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Turning down the volume on cancer

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When the audio on your television set or smart phone is too loud, you simply turn down the volume. What if we could do the same for the signaling in our bodies that essentially causes normal cells to turn cancerous?

New discoveries by researchers at the Stephenson Cancer Center at the University of Oklahoma may point to new ways to do just that.

Hiroshi Y. Yamada, Ph.D., and his team zeroed in on chromosome instability as a potential precursor to colon cancer.

"Chromosome instability is a major cause of genomic instability and occurs in many cancers. It is seen in 80 to 90 percent of human colon cancers. In fact, our data suggest that it may be a key player in the process by which healthy cells in the colon become cancerous," Yamada said.

The team first developed a laboratory model with a mutation that essentially makes cell division sloppy, resulting in chromosome instability.

"The simple premise is that if we test a drug or diet on this laboratory model which we know is at greater risk for colon cancer and we see fewer cancers, then that drug or diet may be promising in terms of preventing or curing cancer. It's a type of research called translational oncology and it's an essential pre-clinical step for developing new drugs for cancer prevention and therapy," he explained.

As predicted, the laboratory model proved cancer-prone, quickly developing small tumors and lesions. After a while, tumor suppressors appeared to do their job and most of the small tumors regressed. The tumors that grew, though, were found to be carrying more than ten times the number of mutations of tumors in the controls. These tumors also were likely malignant and more difficult to cure.

"There seemed to be a tug-of-war at the molecular level influencing whether the mutated cells would become cancerous. That's when we decided to introduce a systems biology approach in our analysis and that brought many surprising and promising findings," Yamada said.

In fact, by tapping into the cutting-edge technologies within the bioinformatics core at the University of Oklahoma Health Sciences Center, the team discovered different gene expression signatures - signatures similar to those in cancer - in the laboratory model with chromosome instability. In addition, many of the pathways that lead to cancer were upregulated, like turning up the volume on the TV.

Another surprise was that the genes involved in immune function, which is the biologic system that helps the body police for cancer, were downregulated.

"This was something new," Yamada said. "We had assumed that the effects of chromosome instability would be based more on individual cells. Instead, our research showed chromosome instability may be able to influence the genesis of cancer in many different ways. It's actually good news because with the bioinformatics information, we can formulate novel intervention strategies aimed at these previously unknown targets."

The findings bring a lot of excitement for Yamada, his team and for the field of cancer prevention and treatments. There may be other

applications for their work too.

"Genomic instability also is a hallmark of aging. So we intend to look into the effect of this in the aging process and in age-associated cancers," Yamada added.

Provided by University of Oklahoma