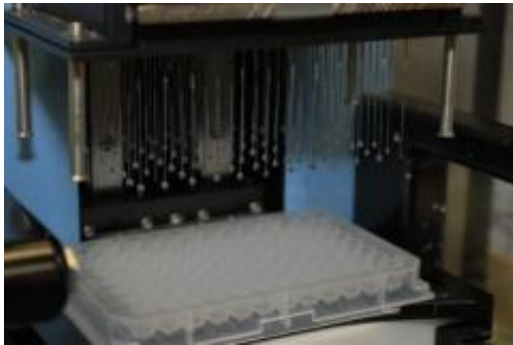


# Gene mutations increase risk for aggressive prostate cancer

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Dispensing DNA samples for high-throughput BRCA1/2 analyses. Credit: Albert Einstein College of Medicine

Men who develop prostate cancer face an increased risk of having an aggressive tumor if they carry a so-called breast cancer gene mutation, scientists from the Albert Einstein College of Medicine of Yeshiva University report in today's issue of *Clinical Cancer Research*. The findings could help to guide prostate-cancer patients and their physicians in choosing treatment options.

The study, involving 979 men with prostate cancer and 1251 men without the disease, looked at whether participants carried mutations for either of two genes, BRCA1 and BRCA2. Women carrying mutations in either gene face an increased risk of developing breast cancer, ovarian cancer, or both.

All the people enrolled in the Einstein study were of Ashkenazi Jewish descent. The study focused on them because they are five times likelier than people in the general population to carry a mutation of any kind in the BRCA1 or BRCA2 genes. The researchers looked for the presence of three particular mutations—two in BRCA1 and one in BRCA2. Scientists believe that genetic discoveries among the Ashkenazi can benefit society as a whole in terms of preventing and

treating major diseases.

Having any of the three mutations did not increase a man's risk of developing prostate cancer, the study found. But for those men who did develop prostate cancer, two of the mutations—BRCA1-185delAG and the mutated BRCA2 gene—increased the risk that tumors would be aggressive or high-grade, as defined by a Gleason score of 7 or above. The Gleason score, based on the microscopic appearance of prostate tissue removed during a biopsy or surgery, assesses the aggressiveness of a prostate tumor on a scale from 2 (least aggressive) to 10 (most aggressive).

Specifically, prostate cancer patients with high-grade, aggressive tumors (Gleason scores of 7 or above) were 3.2 times more likely to carry the BRCA2 gene mutation than were men in the control group. Carriers of the BRCA1-185delAG mutation were also at increased risk of having an aggressive prostate cancer.

Previous investigations into a possible link between prostate-cancer risk and the BRCA1 and BRCA2 genes have yielded conflicting results—perhaps because they involved small numbers of subjects and lacked well-matched control groups. "Our large study shows conclusively that prostate cancer patients with either the BRCA2 gene mutation or the BRCA1-185delAG mutation are more susceptible to aggressive cancers than people without that mutation," says Robert Burk, M.D., professor of pediatrics (genetics) at Einstein and senior author of the study.

Routine genetic testing for BRCA mutations—done by analyzing blood samples or cells swabbed from the inside of one's cheeks—wouldn't be justified for most men, says Dr. Burk: the prevalence of the mutations in the general population is very low; and men with high Gleason scores already know that their prostate cancer is aggressive. But, notes Dr. Burk, "our findings might have practical implications

for some men diagnosed with early-stage (low Gleason score) prostate cancers—particularly Ashkenazi Jewish men, who are much more likely to have these mutations."

"One of the biggest problems with early-stage prostate cancer is being able to distinguish between tumors with the potential to become aggressive and those that may persist for many years without enlarging or spreading," notes Dr. Burk. For that reason, he says, Ashkenazi men diagnosed with early-stage prostate cancer might want to consider getting tested for the BRCA2 and BRCA1-185delAG mutations.

Knowing they have the mutation—and that their tumor may become aggressive—may influence treatment options that patients pursue. For example, a prostate cancer patient who has the BRCA2 mutation might vote against 'watchful waiting'—in which the growth of the cancer is monitored and treatment is held in abeyance—and instead opt for surgery or radiation treatments with or without hormone blockade therapy.

For early-stage prostate cancer patients in the general population, knowing they carry the BRCA1 or BRCA2 mutation would also be useful, says Dr. Burk. But these mutations are so rare in the general population—a prevalence of far less than one percent—that testing is unlikely to reveal their presence.

Source: Albert Einstein College of Medicine

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