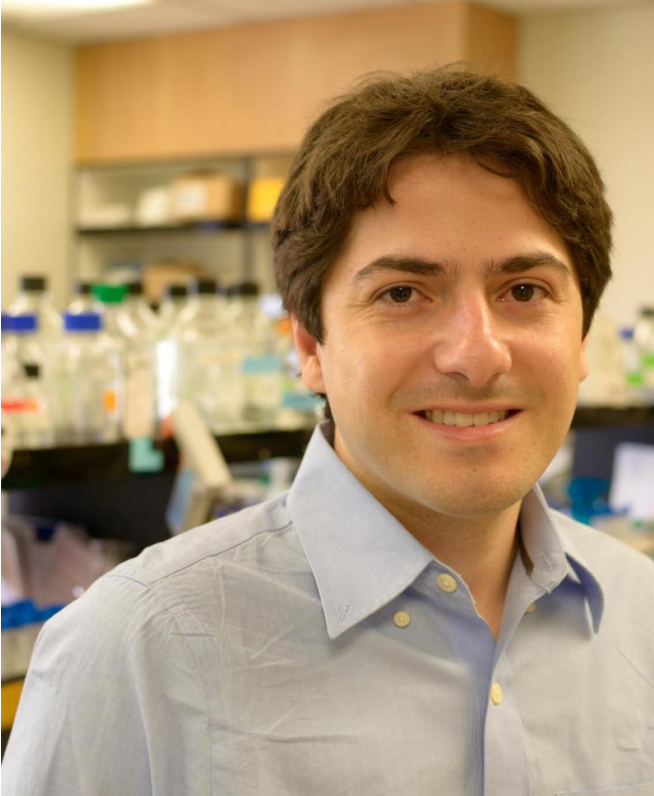


Researchers mimic viral infection in colon cancer stem cells

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Principal investigator and lead author of the study, Dr. Daniel De Carvalho, is a scientist at Princess Margaret Cancer Centre, University Health Network. Credit: UHN

Researchers targeting colorectal cancer stem cells - the root cause of disease, resistance to treatment and relapse - have discovered a mechanism to mimic a virus and potentially trigger an immune response to fight the cancer like an infection.

The discovery, published online today in *Cell*, illuminates a major shift in understanding anti-tumour mechanisms and identifies a promising druggable target against colorectal [cancer stem cells](#), says principal investigator and lead author Dr. Daniel De Carvalho, a scientist at Princess Margaret Cancer Centre, University Health

Network. He is also Assistant Professor in the Department of Medical Biophysics, Faculty of Medicine at University of Toronto. Dr. De Carvalho talks about his research in a video below.

"By mimicking a virus the potential is to trick the immune system into 'seeing' the [cancer cells](#) as an infection that needs to be destroyed," says Dr. De Carvalho. "Our work demonstrates that viral mimicry is a viable anti-tumour strategy." Currently, colorectal cancer recurs in about 50% of patients and is among the top three leading causes of cancer-related deaths.

In the laboratory, the research team replicated human colorectal cancer in pre-clinical experiments and used bioinformatics analysis to demonstrate that a low-dose of the chemotherapy drug decitabine targeted the cancer [stem cells](#) by inducing viral mimicry.

Decitabine is approved by the U.S. Food and Drug Administration to treat myelodysplastic syndromes and leukemia, and for use in clinical trials for several types of solid-tumour cancers including colorectal. In Dr. De Carvalho's research, the team discovered that this drug - known as an epigenetic therapy because it chemically modifies DNA - activates a pathway that recognizes viruses.

"We have found a switch to turn on an anti-viral response in colorectal cancer stem cells, which seem to be especially sensitive to it," says Dr. De Carvalho. This discovery builds on earlier published research from other Princess Margaret scientists, Dr. John Dick, the pioneer of the cancer stem cell field, and Dr. Catherine O'Brien, whose 2007 study established that not all [colorectal cancer](#) cells are equal; rather, they are organized in a hierarchy sustained by a subpopulation of stem cells that initiate disease, resist treatment, then self-renew to regrow tumours.

Dr. De Carvalho says: "Another important

implication of our finding is that since decitabine induces an anti-viral response, which is highly immunogenic, it may be useful to combine this agent with immune therapy to further advance personalized cancer medicine by boosting an individual's natural defenses to fight disease. The next step is to start clinical trials to find out if targeting colon cancer stem cells in this way will result in durable cures."

Provided by University Health Network

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