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Researchers discover biomarkers for prostate cancer detection, recurrence

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Alterations to the "on-off" switches of genes occur early in the development of prostate cancer and could be used as biomarkers to detect the disease months or even years earlier than current approaches, a Mayo Clinic study has found. These biomarkers — known as DNA methylation profiles — also can predict if the cancer is going to recur and if that recurrence will remain localized to the prostate or, instead, spread to other organs. The study, published in the journal *Clinical Cancer Research*, is the first to capture the methylation changes that occur across the entire human genome in prostate cancer.

The discovery could someday help physicians diagnose prostate cancer earlier and make more effective treatment decisions to improve cure rates and reduce deaths. It also points to the development of new drugs that reverse the DNA methylation changes, turning the "off" switch back "on" and returning the genetic code to its normal, noncancerous state.

"Our approach is more accurate and reliable than the widely used PSA (prostate-specific antigen) test," says senior author Krishna Donkena, Ph.D., a Mayo Clinic molecular biologist.

The PSA test detects any prostate abnormality, whether inflammation, cancer, infection or enlargement, while the DNA methylation changes are specific to prostate cancer, she says.

Though the instructions for all the cell's activities lie within the genes, whether a particular gene is turned "off" or "on" is determined by the

presence or absence of specific chemical tags or methyl groups — methylation — along the underlying DNA of cells. When this process of DNA methylation turns off the activity of tumor suppressor genes, cancer develops.

Dr. Donkena and her colleagues analyzed the methylation status of 14,495 genes from 238 prostate cancer patients. The patients included people who remained cancer-free after treatment, those who had a localized tumor recurrence and those whose cancer spread. The researchers found that the DNA methylation changes that occurred during the earliest stages of prostate cancer development were nearly identical in all patients.

Having discovered DNA methylation patterns that could distinguish between healthy and cancerous tissue, the researchers then searched for similar biomarkers that could distinguish between patients with varying levels of recurrence risk. They found distinct methylation alterations that corresponded to whether a patient had a slow-growing tumor known as an indolent tumor, or had a more aggressive one.

If physicians can determine what type of tumor patients have, they can avoid exposing patients with indolent tumors to unnecessary treatment, and can treat those with aggressive tumors earlier and more effectively, Dr. Donkena says.

Dr. Donkena and her colleagues are working to develop a DNA methylation test that is more cost-effective and practical for use in clinical settings. Currently, the test relies on microarray or gene "chip" technology that assesses methylation status of genes across an entire genome. The researchers are trying to generate more economical custom microarray to specifically look at only the genes that predict the development of prostate cancer or recurrence.

They also hope to develop drugs that can reverse DNA methylation in prostate cancer cells. Similar drugs are already being used to treat certain forms of leukemia.

Provided by Mayo Clinic