What is Tissue?

Why is it Important?

A concept paper to increase your understanding

When you give permission to have some kind of medical procedure like a blood draw, a biopsy, or surgery you also give permission for your doctor to use your tissue or specimen to help make a diagnosis or check how you are progressing. Most people don't think about the tissue or specimens that remain after they have analyzed for diagnosis and treatment.

You may be asked to donate some of your tissue that is not needed for your medical care. Before you make your decision it may be helpful for you to learn more about tissue and why it is so important.

The use of tissue or specimens in research is vital for medical science to advance. We are now in the age of understanding how normal cells and cancerous cells actually work. Much of what we know to date has come from researchers' ability to study tissue. This is especially true in the last 10 years.

What is Tissue?

Tissue used for research can be called many different things: specimen, biological samples or human biological material. All of these terms refer to a small piece or sample of tissue or fluid and are used interchangeably. When researchers say tissue they can mean blood, urine, saliva, feces, fluid from the spine and brain, organ tissue, bone marrow, tumor tissue, lymph nodes, lymphatic fluid, and many others.

Tissue is a group of cells or fluid that work together to perform a specific job in the body like cells in an organ like the kidney or heart or blood cells that carry oxygen to and waste materials from the cells in the body.

Individual Uses of Tissue

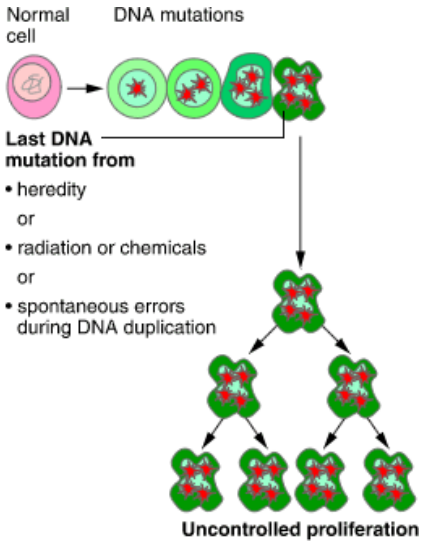
Tissue can be used to diagnose and classify diseases, e.g., to identify that a patient has cancer, what kind of cancer (e.g., kidney, prostate) and the characteristics of the cancer (e.g., Stage II, grade or subtype of lung cancer). Tissue can also be used to monitor responses to treatments to determine if the cancer is progressing or responding or what side effects of treatment are occurring.

Research Uses of Tissue

Scientists use tissue in several ways. They can retrospectively (looking back) compare characteristics of tissue with patient information and how well the patient responded. This gives them information about how well a certain drug worked. They can prospectively (going forward) develop a theory about how a drug will work and then use tissue to determine if they were correct. In the last 10 years the information about how cancer cells work has exploded. One of the most important research uses of tissue is to use saved (archived) tissue to test new discoveries.

Research using tissue is essential to understand the causes of cancer, identify targets for treatments, discover biomarkers that can identify characteristics of a cancer and develop treatments that target a specific gene or signaling process.

Causes of Cancer



We know that cancer arises when there are mutations (changes) in the genes of a cell. Mutations in genes that control the normal growth of cells often contribute to the development of cancer. A person can inherit (be born with) a gene mutation. Some inherited mutations cause a disease or condition. Other mutations only increase our chances (predisposition) of developing a disease. Mutations in genes can be caused by things in the environment, such as: chemicals (e.g., from smoking or diet), radiation and viruses or bacteria (e.g., human papillomavirus (HPV) and cervical cancer; Hepatitis B and liver cancer; H.pylore (bacteria) and gastric cancer). However, most cancer-causing mutations are simply spontaneous errors. Before a cell divides, the normal DNA is replicated (copied) and during this replication, mistakes can be made. When the mistake is not corrected and the cell divides the mistake can persist in the next generation of cells.

What we know so far about the causes of cancer has been learned from studying tissue. If we are to continue to learn more about what causes cancer, we must have patients willing to donate tissue for study.

How Cancer Cells Work

Researchers learn how cancer cells work by studying them in a laboratory. Investigators usually work with individual genes to learn what they do. A good example of this is what was learned about a gene, HER2/neu. When researchers began looking for genes involved with cancer in the 1970's, some focused on understanding oncogenes and the

role they played in cancer. Researchers were able to identify that the HER2/neu gene in a normal cell makes a protein that tells the cell to create receptors for a growth factor. Researchers learned that some breast cancers have too many copies of the HER2/neu gene. The multiple copies of the gene produced an increase in the protein that tells the cell to create growth factor receptors. The more growth factor receptors on the surface of the cell, the faster the cell will grow and divide.

Researchers learned about the HER2/neu gene by studying the tumor tissue in samples or blocks donated from women who had breast cancer. From this they could also match the tumor tissue samples with how well the patient did after treatment. Patients who had multiple copies of the HER2/neu gene had more aggressive cancers and poorer survival rates.

Identify Targets for Treatment

It was discovered by using donated tissue samples that about 25 to 30% of women with breast cancer had the HER2/neu gene mutated. When the HER2/neu gene mutates it makes more copies of itself than there are supposed to be. This is called gene amplification or overexpression.

By studying tissue samples, researchers knew that in some breast cancers there were more growth factor receptors than in normal or in other breast cancer cells. These cancers are called HER2 positive (HER2+). Researchers had identified a target for the treatment of HER2+ breast cancer. If they could block the extra receptors on the surface of the cell, they could slow down how fast the cell was growing and dividing.

Developing Treatments

In the development of a treatment for HER2/neu positive breast cancer, researchers had to find a chemical that would block the many extra growth factor receptors on the surface of the cell. One of the things they tried was a monoclonal antibody, which binds to a single target in the body. In this case the target is the extra receptors on the surface of some cancer cells.

Much of the beginning work of developing a new treatment took place in the laboratory with tissue donated from cancer patients. Researchers identified a chemical, later called Herceptin that blocked the extra growth factor receptors in HER2+ cancers. After many experiments with tissue and animals (usually laboratory rats), researchers were ready to see if Herceptin worked in patients.

Clinical trials (research done with people) were conducted to make sure Herceptin was safe and effective. These trials could not have been done without patients who volunteered to participate and who donated some of their tissue.

The results of the clinical trials showed that Herceptin did work for some women with HER2+ breast cancer. Remarkably, this happened when almost all other treatments had stopped working. In addition, Herceptin did not have as many side effects as other drug treatments. The reason for this is because many chemotherapies target all fast growing cells including bone marrow, hair, and the lining of the gastrointestinal system. This causes low blood cell counts, hair loss, and nausea, vomiting and bowel problems. Herceptin, however, only acts on the HER2/neu growth factor receptors on the surface of the breast cancer cells and very few other cell types in the body, so it has very few side effects.

Discovering Biomarkers

A biomarker is a biological substance (a molecule made by a cell) the tumor that can be used to predict the biological behavior (prognosis) of a disease, measure the progress of a disease, or measure the effectiveness of treatment

If no biomarker had been developed, doctors would not know which patients should take Herceptin. Now even newly diagnosed breast cancer patients are given one, and sometimes two, tests for HER2 mutation (amplification or overexpression). The results of these tests can help determine the best treatment for the patient.

A second good example is Epidermal Growth Factor Receptor (EGFR) mutations in lung cancer. Patients with mutated EGFRs are responsive to an EGFR inhibitor drug called Iressa.

Tissue and You

This handout has shown you how tissue is used in research to understand the causes of cancer, Identify targets for treatments, develop treatments that target a specific gene or signaling process and discover biomarkers that can identify characteristics of a cancer.

The story of Herceptin would not exist without patients who were willing to donate tissue for research. If you or someone you know is considering donating tissue you should learn about the risks, benefits and protections by reading, *Why it is important for me to consider donating my tissue for research*? (available at http://www.researchadvocacy.org).

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Research Advocacy Network

Advancing Patient-Focused Research

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