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Scientists Confect New Cancer Treatment

Study goes after sugars on outside of cells

By Adam Marcus
HealthScoutNews Reporter

MONDAY, Jan. 21 (HealthScoutNews) -- Opening the prospect for a novel frontier in cancer treatment, a new study says snipping sugars that fringe the outside of cells can either promote or retard tumor growth.

The finding hinges on enzymes whose job it is to cut sugar chains that make up the extracellular matrix, the fuzzy tutu ringing the cell wall that helps it interact with its chemical environment.



"Virtually all cells express these sugars, and they are known to play a fundamental role in how they process signals from the outside," says Ram Sasisekharan, a bioengineer at the Massachusetts Institute of Technology and a co-author of the study. As a result, he says, targeting sugars as a way to control cancer is likely to be viable for almost every form of the disease.

Moreover, matrix sugars double as the identity cards for cells and thus help give tissues their uniqueness. So a therapy that leverages these molecules would be highly specific and might avoid the system-wide toxicity that plagues most current cancer treatments. A report on the findings appears in the Jan. 22 issue of the *Proceedings of the National Academy of Sciences*.

Sugars are the least understood member of the triumvirate of information-bearing molecules in the body, a group that also includes DNA, which carries genes, and proteins, which do a cell's heavy lifting. Whereas DNA has four basic building blocks and proteins have 20 (the amino acids), sugars have at least 32, giving them the ability to combine into a numbingly vast catalog of structures that help dictate their function. It's no wonder, therefore, that scientists "know very little about sugars," Sasisekharan says.

What is clear, though, is that sugars in the extracellular matrix are a cell's eyes and ears. By virtue of their structure, they provide a means for signaling molecules to do their job. [Viruses and other pathogens have learned to exploit this structural identity by homing in on specific sugar targets.]

One matrix sugar is heparan sulfate-like glycosaminoglycans (HSGAG), which the researchers describe as a "molecular sponge" that collects various signaling chemicals, including growth factors, that float its way.

In the latest study, Sasisekharan and his colleagues sought to learn whether they could change the growth properties of various mouse tumor cells by altering the structure of HSGAG. To do so, they dosed the cells with two forms of a family of enzymes called heparinases -- Hep I and Hep III -- that cut the sugar at different places.

The addition of Hep I to cancerous tissue -- melanoma and lung and prostate tumors -- encouraged growth. But Hep III markedly retarded the formation of tumors, the researchers say, stalling them by as much as 85 percent with only a little of the enzyme. It also blocked the spread of cancer cells to other sites. "We used a fairly low amount to get that much inhibition. That was pretty surprising to us," Sasisekharan says.

Intriguingly, the researchers found that when they injected the mice with the corresponding sugar fragments they had the same effect as the whole enzyme. "This raises the exciting possibility of using fragments as a potential therapeutic drug," Sasisekharan says.

Phil Robbins, a cell biologist at Boston University who is familiar with the new study, calls it "very nice work" that's worthy of pursuing.

However, Robbins says the researchers certainly haven't found a cure for cancer, because they were able only to slow its progression. On the other hand, he adds, the researchers do point the way to a "new paradigm" in cancer treatment that might one day prove valuable.

What To Do

For more on Sasisekharan's work, try his lab at [MIT](http://web.mit.edu/tox/sasisekharan/healthscout.html).

To find out more about cancer and cancer treatments, visit the [National Cancer Institute](#) or the [American Cancer Society](#).

SOURCES: Interviews with Ram Sasisekharan, Ph.D., associate professor of bioengineering, Massachusetts Institute of Technology, Cambridge, Mass.; Phil Robbins, Ph.D., professor of molecular and cell biology, Boston University; Jan. 22, 2002, *Proceedings of the National Academy of Sciences*

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