell recruitment shows just how sophisticated cancer cells can become in finding ways to establish a foothold in the body. Fighting cancer will require researchers to become equally adept in devising new weapons for battle.