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# Understanding the Role of Personalized Medicine

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# Understanding the Role of Personalized Medicine

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# *Growing knowledge about the genetic makeup of tumors is leading to a revolution in cancer treatment.*

**Through research, more effective tailored cancer treatments are now available.** This means that we are beginning to move away from the use of "one-size-fits-all" chemotherapy and toward the use of targeted drugs designed for specific patients and tumors—that is, personalized medicine.

For many years, doctors knew that certain groups of people benefited from certain types of treatments. For example, older women with breast cancer tended to benefit more from hormone treatments than younger women with breast cancer. But in recent years, scientists discovered that not all cancers are alike. There are variations of each type of tumor. This was discovered when researchers focused on the genetics of tumors. Our genes are the blueprint for control of every cell in the body. A better understanding of this blueprint means we can find out how different types of tumors work, how they grow, and how to stop them from growing.

Medicines are being designed to target a number of different tumor cell growth mechanisms. With targeted drugs, doctors can select the treatment that is most likely to work for a certain patient and his or her particular type of tumor. This information also means that people for whom the drug would not work can avoid taking it and risking side effects.

# How Targeted Treatments Work

Standard chemotherapy drugs are powerful medications that can kill cancer cells. They offer an effective way to treat tumors, but they can also harm healthy tissues. One day, targeted treatments may replace chemotherapy. But for now, doctors will continue to use chemotherapy, sometimes in combination with targeted drugs. (In some cases, doctors combine two targeted treatments without chemotherapy.)

There are many targeted treatments already available, and many more drugs are being studied in laboratories and clinical trials. A number of these medications are oral drugs, which are easier and more convenient for patients to take. To kill a cancer cell, targeted treatments disrupt many different types of cell mechanisms.

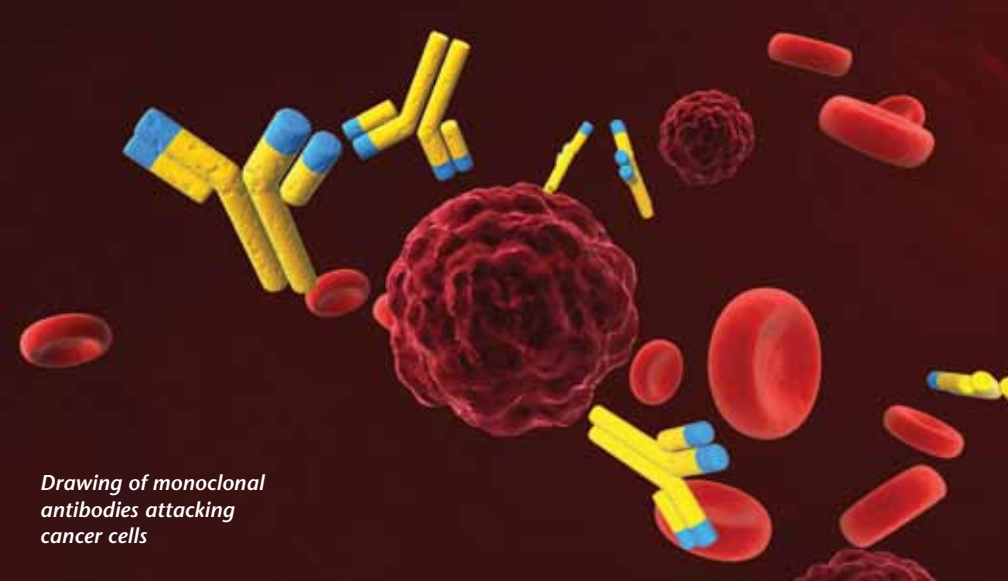
**Drugs made of small molecules are able to get past the tumor cell's outer layer and interfere with cell growth from the inside.** These small molecules block signals from proteins that tell cancer cells to grow and divide. (Proteins are controlled by genes.) This type of targeted treatment can help stop tumor growth and may cause cancer cells to die.

Examples of small-molecule targeted treatments include dasatinib (Sprycel), which is approved by the U. S. Food and Drug Administration (FDA) to treat people with chronic myelogenous leukemia (CML) or acute lymphoblastic leukemia, and nilotinib (Tasigna), which is approved to treat some people with CML.

Other types of small-molecule drugs disrupt tumor cells by changing some of their cell functions or by directly causing their death in a process known as apoptosis. Two examples are romidepsin (Istodax), approved by the FDA for the treatment of cutaneous T-cell lymphoma, and bortezomib (Velcade), approved for the treatment of multiple myeloma.

Some small-molecule drugs block the growth of blood vessels to tumors. To grow beyond a certain size, tumors must have a blood supply to get oxygen and nutrients. Treatments that interfere with the formation of these blood vessels may block tumor growth. An example of this type of drug is pazopanib (Votrient), approved by the FDA for the treatment of advanced kidney cancer.

**Monoclonal antibodies track down tumor cells and bind to their surface to disrupt the cells' function from the outside.** Made in the laboratory, monoclonal antibodies are a type of protein. Although they cannot get past a tumor cell's outer layer, monoclonal antibodies can attach themselves to the cell surface and block its receptors, or doorways. When receptors



*Drawing of monoclonal antibodies attacking cancer cells*

are blocked, growth signals cannot get in and the cell dies. There are many types of monoclonal antibodies. Each type is designed to find a specific kind of tumor cell.

**Sometimes, monoclonal antibodies are used to carry an anti-cancer medicine directly to the tumor cell to kill it.** The advantage of using this technique is that the treatment bypasses healthy tissue and goes directly to the tumor. Brentuximab vedotin (Adcetris) is an example of an antibody combined with a targeted treatment. Hitching a ride on the monoclonal antibody, the drug enters the cell and kills it. Brentuximab vedotin is approved by the FDA for the treatment of Hodgkin's lymphoma and systemic anaplastic large cell lymphoma.

**Some monoclonal antibodies are designed to trigger the immune system to fight the cancer.** In the case of ipilimumab (Yervoy), the antibody seeks out a substance on tumor cells called CTLA-4, which blocks the immune system. By blocking CTLA-4, ipilimumab stimulates the immune system to attack melanoma cells. This medication has been approved by the FDA for treating melanoma that has spread.

# The New Diagnostics

In cancer, a pathologist is the physician who diagnoses the type of tumor a person has by studying cells and tissues under a microscope. The pathologist also provides information on how the tumor may grow, its stage or grade, and other basic characteristics. But now, because of personalized medicine, pathologists have a new and important role to play: helping to guide oncologists in choosing the most effective personalized treatment.

There are a number of different tests that pathologists can perform to learn more about the genetics of a tumor and the subclass it belongs to. This information helps point the way to the best personalized treatment. Through a fairly new field called proteomics, powerful new tools are being developed to find the genetic features of tumor cells. The "proteome" (a blend of the words "**prote**in" and "gen**ome**") is all the proteins our genes make; proteins do most of the work in cells. The genome is our complete genetic material.

New technologies allow pathologists to extract genetic material from stored tumor samples and to sort out thousands of pieces of genetic material in new tissue samples from a tumor. These techniques enable doctors to identify specific genes. It is a rapidly growing area of medicine that is vital to cancer treatment.

With proteomics, doctors can also identify the proteins that govern how each person will process, or metabolize, drugs. This is another important part of choosing effective treatment. For example, those with a mutated (changed) form of the *DPD* gene have difficulty metabolizing 5-fluorouracil, a common

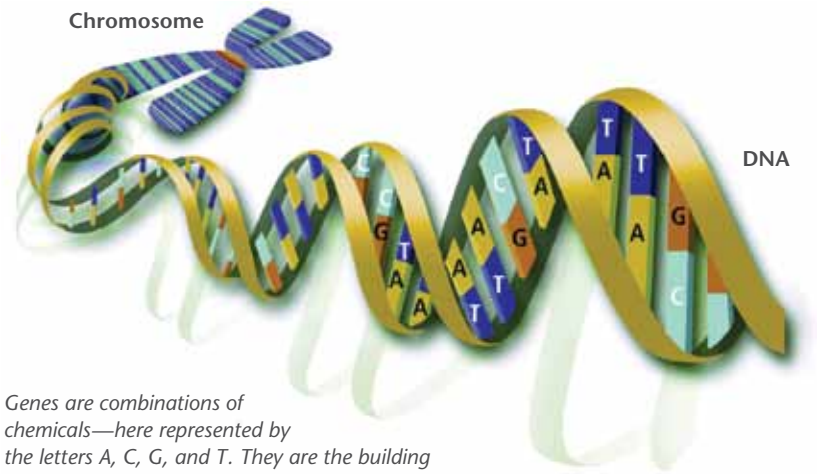
anti-cancer drug. That's because the mutated gene does not make the needed DPD protein. As a result, people with a mutated *DPD* gene experience more side effects from this chemotherapy. This drug is used to treat a number of cancers including breast, stomach, pancreas, and certain types of colorectal and head and neck cancers. If a doctor knows the patient has a mutated *DPD* gene, he or she can choose another treatment or reduce the dose of 5-fluorouracil. In another example, people who are "fast metabolizers" of anti-nausea drugs can be given a higher dose so the medicine will stay in their system longer and work better.

The more your doctor knows about your genetic makeup, the more effective treatment you can receive.

# Genes Matter

Genetic changes, or mutations, present a target that the new personalized treatments can zero in on to stop the growth and spread of cancer cells. Some gene mutations play a role in multiple cancers. Just a few examples include:

| Cancer | Gene mutation | Targeted treatment |
|---|---|---|
| **Lung** | *EGFR*<br>*EML4-ALK* | Erlotinib (Tarceva)<br>Crizotinib (Xalkori) |
| **Skin** | *BRAF* | Vemurafenib (Zelboraf) |
| **Colon** | *EGFR*<br>*KRAS* | Cetuximab (Erbitux)<br>Panitumumab (Vectibix) |
| **Breast** | *HER2* | Trastuzumab (Herceptin)<br>Lapatinib (Tykerb) |




*Genes are combinations of chemicals—here represented by the letters A, C, G, and T. They are the building blocks of DNA, our genetic blueprint.*

# Side Effects of Targeted Treatments

## Although targeted treatments don't affect the body in the same ways as chemotherapy, they can lead to different types of side effects.

Drugs that target the EGFR protein often lead to skin rash. (In fact, a rash may be a sign that the targeted treatment is working.) The EGFR protein tells cancer cells to grow and divide. But healthy skin cells have a lot of EGFR too, and these cells must continue to grow quickly so they can maintain the skin's surface layer. Drugs that block EGFR often affect skin cells by "turning off" their growth signal.

Because these changes to the skin can range from mildly annoying to severe, it's important to work closely with your health care team to treat the symptoms promptly so they don't worsen or lead to infection or other problems.

You should note that skin rash usually develops slowly over days to weeks. If you develop symptoms quickly—within minutes to a few hours after receiving a targeted treatment—it probably means you are allergic to it. Allergic reactions include hives (raised skin bumps or welts that typically go away within a day or so) and intense itching.

***If you develop trouble breathing, dizziness, tightness in the throat or chest, or swelling of the lips or tongue, get emergency help and call your doctor right away.***

Talk with your doctor if you notice any of the following symptoms:

**Changes in how the skin feels** Before any redness or rash shows up, skin may start feeling like it's sunburned.

**A rash that looks like acne (but with no blackheads) on the scalp, face, neck, chest, and upper back** In severe cases, it can affect other parts of the body. The rash usually starts as skin redness and swelling and is often most severe within the first few weeks of treatment.

**Dry skin** Skin may become very dry and scaly and may even crack open.

**Itchy skin** Many of the skin changes, like rash or dryness, can cause itching.

**Red, sore cuticles around the fingernails and toenails** Some targeted treatments can cause painful skin sores in these areas. These sores may become infected. Nails may also become brittle and grow more slowly.

**A painful sensitivity of the hands and feet** Sensitivity is an early symptom of hand-foot syndrome, a side effect marked by redness, swelling, numbness, and tingling of the hands or feet.

**Changes in hair growth** Hair on the head may become thin, dry, and brittle, or even curly. Long-term use of targeted treatments may lead to bald patches or hair loss. Facial hair for both men and women may grow faster than usual, including longer, thicker, curly eyelashes that may need to be trimmed. In some men, facial hair may grow slowly. In addition, the eyebrows may thin out.

**Changes in hair or skin color** Some medications can cause the skin or hair to turn a yellowish color during treatment. In a few people, hair color can become darker. These changes tend to go away once treatment is finished.

**Changes in and around the eyes** The eyes may burn and become dry or red. The eyelids may get tender, swollen, or inflamed, and crusts may be seen in the lashes. Prolonged dryness can damage the clear part of the eye (the cornea). In order to avoid injury, it's important to work with your doctor or nurse to manage these changes.

# Personalized Medicine and Quality of Life

By defining specific types of cancer, and directing the right treatment to the right person, doctors are working to improve the quality of life for all people with cancer. Targeted treatments are potentially less harmful to healthy cells, may cause fewer serious side effects, and could be more effective than standard chemotherapy. In addition to treating cancer, the goal of oncologists is to help people live better during treatment and as survivors after treatment.

The more active a role you play in your treatment, the more control you will have over side effects. Good communication with members of your health care team is especially important so that they can prevent and treat side effects before they affect your quality of life.

# The Importance of Clinical Trials

The exciting advances in personalized medicine have all come about because of clinical trials and the thousands of people with cancer who have taken part in them. These studies also increase the knowledge of tumor genetics through blood and tissue samples examined by pathologists. Some clinical trials are designed to learn more about side effects and quality-of-life issues. Talk to your doctor about whether a clinical trial is right for you.

Here are a number of questions you should ask your doctor about clinical trials. You may want a friend or family member to sit with you during the discussion to take notes.

- What is the purpose of the study?
- What is the phase of the trial?
- What kinds of tests and treatments are involved?
- How do the possible risks, side effects, and benefits of the study compare with my current treatment?
- How might this study affect my daily life?
- How many visits per week or month will I need to make?
- How long will the study last?
- Is a hospital stay required?
- Who will pay for the treatment?
- Will I be reimbursed for any expenses, such as transportation?

- What type of long-term follow-up care is part of this study?
- How will I know that the treatment being studied is working? Will the results of the trial be given to me?
- Who will be in charge of my care?
- Are there other experts I can talk to about this study?
- Can I take the informed consent form home to talk it over with my family or partner?

See the resources on page 17 of this booklet to learn where you can get more information about clinical trials.

# Frequently Asked Questions

**Q.** I've heard that it's very expensive to have a tumor tested for gene mutations. Will my insurance plan pay for genetic testing?

**A.** It depends on the type of test. For instance, doctors have official treatment guidelines for testing the *BRCA* gene in breast cancer, and many insurance plans cover that. If your doctor believes other genetic tests, not covered under the guidelines, are needed in order to make a treatment decision, insurance plans often will cover the cost. A number of large cancer centers conduct these tests as part of the care they provide. Even if a genetic test is approved by the FDA, health care plans may vary. You should note that tumor testing for research purposes generally is not paid for by health insurance, but the sponsors of the clinical trial will cover that cost.

**Q.** When a lab tests a tumor for one type of mutation, can it test for other mutations at the same time?

**A.** Yes, and it is important to do that because additional testing may provide more information about the tumor. It is more cost effective to look for many different mutations than to search just one particular mutation. Often, pathologists ask for a second biopsy so that more tissue can be studied. Retesting a tumor helps guide treatment as the patient progresses through treatment.

**Q. Do doctors keep biopsy material in case a more sophisticated test is developed in the future?**

**A.** Some cancer centers maintain their tissue samples permanently. But every state has different requirements for keeping tumor tissue. Some of those guidelines may be changing because of personalized medicine. We know that biopsy material could be important a few years down the line as we gain more knowledge.

**Q. Before my next visit to the doctor, how should I prepare so that I can make the most out of our discussion about personalized medicine?**

**A.** Try to find out as much as possible about your cancer and its treatment. Your doctor's office is another good place to gather information. Some practices provide written materials to their patients. Come with a list of questions written down. Your doctor may cover some of the topics, but if you have prepared some notes, you won't forget to ask about subjects he or she did not discuss. Have a list of your medications as well as your personal and family medical histories. They are important factors for your doctor to take into account when it comes to personalizing your treatment. It's always a good idea to bring someone with you to the visit, so you have a second set of ears. Ask your friend or loved one to bring a paper and pen. Finally, keep the dialogue going. Your doctor or a staff member should be available to answer questions, even if you think of them after your office visit.

# Resources

**Cancer*Care***
800-813-HOPE (4673)
www.cancercare.org

**American Cancer Society**
800-227-2345
www.cancer.org

**Cancer.Net**
Patient information from the American Society of Clinical Oncology
www.cancer.net

## FINANCIAL ASSISTANCE

**Cancer*Care***
800-813-HOPE (4673)
www.cancercare.org

**Cancer Financial Assistance Coalition**
www.cancerfac.org

**Partnership for Prescription Assistance**
888-477-2669
www.pparx.org

**U.S. Social Security Administration**
800-772-1213
www.socialsecurity.gov

## TO FIND OUT ABOUT CLINICAL TRIALS

**Coalition of Cancer Cooperative Groups**
www.CancerTrialsHelp.org

**National Cancer Institute**
www.cancer.gov/clinicaltrials

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