Cancer relapse linked to body's own immune system

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Cancer cells that survive after treatment may use the body's own immune system to wake themselves up and fuel their growth, a new study shows.

The research sheds new light on how the immune system loses its ability to keep cancer in check, leading to the patient relapsing.

And the researchers found immunotherapy could be effective at preventing relapse, by getting the body's immune response back on track.

Scientists at The Institute of Cancer Research, London, with colleagues in Leeds, Surrey and the US, aimed to understand how a small number of cancer cells that resist treatment can turn deadly after lying dormant for long periods.

The researchers studied the immune response in mice to investigate how the cells of the immune system behaved before initial treatment, after treatment appeared to have worked, and when tumours returned.

The study is published today (Monday) in the journal *Cancer Immunology Research* and was funded by the European Research Council, the Richard M Schulze Family Foundation, the Mayo Foundation, Cancer Research UK, and the US National Institutes of Health.

Immune cells normally release signals that trigger inflammation in response to trauma or infection which, in some circumstances, can help the immune system kill cancer cells.

But the new research suggests these signals are subverted by leftover cancer cells after treatment, and used to drive their aggressive growth during relapse.

Crucially, the researchers showed that immunotherapies that target this response could either delay or prevent cancer returning in mice - suggesting that this approach could be effective in patients at risk of relapse.

Researchers found that a chemical signal called TNF-alpha switches in its effect from an anti-tumour agent that supports the immune response to eliminate cancer cells, to a new type of signal that promotes cancer relapse.

Resistant cells were also able to tell immune cells called natural killer cells to turn a blind eye, so that the relapsing cancer cells could grow unchecked.

Researchers found that the resistant cancer cells had high levels of a molecule called PD-L1 on their surface, which interacts with PD-1 on immune cells called T cells to tell them not to attack.

PD-1 is the target for highly successful immune checkpoint inhibitor drugs, and the researchers showed these treatments could delay or prevent relapse in mice.

Study co-author Professor Alan Melcher, Professor of Translational Immunotherapy at The Institute of Cancer Research, London, said:

"Our study finds the body's own immune system seems to play a crucial role when cancer relapses. The immune system goes from keeping cancer cells in check to awakening and feeding residual cells, while turning a blind eye to their growth.

"Excitingly, many of the methods employed by treatment-resistant tumours to re-grow and hide from the immune system can be blocked using existing immunotherapies. This idea is, in fact, supported by emerging data from clinical trials, showing that immunotherapies can reduce the risk of cancers coming back."

Study co-author Professor Kevin Harrington, Professor of Biological Cancer Therapies at The

Institute of Cancer Research, London, said:

"It is becoming increasing clear that the immune system is at the core of the puzzle of how we can treat cancer more effectively.

"This fascinating new study helps explain why sometimes a patient's immune system can be effective against cancer cells while at other times it is not. It also shows there is a lot more to learn about the nature of those cancer cells that lie dormant as a way of resisting the killing effects of cancer treatments. Changes must occur in these cells that make them better able to manipulate the immune system - and understanding this could open up new treatment options to prevent relapse."

Provided by Institute of Cancer Research