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# How tumors caused by STD quickly regress in dogs

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The canine transmissible venereal tumor is a contagious cancer that has spread by mating among dogs worldwide. One unique feature of this cancer is that, for unclear reasons, it regresses spontaneously or a few weeks after a single treatment of radiotherapy or chemotherapy. A study published April 9 in the journal *Cancer Cell* shines a light on this mystery, revealing a key role for the immune system in triggering fast cancer rejection in chemotherapy-treated dogs. Because the canine transmissible venereal tumor shares many similarities with various human cancers, the findings could point to more effective therapeutic strategies.

"We found that activation of the innate immune system and production of certain molecules called chemokines by the host tissue around the tumor is critical to attract immune cells within the tumor and trigger a chain reaction that leads to the rejection of the cancer and its elimination," says senior author Professor Ariberto Fassati of UCL (University College London). "We hope that this study will encourage the clinical testing of combined approaches to improve immunological therapies against cancer, in animals and humans alike."

First described in the 1800s, the canine transmissible venereal tumor rapidly grows into a cauliflower-like mass on genitalia, and it is naturally transmitted between dogs by coitus, biting, or licking tumor-affected areas. It is one of three known clonally transmissible cancers in nature, along with Tasmanian devil facial disease and leukemias in soft-shell clams. Because it originated from a single common ancestor, the canine

transmissible venereal tumor consists of genetically identical cells in all affected dogs, making it easier to identify key factors driving cancer regression. Yet few labs have investigated this topic, leaving it unclear how cancer rejection occurs.

To answer this question, Fassati and his collaborators collected biopsies from canine transmissible venereal tumors in eight dogs before treatment as well as 6 days and 14 days after receiving a chemotherapy drug called vincristine. The researchers performed systematic genome-wide analyses to compare gene activity in tumors that fully regressed with those that did not regress.

They discovered that regression occurs in sequential steps. First, vincristine treatment led to a strong inflammatory response and the proliferation of host skin cells, which may represent an attempt by the tissue surrounding tumors to contain or replace the malignant tissue. "We were expecting that most changes leading to regression of this dog tumor would occur in the cancer cells," Fassati says. "Instead, we realized that the host cells were more important."

This early stage of regression was also characterized by an increase in the production of a chemokine called CCL5—a signaling protein that attracted cancer-fighting immune cells to the tumor. Ultimately, this process resulted in immune rejection of the tumor and repair of tissue damage.

"There are two key messages of our study," Fassati says. "First, we should not focus on the cancer cells only but also understand the importance of normal tissue around the cancer in promoting rejection. Second, we must be able to induce the production of large amounts of certain chemokines to attract loads of immune cells to the tumor site."

In the end, this research could have implications for human cancers,

such as skin cancer, bone cancer, and certain blood cancers. For his own part, Fassati plans to investigate whether it's possible to stimulate chemokines that attract immune cells to tumors in human cancers. "However, it may take some time before these approaches are tested in the clinic," he says. "So the general audience should not take away the message that we have found the magic wand to make cancer disappear."

Despite these limitations, this research could help guide ongoing and future clinical investigations. "There might be ways to improve the efficacy of immunological therapies against cancer by combining different approaches, such as releasing the breaks of the immune system through checkpoint inhibitors and inducing host cells surrounding the tumor to attract the unleashed immune cells to the tumor site," Fassati says. "Indeed, there are already ongoing trials that combine low-dose radiotherapy or chemotherapy with immunological therapies, precisely to stimulate a strong inflammatory response in the tumor."

**More information:** *Cancer Cell*, Frampton et al.: "Molecular Signatures of Regression of the Canine Transmissible Venereal Tumor" www.cell.com/cancer-cell/fullt … 1535-6108(18)30071-0 , DOI: 10.1016/j.ccell.2018.03.003

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