H-30755- INCORPORATION OF GENOMIC SEQUENCING INTO PEDIATRIC CANCER CARE

Background

You are currently taking part in this research study. Permission for you to take part in this research study was given by one of your parents or your legally authorized representative. Now that you have reached the age of majority (which in the State of Texas is 18 years of age), we are asking for your consent for continued participation in this research study. The age of majority means you are considered adult enough to sign legal contracts and consents for yourself. Your participation in this study is entirely voluntary. Should you choose to withdraw from this study, your decision will in no way affect the care you receive. We feel that it is important to remind you of the study, and this consent form describes the research study including some procedures that may have already been done. Please read the consent form carefully and feel free to ask any questions before you decide to continue your participation. You will be given a copy of the consent form to keep if you decide to continue your participation in this study.

Cancer is a disease caused by changes (mutations) in the genetic code of a cell. The genetic code is like a set of instructions that tell our cells how to grow properly. These instructions are referred to as genes. The mutations in genes found in cancer cells cause cells to grow and spread abnormally. Sometimes one of these mutations is present in every cell of the body ("inherited mutations") and can be found in a blood sample, while others are only found in the cancer cells ("tumor mutations"). A clinical test is now available to look for certain kinds of mutations in all 20,000 genes in a cell. This test is called "exome sequencing." It is important to understand that exome sequencing cannot find all types of mutations that might occur in your tumor or blood.

In this study we will use exome sequencing to look for inherited and tumor mutations occurring in you. The exome sequencing test is not experimental and is performed in a clinically certified laboratory. However, most patients with cancer do not have it done as part of their regular cancer care, and no one knows the best way to use the tests for cancer patients yet.

This research study is funded by the National Institutes of Health (NIH)

Purpose

The main goal of this study is to learn how to best report and use the clinical exome sequencing test results for childhood cancer patients at the Texas Children's Cancer Center (TCCC). We plan to study how these results can best be explained to physicians and parents of cancer patients. We want to learn what both groups prefer in receiving the results. We want to learn whether the results can help us to: (1) better understand the future cancer risk of childhood cancer patients and their family members so that better methods of screening and prevention can be developed and (2) make treatment decisions for our patients if their cancer returns.

A second goal of this study is to learn more about the biology of childhood cancer and develop better ways to prevent, detect, and treat these cancers. To complete this goal we will use additional research methods to find new inherited mutations and tumor mutations occurring in childhood cancers and we will combine these results with clinical information from patients' medical records.

Procedures

The research will be conducted at the following location(s): Baylor College of Medicine, TCH: Texas

Children's Hospital, TCH: Texas Children's Hospital, Clinic, Texas A&M University.

We will enroll 308 patients and their parents in this study.

COLLECTION OF STUDY SAMPLES

We obtained your parent's permission to use your tumor and blood samples. These were obtained at (or near) the time of your tumor surgery and sent to the Baylor College of Medicine Whole Genome Laboratory (WGL) for exome sequencing. In addition, we requested blood samples from both parents so that the WGL could confirm inherited mutations identified in you. The WGL handled your samples the way any regular medical samples are handled, following all standard procedures for sample tracking, storage, and confidentiality.

1. Your tumor sample. This sample was collected to find the tumor mutations using exome sequencing. Only tumor tissue that was removed as part of your routine diagnosis and treatment and was left over after all necessary clinical tests were completed was used for this study. No extra surgery was performed.

2. Your blood sample. This sample was collected to find the inherited mutations using exome sequencing. We obtained 1-2 teaspoons of blood.

WILL I GET TO SEE THE RESULTS OF GENETIC TESTING?

You may have already received the results of this genetic testing. If not, the information below describes the process for returning exome sequencing test results and the types of results we may or may not find.

Clinical Exome Test Results:

The exome test takes a long time to finish. We think it will be about 3 months after we take the sample until the results are ready. The results of the exome test will be given to your cancer doctor and also placed into your electronic medical record. Before your doctor meets with you and your parents to review the results, he or she will be able to discuss them with the investigators on this study who are experts in exome tests. Your cancer doctor will then explain the results to you and your parents and work with you to decide whether anything about your care should change based on the results. A genetic counselor will work with your cancer doctor to explain the inherited mutations to you and your parents. These results will be explained to you and your parents in one or two meetings scheduled at the same time as your regular clinic visits whenever possible.

These tests are very new and we do not know yet how to use exome testing to guide children's cancer treatment. Because the test takes so long to do, the results will not be available until after you begin your treatment. We do not expect the test results to change anything your doctor planned to do for treatment. Therefore we do not think that getting the results is likely to make your treatment better or make it more likely for you to be cured. It is possible, however, that the results might reveal tumor or inherited mutations that matter to your clinical care or family such as:

1. Tumor mutations that are normally found in a different type of tumor from what you were diagnosed with. We think this will be rare, but if it does happen, your doctor may talk to you about changing your treatment plan.

2. Tumor mutations that make your doctor think your tumor will respond better or worse to a particular cancer treatment. We think this will be very rare for most patients. It might be more common in cases where a patient's tumor has returned after standard treatment and additional treatment options are being considered.

3. Inherited mutations that might affect how your body responds to certain medicines. This information might help your doctors choose the dose of some of your medicines.

4. Inherited mutations that cause you to have an increased risk of developing other cancers (or a second cancer of the same type). This information may also provide information about the risk of cancer in close family members. For example, children and adults who inherit mutations in the gene called p53 are at increased risk for multiple different types of cancer. If an inherited mutation in this gene is found in you, then additional cancer screening would be recommended and close family members should also be checked for the mutation so that they can be screened as well if necessary.

5. Inherited mutations that are unrelated to cancer but provide information about a different medical condition for which treatment is available and recommended as standard medical care. For example, we might find a patient who inherited a mutation that puts himself or herself at high risk of life-threatening bleeding from a blood vessel (called an aneurysm). If that type of mutation were found we would recommend additional follow-up testing and/or treatment as part of standard medical care.

If we find any of these kinds of mutations, your cancer doctor and a genetic counselor will explain them to you and your parents and work with you to determine the most appropriate screening or treatment (if any) for yourself and family members.

Exome sequencing can also reveal information about whether you are a carrier of a genetic disorder such as Cystic Fibrosis. This information may not affect your health but it may be helpful to know later in life. If you have one of these kinds of mutations, you probably inherited it from a parent. Therefore your parents might want to be screened to see if there is a risk of having a child who has a genetic disorder. However, some people do not want to know this kind of information. This type of genetic information will only be included in your exome sequencing report if that option was chosen in your consent form by your parents.

PROCEDURES TO HELP US LEARN THE BEST WAY TO COMMUNICATE CLINICAL EXOME TEST RESULTS

Because we want to learn more about how doctors and patients discuss exome test results, we will include the following activities if you decide to continue your participation in the study:

1. If your exome sequencing tests are not yet complete and/or the test results have not yet been discussed with you and your parents, we will audiorecord the clinic visit(s) where you and your parents learn about the results of exome sequencing. By studying how doctors and patient families talk about genetic test results this will help us learn how to improve communication and understanding about these results between cancer doctors and patient families. The audiorecording of this clinic visit may have already been completed.

2. Age of Majority Interview. Whether you decide to continue your participation in this study or withdraw, we would like to invite you to participate in an interview. This interview will ask more detailed questions about (get this information from Project 3). This interview will be conducted in a place and at a time that is convenient for you. This interview will last approximately 1 hour and will be audiorecorded.

We will also collect information from your medical records, including your age, ethnic background, diagnosis, disease history, medical treatments, and response to treatments. We hope this will help us understand whether the exome results are related to how children with cancer do. Some of this information may have already been collected, and we are now asking for your permission to continue collecting this information.

ADDITIONAL LABORATORY RESEARCH STUDIES

After the exome sequencing test was performed on your tumor sample, there may have been some sample left over. If so, and your parents gave us permission, we may have done or still plan to do some additional genetic research tests. If your parents gave us permission, we also requested an additional blood sample that was used or may be used for research. This may have included or will include using newer methods of sequencing, or sequencing parts of the DNA that doesn't contain genes or studying the RNA and proteins that are coded by your DNA as well as grow blood cells in the laboratory to test for gene function. We may have also grown or plan to grow tumor or blood cells in the laboratory. Any results of these research tests are preliminary and would not be reported to you or placed in the medical record. If research from this project is presented at research conferences or published in professional journals, we will not use any information such as name, address, telephone number, or social security number, included in the presentations or publications.

If we identify a genetic change that we think is clinically important, we will share those results with your cancer doctor so that they can discuss them with you and make follow-up plans. It is important to realize that these are research results and must be confirmed in a clinical laboratory in order to be used for clinical purposes.

If your parents consented to have your samples submitted to the Texas Children's Cancer Center Tissue Bank (in a separate consent document), we gave or we will give any leftover samples to the Tissue Bank.

Patient tumor samples from additional tumor surgeries at TCH:

We also asked your parent's permission to collect research samples from any future surgeries that may have already occurred or might occur so that we may study how tumor mutations change over time as tumors are treated. These samples were not required for enrollment on the study. Only tumor tissue that has been removed (or will be removed) as part of your routine diagnosis and treatment and is left over after all necessary clinical tests have been completed were used or will be used for this study. No extra surgery was done or will be done.

If your parents agreed to participate in this portion of the study, these biological samples were obtained and used for research. This research material was not available to use for other clinical testing.

Who will have access to your additional study information?

As we explained, the clinical exome report is handled like any other clinical test and was placed or will be placed in your medical record and was explained or will be explained to you and your parents by your physician. For the laboratory research studies, audiotape and interview information, these results were stored or will be stored in a confidential computer database along with all data about your biological samples and parents' biological samples (if provided). These biological samples and medical information were labeled or will be labeled with a code, meaning that names and other identifying information were or will be removed and samples were or will be given computer-assigned numbers that the research team can use to access them. Only the investigators and selected research staff are able to match the code to a particular person. Only the investigators and selected research staff are able to access the database.

In order to speed research, other researchers would like to be able to study your blood and tumor samples and have access to your genetic information so that they can compare it to the genetic information of others from other research studies and use it to answer future research questions. This information is most valuable when it is linked to some information about your medical history (clinical information). It would also be helpful to use your blood samples and genetic and clinical information for this research. Your parents may have already given permission for de-identified research blood and leftover tumor samples, as well as de-identified parts of your genetic information, and in some instances, clinical information, to be shared with other researchers at Baylor College of Medicine (BCM) who are conducting approved research studies. In addition, your parents may have already given permission for your genetic and clinical information to be shared by releasing it into scientific databases including those maintained by BCM and some maintained by the National Institutes of Health. These databases are restricted and can only be accessed by approved researchers. Sharing this information will help advance medicine and medical research by allowing other researchersto use this information to help solve questions of what causes cancers and other diseases.

There is a risk that others will be able to trace this information back to you, which may impact the ability of you or other family members to obtain life insurance, health insurance, or other products that may take into account the result of these genetic studies. Nobody will be able to know just from looking at a database that the information belongs to you. However, because your genetic information is unique, there is a small chance that someone could trace the information back to you

or close biological relatives. The current risk of this happening is very small, but may grow in the future as new ways of tracing the information back to you or your close biological relatives are developed. Thus, the risk that your privacy would be breached may increase over time. Researchers who access your genetic and clinical information will have a professional obligation to protect your privacy and maintain your confidentiality.

Permission for future recontact by study investigators

We will follow each patient in the study for 2 years to determine if their cancer doctor has found the exome information useful in their care. In the future, it may be helpful to our research to be able to recontact you to obtain additional clinical information or to ask your permission to collect another research sample. Please initial below if we may recontact you after those 2 years are completed to discuss these research opportunities.

Yes_____ No_____ I consent to be contacted in the future for research study purposes.

Can I change my mind after my parents agreed to let my samples be used?

You can withdraw from this study for any reason at any time. If you decide to withdraw from the study, your samples will be discarded. If your parents had agreed to let your samples be submitted to the TCCC Tissue Bank, you will be asked at the time of withdrawal from this study whether you would like these samples to be discarded or kept in the Tissue Bank for future research.

If you decide to withdraw from this study after your genetic code has been analyzed, your genetic information will be discarded and will not be used in this study. However, if your tumor and inherited exome sequencing reports have already been submitted into the medical record, it will not be possible to remove these reports from the medical record. In addition, if your parents agreed to have your genetic and clinical information shared with other investigators or released into scientific databases, it may not be possible to remove this data from the database.

You can see and get a copy of your research related health information. Your research doctor may be able to provide you with part of your information while the study is in progress and the rest of your information at the end of the study.

Potential Risks and Discomforts

If the exome tests show a risk of you developing a second cancer, a risk of cancer in family members, or a risk of developing other types of diseases unrelated to cancer, you might feel anxious or upset by the results. Your cancer doctor can discuss these risks with you and determine any medical follow-up that is indicated. There is also a potential risk in this type of genetic analysis for uncovering and conveying unwanted information regarding the biological relationship of parents and their children.

There is also the risk of a loss of privacy of your genetic information. The exome report will be placed in the electronic medical record and may be seen by your other doctors and health care workers. Health insurance companies may also have access to this information. There are laws to

protect against the use of this information in making decisions about health insurance and employment. However, you may be asked to provide medical record information when you apply for life insurance or disability insurance.

As described earlier, all research genetic and clinical information for the study will be stored in a confidential access-controlled computer database. In addition, there are additional risks of loss of privacy if you consent to the sharing of this data with other BCM investigators, or to the de-identified release of your genetic information into scientific databases for other scientists to use.

While we believe that the risks to you and your family from participating in this study are low, we are unable to tell you exactly what all of the risks are. We believe that the benefits of learning more about cancer outweigh these potential risks.

Study staff will update you in a timely way on any new information that may affect your decision to stay in the study.

Potential Benefits

The benefits of participating in this study may be: Tumor and/or inherited mutations may be discovered by exome sequencing that would not have been found by other standard tests. Although we do not think that the mutations that are found are likely to change the planned cancer treatment for most patients, it is possible that they may have implications for the clinical care for yourself as well as other family members. For example, tumor mutations may rarely be identified that change the type of tumor that is being diagnosed. Alternatively, tumor mutations may be found that indicate that your tumor may respond better or worse to a particular cancer treatment. We think this will be very rare for most patients. It might be more common in cases where a patient's tumor has returned after standard treatment and additional treatment options are being considered. In both cases, your cancer doctor may make changes to your treatment plan based on the results of tumor exome sequencing. Similarly, inherited mutations may be identified that indicate an increased risk for you and potentially other family members to develop additional cancers and/or diseases other than cancer. If inherited mutations of this type are found, additional follow-up testing or treatment would be recommended if these interventions would be considered standard medical care . However, you may receive no benefit from participating.

Alternatives

You may choose to not participate in this study.

Subject Costs and Payments

You will not be asked to pay any costs related to this research.

You will be paid $25 if you complete the Age of Majority patient interview.

This institution does not plan to pay royalties to you if a commercial product is developed from blood or tissue obtained from you during this study.

Research Related Injury

If you are injured as part of your participation in this study, there are no plans to compensate you.

Research personnel will try to reduce, control, and treat any complications from this research. If you are injured because of this study, you will receive medical care that you or your insurance will have to pay for just like any other medical care.

Subject's Rights

Your signature on this consent form means that you have received the information about this study and that you agree to volunteer for this research study.

You will be given a copy of this signed form to keep. You are not giving up any of your rights by signing this form. Even after you have signed this form, you may change your mind at any time. Please contact the study staff if you decide to stop taking part in this study.

If you choose not to take part in the research or if you decide to stop taking part later, your benefits and services will stay the same as before this study was discussed with you. You will not lose these benefits, services, or rights.

Your Health Information

We may be collecting health information that could be linked to you (protected health information). This protected health information might have your name, address, social security number or something else that identifies you attached to it. Federal law wants us to get your permission to use your protected health information for this study. Your signature on this form means that you give us permission to use your protected health information for this research study.

If you decide to take part in the study, your protected health information will not be given out except as allowed by law or as described in this form. Everyone working with your protected health information will work to keep this information private. The results of the data from the study may be published. However, you will not be identified by name.

People who give medical care and ensure quality from the institutions where the research is being done, the sponsor(s) listed in the sections above, representatives of the sponsor, and regulatory agencies such as the U.S. Department of Health and Human Services will be allowed to look at sections of your medical and research records related to this study. Because of the need for the investigator and study staff to release information to these parties, complete privacy cannot be guaranteed.

The people listed above will be able to access your information for as long as they need to, even after the study is completed.

If you decide to stop taking part in the study or if you are removed from the study, you may decide that you no longer allow protected health information that identifies you to be used in this research

study. Contact the study staff to tell them of this decision, and they will give you an address so that you can inform the investigator in writing. The investigator will honor your decision unless not being able to use your identifiable health information would affect the safety or quality of the research study.

The investigator, SHARON E PLON, and/or someone he/she appoints in his/her place will try to answer all of your questions. If you have questions or concerns at any time, or if you need to report an injury related to the research, you may speak with a member of the study staff: SHARON E PLON at 832-824-4251 during the day. After hours call (832) 824-2099 and ask to page Dr. Plon or Dr. Parsons.

Members of the Institutional Review Board for Baylor College of Medicine and Affiliated Hospitals (IRB) can also answer your questions and concerns about your rights as a research subject. The IRB office number is (713) 798-6970. Call the IRB office if you would like to speak to a person independent of the investigator and research staff for complaints about the research, if you cannot reach the research staff, or if you wish to talk to someone other than the research staff.

National Institutes of Health and the National Cancer Institute may have access to your records for research purposes. Coded information may be provided to the NIH/NCI such as Patient ID, Patient Zip code, Patient country code and Patient Birth date (month/year). However, in the event of an audit NIH/NCI might have access to more information that is part of your research record.

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Signing this consent form indicates that you have read this consent form (or have had it read to you), that your questions have been answered to your satisfaction, and that you voluntarily agree to participate in this research study. You will receive a copy of this signed consent form.

Subject	Date
Investigator or Designee Obtaining Consent	Date
Witness (if applicable)	Date
Translator (if applicable)	Date