UNIVERSITY OF WASHINGTON
PARENT CONSENT FORM
INTERNATIONAL REGISTRY OF WERNER SYNDROME
AND OTHER PREMATURE AGING SYNDROMES

Investigators:

_____, Referring Physician
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INVESTIGATOR'S STATEMENT

We are asking your child to be in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether you wish your child to be in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask your child to do, the possible risks and benefits, your child's rights as a volunteer, and anything else about the research or this form that is not clear. When we have answered all your questions, you can decide if you want your child to be in the study or not. This process is called 'informed consent.' We will give you a copy of this form for your records.

PURPOSE OF THE STUDY

The purpose of this research project is to identify genes that cause aging syndromes and to understand how those genes normally function and how abnormal forms of the genes can lead to a number of disorders commonly associated with aging, particularly tumors and cardiovascular disease. We would like to study patients with Werner's Syndrome or other syndromes with symptoms of premature aging and their close family members.

PROCEDURES

If you agree to let your child participate, we will ask you for permission to allow your child's physician(s) to obtain information from his/her medical records in order to complete the Registry Form now and for periodic updates (typically at approximately five-year intervals) of the data included in that form. This form includes your child's name and contact information in addition to personal medical information related to symptoms of Werner syndrome and other progeroid (aging) syndromes. For example, we will collect information about how tall your child is, whether he or she has different colors of skin pigmentation, if he/she has had ulcers, or if he or she has lost any of their hair. We ask for information about your immediate family as it related to gender, whether they are living or have died and whether they have any symptoms of premature aging. If your child is not alive at the time an update is requested, we would seek permission to view autopsy records, if available, from you.

We will also request that your child donate 20 to 30 cubic centimeters (less than two tablespoons) of blood from a vein in his/her arm. In some cases DNA prepared from a previous blood draw would be adequate for our study. Tissue from surgery in the form of paraffin blocks may also be requested if available.

We may also request a very small biopsy of skin from the inner surface of your child's arm. The sample should be no bigger than a grain or two of rice (2 to 3 mm or no more than 1/8th of an inch). The skin is first numbed by the injection of a local anesthetic and the sample is taken with a small punch instrument.

If your child's symptoms or those of your family member are consistent with Werner Syndrome, our laboratory will use the blood and/or skin samples to determine if your child carries a copy of the mutant gene which, when

present in two copies, causes the Werner syndrome. (There are no known clinical abnormalities associated with having only a single copy of the mutant gene.) If there is no change in the Werner gene found, or symptoms are not consistent with Werner syndrome, we will investigate various other genes. The data collected on the Registry Form and in the follow-ups will be used to analyze the pattern of features in association with specific gene mutations.

Once the studies are completed on the Werner gene, these results will be shared with your child's doctor and with you if you wish to know, as our laboratory is certified for clinical testing of the Werner gene. Interpretation of the test result in light of your child's medical history can be provided by your physicians, who may consult with Dr. Martin or Dr. Oshima. If we find a change in a gene besides the Werner gene, we will share these results with your child's physician and with you if you wish to know. However, these results must be verified in a laboratory certified for clinical testing of research genes.

Cell lines from blood or skin may also be grown in the laboratory and preserved in liquid nitrogen for further studies regarding aging syndromes. Any such cell lines would become the property of the University of Washington. These lines are very unlikely to be of any commercial value, however. The blood drawing or skin biopsy procedures should only take a few minutes. Our research project is ongoing. The clinical data and samples from this study will be kept for further studies of Werner syndrome and other aging syndromes. We will keep the link to your child's personal information (identifiers) for ten years or until the end of the study, whichever comes first. De-identified cell lines and DNA will be kept indefinitely. The investigators may contact you or your child's referring physician to update his/her medical history information in order to better understand the natural history of the condition.
We may do gene analysis that looks at large areas (exome) or even the entire area of your child's DNA (genome). Usually researchers study just a few areas of the DNA that are thought to be linked to a disease or condition. New technology for exome or genome studies allow for most or all of the genes to be analyzed and used by researchers to study links to the disease. No direct benefit can be promised from your child's participation. Some people might find satisfaction in helping to find scientific knowledge about genetic problems and medical conditions.

In order to allow researchers to share test results, the National Institutes of Health (NIH) and other central repositories have developed special data (information) banks that collect the results of whole exome or genome studies. The NIH and other data banks will store your child's genetic information and give it to other qualified researchers to do more studies. Qualified researchers that can access the national databases can be from the government, academic, or commercial institutions. We do not think that there will be further risks to your child's privacy and confidentiality by sharing whole-genome analysis with these databanks; however, we cannot predict how genetic information will be used in the future. The information will be sent with only a code number attached. Your child's name and other information that could identify him/her will never be given to them. There are many safeguards in place to protect your child's information while it is stored in repositories and used for research.

There is a small chance that your child's genetic information could be shared with others by mistake. In the unlikely event that happened and if it were linked with a medical condition, this could affect your child's ability to get or keep some kinds of insurance. There is also the risk that data could be released to the public, employers, or law enforcement agencies. If family members saw this information it could also affect them. This could hurt family relationships. It is also possible that your child could be identified from the sample is someone has another DNA sample to compare. The two samples could be matched to identify your child from the sample given for this study.

You should not sign this consent form if you are not comfortable sharing your child's coded DNA information with other researchers.

You will not receive any results produced from your child's participation in the national databases unless it is considered medically relevant.

You can withdraw your consent at anytime you no longer want your child's data shared in the national databases. Your child can decide to withdraw consent when he/she reaches 18 years. There will be no consequences for withdrawing consent. However, data that has already been sent to researchers cannot be retrieved from those researchers.

RISKS, STRESS, OR DISCOMFORTS

The withdrawal of blood will cause a slight discomfort from the needle puncture, the possibility of a small bruise around the puncture site, and a very low risk of infection at the puncture site. There is also a risk of fainting from the blood draw. If your child has a skin biopsy, it will cause a slight discomfort and is also associated with a very low risk of infection. A local anesthetic (about a quarter of a milliliter or a twentieth of a teaspoon of xylocaine 1 % strength in saline or an equivalent anesthetic) will be used to minimize discomfort. In some individuals this anesthetic may cause an allergic reaction. For the case of family members, there is no known risk to insurability if the results of our tests go into your child's medical records. **You have the right, however, to prevent such information from appearing in your medical records by notifying your referring physician**. Involvement in any medical activity is often stressful and there may be anxiety that precedes each portion of this study. Some people find it stressful to learn, even though they are clinically affected, that they have an identifiable alteration in a gene in their body. Some people feel that providing samples for research is an invasion of privacy.

ALTERNATIVES TO TAKING PART IN THIS STUDY

Taking part in this study is voluntary. If you choose for your child not to take part, it will not change his or her regular medical care. If you choose for your child to be in the study, he or she may quit at any time without changing their medical care. You can choose not to be contacted about taking part in this study in the future.

BENEFITS

Your child may or may not benefit directly from this study. The study may be of benefit to your child if we learn that there are mutations in the specific genes we examine because it may provide you with more information about what you can expect and allow you to use the information for family planning, if you so choose. If your child is clinically affected and we are unable to identify an alteration, it may mean that the diagnosis is not correct and additional consultation should be sought. If your child is clinically unaffected and we can show that he/she does not have alterations in the genes we study then this would mean that their offspring have little risk for the condition and that they would not develop it as they get older. We hope that, by understanding the genetic basis of inherited disorders of aging syndromes, we may someday be able to develop effective treatments and even cures for these disorders. There are currently no available treatments that address the underlying mutational basis of the disease. The results of this study may also lead to new approaches in the prevention and treatment of a number of common disorders in older people.

COMPENSATION FOR INJURY

If you think your child may have an injury or illness related to this study, contact the study staff [Junko Oshima, 206-543-5088] right away. The researchers will treat your child or refer him/her for treatment. The UW will pay up to $10,000 to reimburse for treatment of physical injury or illness resulting from the study. No money has been set aside to pay for things like lost wages, lost time, or pain. However, you do not waive any rights by signing this consent form.

OTHER INFORMATION

You will not be paid for your child's participation, nor will you be charged any extra fees as a result of participation in this study. Your child's participation is entirely voluntary; you may refuse to allow your child to participate or he/she may withdraw from the study at any time and request that all samples be destroyed. To do this you would contact the Werner Registry investigator. You can contact the investigator by phone (206-543-5088 or toll-free 888-288-7362), email (picard@u.washington.edu), or by mail (Junko Oshima., Dept of Pathology, 1959 NE Pacific St. Box 357470, Seattle, WA 98195). Please note that after the link to your child's name is destroyed, we will not be able to destroy his or her samples. We cannot ensure the confidentiality of information sent via e-mail. Refusal or withdrawal would be without penalty or loss of benefits to which you are otherwise entitled. Your child's identity as a blood or tissue donor will remain confidential. Samples will be coded and not identified by subject's name. Only Dr. Martin, Dr. Oshima, and three senior technical associates will have access to patient identities linked with this data. Unidentified cell lines and clinical data may be shared with other non-profit repositories for research on aging. Samples and clinical information will be kept in order to investigate new hypotheses concerning the functions of the various gene products associated with aging syndromes.

All information collected will be strictly confidential. All records with identifying information will have this information blacked out and will be given a study number. These files will be kept in a locked filing cabinet. The code that links your name to the study number will be kept in a computer file that will need a password to enter and will be kept indefinitely. The investigators in this study will have access to the password or study files.

Although we will make every effort to keep your information confidential, no system for protecting your confidentiality can be completely secure. There is still the possibility that unauthorized persons might discover your participation in this study and information about you. Government or university staff sometimes reviews studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm.

Government or university staff sometimes reviews studies such as this one to make sure they are being done safely and legally. If a review of this study takes place, your records may be examined. The reviewers will protect your privacy. The study records will not be used to put you at legal risk of harm. To further protect your privacy we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation for Federally funded projects or for information that must be disclosed in order to meet the requirements of the Federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your Involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information.

Exceptions:
A Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information about you, without your consent in incidents such as child abuse, and intent to harm yourself or others.

Medical photographs will be requested of some subjects. Those in which the face or other identifying parts are visible will be marked so as to obscure the identity of the individual if that is the wish of the subject. In some instances those features are the important ones to illustrate, however. Permission for use in medical publication and for illustration of medical lectures will be obtained with a separate release form specific to this research project. The photographs will be retained by the investigators and will be used only for purposes specified by the participant. At any time, the subject of the photographs may review them, may withdraw permission for their use, or may delete portions.

Printed name of researcher | Signature of researcher | Date

Printed name of referring physician | Signature of referring physician | Date

SUBJECT'S STATEMENT

This study has been explained to me. I give permission for my child to take part in this research. I have had a chance to ask questions. If I have questions later about the research, I can ask one of the researchers listed above. If I have questions about my child's rights as a research subject, I can call the Human Subjects Division at (206) 543-0098. I give permission to the researchers to use my child's medical records as described in this consent form. I will receive a copy of this consent form.

Printed name of subject | Signature of Parent | Date

Printed name of parent

ADDENDUM:
If you agree to any of the following, we would contact you for permission to release your information in each individual case. This is a service to you and others, not a part of our research study.

We are at times contacted by individuals in the media or educators who wish to feature a person with Werner syndrome in various projects. If we learn of such an opportunity would you like us to contact you and offer the chance to participate? YES NO

Some of our participants ask if they might be able to speak with another person with the same condition. Would you wish to be contacted with such a request? YES NO

Other researchers in the field of aging conditions can request samples from us for study without identifying information. If there were a research study that would require contact with you and a separate consent form, would you wish to be notified? YES NO

Copies to: Subjects
Investigator's File

Revised: 2/2012