Shared survival mechanism explains why 'good' nerve cells last and 'bad' cancer cells flourish

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Cancer cells and nervous system neurons may not look or act alike, but both use strikingly similar ways to survive, according to new research from the University of North Carolina at Chapel Hill School of Medicine.

The study published in the December issue of *Nature Cell Biology* is the first to describe how neurons (nerve cells) and cancer cells achieve the common goal of inhibiting the series of biochemical events called apoptosis that eventually causes cells to break down and die.

That's good in the case of neurons, but bad when it comes to cancer.

"In neurons, inhibiting cell death is physiologically important to ensuring their long term survival," said the study's lead author, neurobiologist Mohanish Deshmukh, Ph.D., associate professor of cell and developmental biology and member of the Lineberger Comprehensive Cancer Center. "In cancer cells, blocking cell death allows them to evade the host defense systems and proliferate uncontrollably."

Both neurons and cancer cells do have something in common: relying extensively on the metabolism of glucose, a simple sugar. But until now, the advantages of this common characteristic have remained unclear.

"One reason why these results are so interesting is that neurons and

cancer cells are as different from each other as you can imagine. For example, cancer cells divide continuously, whereas neurons don't divide at all," Deshmukh said.

In their research, Deshmukh and UNC graduate student Allyson Vaughn (currently a postdoctoral scientist at MIT) found that to prevent death, neurons and cancer cells use a specific metabolic pathway, or series of chemical reactions. This pathway – the pentose phosphate biochemical pathway – inhibits the activation of a key protein involved in the process of cell death called cytochrome c. "What we show is that both neurons and cancer cells inhibit the cell death process mediated by cytochrome c," Deshmukh said.

Specifically, according to the study, cytochrome c's ability to induce death can be turned off if the cellular environment contains high levels of antioxidants. Healthy neurons and cancer cells have increased levels of the antioxidant glutathione (GSH), which is generated by glucose metabolism through the pentose phosphate pathway. Thus, both neurons and cancer cells are able to resist cell death in part via their reliance on glucose metabolism.

"For neurons and cancer cells, evolution has come up with ways to restrict the cell death pathway. Our results provide insight into the mechanism behind this adaptive advantage," Deshmukh said. "They also bring together the fields of cancer and neurobiology and suggest that the mechanisms used by neurons to evade cell death could be the same ones adapted by dividing cells during their progression toward cancer."

The UNC scientist said his lab's further systematic explorations for other similarities between these cell types may offer insights into turning the cell death process back on in cancer cells.

Source: University of North Carolina