MedicalXpress

New approach to cancer: Find most tightly controlled genes

July 18 2008

Scientists at a Duke University medical school in Singapore have found a new way to study cancer that could be very useful for developing targeted therapies against cancer and possibly many other diseases.

"Because all you need for this approach is gene expression data to compare both diseased and normal tissues, you could apply it to cancer or any other disease, if you have the data," said co-author and researcher Patrick Tan, M.D., Ph.D., associate professor of Duke-NUS Graduate Medical School Singapore. "Just replace the word 'cancer' with 'diabetes,' 'obesity,' and so on."

Surveying large amounts of genetic data, the scientists analyzed both cancerous and healthy, normal tissue for genes with tightly controlled activity.

They defined "tightly controlled" as genes that varied the least during their expression. Gene expression is the process through which a gene is turned on to make certain products, such as proteins.

In cases where the same genes were active in both diseased and normal tissue, they narrowed their search to the genes that are more tightly controlled in cancerous tissue. The diseased and normal samples used came from lung, thyroid, liver, esophagus, colon and breast tissues.

"We thought that since the tumors were spending costly cellular resources and energy to control the expression of these particular genes,

they must have functional importance in cancer," said Dr. Tan, who is also a principal investigator with the National Cancer Centre and group leader in the Genome Institute of Singapore.

The work, published in the July 18 issue of *PLoS Genetics*, was funded by the National Cancer Centre of Singapore and a grant from the Biomedical Research Council of Singapore.

Forty-eight genes that are tightly controlled in tumors emerged from the analysis. The scientists referred to this collection as a "poised gene cassette" or PGC.

"We view the PGC genes as an exciting new class of genes, in which you would only need to slightly affect gene function to elicit a sizeable effect on the tumor," Tan said. "This would make the PGC genes attractive targets."

For example, a treatment targeting a PGC gene might only need to inhibit protein activity by 10-20 percent in order to gain the desired effect. This contrasts with other genes, where a near-complete inhibition (90-100 percent) might be required before effects on tumors are seen.

The scientists studied what happens with some of these genes in the PGC by comparing different samples of tumor tissue that were known to be more or less metastatic (able to spread to other places in the body). They found that the PGC expression was subtly yet significantly lower in highly metastatic cells.

"Beyond cancer, we could easily apply this approach to other diseases," Tan said. "With the right data, researchers could find genes related strictly to disease progression and explore how they can be manipulated to our benefit."

Source: Duke University