Scientists find common trigger in cancer and normal stem cell reproduction

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Researchers at Stanford University School of Medicine have discovered, for the first time, a common molecular pathway that is used by both normal stem cells and cancer stem cells when they reproduce themselves.

In a paper to be published Aug. 7 in the journal *Cell,* Michael Clarke, MD, the Karel H. and Avice N. Beekhuis Professor in Cancer Biology, and his colleagues showed that breast cancer stem cells and normal breast stem cells turn down the creation of a specific group of cell signals when they are reproducing. Increasing the amount of one of these signals, called miR-200c, strongly suppressed the ability of both cancer stem cells and normal stem cells to divide and reproduce.

The discovery of a common regulatory pathway in both kinds of stem cells supports the idea that cancer stem cells and normal stem cells share fundamental properties. "This very strongly supports the cancer stem cell hypothesis," said Clarke, who is associate director of the Stanford Stem Cell Biology and Regenerative Medicine Institute and a member of the Stanford Cancer Center. "A lot of people have speculated that there was this molecular link between these two kinds of cells (cancer stem cells and normal stem cells), but this is the first time we have actually identified it."

The cancer stem cell hypothesis states that cancers are a collection of many different kinds of cells, only a very few of which create and sustain the cancer. These are the cancer stem cells, which share many

traits with normal stem cells.

While most cells in the body cannot reproduce themselves, stem cells have the ability to do so, and can also create the cells that mature into various tissues. Blood stem cells, for instance, which reside in the bone marrow, have the ability to create new blood stem cells and also to create all the different types of mature blood cells.

While the current discovery is important evidence of how cancer stem cells operate, it does not automatically lead to new cancer therapies. "The problem is that if we attack cancer using this mechanism, it is also going to affect normal stem cells which are essential for our survival," Clarke said. But understanding how cancer cells sustain themselves may in the future offer new ways of attacking the disease. "The hope is that we can find nuances that distinguish between how normal stem cells renew themselves and how cancer stem cells do so, and then use those differences to attack only the cancer," said Clarke.

The research also demonstrates the power of conducting studies that zero in on cancer stem cells rather than screen all cancer tumor cells. In the past, for instance, scientists tried to gain insight into how cancer cells reproduce by looking at molecular signals in all the cancer cells in a tumor. But this molecular detective work did not reveal cancer stem cells' use of the miR-200c pathway, probably because signals from cancer stem cells were lost in a crowd of molecular signals from the far more numerous non-stem cells.

Clarke and his colleagues therefore isolated the cancer stem cells first and then did the analysis. Clarke noted that it is technically challenging to isolate cancer stem cells, which can be outnumbered by generic tumor cells 100 to 1, but the rewards can be dramatic.

By analyzing only stem cells, the link between the molecular signals that

control reproduction in cancer stem cells and normal stem cells became apparent.

"If you are looking at all the cells in a tumor, it's like looking for a crying child lost in an auditorium of cheering people," Clarke said. "You can't hear the child crying until you remove everyone else from the auditorium, and then the sound will pop out."

Source: Stanford University Medical Center (news : web)