



Research project summary

The checkpoint receptor PD-1 inhibits Natural Killer cell responses to cancer

- Principal Investigator: Michele Ardolino
- Awarded \$841,500 from the Canadian Institutes of Health Research (CIHR) in January 2018

The body has an extraordinary weapon against cancer: the immune system. Unfortunately, tumors often learn how to evade the immune response. We recently discovered one of these mechanisms, namely an inhibitory network that suppresses a population of immune cells called Natural Killer cells. As implied by their name, Natural Killer cells effectively kill tumor cells. To develop, tumors need to inactivate Natural Killer cells, but it is not clear how they do so. We found that tumors cause Natural Killer cells to produce inhibitory molecules. When Natural Killer cells express these inhibitory molecules, called checkpoint receptors, they no longer effectively fight cancer. We are requesting support to i) determine how checkpoint receptors suppress Natural Killer cells, ii) understand how checkpoint receptors are induced on Natural Killer cells in the tumor environment and iii) design and test novel immunotherapies to rescue the anti-tumor activity of Natural Killer cells. Our studies will involve both mouse models of cancer and experimentation with samples from cancer patients. Our goal is to understand the inhibitory circuits that suppress the immune system in cancer in order to develop new strategies to activate our own immune cells against tumors.

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