

## Gene mutation can allow proteins to gather, spark tumor growth

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Prostate cancer is generally treated as if it's a single disease. But researchers have discovered a new type of the cancer that appears to affect 15 percent of patients, a finding that paves the way for better diagnosis and more targeted therapies down the road.

The new pathway for <u>prostate cancer</u> development was discovered after a team of scientists identified unique mutations in a gene known as SPOP (pronounced 'S-Pop') while examining patient tumors. These <u>aberrations</u> may lead to a dangerous accumulation of proteins that spark <u>tumor growth</u>, forming a distinct kind of cancer, according to the study, published in the journal *Nature Genetics*.

The discovery of a second way for cancer to grow means we might one day "think of prostate cancer not as one disease but as a collection of molecularly defined subtypes, similar to breast and <u>lung cancer</u>," said Dr. Mark Rubin, vice chair for <u>experimental pathology</u> at Weill Cornell Medical College and a co-senior investigator of the study.

Along with previous research, the study is helping flesh out the overall genetic landscape of prostate cancer - the most common cancer in men with the exception of <a href="skin cancer">skin cancer</a>.

About one-sixth of men will be diagnosed with prostate cancer in their lifetime; two-thirds when they are older than 65. Prostate cancer is the second leading cause of cancer deaths in men.



Some speculate that the finding of an SPOP mutation may be one of the breakthroughs oncologists have been seeking. "Knowing what these mutations mean may give us huge clues about how the patient's cancer will progress and how they might be best treated in the future," said study co-author Christopher Barbieri, chief resident in urology at Weill Cornell who spent a research year in Rubin's laboratory.

About half of all prostate cancers are characterized by the presence of socalled ETS <u>fusion genes</u>. A <u>gene fusion</u> occurs when two genes located in different parts of the genome become attached together, leading to a new function.

The new subtype of prostate cancer is defined by two factors: the presence of a mutation in the SPOP gene and the loss of DNA in an area harboring another gene.

"Alterations in these two major gatekeepers lead to a cascade of downstream events that make these tumors distinct from other prostate cancers," said Rubin, who noted that SPOP mutations and fusion genes never occur in the same tumor, implying two distinct molecular classes of prostate cancer.

The SPOP gene belongs to a family whose job is to regulate other proteins by tagging or marking them for disposal. The team discovered the mutations occur where the SPOP protein binds to the other proteins it should tag.

"That suggests that there might be an accumulation of proteins in the cell that aren't cleaned out and this might lead to cancer growth, or the mutations could be removing proteins that help prevent unchecked cell growth," said Rubin.

Rubin predicted that within a year, men already confirmed with prostate



cancer will be able to get tested to see what kind of subtype of prostate cancer they have and then receive tailor-made treatment. Rubin predicts future screening tests will include panels of such cancer specific markers to ensure accurate diagnosis of cancer.

Still, others say that although the discovery is exciting, the test wouldn't be clinically available for quite some time - if ever. Additionally, it would never be used as a screening tool because it's present in only a small portion of all prostate cancers.

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