Scientists reveal mechanism that regulates cancer-causing gene

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Two University of Rhode Island scientists have revealed how a cancer causing protein is regulated by reactive oxygen species (ROS) -- a type of stress signal. Their findings provide new insight into how this protein normally behaves in human cells and may help in the design of drugs targeting specific cancers.

Doctoral student David J. Kemble and Professor Gongqin Sun in the URI Department of Cell and Molecular Biology are the first to provide a biochemical mechanism describing how certain protein tyrosine kinases sense and respond to oxidation. This sensing system was found to uniquely apply to two families of proteins implicated in numerous cancers: the Src and Fibroblast Growth Factor Receptor families of tyrosine kinases.

Their results were published online March 9 in the Proceedings of the National Academy of Sciences.

Src was the first enzyme identified as a cancer-causing gene in the early 1900's. For years scientists have been studying how the enzymes are expressed in cancer cells - what do they do and what controls them.

According to Kemble and Sun, Src is a master regulator of cell function, controlling cell metabolism, division, and death. In normal cells, the function of Src is turned off, and it is turned on only when certain stimulatory signals activate it. When the regulatory mechanisms that control Src activity are disrupted, Src may be turned on all the time,

which turns the host cell into a cancer cell. Thus, it is crucial to understand how Src function is controlled.

Reactive oxygen species have long been viewed as damaging byproducts of oxygen-based metabolism. However, it is now recognized that ROS are produced when the cells are under growth stimulation, and they in turn regulate other cellular events.
Accumulating evidence indicates that ROS can directly regulate the function of Src function, and thus indirectly control many cellular processes. Yet how Src responds to this regulation has remained elusive.

The URI scientists took a systematic approach, examined all the potential mechanisms, and identified the sensor that enables Src to respond to ROS regulation. They further found that the sensor is also present in several other similar enzymes, mostly in the FGFR family.

"Our results were surprising at first, given that the results contradict some reports in the literature," Kemble said. "But there was always a very clear answer to each question we asked. It was both unusual and exciting to see things progress as smoothly as it did."

According to Sun, this mechanism of regulation represents just a small piece of the large puzzle of how Src is controlled in the cells. "Src function is under the control of several different mechanisms; each one needs to fit in with the others to form a seamless regulatory system." Sun said.

Source: University of Rhode Island (news : web)