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Only a small fraction of tumour-infiltrating immune cells possess special anti-tumour proteins

What is this research about?

Cytolytic lymphocytes (CL) are a group of immune system cells that identify and kill infected and cancerous cells. After recognizing and attaching to a target cell, CL cells utilize a wide range of molecules to achieve target cell death. Perforin and proteins of the granzyme family (which degrade other proteins) play the primary role. Perforin anchors the CL to the target cell and then creates holes in the protective outer covering of the target cell. Next, granzymes flow through these holes and kill the target cell. Tumour infiltrating lymphocytes (TIL) are a type of CL that are commonly found in cancerous tissues, but they are seldom fully effective at causing tumour regression. New cancer treatment methods target TIL, hoping to stimulate this natural cancer defence mechanism into being more effective. Canine cutaneous histiocytoma (CCH) is a benign cancer found in immune cells in the skin of young dogs. CCH regresses naturally without treatment, in a process involving TIL. Studying the maturation process of TIL in CCH can help scientists understand how TIL behave when they are effective.

What did the researchers do?

Tumour samples were taken from 17 dogs with CCH, as well as samples of lymphocyte-rich tissues from dogs without cancer or immunological problems. The CCH samples were placed into one of four categories based on the amount of cancer regression and the corresponding level of TIL infiltration. Special antibodies were used to make the perforin, granzyme, and other proteins glow. The tissue samples were examined under a microscope and the number of lymphocytes containing perforin and granzyme were counted.

What you need to know:

CCH tumour regression was associated with widespread invasion by TILs, despite the fact that only a small fraction of TILs possessed the anti-cancer proteins perforin and granzyme. Since many granzyme-positive TILs did not contain perforin, some TIL may have perforin-independent ways of killing cancerous cells.

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Project supported by:
A program of the OMAFRA-U of G Partnership.

Agri-Food and Rural Link
A program of the OMAFRA – U of G Partnership
Mobilizing Agri-Food and Rural Research Knowledge

What did the researchers find?

Granzyme B was found in 25% of activated TIL in CCH tumours, while perforin was identified in only 4% of overall TIL. Perforin was not found in inactive and immature lymphocytes taken from healthy lymph tissues. GranzymeB density was higher in later stages of tumour regression, while there was no clear relationship with perforin. Most perforin- and granzyme-positive cells showed tight concentration of these proteins in granules in one area of the cell, and this was a reliable marker of TIL maturity and activity. Perforin concentration was greatest during the earlier stages of tumour regression. Since there were a large number of granzyme-positive TIL without perforin, these cells may possess a perforin-independent method of killing target cells.

How can you use this research?

Cancer researchers can use this research to better understand how TILs mature, infiltrate tumours, and kill cancerous cells.

Immunologists can further this research by figuring out how or why some granzyme-positive tumour-infiltrating lymphocytes are able to attack cancerous cells without perforin.

Genetic engineers can use this research to manipulate the expression of perforin and granzyme in tumour-infiltrating lymphocytes in order to make them more effective at killing cancerous cells.

Keywords:

Cancer, tumour regression, lymphocytes, histiocytoma, perforin, granzyme

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Cite this work:

University of Guelph, Institute for Community Engaged Scholarship (2012). Only a small fraction of tumour-infiltrating immune cells possess special anti-tumour proteins. Retrieved from: http://hdl.handle.net/10214/5623

This summary is a project of the Institute for Community Engaged Scholarship (ICES) at the University of Guelph, with project partners: the Catalyst Centre, SPARK Program at the University of Guelph, and the Knowledge Mobilization Unit at York University. This project is part of the Pan-Canadian Research Impact Network.

http://csahs.uoguelph.ca/pps/Clear_Research

Article citation:

[Manuscript submitted for consideration, not yet published]