II. Informed Consent and Assent

UNIVERSITY OF MICHIGAN

CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study. Parents or legal guardians, who are giving permission for a child, please note: in the sections that follow the word 'you' refers to 'your child'.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title: Personalized Medicine Based on Molecular Profiling of Patients with Cancer

1.2 Company or agency sponsoring the study: None

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Principal Investigators:
Rajen Mody, MD, Associate Professor, Department of Pediatrics Hematology/Oncology
Arul M. Chinnaiyan, MD, PhD, Professor, Department of Pathology

Department of Internal Medicine, Hematology and Oncology
Moshe Talpaz, MD, Professor, Department of Internal Medicine
Elena Martinez Stoffel, MD, Assistant professor, Department of Internal Medicine

Department of Pediatrics, Cancer Genetics
Raymond Hutchinson, MD, Professor, Department of Pediatrics
Jeffery Innis, MD, PhD, Professor, Department of Pediatrics
Jessica Everett, MS, Genetic Counselor, Department of Internal Medicine
Victoria Raymond, MS, Genetic Counselor, Department of Internal Medicine
Shanna Gustafson, MS, Genetic Counselor, Department of Internal Medicine
Rhonda McDougall, NP, Department of Pediatrics
Marcia Leonard, NP, Department of Pediatrics
Rama Jasty-Rao, MD, Department of Pediatrics
Aghiad Chamdin, MD, Department of Pediatrics
Nur Akcasu, NP, Department of Pediatrics
Judith Moyer, NP, Department of Pediatrics
Gregory Yanik, MD, Professor, Department of Pediatrics

Michigan Center for Translational Pathology
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Javed Siddiqui, MS, Department of Pathology
Robert Lonigro, MS, Mathematics and Biostatistics, Michigan Center for Translational Pathology

Bioethics
Scott Roberts, PhD, School of Public Health, Center for Bioethics and Social Sciences in Medicine
Scott Kim, MD, PhD, Department of Psychiatry, Center for Bioethics and Social Sciences in Medicine

Department of Radiology
Jonathan Dillman, M.D., Assistant Professor, Department of Radiology

Department of Pathology:
Raja Rabah, MD, Professor, Department of Pathology

Research Coordinator (Pediatric Phase-I Program):
Kevin Frank, Department of Pediatrics

Clinical Coordinator
Angela Stovall, Department of Pediatrics

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The goal is to identify key genes important to cancer cells that could potentially influence clinical decision making for managing cancer. You will be asked to provide normal samples (Blood, cheek swab, urine, and spit) and tumor samples (through a biopsy). Genetic material, including DNA and RNA, will be obtained from samples, stored, and used for evaluation of your cancer. Specifically, the study includes DNA sequencing of your tumor and normal cells as a comparison.

However, molecular evaluation is not guaranteed. It is possible that the DNA sequencing process may take longer or in some cases may not be possible. This could be due to unpredictable variation in tissue quality or technical problems. Furthermore, the results are not guaranteed to help your doctor take care of you.

Tumor tissue may be grown and used to create cell lines that allow researchers to maintain cancer cells in the lab for research. These cells can be used for ongoing research towards the development of new therapies.

Clinical information and samples will be collected and stored for ongoing research. This is a necessity because improved diagnosis, prognosis and treatment of cancer in the future depend upon the ongoing analysis of basic research findings and clinical outcomes. This type of research may improve the lives of future patients with cancer.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Your study doctor will review your past medical history, known allergies, current medications, and blood tests, to determine if you are eligible to take part in this study.

1) Inclusion Criteria: A confirmed diagnosis of cancer

1) Any kind of advanced cancer
2) Less than or equal to 25 years of age
3) Patients are undergoing standard of care surgeries or procedures

OR

Patients have tumor that is suitable for research biopsy (as assessed by trained specialists in radiology) AND Patients are medically fit to safely undergo a biopsy

4) Procedure-specific signed informed consent prior to initiation of any study related procedures
5) Women and minorities are included in this protocol
6) Patients with multiple malignancies remain eligible
7) Patients with an inherited cancer syndrome or a medical history suggestive of an inherited cancer syndrome remain eligible

2) Exclusion Criteria:

1) If enrolling study physician feels you are unable to undergo biopsy
2) Patients who are in prison are not eligible to participate
3) Women who are pregnant

3.2 How many people (subjects) are expected to take part in this study?

For the first phase of this study, we are enrolling 40 patients. We intend to expand the study and anticipate enrolling of up to 200 patients from all parts of the study in the next four years.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

A Clinical Investigator from the Study Team and Genetic Counselor will explain the study to you. The study doctors and coordinators will review your history to determine if you are eligible to take part in the study. You will have the opportunity to ask any questions about the study. You must complete this informed consent form in order to participate.

- Study Investigators will take your complete history and perform a routine examination.
- The study involves collection of tumor tissue, typically through a biopsy procedure. The type of biopsy procedure varies for person to person and the type of cancer they have.
- You will be asked to provide additional samples including blood, cheek swab, spit, and urine.
- Your clinical information will be recorded and updated.

- Your tumor will undergo DNA sequencing in the Department of Pathology's Michigan Center for Translational Pathology at the University of Michigan.

Samples:
A) Blood Collection: Four tablespoons of blood will be drawn from your vein, using regular blood drawing techniques. When possible, these samples will be obtained at the same time as routine blood work through your doctor.
B) Buccal or "Cheek" Swab: A sterile brush will be used to gently swipe the inside of your cheek ten times avoiding the gum line. This process will be repeated with two more brushes.
C) Saliva Collection: You will be asked to spit into a small container several times.
D) Urine Collection: We will ask that you provide a urine sample.
E) Previously Collected Tumor Specimens. You will be asked to sign a release for retrieving previously collected tumor specimens here or at other hospitals and clinics. We will make arrangements to retrieve these materials, at no cost to you.
F) Tumor Tissue or Bone Marrow Biopsy: The study doctor will arrange for tumor tissue to be collected through the least invasive procedure possible. This will generally involve a needle biopsy.

Important: If you are currently taking a medicine called **warfarin** sodium (also called Coumadin) or other **blood thinners**, you must tell your study doctor. Blood thinners may increase the risk of bleeding after biopsy. In order to undergo biopsy, your study doctor will confer with your primary care doctor if it is safe to temporarily stop your blood thinner before a biopsy.

Exception: During the course of the study, if you're cancer should become resistant to your current therapy, you will be eligible to have another tumor biopsy and blood sample to re-evaluate the tumor. If you wish to participate by having another biopsy, you will be asked to complete another consent form, agreeing to the repeat biopsy. The same eligibility criteria will apply.

What will happen to the samples that are collected?
Genetic material, including DNA and RNA, will be obtained from samples, stored in freezers, and used for profiling and analyzing your cancer. Specifically, the study includes DNA sequencing of your tumor and normal cells as a comparison. The goal is to identify key changes in the genes important to cancer cells that could potentially influence clinical decision making for your cancer. However, success or clinical benefits from the profiling of your cancer DNA is **not** guaranteed.

Some cells from your tumor may be grown and used to create cell lines that can be used as an ongoing source of genetic material or used for laboratory research. Additional analysis of the sequencing data will be used for research purposes, for example to discover new, unknown associations between genes and cancer. This type of research may affect the lives of future patients with cancer.

Are there additional costs to me or my insurance?
As a participant in this study, you will **not** be billed for the collection, processing, storage, DNA sequencing, or analyses of these samples. You will **not** be billed for the tissue biopsy.

In some instances, if certain genetic changes are found, more testing may be needed. When clinically indicated, the treating physician may order additional testing at a CLIA certified laboratory. This would **not** be part of the study and would be billed to your insurance.

4.2 How much of my time will be needed to take part in this study?

- **Samples.** Blood, buccal, and urine samples can be collected at one of your clinic visits, and may add up to 1 hour of time.
- **Tumor biopsy.** A tumor biopsy will be scheduled and generally takes several hours, including check-in time, preparation, the procedure, and observation.
- **Follow up.** The study involves periodic follow-up to update our records. After enrollment, medical records will be requested after 4 months, 8 months, 12 months, 18 months, 24 months, and then every 12 months indefinitely. Generally this follow up is completed by review of your medical records which will not require your time or effort, but on occasion we may require additional phone contact.

4.3 When will my participation in the study be over?

Study participation is **indefinite**. This involves periodically updating our database through retrieval of your medical records at regular intervals (as described in the previous section).

However, you are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information” (below).

4.4 Will the researchers give me results?

Our goal is to offer results that have **clinical value** based on available information and our best clinical judgment. A Board consisting of **experts in oncology (cancer), genetics, and ethics** from the University of Michigan will serve on a “Sequencing Tumor Board” will review the results and determine what results are important.

In this study, you will receive results if they are felt to be **clinically important (information that can help your doctor manage your cancer)** and the results have been confirmed through clinically-certified lab. Since you are participating in a cancer study, **we will always tell you about any results that have a “Direct impact on care of your current cancer.”**

The initial results of our research studies will be sent to the referring physician. Our research results may find a result that can be confirmed with a clinically validated medical test. This is typically available through a genetic testing lab. These tests typically cost hundreds or thousands of dollars. If you and your physician decide to do any type of confirmatory testing, you or your insurance may be charged for the cost of a new sample collection or for laboratory tests to confirm the research results. Specifically, the University of Michigan will not participate in the decision whether to validate the research findings through a commercially available test.

However, this study may uncover additional information that **may** or **may not** be important to you. Some patients may find this extra information to be overwhelming, while others may want

to have all information given to them. Therefore, we give you the choice to say "Yes" or "No" to these other results **before** you begin the study.

4.5 What choices do I have for receiving these other results that do not have direct impact on care of my current cancer?

There are at least two kinds of information that do not have direct impact on your cancer care but which you may or may not wish to know about:

1) Results that may have significance for biological family members.

Example 1: The researchers may discover that you have a gene that, if inherited by biologically-related family members, could increase their risk of cancer. These family members may or may not have the gene; they would need to be tested to find that out. Is the possibility that they might have such a gene something that you and/or your family member(s) would want to know?

Example 2: The researchers might discover that you carry a gene for another medical condition. Your biological family members may also have such a gene. Is this something that you and/or your family member(s) would want to know?

2) Results that are not related to your cancer, but may have potential medical impact for you.

Example: The researchers may discover that you have a gene that significantly increases your risk for another medical condition, not related to your cancer. We cannot know ahead of time what that condition might be. Is this something that you would to know?

We realize that whether or not you want to be told about these results that do not have direct impact on the care of your current cancer will be a very personal decision.

If you do not do anything, then you will be given the results by default. However, if you do not wish to be told, you can direct us not to disclose these types of results.

Please feel free to ask questions and discuss your preferences with the study team members. They will help you complete the table. If you do nothing, you will be told. However, if you wish not to be told, please initial where indicated below.

What choices do I have for receiving these other results that do not have direct impact on care of my current cancer?	**If you do NOT want to be told of these results, please initial the boxes below.**
1) Results that may have **significance for biological family members**.	
2) Results that are **not related to your cancer,** but may have **potential medical impact for you**.	

As with any research study, there may be additional outcomes or risks that are unknown or unexpected. These will be handled on a case by case basis by the Sequencing Tumor Board.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:

A) Blood Collection: Blood collection usually causes minor discomfort at the site where blood is taken.

- You may experience bleeding, bruising, lightheadedness, or fainting (1-10% of patients).
- Rare side effects (less than 1%) include serious bleeding or infection.

To reduce these risks, the research team will draw blood at the same time as your doctor orders them for your routine care and ensure proper blood drawing techniques is performed by a trained individual.

B) Buccal "Cheek" Swab Collection: Buccal swabs may rarely (less than 1% of patients) cause some irritation at the swab site.

C) Saliva Collection: There are no known risks to providing a saliva sample.

D) Urine Collection: There are no known risks to providing a urine sample.

E) Previously Collected Tumor Specimens: There are no known risks to providing previously collected tumor specimens.

F) Tumor Biopsy or Bone Marrow Aspirate: If necessary, your study doctor or a member of the study team will perform or arrange for the tumor biopsy. Procedures are performed by experienced personnel with the proper technique that will minimize the risks of the procedure. You could experience pain, inflammation, bleeding, swelling, or infection at the site where the tumor tissue is removed. The person that performs your biopsy, whether your study doctor or another healthcare professional, will tell you about the biopsy procedure and any specific risks associated with the biopsy. They will also obtain your consent for the biopsy according to the standard process.

The most common side effects (occurring in more than 10% of patients) are:

- Pain
- Inflammation
- Swelling
- Minor bleeding

Rare side effects (occurring in less than 1% of patients) are:

- Serious Bleeding
- Infection

Some data collected from you may be deposited into dbGAP but all identifiable information will be removed prior to submission so that the data cannot be linked to you in any way. The database of Genotypes and Phenotypes (dbGaP) is a database developed by the National Center for Biotechnology Information (a division of the National Library of Medicine) to archive and distribute the results of studies that have investigated the interaction of genotype and phenotype. All data submitted from this study will only be available through controlled access and restricted to cancer research studies. Any researcher requesting access to the data must

formally apply to dbGAP and present a research study rationale for why they need access to the data. The data may also be submitted to other future database systems which will have similar access controls as dbGAP utilizes.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 .What are the risks of genetic research?

There are some risks to receiving genetic results. Participants could experience risks such as psychological or emotional distress, loss of insurance, loss of employment, discovery of previously unknown health conditions, discovery that you are not the biological parent of a child(ren), or discovery that you could carry a gene for a certain disease, etc. Therefore, we offer **genetic counseling** before participation in the study as part of the informed consent process.

Patients may be referred to additional Genetic Counseling as part of their routine clinical care. This is typically covered by most insurance agencies. If this is not covered, you will have to pay out of pocket for this service, typically around $300 to $400 for a visit.

What is the Genetic Information Nondiscrimination Act (GINA)?
The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment
- GINA does not apply to the following groups, however these groups have policies in place that provide similar protections against discrimination:
  - Members of the US Military receiving care through Tricare
  - Veterans receiving care through the Veteran's Administration (VA)
  - The Indian Health Service
  - Federal employees receiving care through the Federal Employees Health Benefits Plans

5.3 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.4 If I take part in this study, can I also participate in other studies?

Since this study does not involve active treatment, participating in this study does not limit your ability to participate in other studies. If you do participate in more than one study, please notify researchers from all studies.

5.5 How could I benefit if I take part in this study? How could others benefit?

If we identify a potentially important result from your DNA analysis that could help your doctor manage your cancer, you and your doctor may pursue a therapy that might work better for you. **Benefits of therapy are not guaranteed**. If we do not identify information that would be important for your cancer then you will not receive any personal benefits from being in this study. However, the tissues donated through this tissue bank will help advance understanding of the genetics of cancer and may lead to new treatments for patients in the future.

5.6 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn new information that could change your willingness to stay in the study, as long as you have agreed to receive that information per section 4.5 The researchers will give you the information they have learned, discuss risks and benefits with you and you will have the option to continue on study or withdraw.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

Your participation in the study is completely voluntary. The alternative is to not participate, in which case there will be no penalty to you or your treatment.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information” (below). If you request removal from the study then your clinical information will be removed from the databases and no new information will be collected. However, previously collected samples and any completed test results will be retained. If you withdraw from the study, it will not be possible to remove any of your data that may have been submitted into dbGAP. This data will remain in the dbGAP repository but will not have any identifiers in it that could link the data to you.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

No

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.

- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Mody immediately, at 734-764-7126. The doctor will either treat you or send you to another doctor for treatment.

You will get free medical care at the UMHS for any hospitalization directly caused by the study drug, device, or procedure. The UMHS and the study doctor are responsible for determining whether your condition was the result of your participation in the study.
The UMHS will pay for your treatment only if it has been caused by the study drug, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

8.2 Will I be paid or given anything for taking part in this study?

No. You will not be paid for taking part in this study.

8.3 Who could profit or financially benefit from the study results?

If a new discovery, diagnostic test, or treatment results because of research done on the tissue

you donated, the University of Michigan Researchers could profit by filing a patent. Should any product developed from participant samples, participants will not be responsible for any costs of development, nor will they obtain any profit from the commercial use.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

9.1 How will the researchers protect my privacy?

Patient information kept within the University of Michigan Health System medical record is protected by the Health System's privacy policies. Research information is protected by being kept in a separate research record not included with the patient's medical chart, and stored in a locked office and in a password-protected database.

Your samples will be stored in a manner in which your personal identification is not known to those storing it. Specimens will be stored without any labels that directly identify you, and are only identified by a research code number. The electronic database that contains your personal data is separate from the database with the data from your samples, and is password protected (can only be accessed by a small number of identified individuals). All of the personnel handling the specimens will be adequately educated about and agree to the confidential handling of your samples. The samples will be stored in a secure, limited access area.

We shall keep your research record confidential, to the extent provided by federal, state, and local law. We shall not allow anyone to see your record, other than people who have a right to see it. You will not be identified in any reports from this study.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Your AIDS/HIV status
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.

- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
  - Make sure the study is done safely and properly
  - Learn more about side effects
  - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.med.umich.edu/hipaa/npp.htm. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

This Authorization does not have an expiration date. The University of Michigan study team may need to correct or provide missing information about you even after your study participation is over. The review of your medical records (described above) may also take place after the study is over.

You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

You have the right to take back (revoke) your Authorization at any time by writing. Please tell one of the persons listed in Section 10 “Contact Information” (below).

If you revoke your Authorization, the University of Michigan study team will not collect any new study data and/or health information about you. However, they can continue to use and disclose any already collected information before you cancelled the study if that is necessary for the reliability of the study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Rajen Mody, MD
Mailing Address: 1500 East Medical Center Drive, D4202 MPB
Ann Arbor, MI 48109-5718
Telephone: 734-764-7126

Study Coordinator: Kevin Frank
Mailing Address: 1500 East Medical Center Drive, D4202 MPB
Ann Arbor, MI 48109-5718
Telephone: 734-764-9306

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
28 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details

about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*
- Other (specify): Assent for 10-13 year old subjects (next page)

Assent for Children 10-13 Years of Age

(Minors 14-17 can choose to sign to give assent on the next page)

My study doctor has explained to me what this research study is about. I understand how it may or may not help me. I understand that this research may help doctors understand more about the DNA sequencing of tumor samples. I understand that there are risks and discomforts that may happen to me if I participate and these have been explained to me.

I have been given time to think about being in this research study. I have asked questions and had time to have them answered. If I think of more questions later, I can call Dr. Rajen Mody at 734-764-7126 or ask him next time.

I know I don't have to agree to be in this research study and no one will be upset with me and I will not be treated any different if I choose not to participate.

Even though I agree now, I may feel differently later on. If I change my mind it will be okay and I will still be taken care of by the doctors and nurses. I know that I may talk with my parents and/or my doctors if I change my mind about being in the study at any time.

The doctors will tell me if they find out new things that they didn't know about when they first explained this study to me. Participation in this study will go on for many years. At times, my records will be updated in our database by looking at my medical records.

All the information collected about me for this study will be kept private.

If I put my name at the end of this form it means I agree to be in this study. I will be given a copy of this form to keep after I sign it and so will my parents.

Name (printed): _____

Signature: _____

Date: _____

12. SIGNATURES

By signing this consent, I understand that I agree to the following:

- I agree to undergo a complete **history and routine examination** and have this information entered into a clinical database.
- I understand that I am providing **samples** for blood, urine, cheek swabs, saliva, and tumor biopsy. If previously obtained tumor samples are available, I agree to their release for the study.
- I agree to be re-contacted by phone or mail to **update my personal medical information**.
- In the event that clinically significant results are identified, I understand that I will be contacted in the future regarding results related to my **"Cancer of Interest."**

What is your preferred means of contact? _____Phone_____Email_____Postal Mail
Email address:_____ Preferred Phone:_____
Preferred Postal address:_____

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of (Assenting 14-17) Subject: _____Date: _____

Name (Print legal name): _____

Patient ID:_____ Date of Birth: _____

Legal Representative (if applicable):

Signature of Person Legally Authorized to Give Consent _____

Date of signature: _____

Name of Person Legally Authorized to Give Consent (print legal name): _____

Address of Legal Representative: _____

Relationship to Subject (check): ☐ Parent ☐ Spouse ☐ Child ☐ Sibling ☐ Legal Guardian ☐ Other: _____

If this consent is for a child who is a ward of the state (for example a foster child), please tell the study team immediately. The researchers may need to contact the IRBMED.

Reason subject is unable to sign for self: _____

***For Standard of care procedures where there is no direct benefit to the patient, obtain second parent permission**

Second Parent Permission

Print Legal Name: _____

Signature: _____

Address: _____

Date of Signature (mm/dd/yy): _____

Genetic Counselor:

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study. Parents or legal guardians, who are giving permission for a child, please note: in the sections that follow the word 'you' refers to 'your child'.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title: Personalized Medicine Based on Molecular Profiling of Patients with Cancer

1.2 Company or agency sponsoring the study: None

1.3 Names, degrees, and affiliations of the researchers conducting the study:

Principal Investigators:
Rajen Mody, MD, Associate Professor, Department of Pediatrics Hematology/Oncology
Arul M. Chinnaiyan, MD, PhD, Professor, Department of Pathology

Department of Internal Medicine, Hematology and Oncology
Moshe Talpaz, MD, Professor, Department of Internal Medicine
Elena Martinez Stoffel, MD, Assistant professor, Department of Internal Medicine

Department of Pediatrics, Cancer Genetics
Raymond Hutchinson, MD, Professor, Department of Pediatrics
Jeffery Innis, MD, PhD, Professor, Department of Pediatrics
Jessica Everett, MS, Genetic Counselor, Department of Internal Medicine
Victoria Raymond, MS, Genetic Counselor, Department of Internal Medicine
Shanna Gustafson, MS, Genetic Counselor, Department of Internal Medicine
Rhonda McDougall, NP, Department of Pediatrics
Marcia Leonard, NP, Department of Pediatrics
Rama Jasty-Rao, MD, Department of Pediatrics
Aghiad Chamdin, MD, Department of Pediatrics
Nur Akcasu, NP, Department of Pediatrics
Judith Moyer, NP, Department of Pediatrics
Gregory Yanik, MD, Professor, Department of Pediatrics

Michigan Center for Translational Pathology
Michigan Institute for Clinical and Health Research
Javed Siddiqui, MS, Department of Pathology
Robert Lonigro, MS, Mathematics and Biostatistics, Michigan Center for Translational Pathology

Bioethics
Scott Roberts, PhD, School of Public Health, Center for Bioethics and Social Sciences in Medicine
Scott Kim, MD, PhD, Department of Psychiatry, Center for Bioethics and Social Sciences in Medicine

Department of Radiology
Jonathan Dillman, M.D., Assistant Professor, Department of Radiology

Department of Pathology:
Raja Rabah, MD, Professor, Department of Pathology

Research Coordinator (Pediatric Phase-I Program):
Kevin Frank, Department of Pediatrics

Clinical Coordinator
Angela Stovall, Department of Pediatrics

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The goal is to identify key genes important to cancer cells that could potentially influence clinical decision making for managing cancer. You will be asked to provide normal samples (Blood, cheek swab, urine, and spit) and tumor samples (through a biopsy). Genetic material, including DNA and RNA, will be obtained from samples, stored, and used for evaluation of your cancer. Specifically, the study includes DNA sequencing of your tumor and normal cells as a comparison.

However, molecular evaluation is not guaranteed. It is possible that the DNA sequencing process may take longer or in some cases may not be possible. This could be due to unpredictable variation in tissue quality or technical problems. Furthermore, the results are not guaranteed to help your doctor take care of you.

Tumor tissue may be grown and used to create cell lines that allow researchers to maintain cancer cells in the lab for research. These cells can be used for ongoing research towards the development of new therapies.

Clinical information and samples will be collected and stored for ongoing research. This is a necessity because improved diagnosis, prognosis and treatment of cancer in the future depend upon the ongoing analysis of basic research findings and clinical outcomes. This type of research may improve the lives of future patients with cancer.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished,

there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Your study doctor will review your past medical history, known allergies, current medications, and blood tests, to determine if you are eligible to take part in this study.

1) Inclusion Criteria: A confirmed diagnosis of cancer.

1) Any kind of advanced cancer.
2) Less than or equal to 25 years of age
3) Patients are undergoing standard of care surgeries or procedures

OR

Patients have tumor that is suitable for research biopsy (as assessed by trained specialists in radiology) AND Patients are medically fit to safely undergo a biopsy

4) Procedure-specific signed informed consent prior to initiation of any study related procedures
5) Women and minorities are included in this protocol
6) Patients with multiple malignancies remain eligible
7) Patients with an inherited cancer syndrome or a medical history suggestive of an inherited cancer syndrome remain eligible

2) Exclusion Criteria:

1) If enrolling study physician feels you are unable to undergo biopsy
2) Patients who are in prison are not eligible to participate
3) Women who are pregnant

3.2 How many people (subjects) are expected to take part in this study?

For the first phase of this study, we are enrolling 40 patients. We intend to expand the study and anticipate enrolling of up to 200 patients from all parts of the study in the next four years.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

A Clinical Investigator from the Study Team and Genetic Counselor will explain the study to you. The study doctors and coordinators will review your history to determine if you are eligible to take part in the study. You will have the opportunity to ask any questions about the study. You must complete this informed consent form in order to participate.

- Study Investigators will take your complete history and perform a routine examination.
- The study involves collection of tumor tissue, typically through a biopsy procedure. The type of biopsy procedure varies for person to person and the type of cancer they have.
- You will be asked to provide additional samples including blood, cheek swab, spit, and urine.
- Your clinical information will be recorded and updated.
- Your tumor will undergo DNA sequencing in the Department of Pathology's Michigan Center for Translational Pathology at the University of Michigan.

Samples:
A) Blood Collection: Four tablespoons of blood will be drawn from your vein, using regular blood drawing techniques. When possible, these samples will be obtained at the same time as routine blood work through your doctor.
B) Buccal or "Cheek" Swab: A sterile brush will be used to gently swipe the inside of your cheek ten times avoiding the gum line. This process will be repeated with two more brushes.
C) Saliva Collection: You will be asked to spit into a small container several times.
D) Urine Collection: We will ask that you provide a urine sample.
E) Previously Collected Tumor Specimens. You will be asked to sign a release for retrieving previously collected tumor specimens here or at other hospitals and clinics. We will make arrangements to retrieve these materials, at no cost to you.
F) Tumor Tissue or Bone Marrow Biopsy: The study doctor will arrange for tumor tissue to be collected through the least invasive procedure possible. This will generally involve a needle biopsy.

Important: If you are currently taking a medicine called **warfarin** sodium (also called Coumadin) or other **blood thinners**, you must tell your study doctor. Blood thinners may increase the risk of bleeding after biopsy. In order to undergo biopsy, your study doctor will confer with your primary care doctor if it is safe to temporarily stop your blood thinner before a biopsy.

Exception: During the course of the study, if you're cancer should become resistant to your current therapy, you will be eligible to have another tumor biopsy and blood sample to re-evaluate the tumor. If you wish to participate by having another biopsy, you will be asked to complete another consent form, agreeing to the repeat biopsy. The same eligibility criteria will apply.

What will happen to the samples that are collected?
Genetic material, including DNA and RNA, will be obtained from samples, stored in freezers, and used for profiling and analyzing your cancer. Specifically, the study includes DNA sequencing of your tumor and normal cells as a comparison. The goal is to identify key changes in the genes important to cancer cells that could potentially influence clinical decision making for your cancer. However, success or clinical benefits from the profiling of your cancer DNA is **not** guaranteed.

Some cells from your tumor may be grown and used to create cell lines that can be used as an ongoing source of genetic material or used for laboratory research. Additional analysis of the sequencing data will be used for research purposes, for example to discover new, unknown associations between genes and cancer. This type of research may affect the lives of future patients with cancer.

Are there additional costs to me or my insurance?
As a participant in this study, you will **not** be billed for the collection, processing, storage, DNA sequencing, or analyses of these samples. You will **not** be billed for the tissue biopsy.

In some instances, if certain genetic changes are found, more testing may be needed. When clinically indicated, the treating physician may order additional testing at a CLIA certified laboratory. This would **not** be part of the study and would be billed to your insurance.

4.2 How much of my time will be needed to take part in this study?

- **Samples.** Blood, buccal, and urine samples can be collected at one of your clinic visits, and may add up to 1 hour of time.
- **Tumor biopsy.** A tumor biopsy will be scheduled and generally takes several hours, including check-in time, preparation, the procedure, and observation.
- **Follow up.** The study involves periodic follow-up to update our records. After enrollment, medical records will be requested after 4 months, 8 months, 12 months, 18 months, 24 months, and then every 12 months indefinitely. Generally this follow up is completed by review of your medical records which will not require your time or effort, but on occasion we may require additional phone contact.

4.3 When will my participation in the study be over?

Study participation is **indefinite**. This involves periodically updating our database through retrieval of your medical records at regular intervals (as described in the previous section).

However, you are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information” (below).

4.4 Will the researchers give me results?

Our goal is to offer results that have **clinical value** based on available information and our best clinical judgment. A Board consisting of **experts in oncology (cancer), genetics, and ethics** from the University of Michigan will serve on a “Sequencing Tumor Board” will review the results and determine what results are important.

In this study, you will receive results if they are felt to be **clinically important (information that can help your doctor manage your cancer)** and the results have been confirmed through clinically-certified lab. Since you are participating in a cancer study, **we will always tell you about any results that have a “Direct impact on care of your current cancer.”**

The initial results of our research studies will be sent to the referring physician. Our research results may find a result that can be confirmed with a clinically validated medical test. This is typically available through a genetic testing lab. These tests typically cost hundreds or thousands of dollars. If you and your physician decide to do any type of confirmatory testing, you or your insurance may be charged for the cost of a new sample collection or for laboratory tests to confirm the research results. Specifically, the University of Michigan will not participate in the decision whether to validate the research findings through a commercially available test.

However, this study may uncover additional information that **may** or **may not** be important to you. Some patients may find this extra information to be overwhelming, while others may want to have all information given to them. Therefore, we give you the choice to say “Yes” or “No” to these other results **before** you begin the study.

4.5 What choices do I have for receiving these other results that do not have direct impact on care of my current cancer?

There are at least two kinds of information that do not have direct impact on your cancer care but which you may or may not wish to know about:

1) Results that may have significance for <u>biological family members</u>.

Example 1: The researchers may discover that you have a gene that, if inherited by biologically-related family members, could increase their risk of cancer. These family members may or may not have the gene; they would need to be tested to find that out. Is the possibility that they might have such a gene something that you and/or your family member(s) would want to know?

Example 2: The researchers might discover that you carry a gene for another medical condition. Your biological family members may also have such a gene. Is this something that you and/or your family member(s) would want to know?

2) Results that are <u>not related to your cancer</u>, but may have potential medical impact for <u>you</u>.

Example: The researchers may discover that you have a gene that significantly increases your risk for another medical condition, not related to your cancer. We cannot know ahead of time what that condition might be. Is this something that you would to know?

We realize that whether or not you want to be told about these results that do not have direct impact on the care of your current cancer will be a very personal decision.

If you do not do anything, then you will be given the results by default. However, if you do not wish to be told, you can direct us not to disclose these types of results.

Please feel free to ask questions and discuss your preferences with the study team members. They will help you complete the table. If you do nothing, you will be told. However, if you wish not to be told, please initial where indicated below.

What choices do I have for receiving these other results that do not have direct impact on care of my current cancer?	**If you do NOT want to be told of these results, please initial the boxes below.**
1) Results that may have **significance for biological family members**.	
2) Results that are **not related to your cancer,** but may have **potential medical impact for you**.	

As with any research study, there may be additional outcomes or risks that are unknown or unexpected. These will be handled on a case by case basis by the Sequencing Tumor Board.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:

A) Blood Collection: Blood collection usually causes minor discomfort at the site where blood is taken.

- You may experience bleeding, bruising, lightheadedness, or fainting (1-10% of patients).
- Rare side effects (less than 1%) include serious bleeding or infection.

To reduce these risks, the research team will draw blood at the same time as your doctor orders them for your routine care and ensure proper blood drawing techniques is performed by a trained individual.

B) Buccal "Cheek" Swab Collection: Buccal swabs may rarely (less than 1% of patients) cause some irritation at the swab site.

C) Saliva Collection: There are no known risks to providing a saliva sample.

D) Urine Collection: There are no known risks to providing a urine sample.

E) Previously Collected Tumor Specimens: There are no known risks to providing previously collected tumor specimens.

F) Tumor Biopsy or Bone Marrow Aspirate: If necessary, your study doctor or a member of the study team will perform or arrange for the tumor biopsy. Procedures are performed by experienced personnel with the proper technique that will minimize the risks of the procedure. You could experience pain, inflammation, bleeding, swelling, or infection at the site where the tumor tissue is removed. The person that performs your biopsy, whether your study doctor or another healthcare professional, will tell you about the biopsy procedure and any specific risks associated with the biopsy. They will also obtain your consent for the biopsy according to the standard process.

The most common side effects (occurring in more than 10% of patients) are:

- Pain
- Inflammation
- Swelling
- Minor bleeding

Rare side effects (occurring in less than 1% of patients) are:

- Serious Bleeding
  Infection

Some data collected from you may be deposited into dbGAP but all identifiable information will be removed prior to submission so that the data cannot be linked to you in any way. The database of Genotypes and Phenotypes (dbGaP) is a database developed by the National Center for Biotechnology Information (a division of the National Library of Medicine) to archive and distribute the results of studies that have investigated the interaction of genotype and phenotype. All data submitted from this study will only be available through controlled access and restricted to cancer research studies. Any researcher requesting access to the data must formally apply to dbGAP and present a research study rationale for why they need access to the data. The data may also be submitted to other future database systems which will have similar access controls as dbGAP utilizes.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 .What are the risks of genetic research?

There are some risks to receiving genetic results. Participants could experience risks such as psychological or emotional distress, loss of insurance, loss of employment, discovery of previously unknown health conditions, discovery that you are not the biological parent of a child(ren), or discovery that you could carry a gene for a certain disease, etc. Therefore, we offer **genetic counseling** before participation in the study as part of the informed consent process.

Patients may be referred to additional Genetic Counseling as part of their routine clinical care. This is typically covered by most insurance agencies. If this is not covered, you will have to pay out of pocket for this service, typically around $300 to $400 for a visit.

What is the Genetic Information Nondiscrimination Act (GINA)?
The federal Genetic Information Nondiscrimination Act (GINA) generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance. Under this law:

- Health insurance companies and group health plans may not request your genetic information that we obtain from this research
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums
- Employers with 15 or more employees may not use your genetic information that we obtain from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment
- GINA does not apply to the following groups, however these groups have policies in place that provide similar protections against discrimination:
  - Members of the US Military receiving care through Tricare
  - Veterans receiving care through the Veteran's Administration (VA)
  - The Indian Health Service
  - Federal employees receiving care through the Federal Employees Health Benefits Plans

5.3 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors**.**

5.4 If I take part in this study, can I also participate in other studies?

Since this study does not involve active treatment, participating in this study does not limit your ability to participate in other studies. If you do participate in more than one study, please notify researchers from all studies.

5.5 How could I benefit if I take part in this study? How could others benefit?

If we identify a potentially important result from your DNA analysis that could help your doctor manage your cancer, you and your doctor may pursue a therapy that might work better for you. **Benefits of therapy are not guaranteed**. If we do not identify information that would be important for your cancer then you will not receive any personal benefits from being in this study. However, the tissues donated through this tissue bank will help advance understanding of the genetics of cancer and may lead to new treatments for patients in the future.

5.6 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn new information that could change your willingness to stay in the study, as long as you have agreed to receive that information per section 4.5 The researchers will give you the information they have learned, discuss risks and benefits with you and you will have the option to continue on study or withdraw.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?

Your participation in the study is completely voluntary. The alternative is to not participate, in which case there will be no penalty to you or your treatment.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 “Contact Information” (below). If you request removal from the study then your clinical information will be removed from the databases and no new information will be collected. However, previously collected samples and any completed test results will be retained. If you withdraw from the study, it will not be possible to remove any of your data that may have been submitted into dbGAP. This data will remain in the dbGAP repository but will not have any identifiers in it that could link the data to you.

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

No

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. If you are not sure what these are, see Section 4.1 above or ask the researchers for a list. If you get a bill you think is wrong, call the researchers' number listed in section 10.1.

You or your health plan will pay for all the things you would have paid for even if you were not in the study, like:

- Health care given during the study as part of your regular care
- Items or services needed to give you study drugs or devices
- Monitoring for side effects or other problems
- Deductibles or co-pays for these items or services.

If you do not have a health plan, or if you think your health plan may not cover these costs during the study, please talk to the researchers listed in Section 10 below or call your health plan's medical reviewer.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Mody immediately, at 734-764-7126. The doctor will either treat you or send you to another doctor for treatment.

You will get free medical care at the UMHS for any hospitalization directly caused by the study drug, device, or procedure. The UMHS and the study doctor are responsible for determining whether your condition was the result of your participation in the study.
The UMHS will pay for your treatment only if it has been caused by the study drug, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

8.2 Will I be paid or given anything for taking part in this study?

No. You will not be paid for taking part in this study.

8.3 Who could profit or financially benefit from the study results?

If a new discovery, diagnostic test, or treatment results because of research done on the tissue you donated, the University of Michigan Researchers could profit by filing a patent. Should any product developed from participant samples, participants will not be responsible for any costs of development, nor will they obtain any profit from the commercial use.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

9.1 How will the researchers protect my privacy?

Patient information kept within the University of Michigan Health System medical record is protected by the Health System's privacy policies. Research information is protected by being kept in a separate research record not included with the patient's medical chart, and stored in a locked office and in a password-protected database.

Your samples will be stored in a manner in which your personal identification is not known to those storing it. Specimens will be stored without any labels that directly identify you, and are only identified by a research code number. The electronic database that contains your personal data is separate from the database with the data from your samples, and is password protected (can only be accessed by a small number of identified individuals). All of the personnel handling the specimens will be adequately educated about and agree to the confidential handling of your samples. The samples will be stored in a secure, limited access area.

We shall keep your research record confidential, to the extent provided by federal, state, and local law. We shall not allow anyone to see your record, other than people who have a right to see it. You will not be identified in any reports from this study.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study. Information about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Mental health care records (except psychotherapy notes not kept with your medical records)
- Alcohol/substance abuse treatment records
- Your AIDS/HIV status
- All records relating to your condition, the treatment you have received, and your response to the treatment
- Billing information

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.

- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.med.umich.edu/hipaa/npp.htm. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

This Authorization does not have an expiration date. The University of Michigan study team may need to correct or provide missing information about you even after your study participation is over. The review of your medical records (described above) may also take place after the study is over.

You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

You have the right to take back (revoke) your Authorization at any time by writing. Please tell one of the persons listed in Section 10 "Contact Information" (below).

If you revoke your Authorization, the University of Michigan study team will not collect any new study data and/or health information about you. However, they can continue to use and disclose

any already collected information before you cancelled the study if that is necessary for the reliability of the study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Rajen Mody, MD
Mailing Address: 1500 East Medical Center Drive, D4202 MPB
Ann Arbor, MI 48109-5718
Telephone: 734-764-7126
Study Coordinator: Kevin Frank
Mailing Address: 1500 East Medical Center Drive, D4202 MPB
Ann Arbor, MI 48109-5718
Telephone: 734-764-9306

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
28 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

By signing this consent, I understand that I agree to the following:

- I agree to undergo a complete **history and routine examination** and have this information entered into a clinical database.
- I understand that I am providing **samples** for blood, urine, cheek swabs, saliva, and tumor biopsy. If previously obtained tumor samples are available, I agree to their release for the study.
- I agree to be re-contacted by phone or mail to **update my personal medical information**.
- In the event that clinically significant results are identified, I understand that I will be contacted in the future regarding results related to my **"Cancer of Interest."**

What is your preferred means of contact? _____Phone_____Email_____Postal Mail
Email address:_____ Preferred Phone:_____
Preferred Postal address:_____

Research Subject:

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Signature of Subject: _____Date: _____

Name (Print legal name): _____

Patient ID:_____ Date of Birth: _____

Legal Representative (if applicable):

Signature of Person Legally Authorized to Give Consent _____

Date of signature: _____

Name of Person Legally Authorized to Give Consent (print legal name): _____

Address of Legal Representative: _____

Relationship to Subject (check): ☐ Parent ☐ Spouse ☐ Child ☐ Sibling ☐ Legal Guardian ☐ Other: _____

If this consent is for a child who is a ward of the state (for example a foster child), please tell the study team immediately. The researchers may need to contact the IRBMED.

Reason subject is unable to sign for self: _____

***For Standard of care procedures where there is no direct benefit to the patient, obtain second parent permission**

Second Parent Permission

Print Legal Name: _____

Signature: _____

Address: _____

Date of Signature (mm/dd/yy): _____

Genetic Counselor:

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____

Principal Investigator (or Designee):

I have given this research subject (or his/her legally authorized representative, if applicable) information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____