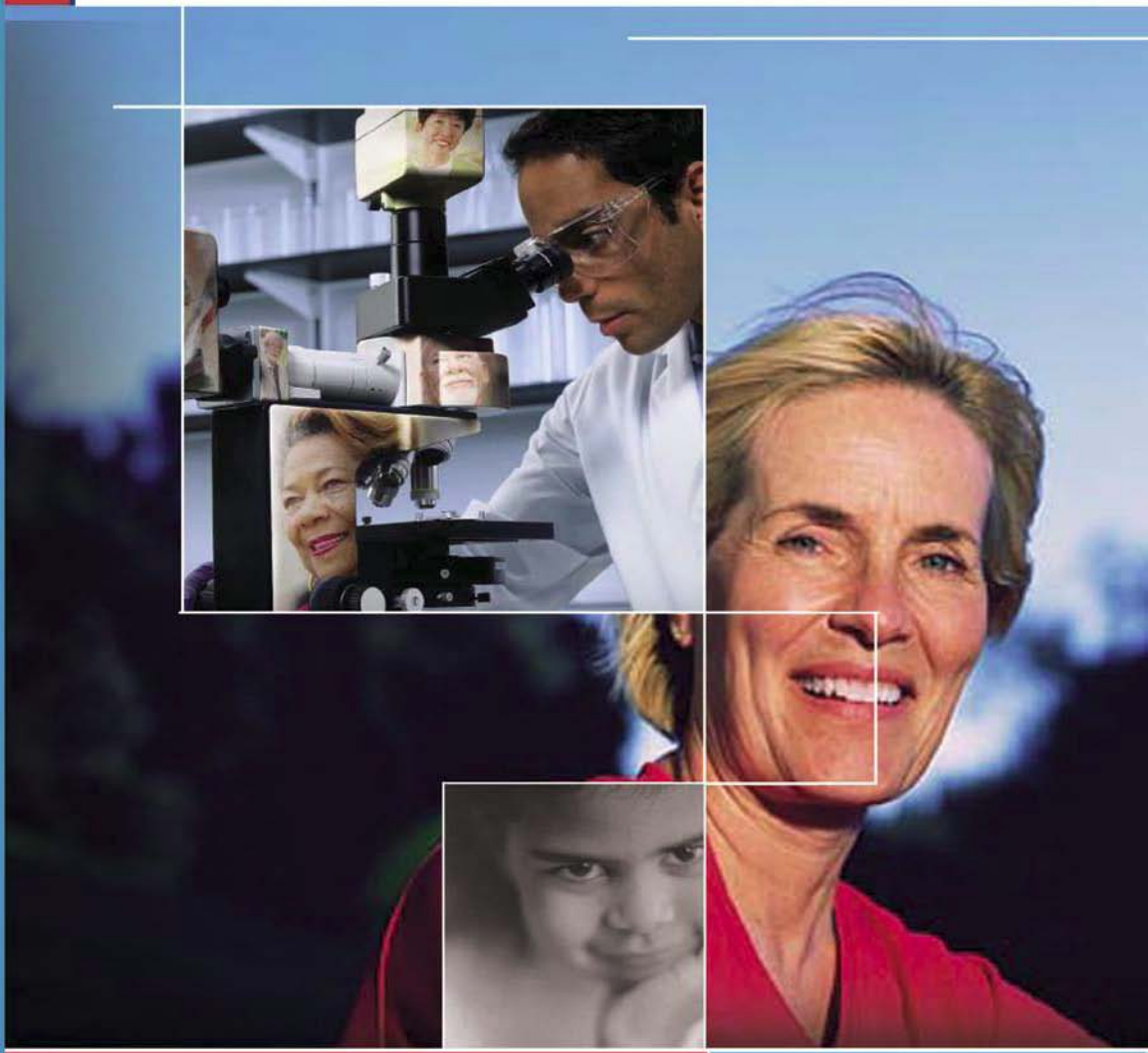
Why is it important for me to consider donating my tissue for research?

A booklet for prospective donors

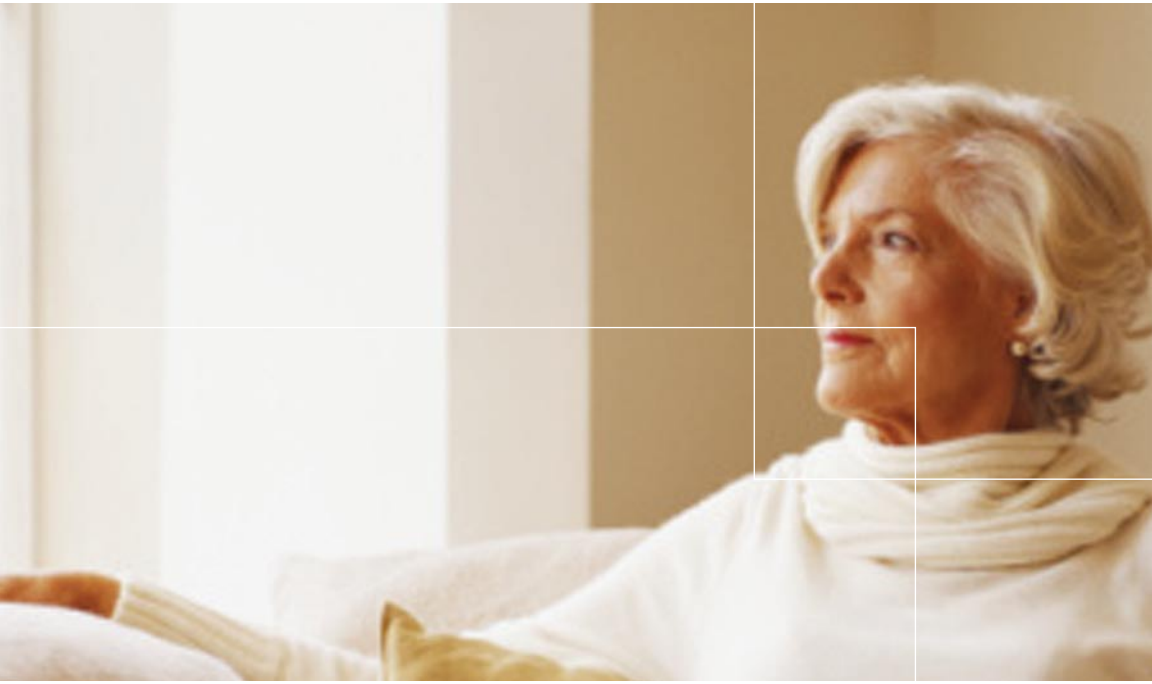


Research Advocacy Network

Advancing Patient-Focused Research

Background

Tissue comes from people and is defined as a group of cells or fluids such as, muscle, organ, blood, etc. that perform a specific function. Tissue provides information that helps clinicians diagnose cancer and make appropriate treatment decisions for people. The tissue collected for staging and diagnosis may include a small a portion of the tumor. Blood, urine, bone marrow, lymph nodes, fluid or sputum may also be used for diagnosis. All of these things are referred to as tissue in this booklet.



At least three kinds of tissue are used in research.

- Residual or extra tissue taken for the patient's diagnosis and treatment.
- Tissue taken specifically for research purposes, e.g., blood.
- Excess normal tissue.

Research on tissue may provide information that will help prevent, diagnose and treat cancer patients in the future.

Why should I consider donating my tissue for research?

Tissue is critical to the accurate diagnosis and staging of your cancer. It helps you and your doctor make good treatment decisions giving you the best chance

of disease-free survival. The study and analysis of tissue by researchers is necessary for cancer research. Studying tissue could ultimately lead to scientific discoveries that will prevent cancer and aid in the diagnosis and treatment for cancer patients in the future. For example, finding which patients respond better to or have fewer side effects from a drug. You may not directly benefit from donating your tissue but the research on your tissue may benefit cancer patients in the future.

Scientific discoveries through tissue

Learn how cancer cells work
The study of tissue allows us to learn more about how cancer cells work. The knowledge of how cells work and the outcomes of treatment for people who donate their tissue provide valuable information for future treatment. An excellent example of this is understanding the role of estrogen receptors in breast cancer cells. Through the analysis of tissue from breast cancer patients, scientists were able to identify that some breast cancer tumors had multiple estrogen receptors in their cells. This confirmed the theory that the body's own estrogen was "fueling" tumor growth. In estrogen receptor positive (ER+) tumors, blocking the estrogen receptor with drugs such as tamoxifen or decreasing the amount of hormones in the body with drugs like anastrozole could reduce the recurrence of cancer. It was only through the generosity of women with breast cancer who donated their tissue that researchers were able to improve treatment.

Other examples of cancer discoveries:

Iressa and Tarceva:
Iressa and Tarceva are so-called targeted therapies, in that they stop the growth of certain cancers by acting on a signaling molecule critical to the survival of those cancer cells. They target a gene in tumors called the epidermal growth factor receptor (EGFR). EGFR is a receptor, found on the surface of some lung, pancreatic and other cancer cells, that helps tumors grow and spread. Iressa and Tarceva block this receptor.

Both drugs have been tested in patients with non-small cell lung cancer (NSCLC), however the two drugs are effective in only 10% of patients. To understand why only a small number of patients responded, researchers analyzed tumor samples from NSCLC patients. Scientists found that the two drugs worked specifically in patients whose cancers contain mutations in the epidermal growth factor receptor (EGFR) gene. Because of the difference in how patients responded to these drugs, it was hoped that a test could be done to determine which patients had the mutation in the EGFR gene. In a larger study done in Canada, tissue was analyzed for mutations in the EGFR gene and then compared to the response of NSCLC patients to Tarceva. Researchers found that the presence of the mutation did not predict responsiveness to Tarceva.

It is too early to tell if this mutation in the EGFR gene will be able to predict which patients will respond to these new drugs. The tissue donated from patients and studied by researchers will ultimately give us an answer.

Gleevec:
Gleevec represents a new approach to cancer treatment, one that targets the unique genetic defects present in tumors. It was approved in 2001 for the treatment of some types of leukemia. Gleevec appears also to work in a rare type of cancer called gastrointestinal stromal tumor (GIST).

The majority of GISTs have a mutation in a protein known as KIT, which is responsible for the processes that regulate growth and multiplication of cells. In the treatment of GIST Gleevec is thought to work by blocking the KIT pathway, which then stops the cancer from growing. Because of how different patients respond to Gleevec, researchers wanted to know if understanding KIT mutations would help provide a link between responders and non-responders after treatment. Scientists obtained tumor samples from 324 patients diagnosed with GIST. Of the 324 patients, 280 were found to have KIT mutations. Researchers concluded that certain KIT mutations are associated with significantly higher response rates to and longer time to cancer progression intervals among patients treated with Gleevec. Genetic mutations in the tumor appear to predict which tumors will respond to the drug. The study indicates the importance of profiling patients in order to individualize therapy, which ultimately may provide a better outcome for the patient. This is one more example of a study that was done analyzing tissue donated by patients.

Identify causes of cancer

The information gained from the analysis of tissue samples may help identify the causes of cancer. Linking genetic factors and environmental exposures, such as, diet, culture, toxins, microorganisms and parasites, and life style choices may tell us more about what causes or contributes to the development of cancer. Information from tissue may help us understand how personal, familial and ethnic factors affect our susceptibility to diseases like cancer.

All cancer is genetic. This does not mean that all cancer is inherited but rather all cancer is caused by changes in our genes. Most of these changes or mutations can occur in any type of cell (e.g., lung, colon, brain, breast, liver) at any point in our lifetimes. The changes can give rise to cancer in those particular cells.

Whether or not a mutation can be passed on to the next generation depends on the type of cell in which it occurs. Mutations can occur in our germ cells or somatic cells. Germ cells are the reproductive cells in our bodies, either egg or sperm cells. In contrast, somatic cells are all of the non-reproductive cells in our bodies such as liver cells, skin cells, and muscle cells.

Because only our reproductive cells form an embryo, only mutations in these cells can be passed on to the next generation. Mutations that can be passed on to the next generation are called hereditary or germline mutations. There may be emotional risks and benefits in knowing that you have a genetic mutation and emotional benefits in knowing you do not have a genetic mutation that could indicate cancer in the future. The history of BRCA1 and BRCA2 is a good case study on germline mutations and the emotional impact of knowing you carry a gene for cancer. [i] [ii]

In contrast, mutations in somatic cells such as our liver cells, blood cells, stomach cells, and all other non-reproductive cells cannot be transmitted to the next generation. These are called somatic mutations.

What are the risks to me in donating tissue?

Physical Risks

Depending on the type of tissue being taken and the way it is taken, you may experience:

- Pain at the biopsy site or needle puncture site
- Bruising/swelling at the place where the tissue is taken
- Risk for infection

Your doctor will be able to answer any questions you have about the risks of taking a tissue sample for research.

For other types of research a biopsy or blood sample will not need to be taken. Instead, a small portion of the tissue previously taken to diagnose your cancer will be obtained. The tissue taken to diagnose your cancer is saved by being stored in hard wax and called a tissue block. The tissue block is stored in the pathology department of the hospital where you were diagnosed. Only a few small slivers of your tissue block are needed for most research projects.

Non-physical Risks
Most research does not provide the type of individual medical information that would affect your family, insurance or employment situation. Your doctor will be able to answer any concerns you have over the social risks of giving your tissue for research. However, you should know about possible risks, in order to make the right decision for you.

Social Risks
The social risks of donating tissue include:

- Loss of privacy – How researchers identify the medical information may allow others to know that information.
- Breach of confidentiality – If researchers disclose medical information in an unauthorized way, others may have access to information and use it in a way that is harmful to the individual.

Some types of medical research raise concerns over:

- Insurance discrimination – An insurer refuses to provide you with insurance.
- Employment discrimination – An employer refuses to hire or promote you.
- Family conflicts –Some family members may not want certain medical information from your tissue sample disclosed, while other family members may want medical information disclosed to them.

Other concerns:

- Use of tissue for purposes you would not want
- Tissue may be used for research you feel is religiously or philosophically objectionable.

One question that arises when people donate their tissue is the question of ownership. Who owns the product or intellectual property that could come from using or analyzing tissue and who will profit from that ownership? The current legal precedent holds that the possession of tissue alone does not constitute intellectual property. Something must be done to, or with, the tissue that adds commercial value and it is this value-added that is considered intellectual property and protected by law. It is the analysis of many tissue samples that leads to most discoveries. Therefore, the patient usually gives up all ownership rights when they donate their tissue for research.

Will I get the results from the research on my samples?

You will probably not get the results of research done on your tissue sample. The value of research using tissue comes from combining all the individual results and identifying patterns, e.g. most people with gene Q have a higher survival rate; only a very small percentage of people with gene K have cancer that spreads. It is the overall finding or patterns that are then reported by being published in scientific journals or made available on company websites. Your doctor will be able to tell you if your results will be available to you.

What protections exist to ensure my privacy and the confidentiality of my medical information?

There are laws and regulations that govern:

- How your tissue is collected and stored.
- The type of information researchers must provide to you before you agree to participate or donate tissue.
- How medical information from your tissue may be provided to others and under what circumstances.

Protections for collection of tissue

Ethically all research of any kind should be reviewed by an Institutional Review Board (IRB) or Ethical Review Boards (ERBs). These review boards ensure that the rules and regulations that apply to research with people are strictly followed. All drug research requires some level of IRB or ERB approval. The review boards analyze whether the anticipated benefits of research are worth the risks. They protect you as a tissue donor by requiring your voluntary participation and full disclosure of research procedures, risks, rights, and responsibilities.

Protections for tissue storage

While not directly protecting research participants, protecting tissue storage and handling assures you that your tissue will not be lost to poor practices. A number of professional organizations have or are developing standards and "best practices" for tissue repositories or banks. Such organizations include the International Society for Biological and Environmental Repositories (ISBER), the National Committee for Clinical Laboratory Standards. These standards and "best practices" detail policies and procedures that emphasize quality assurance and cover collection, freezing/fixing, storing and shipping of specimens.

Protections for privacy of health care information

Every country has laws and regulations that protect the privacy of identifiable health care information. For example, The Health Insurance Portability and Accountability Act (HIPAA) in the USA, the European Union Data Protection Directive (95/46/ED) and Japan's Personal Information Protection Act. These laws provide safeguards against the inappropriate dissemination of your medical information. Your doctor will be able to answer questions on the laws and regulations that exist in your country to protect the privacy of your health care information.

Privacy regulations require that medical information or tissues be stripped of any personal health information such as name, age, address, social security number, etc. One way of stripping tissue samples of personal health information is to assign a code number to the tissue sample. In this way, researchers can study patterns or identify new markers that may help understand cancer causes and how and why people respond differently to cancer treatments without knowing personal details of the tissue donor. If a researcher wants to link medical information with tissue at a later date they would have to gain permission to access the code.

How does informed consent protect my privacy and confidentiality?

Laws and regulations require that people be fully informed of how their tissue will be taken and how it will be used. The researcher conducting the study is responsible for providing the information. This process is called informed consent and it requires researchers to explain to you:

- The risks and benefits of donating tissue.
- The voluntary nature of agreeing to donate tissue – it is your choice to participate or not to participate.
- How the tissue will be collected and used in research.
- How medical information will be stored.
- What information will be provided to other researchers if they receive your tissue to conduct their research.
- Information about who may profit from any product or intellectual property created through the use or analysis of your tissue.
- If samples of normal tissue will be collected and used.
- How long your tissue may be stored for research.
- How and if you can withdraw your consent for research to be performed on your stored tissue sample.

The information explained to you by the research staff will allow you to make an informed decision about being a donor. To ensure that you are fully informed you must sign an informed consent document. You may be asked to participate in different types of studies. One type of study may involve you only consenting to donate your tissue for research. Another type of study may involve you being a participant in a clinical study in which a new drug is being tested to treat patients with your type of cancer. In these studies, your agreement to donate your tissue samples for research may be voluntary or it may be a mandatory requirement for participating in the study. Your doctor will explain whether or not you are required to donate tissue in order to participate in the study.

By signing the informed consent and having it witnessed by a third party, you indicate that you understand all the information given to you and your willingness to donate tissue. After you sign the informed consent document for the use of your tissue for research purposes, the tissue is collected (the tissue needed may have already been collected as part of your diagnosis) and then sent to a tissue repository or research laboratory. This repository or laboratory may be located at a hospital or a central location and should meet certain standards. Researchers wanting use of this tissue must have IRB or ERB approval and your approval before requesting your tissue for research.

Other research uses of your tissue

You may be asked if you want to restrict the use of your tissue to:

- Research specified in the consent;
- Cancer research done at a later date;
- Other health related research done at a later date.

You can reply yes or no to these separate requests. When you agree to the use of your tissue in research other than what is specified in the consent form, your tissue may be sent to other researchers. If this happens, no identifying information will be sent with the tissue. The only identification will be a code number known only to the tissue bank.

[i] Lynch HT, Lemon SJ Stephen, Durham C. et al. A descriptive study of BRCA1 testing and reactions to disclosure of test results. Cancer 1997; 79:2219-2228. . http://www3.interscience.wiley.com/cgi-bin/abstract/73502935/ABSTRACT?CRETRY=1&SRETRY=0

[ii] Wilson BJ, Forrest K, Van Teijlingen ER, et al. Family communication about genetic risk: the little that is known. Community Genetics 2004; 7:15-24. http://content.karger.com/ProdukteDB/produkte.asp?Aktion=ShowPDF&ProduktNr=224224&ArtikelNr=80300&filename=80300.pdf

For more information, please see the following:

- Health Insurance Portability and Accountability Act (HIPAA) *http://www.hipaa.com/*
- European Union Data Protection Directive (95/46/ED) *http://www.cato.org/pubs/wtpapers/991201paper.html*
- Japan Personal Information Protection Act (2003) *www.privacyexchange.org/japan/JapanPIPA2003v3_1.pdf*
- NIH Office of Human Research Protections *http://www.hhs.gov/ohrp/*
- Belmont Report, *http://www.med.umich.edu/irbmed/ethics/belmont/ BELMONTR.HTM*
- Moore Case, *http://www.forhealthfreedom.org/Publications/Informed/ WhoOwns.html http://www.bioethics.uu.se/chapters/JDRendtorff.pdf*
- National Bioethics Advisory Commission Report (1999) Research Involving Human Biological Materials: Ethical Issue and Policy Guidance, *http://www.nlm.nih.gov/pubs/cbm/hum_exp.html*
- National Dialogue on Cancer National Biospecimen Network Blueprint, *http://prostatenbnpilot.nci.nih.gov/blue_full6.asp*
- International Society for Biological and Environmental Repositories, *http://www.isber.org*

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