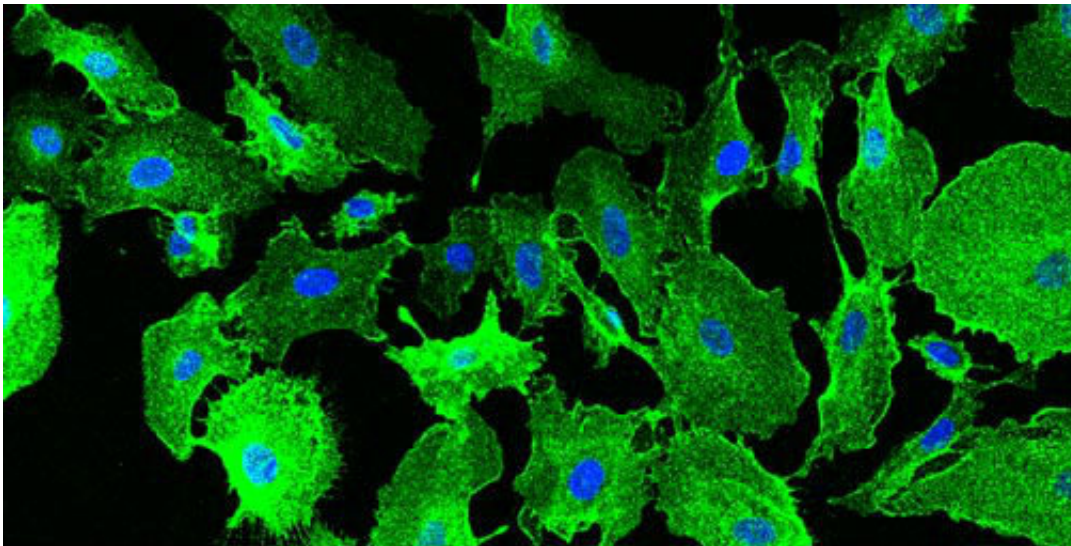


The battle between cancer and the immune system—who switches the off signals off?

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Research centred on PDL1, an ‘immune checkpoint’ protein and prominent target of cancer immunotherapies. Credit: University of York

Scientists have discovered key new information about how to boost our immune system's fight against cancer.

Their research revealed a trick that healthy [cells](#) use to prevent undue suppression of the immune response.

The study, by scientists from the University of York, the Hull York Medical School and Barts Cancer Institute, Queen Mary University of London, could lead to improved use and management of cancer

immunotherapies.

Our immune system has a remarkable potential to clear pre-cancerous or [cancer cells](#). However, often cancer cells develop the ability to emit 'off' signals to immune cells and fool them into apathy.

Immune checkpoints

These 'off' signals are called 'immune checkpoints'. In the last five years, the way we treat cancer has been transformed by developing drugs that try to stop these off signals and reawaken our immune system.

The research centred on PDL1, an 'immune checkpoint' protein and prominent target of cancer immunotherapies.

The researchers were inspired by the fact that immune checkpoints are not just present in cancer cells. They exist naturally in our body to prevent [immune cells](#) from prolonged or unnecessary immune responses, for example autoimmunity (where our immune system attacks our own cells).

Based on this observation, rather than exploring how immune checkpoints are controlled in cancer cells, the researchers went back and asked how the immune checkpoint protein PDL1 is controlled in normal non-cancerous cells.

By understanding the normal biology of this important drug target, the investigators hoped to gain new insight into ways of "rewiring" cancer cells in a manner that would render them susceptible to [immune attack](#).

Immunologist Dr Dimitris Lagos of the Centre for Immunology and Infection, which is part of the University of York's Department of Biology and Hull York Medical School, led the research.

Dr Lagos said: "We wanted to find mechanisms that suppress the levels of PDL1 in [healthy cells](#). Remarkably, we discovered that miR-155, a tiny biomolecule from a family of genes called microRNAs, keeps a check on PDL1 levels.

"Interestingly, miR-155 has been known to be a key regulator of immunity for almost a decade. However, its connection to the immune checkpoint function has eluded scientists. This discovery has the potential to help us come up with more effective anti-cancer immunotherapies"

New discovery

Dr Tyson V. Sharp of Barts Cancer Institute, Queen Mary University of London, who collaborated with Dr Lagos in the study said: "Immunology, the study of anti-cancer immunity, is a highly active research space in cancer medicine.

"This exciting finding opens up new avenues of investigation that we believe can help us develop novel and more effective treatments for cancer, including cancers of unmet needs, such as lung and pancreatic [cancer](#). More work is needed to reveal the full potential of this new discovery."

The study is published in the *Journal of Biological Chemistry*.

More information: Daniel Yee et al. MicroRNA-155 induction via TNF- α and IFN- γ suppresses expression of programmed death ligand-1 (PD-L1) in human primary cells, *Journal of Biological Chemistry* (2017). [DOI: 10.1074/jbc.M117.809053](https://doi.org/10.1074/jbc.M117.809053)

Provided by University of York

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