What's New in Prostate Cancer Research?

Research into the causes, prevention, detection, testing, and treatment of prostate cancer is being done in many medical centers throughout the world.

- Genetics
- Prevention
- Early detection
- Diagnosis
- Staging
- Treatment

Genetics

New research on gene changes[1] in prostate cancer cells is helping scientists better understand how prostate cancer develops. This could also help design medicines to target these changes. Learning more about these gene changes might be helpful in other ways as well, such as:

- Identifying which men are most likely to develop (or to already have) prostate cancer
- Determining which men might need a second prostate biopsy, even if an initial biopsy doesn't find cancer
- Determining which prostate cancers are most likely to grow and spread[2] (and therefore should be treated)
- Determining if specific treatments such as newer targeted therapy drugs[3] might be helpful
- Identifying which men might benefit from genetic testing[4] to see if they inherited a gene change (and therefore might have a higher risk for other cancers as well)

Some of these uses are discussed in more detail below.

Prevention

Researchers continue to look for foods (or substances in them) that can help lower prostate cancer risk. Scientists have found some substances in tomatoes (lycopenes)

and soybeans (isoflavones) that might help prevent some prostate cancers. Studies are now looking more closely at the possible effects of these compounds.

Scientists are also trying to develop related compounds that are even more potent and might be used as dietary supplements. But so far, most research suggests that a balanced diet including plenty of fruits and vegetables is probably of greater benefit than taking specific substances as dietary supplements.

Some research has suggested that men who regularly take certain medicines (such as aspirin or cholesterol-lowering statins) for a long time might have a lower risk of getting or dying from prostate cancer. More research is needed to confirm this, and to confirm that any benefit outweighs the potential risks.

Scientists have also tested certain hormonal medicines called **5-alpha reductase inhibitors** as a way of reducing prostate cancer risk. This is discussed in Can Prostate Cancer Be Prevented?[5]

Early detection

The prostate-specific antigen (PSA) blood test is not a perfect test for finding prostate cancer early. It misses some cancers, and sometimes it finds cancers that would probably never need to be treated. Researchers are working on strategies to address these issues.

One approach is to try to improve on the test that measures the total PSA level, as described in Screening Tests for Prostate Cancer[6].

Another approach is to develop new tests based on other forms of PSA, or other types of biomarkers. Several newer tests seem to be more accurate than the PSA test, including:

- The **Prostate Health Index (PHI)**, which combines the results of total PSA, free PSA, and proPSA to help determine how likely it is that a man has prostate cancer that might need treatment
- The **4Kscore test**, which combines the results of total PSA, free PSA, intact PSA, and human kallikrein 2 (hK2), along with some other factors, to help determine how likely a man is to have prostate cancer that might need treatment
- Tests (such as **Progensa**) that look at the level of **prostate cancer antigen 3 (PCA3)** in the urine after a digital rectal exam (DRE). The DRE pushes some of the prostate cells into the urine. The higher the level, the more likely that prostate

cancer is present.

- Tests that look for an abnormal gene change called ***TMPRSS2:ERG*** in prostate cells in urine collected after a DRE. This gene change is found in some prostate cancers, but it is rarely found in the cells of men without prostate cancer.
- **ExoDx Prostate(IntelliScore)**, or **EPI**, a test that looks at levels of 3 biomarkers in a urine sample to help determine a man's risk of having aggressive (high-grade) prostate cancer
- **SelectMDx**, which looks at the levels of certain forms of RNA (linked to certain cancer-related genes) in the urine. This test can be used along with other factors to help determine a man's risk of having aggressive (high-grade) prostate cancer.
- **My Prostate Score 2.0 (MPS2)**, which checks the urine after a DRE for changes in 18 genes, including *PCA3* and *TMPRSS2:ERG* (see above), to help determine a man's risk of having Grade Group 2 or higher[7] prostate cancer
- **Sentinel PCa Test**, which looks for certain pieces of RNA in the urine to help determine a man's risk of prostate cancer
- **IsoPSA**, which looks at different forms of PSA in the blood to help determine a man's risk of having high-grade prostate cancer
- **ConfirmMDx**, which is a test that looks at certain genes in the cells from a prostate biopsy sample

These tests aren't likely to replace the PSA test any time soon, but they might be helpful in certain situations. For example:

- Some of these tests might be useful in men with a slightly elevated PSA, to help determine whether they should have a prostate biopsy[8].
- Some of these tests might be helpful in determining if men who have already had a prostate biopsy that didn't find cancer should have another biopsy.

Doctors and researchers are trying to determine the best way to use each of these tests.

Diagnosis

Doctors doing prostate biopsies often rely on transrectal ultrasound (TRUS)[9], which creates black-and-white images of the prostate using sound waves, to know where to take samples from. But standard ultrasound may miss some areas containing cancer. Some newer techniques might help make TRUS more effective in finding prostate cancer.

- **Color Doppler ultrasound:** This technique measures blood flow within the prostate gland. (Tumors often have more blood vessels around them than normal tissue.) It may make prostate biopsies more accurate by helping to ensure the right part of the gland is sampled.
- **Contrasted-enhanced Doppler ultrasound:** Doppler ultrasound might be enhanced even further by first injecting a person with a contrast agent that can help improve the images. Researchers are continuing to look for better contrast agents.
- **Transrectal elastosonography (TRES):** In this technique, ultrasound is used to help determine how stiff different parts of the prostate are. Because tumors tend to be stiffer than normal prostate tissue, this can help guide which parts of the prostate should be biopsied.
- **Micro-ultrasound:** This newer technique uses higher-frequency ultrasonic waves, which can help create more detailed images of the prostate.

Another approach combines MRI and TRUS images to help guide prostate biopsies, especially in men who previously had negative TRUS-guided biopsies but the doctor still suspects have cancer. This test, known as **MRI/TRUS fusion-guided biopsy**, is discussed in Tests to Diagnose and Stage Prostate Cancer[10]. This might be done using multiparametric MRI, which is discussed below.

Staging

Determining the stage (extent) of prostate cancer[11] plays a key role in determining a man's treatment options. But imaging tests for prostate cancer, such as CT[12] and MRI[13] scans, might not detect all areas of cancer, especially small areas of cancer in lymph nodes, so doctors are now looking at newer types of imaging tests.

Multiparametric MRI (mpMRI) can be used to help determine the extent of the cancer and how aggressive it might be, which might affect a man's treatment options. For this test, a standard MRI is done to look at the anatomy of the prostate, and then at least one other type of MRI (such as diffusion-weighted imaging [DWI], dynamic contrast-enhanced [DCE] MRI, or MR spectroscopy) is done to look at other parameters of the prostate tissue. The results of the different scans are then compared to help find abnormal areas.

Enhanced MRI may help find lymph nodes that contain cancer cells. Patients first have a standard MRI. They are then injected with tiny magnetic particles and have another scan the next day. Differences between the 2 scans point to possible cancer cells in the lymph nodes. Early results of this technique are promising, but it needs more research before it becomes widely used.

Newer types of PET scans can also be helpful in detecting prostate cancer in different parts of the body. These newer tests use tracers, such as radioactive sodium fluoride, fluciclovine, choline, or carbon acetate. Some newer tests (known as **PSMA PET scans**) use radioactive tracers that attach to prostate-specific membrane antigen (PSMA), a substance that is often found in large amounts on prostate cancer cells. Some of these newer tests are now being used in many centers, while others are still being studied. For more information, see Tests to Diagnose and Stage Prostate Cancer[14].

Treatment

Newer tests and treatments are being developed, and improvements are being made to current prostate cancer treatment methods.

Determining if treatment is needed

An important area of research is determining which men with early-stage prostate cancer need to be treated right away, and which men might choose monitoring (active surveillance or observation[15]) as a reasonable option.

Some newer molecular tests (also known as genomic tests) look for certain gene or protein changes in prostate cancer cells to help determine how quickly the cancer is likely to grow and spread. The results of one of these tests can be used to help determine if the cancer needs to be treated. To learn more, see Risk Groups and Lab Tests to Help Determine Risk from Localized Prostate Cancer[16].

Surgery

Doctors are constantly improving the surgical techniques[17] used to treat prostate cancer. The goal is to remove all of the cancer while lowering the risk of complications and side effects from the surgery.

Surgery to treat prostate cancer is most often done using **robot-assisted prostatectomy**. In this approach, several small cuts are made in the abdomen to insert long surgical tools, which the surgeon maneuvers while sitting at a control panel. Benefits of this approach include quicker recovery times and less pain after surgery.

In a newer approach, known as **single-incision robotic prostatectomy**, the operation is done through only one small cut near a man's belly button. The hope is that using only one incision might cut down on pain and recovery times even further, although this still needs to be proven in studies.

Radiation therapy

As described in Radiation Therapy for Prostate Cancer[18], advances in technology are making it possible to aim radiation more precisely than in the past.

Current treatment methods, such as **intensity-modulated radiation therapy (IMRT)** and **proton beam radiation,** help doctors avoid giving radiation to normal tissues as much as possible.

In many centers, doctors are now using image-guided approaches to help aim radiation more precisely as well. Because the prostate might be in a slightly different position in the body each day, getting an imaging test (such as MRI) before each treatment (or even during treatment) can help ensure the radiation is aimed exactly where the doctor wants it to go.

These newer methods may increase the effectiveness of radiation therapy while reducing the side effects.

Technology is making other forms of radiation therapy more effective as well. New computer programs allow doctors to better plan the radiation doses and approaches for both external radiation therapy and brachytherapy. Planning for brachytherapy can now even be done during the procedure (intraoperatively).

Newer treatments for early-stage cancers

Researchers are looking at newer forms of treatment for early-stage prostate cancer. These new treatments might be used either as the first treatment or if cancer remains after radiation therapy.

For example, doctors are now looking at whether ablative treatments can be helpful for these cancers. These treatments use extreme heat, cold, or other methods to destroy (ablate) tumors. Examples include **cryotherapy, high-intensity focused ultrasound (HIFU), photodynamic therapy (PDT), focal laser ablation (FLA),** and **irreversible electroporation (IRE).**

The safety and effectiveness of these treatments are now being studied. While some of these are now available, most doctors in the United States don't consider them to be proven first-line treatments for prostate cancer at this time. To learn more, see Cryotherapy, HIFU, and Other Ablative treatments for Prostate Cancer[19].

Nutrition and lifestyle changes

Many studies have looked at the possible benefits of specific nutrients (often as supplements) in helping to treat prostate cancer, although so far none have shown a clear benefit. Some compounds being studied include extracts from pomegranate, green tea, broccoli, turmeric, flaxseed, and soy.

It's important for men thinking about taking any type of nutritional supplement to talk to their health care team first. They can help you decide which ones you can use safely while avoiding those that might be harmful.

Hormone therapy

Several newer forms of hormone therapy have been developed in recent years. Some of these may be helpful when standard forms of hormone therapy are no longer working.

Some examples include abiraterone (Zytiga), enzalutamide (Xtandi), apalutamide (Erleada), and darolutamide (Nubeqa), which are described in Hormone Therapy for Prostate Cancer[20]. Others are now being studied as well.

Chemotherapy

Studies in recent years have shown that many chemotherapy drugs can affect prostate cancer. Some, such as docetaxel (Taxotere) and cabazitaxel (Jevtana), have been shown to help men live longer.

Other new chemo drugs and combinations of drugs are being studied as well.

Immunotherapy

The goal of immunotherapy[21] is to boost the body’s immune system to help fight off or destroy cancer cells.

Vaccines

Unlike vaccines against infections like measles or mumps, prostate cancer vaccines are designed to help treat, not prevent, prostate cancer. One possible advantage of these types of treatments is that they seem to have very limited side effects. An example of this type of vaccine is **sipuleucel-T (Provenge).**

Several other types of vaccines to treat prostate cancer are being tested in clinical trials.

Immune checkpoint inhibitors

An important part of the immune system is its ability to keep itself from attacking other normal cells in the body. To do this, it uses “checkpoint” proteins on immune cells that need to be turned on (or off) to start an immune response. Cancer cells sometimes use these checkpoints to avoid being attacked by the immune system.

Newer drugs that target these checkpoints (known as **checkpoint inhibitors**) have been shown to be useful in treating many types of cancer, including prostate cancers in which the cells have certain types of gene changes.

Chimeric antigen receptor (CAR) T-cell therapy

In this treatment, immune cells called **T cells** are removed from the patient’s blood and altered in the lab so they have **chimeric antigen receptors (CARs)** on their surface. These receptors can be made to attach to proteins on the surface of prostate cells. The altered T cells are then multiplied in the lab and put back into the patient’s blood. The hope is that they can then find the prostate cancer cells in the body and launch a precise immune attack against them.

This technique has shown some encouraging results against prostate cancer in early clinical trials, but more research is needed to see how useful it can be. CAR T-cell therapy is a complex treatment with potentially serious side effects, and it is only available in clinical trials at this time.

Targeted therapy drugs

Newer drugs are being developed that target specific parts of cancer cells or their surrounding environments. Each type of targeted therapy[22] works differently, but they all alter the way a cancer cell grows, divides, repairs itself, or interacts with other cells.

PARP inhibitors

In some men with prostate cancer, the cancer cells have mutations in DNA repair genes (such as *BRCA2*) that make it hard for cancer cells to fix damaged DNA. Drugs called **PARP inhibitors** work by blocking a different DNA repair pathway. Cancer cells are more likely to be affected by these drugs than normal cells.

PARP inhibitors, such as olaparib, rucaparib, niraparib, and talazoparib, can now be used along with hormone therapy to treat advanced prostate cancers if the cells have changes in a DNA repair gene.

Monoclonal antibodies

These are manmade versions of immune proteins that can be designed to attach to very specific targets on cancer cells (such as the PSMA protein on prostate cancer cells).

For prostate cancer, most of the monoclonal antibodies being studied are linked to chemo drugs or to small radioactive molecules. The hope is that once injected into the body, the antibody will act like a homing device, bringing the drug or radioactive molecule directly to the cancer cells, which might help them work better. Several monoclonal antibodies are now being studied in clinical trials.

Treating prostate cancer that has spread to the bones

Doctors are studying the use of several newer approaches to treating prostate cancer that has spread to one or more areas in the bones, especially if radiation therapy isn't working.

Several of these are **ablative treatments**, in which extreme heat or cold is used on bone tumors to help ablate (destroy) them. Examples include:

- High-intensity focused ultrasound (HIFU)
- Radiofrequency ablation (RFA)
- Cryoablation (cryotherapy)

To learn more, see Treatments for Prostate Cancer Spread to Bones[23].

Prostate Cancer Research Highlights [24]
Get the latest research highlights from our prostate cancer research conducted and funded through ACS grants.

Hyperlinks

1. www.cancer.org/cancer/types/prostate-cancer/causes-risks-prevention/what-causes.html
2. www.cancer.org/cancer/types/prostate-cancer/detection-diagnosis-staging/risk-groups.html
3. www.cancer.org/cancer/types/prostate-cancer/treating/targeted-therapy.html

4. www.cancer.org/cancer/risk-prevention/genetics/genetic-testing-for-cancer-risk.html
5. www.cancer.org/cancer/types/prostate-cancer/causes-risks-prevention/prevention.html
6. /cancer/types/prostate-cancer/detection-diagnosis-staging/tests.html
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