

Scientists identify natural defence cells that impede chemotherapy treatment

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As part of the body's front-line defences against infection, white blood cells called macrophages often infiltrate tumours in great numbers. However, according to new research published in the scientific journal *Cancer Discovery*, these cells can make tumours more resistant to chemotherapy treatment.

The international team of scientists involved in the discovery have shown that a depletion of macrophages (TAM) in progressing breast tumours improved the anti-tumour effectiveness of paclitaxel, a chemotherapeutic agent.

When the team treated TAM-depleted tumours (which also had fewer blood vessels, greater numbers of cytotoxic T [cells](#) and more signs of tumour destruction) with paclitaxel they witnessed a greater reduction in the size of the tumour.

"Our findings offer a new approach to improving the efficacy of established [chemotherapy](#) agents," said Dr Donal Brennan from the UCD Conway Institute, who, along with his UCD colleague Professor William Gallagher, was part of the international team led by Professor Lisa Coussens from the University of California San Francisco.

"In addition to identifying a novel therapeutic agent, we have also developed a predictive inflammatory signature which will identify patients likely to respond to anti-CSF1R therapy," said Dr Brennan.

"The inflammatory signature will hopefully allow us to run biomarker driven clinical trials, which should allow for rapid translation of these findings into breast cancer clinics over the next few years."

Commenting on the significance of the findings, a news article in the leading scientific journal *Nature* said: these results "add weight to an emerging compelling case for deciphering the complexity of leukocyte infiltrates in breast cancer." And, "this may provide clinically relevant indications of the

likely response to chemotherapy and thus patient survival."

The predictive signature developed during this research project took advantage of a novel image analysis approach, IHC-MARK, developed by Professor Gallagher's team at the UCD Conway Institute, to quantify inflammatory cell density in cancer tissues. The method is currently being licensed to the spin-out company, OncoMark Limited, which is utilising such automated image analysis approaches for development of companion diagnostics.

More information: "Leukocyte Complexity Predicts Breast Cancer Survival and Functionally Regulates Response to Chemotherapy" published in *Cancer Discovery*. David G. DeNardo; Donal J Brennan, Elton Rexhepaj; Brian Ruffell; Stephen L. Shiao; Stephen F. Madden; William M Gallagher, Nikhil Wadhvani; Scott D. Keil; Sharfaa A. Junaid; Hope S. Rugo; E. Shelley Hwang; Karin Jirstrom; Brian L. West; and Lisa M. Coussens.

Provided by University College Dublin

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