

Cancer stem cells can go it alone

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At the heart of most, if not all cancers, lie a handful of wayward stem cells that feed the ever growing tumor mass, but their scarcity make it difficult for scientists to study them. Now, times of plenty may lie ahead as a breast cancer cell line – established long ago – turned out to behave a lot like cancer stem cells.

In a study to be published in this week's online edition of the *Proceedings of the National Academy of Sciences* an international group of researchers led by Nobel Laureate Renato Dulbecco, M.D., a distinguished research professor and president emeritus of the Salk Institute, demonstrates that injection of a single cell taken from cultured LA7 cells into mouse breast tissue can seed a new mammary carcinoma.

Their finding supports the observation that although cancer stem cells are rare, in the bulk of a tumor, a single cancer stem cell is sufficient to initiate and maintain a malignant tumor. "We can use single cancer stem cells to study the dynamics and behavior of cancer stem cells and their role in solid tumor formation at the single cell level," says lead author Ileana Zucchi, Ph.D., a molecular cancer biologist at the Institute for Biological Technology (ITB-CNR) in Milan, Italy.

Having a model cancer stem cell system will also allow researchers to identify genes and proteins that will help with the search for human breast cancer stem cells in the future. "As we learn more about tumor formation at the single cell level in tissue, we may be able to specifically target cancer stem cells for destruction while leaving the normal stem cells in the body intact," hopes Zucchi.

Dulbecco had isolated the LA7 cells from a rat mammary adenocarcinoma back in 1979. He and Zucchi have spent the last decade studying their ability to generate the different structures that make up mammary glands. “We initially started to work with LA7 cells because they retain considerable stem cell potential and, therefore, behave like normal adult stem cells. But it wasn’t until later that we could demonstrate that a single LA7 cell can also form heterogenous tumors and behave also as a cancer stem cell,” remembers Zucchi.

The fact that tumor cells and stem cells share many properties has been known for quite some time. The ability of adult stem cells or cancer stem cells to divide and generate both new stem cells (called self-renewal) as well as specialized cell types (called differentiation) is the key to maintaining healthy tissues, and to keep tumors growing indefinitely in the case of cancer stem cells.

There’s a major difference, though. “Although normal stem cells show significant stem cell renewal, they are usually not associated with uncontrolled cell proliferation when they reside within their normal environment or niche. Cancer stem cells, however, are not equally responsive to environmental cues that repress uncontrolled cell proliferation of the stem cells,” explains Zucchi.

When grown in culture dishes, LA7 cells act just like normal stem cells and, when prodded with appropriate cues, differentiate into all the cell lineages found in the mammary gland. Given enough time, the cells form complex, three-dimensional structures resembling the milk-producing alveoli and ducts in normal breast tissue and start to produce milk proteins.

To assess the cells’ tumorigenic potential, the researchers injected the cells into the breast tissue of female mice. Unable to respond to conditions that prevent normal stem cells from spinning out of control,

even a single LA7 cell started to form tumors. “If tumor induction was dependent on injecting more than one cell, it would be difficult to determine whether cells that appear to be resistant to these conditions are simply cell types different from cancer stem cells,” Zucchi says. “But since we start with a single cancer stem cell for injection, we know that the resistance must derive from the original cancer stem cell.”

Source: Salk Institute

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