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Cancer's potential on-off switch

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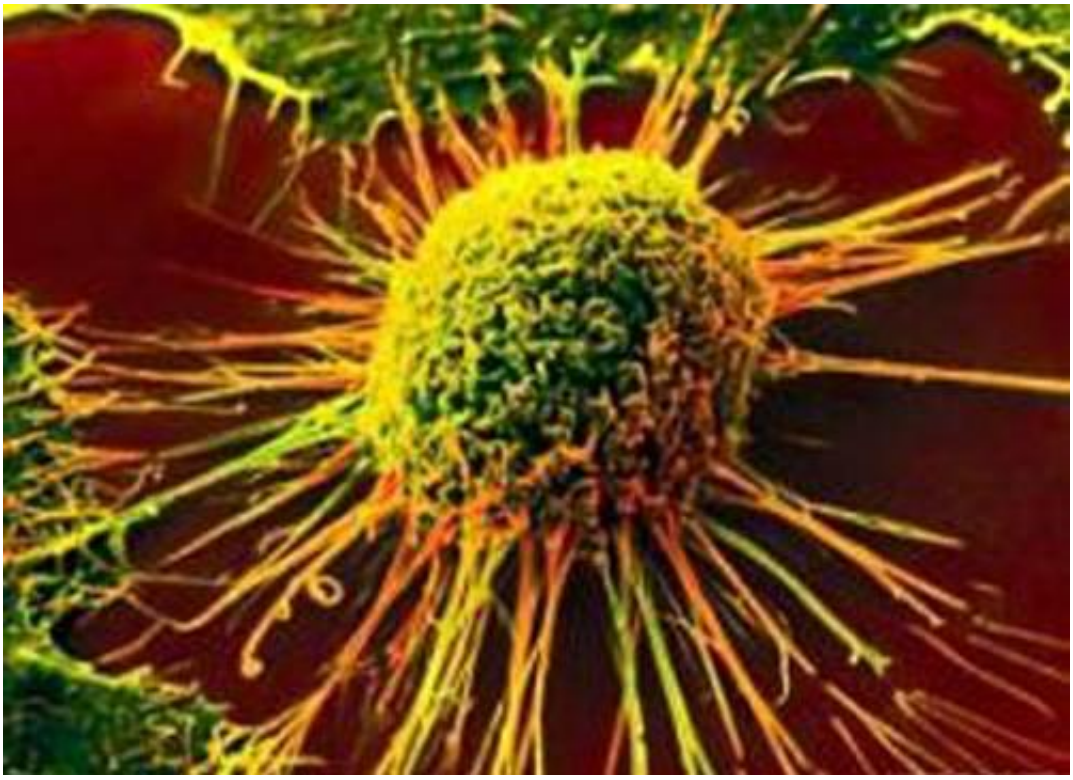

A team of Boston University School of Medicine (BUSM) researchers have proposed that an "on and off" epigenetic switch could be a common mechanism behind the development of different types of cancer. Epigenetics is the phenomena whereby genetically identical cells express their genes differently, resulting in different physical traits.

Researchers from the Boston University Cancer Center recently

published two articles about this in *Anticancer Research* and *Epigenomics*.

The current paradigm states that cancer develops from environmental and genetic changes to cancer progenitor cells. These changes are the result of mutations, exposure to toxic substances or hormonal imbalances.

Cancer progression is extremely complex, however. It also is well known that new mutations and the activation of more cancer causing genes occur throughout the development and progression of cancer.

"If we believe that everything in nature occurs in an organized fashion, then it is logical to assume that cancer development cannot be as disorganized as it may seem," said Sibaji Sarkar, PhD, instructor of medicine at BUSM and the articles corresponding author. "There should be a general mechanism that initiates cancer progression from predisposed progenitor cells, which likely involves epigenetic changes."

The existence of this epigenetic switch is indirectly supported by the fact that tumors develop through different stages. When cells rapidly grow during cancer progression, they become stuck in their current stage of development and their cell characteristics do not change. This is the reason that there are so many types of leukemia—the characteristics that a leukemia cell possesses when it begins to rapidly grow and expand are the characteristics that it will keep until the rapid growth stops.

"If we believe that all of the irreversible changes, mutations and effects of carcinogens make cells rapidly grow, then the mechanism that allows cells to stop growing and assume new changes in character must be of great importance," added Sarkar. "The study of cancer progression is key to understanding how cancer cells continue to differentiate."

During cancer progression, there are different stages of rapid growth and

differentiation. The control that allows for this switch between growth and differentiation can only be achieved through reversible mechanisms, such as epigenetic changes.

Sarkar and colleagues have previously proposed that epigenetic changes are involved in cancer progenitor cell formation and cancer progression. They also believe that epigenetic changes have the ability to control rapid growth and change of characteristics (different grades/types of tumors).

Sarkar compares the stages of cancer growth to a rocket orbiting in space – that is, that an object within an orbit continues to circle a given path, until it is given a signal (or additional fuel) to propel itself into a further orbit. This comparison can be made for cancer progenitor cells and epigenetics. A specific cell continues to grow at a certain stage until it is given a signal – in this case, an epigenetic switch – that propels it to differentiate into a new orbit, or further differentiated cell.

"While the specific details of the epigenetic code that regulates these changes has not been discovered, the fact that we have a possible explanation for the reversible and ever-changing characteristics for cancer progenitor cells is very exciting," said Sarkar. "Future epigenetics findings hold the key to develop drugs which could possibly kill cancer progenitor cells to reduce cancer relapse and drug-resistant cancer cells."

Provided by Boston University Medical Center