Personalized Cancer Treatment

Printed from https://www.cancerquest.org/patients/treatments/personalized-cancer-treatment on 11/02/2026

Personalized cancer treatment, sometimes called precision medicine, is changing cancer care for the better. Historically, cancers arising in the same place (i.e. the lungs or colon) were considered to be very similar to each other and were treated in a similar way. This is not ideal, because the same treatments work better for some people than others. This is because much as no two people are alike, no two cancers are alike. Fortunately, cancer treatment is rapidly shifting to a more personalized approach. Personalized cancer treatment takes into account differences between cancer cases and patients. As a result, treatment effectiveness can be increased and the risk of side effects can be reduced. Personalized cancer treatment can improve cancer outcomes and the quality of life of cancer patients.

The list below is incomplete, but gives an idea of the types of things that allow for cancer patients to be treated individually. Often several of the tests below are used in combination to create the most detailed possible picture of the patient and the cancer.

What are the tools of personalized medicine?

Improved cancer treatments depend on those treating it having a better understanding of the diseases they're treating. The knowledge comes from advances in the ways cancer is studied (called cancer model systems). While no cancer model system can fully represent an actual human tumor, models allow clinicians to study different cancer treatments and predict the most effective treatment for a cancer type or the cancer in an individual patient.

Cancer Model Systems

Cancer model systems allow us to test new treatments without the need for human volunteers. Examples of ways cancer is studied include microscopic analysis via biopsy, cell lines, organoids, animal models, patient-derived xenografts (PDX), and computer-based models.

Information from model systems allows clinicians to tailor cancer treatment to an individuals' unique characteristics, increasing cure rates and reducing treatment resistance. Importantly - individual patients can have their cancers studied in real time allowing them to receive the treatments best suited for their particular case.

Microscopic Examination of Cancer Cells and Tissues

Biopsies, small samples taken during surgery or with a needle, allow clinicians to examine cancers under a microscope. Cancer cells often look different from normal cells of the same type. Looking at cancer up close provides several kinds of information, including:

1. How different do the cancer cells look from normal cells? By examining cancer cells and their normal counterparts in a sample of tissue, it is possible to group cancers by how abnormal they appear. This is called the 'differentiation' of the cancer cells.
2. How rapidly are the cancer cells reproducing? By looking at a group of cells, it is possible to estimate the percentage of the cancer cells that were in the process of reproducing (dividing) at the time the sample was taken. The higher the percentage of dividing cells, the more rapidly the cancer is growing.

The information gained from examining cancer cells/tissues is used to diagnose cancers and can also be used to help guide treatment decisions.

Detection of Cellular Proteins

It is possible to detect particular proteins on the surface or inside cells. Often this involves the use of antibodies that have been altered so they can be detected when they stick to their targets. The use of antibodies (an immune protein) to detect proteins on a biopsy is called immunohistochemistry (IHC). If the proteins of interest are found, they can be targeted with drugs. An example is a protein called programmed death ligand 1 or PD-L1. This protein allows cancer cells to bind to, and shut down, immune cells. This prevents the immune cells from recognizing and killing the cancer. Patients whose cancer cells have enough PD-L1 on their surface may be candidates for treatments designed to block that protein. Cancer treatments targeting immune checkpoint proteins include nivolumab (Opdivo®), pembrolizumab (Keytruda®) and ipilimumab (Yervoy®).

Learn more about immunohistochemistry.

Learn more about PD-L1 and immune checkpoint inhibitors.

Genetic Analysis

All cancers are caused by combinations of changes (mutations) in important cell growth genes. The combination of defective genes is different for every cancer but some cancers (i.e. lung or breast) are more likely to have specific mutations targeted by drugs. Cancers that develop in different locations can be treated with the same drug if they share the right mutation. Almost all cancers are tested for changes (mutations) in at least a few important genes.

Many targeted cancer drugs are designed to block the activity of proteins called 'growth factor receptors'. Growth factor receptors are found on and inside all cells. There are many different kinds, but they all function like cellular antennas. When activated, receptors trigger cells to do a wide variety of things. Drugs now exist that can block the activity of some receptors. Knowing whether a particular growth factor receptor is found on a patient's cancer cells (and how much) is a key way that treatments can be tailored to an individual's cancer. A few examples of growth factor receptors, and the drugs that target them include:

1. **The epidermal growth factor receptor (EGFR)**: The EGFR receptor is often altered (mutated) in lung cancer. The altered form is very active, causing the cancer cells to reproduce. The mutant form of the EGFR is the target of erlotinib (Tarceva®) and afatinib (TAGRISSO®).
2. **HER2/neu**: HER2/neu is similar to EGFR. This particular receptor is found at high levels on some breast cancer and stomach cells. The receptor is targeted with an antibody drug - trastuzumab (Herceptin®). Changes in the gene that make the HER2 protein can be detected with genetic tests and the proteins can be detected with antibodies, as described in the previous section.
3. **The estrogen receptor (ER)**: One of the first of the growth factor receptors to be targeted, the estrogen receptor can drive the growth of breast cancer cells. ER production and activity are targets of several different cancer drugs, including tamoxifen (Nolvadex®) and anastraxole (Arimidex®).
4.

The genetic testing allows the treatment to be personalized - the medications are only used if the cancer has the right target protein.

Advanced Model Systems

Currently, almost all cancers are studied with one or more of the methods described above. There are some personalized medicine tools that are used much less often because of their cost, the time it takes to perform the testing or the experimental nature of the tests. Examples include the use of cell lines, cancer organoids and growing cancer in animal hosts (xenotransplantation).

Learn more about cancer models.

Additional Ways to Personalize Cancer Treatment

The methods described above are all different ways of learning about the cancer. There are differences between patients that can also be important in determining how well a treatment works. Some of these differences can be detected and taken into account when treatments are being planned.

One important factor in treatment success is getting the dosage of the medicine correct. Larger people may need increased amounts of medication, Factors that influence drug dosage inlcude age, sex, race, and physical condition. Also , different people break down drugs at the same rate. It is important to consider genetic differences between patients. This includes the genes which control the processing of the drugs being used. Some people break down drugs more quickly than others. They may need an increased dosage. A patient who processes drugs more slowly may be more likely to have side effects and need less medication.

The study of how genes that control drug metabolism affect patients is called *pharmacogenetics* (or *pharmacogenomics*).1 Pharmacogenetics is relevant to a variety of cancer drugs and medications used to treat other conditions.2, 3, 4, 5 In addition to information collected directly from patients, predictions of drug response can use pharmacogenomic information obtained from cancer cell lines and advanced computer programs.6

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