RIOT
Research Information Outreach Team

Ten Hallmarks of Cancer Series

Hijacked: Cancer Uses Immune Cells to Benefit Tumour Survival - Hallmark #10

Our immune system protects us, right? Immune cells (aka lymphocytes or white blood cells) are supposed to be "the good guys" that fight infection and cancer. Yet, our immune cells may actually help some tumours win the battle.

Tumours are made up of a complex community of different cell types. They create a supportive environment for themselves called the "tumour microenvironment". Immune cells respond to signals produced by this community and dutifully come in to investigate. Imagine these cells as undercover agents infiltrating the enemy. (No kidding: scientists actually call them "tumour-infiltrating lymphocytes"). While these "good" cells should kill the cancerous threat, it's unfortunately not quite so simple.

Our immune system is trained to distinguish "self = good" from "non-self = bad". But, cancer cells are ultimately our own cells gone rogue, so they may not be recognized as "bad". Fortunately, cells gone rogue are imbalanced in ways that immune cells can normally sense. But, cancer cells find ways to "hide" from them. Worse: the tumour microenvironment can convert undercover agents into double agents, tricking immune cells into supporting tumours. This "tumour promoting inflammation" is an emerging hallmark of cancer.

Tumours use immune cells to support their own survival by hijacking the immune cells' natural functions. For example, after successfully fighting infection, the immune response is turned down by "immune suppressor cells". Tumours use suppressor cells like shields to prevent themselves from being killed. Immune cells produce various survival substances (for themselves) that are then stolen by neighbouring cancer cells. Certain factors made by immune cells also help to form new blood vessels that supply tumours with oxygen and nutrients. Finally, some immune cells make chemicals that increase cancer cell mutation rates, helping them to evolve and survive. There are "good" and "bad" (= converted) immune cells in almost every tumour and the balance of these can determine outcome.

We want to understand how tumours "convert" immune cells. What switches turn "good" cells into "bad" cells? Like people, cells respond to signals in their environment that influence how they behave. Figuring out what these signals are can teach us how to promote better behaviour.

My research focuses on special white blood cells called gamma delta ($\gamma\delta$) T cells that naturally kill cancer cells. We have found ways to grow these cells in the lab so that we can learn more about them. Importantly, we are finding ways to harness their impressive cancer-killing abilities to develop $\gamma\delta$ T cell therapies. The idea is to get $\gamma\delta$ T cells from the patient or healthy donor blood, grow them in large numbers and inject them into cancer patients. The $\gamma\delta$ T cells should find and kill cancer cells that may not have been reached by traditional therapies (surgery, chemotherapy, radiation). We are also investigating whether $\gamma\delta$ T cells kill cancer stem cells, which are resistant to many therapies.

Like many other immune cells, $\gamma\delta$ T cells infiltrate tumours and it is possible that the tumour microenvironment dramatically changes how $\gamma\delta$ T cells work. We are determining whether factors in the tumour microenvironment influence the ability of $\gamma\delta$ T cells to kill cancer cells. If so, we want to learn how their anti-tumour capabilities can be recovered. This is very important, as we need to ensure that $\gamma\delta$ T cells injected into patients will kill tumours and not help to support them.

While some immune cells are clearly anti-cancerous, others can help tumours grow. The more we learn about what tips the balance in favour of tumours, the more tools we will gain to counterbalance this and develop better therapies to conquer cancer.

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