UNIVERSITY OF WASHINGTON
LEGAL AUTHORIZED REPRESENTATIVE 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 you to be a proxy for your next of kin in consenting for the use of their tissue in a research study. The purpose of this consent form is to give you the information you will need to help you decide whether allow the tissue to be used in the study or not. Please read the form carefully. You may ask questions about the purpose of the research, what we would ask you to do, the possible risks and benefits, your 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 agree to this use of tissue. 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 use of the sample, we will also ask for permission to allow your family member's physician(s) to obtain information from their medical records in order to complete the Registry Form. This form includes your name and contact information in addition to the subject's (your family member's) personal medical information related to symptoms of Werner syndrome and other progeroid syndromes. For example, we would ask for information on how tall they are, whether they had changes in skin pigmentation, or whether they developed ulcers. We also ask for information about immediate family as it related to gender, whether they are living or have died and whether they have any symptoms of premature aging.

If symptoms of your family member are consistent with Werner Syndrome, our laboratory will use the tissue samples to determine if they carried 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 family member's doctor. As our laboratory is certified for clinical testing of the Werner gene, interpretation of the test result in light of your family's clinical history can be provided by your family member's physicians, who may consult with Dr. Martin or Dr. Oshima. The Registry provides a genetic counselor who is available to discuss the testing process or test result. If we find a change in a gene besides the Werner gene, we will share these results with

your family member's physician. However, these results should 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 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. Our research project is ongoing. We would keep all records and materials for ten years or until the end of the study, whichever comes first. The clinical data and samples from this study will be kept for further studies of Werner syndrome and other aging syndromes. The investigators may contact your family member or their referring physician to update your family's 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 family member'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 family member'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 family member'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 family member'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 family member'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 family member's information while it is stored in repositories and used for research.

There is a small chance that your family member'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 family member'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 family member could be identified from the sample is someone has another DNA sample to compare. The two samples could be matched to identify your family member from the sample given for this study.

You should not sign this consent form if you are not comfortable sharing your family member's coded DNA information with other researchers. You will not receive any results produced from your family member your family member's participation in the national databases unless it is considered medically relevant.

You can withdraw this consent at anytime you no longer want your family member your family member's data shared in the national databases. 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

In the case of family members, there is no known risk to insurability if the results of our tests go into their relative's medical records. **Your family member has the right, however, to prevent such information from appearing in a relative's medical records by notifying the referring physician**. Involvement in any medical activity is often stressful and there may be anxiety that precedes each portion of this study. Some

people might find it stressful to learn, even though their relative is clinically affected, that he or she has 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 your family member chooses not to take part, it will not change their regular medical care. If your family member chooses to be in the study, he/she may quit at any time without changing their medical care. Your family member can choose not to be contacted about taking part in this study in the future.

BENEFITS

The study may be of benefit to your family member if we learn that there are mutations in the specific genes we will examine because it may provide your family member with more information about a their diagnosis. If they were 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. 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 correct the genetic basis of Werner syndrome. 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.

OTHER INFORMATION

Tissue blocks will be returned to the originating laboratory after testing, no later than 6 months after receipt of the tissue (testing typically takes 3-4 months). We would keep all records (pathology reports) until the end of the study. The sample will be used only for research.

Your family member will not be paid for their participation, nor will there be any extra fees charged as a result of participation in this study. Participation is entirely voluntary; your family member may refuse to participate or may withdraw from the study at any time and request that all samples be destroyed. To do this please contact the Werner Registry Genetic investigator. You can contact the investigator by phone (206-685-2719 or toll-free 888-288-7362), email (picard@u.washington.edu), or by mail (Junko Oshima, Research Associate Professor, Dept of Pathology, 1959 NE Pacific St. Box 357470, Seattle, WA 98195). Please note that after the link to your family member'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 from the study would be without penalty or loss of benefits to which your family member is otherwise entitled.

The donor's identity as a blood or tissue donor will remain confidential. Samples will be coded and not identified by subject's name. 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 family member's name to the study number will be kept in a computer file that will need a password to enter. The investigators in this study will have access to the password or study files.

Although we will make every effort to keep your family member's information confidential, no system for protecting confidential information can be completely secure. There is still the possibility that unauthorized persons might discover your family member's participation in this study and information about him/her.

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 family member's records may be examined. The reviewers will protect your family member's privacy. The study records will not be used to put your family member at legal risk of harm. To further protect 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 your family member, 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 your family, 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).
The Certificate of Confidentiality does not prevent your family member or another member of your family from voluntarily releasing information or involvement in this research. If an insurer, employer, or other person obtains your family member's written consent to receive research information, then the researchers may not use the Certificate to with hold that information.

Exceptions:
A Certificate of Confidentiality does not prevent researchers from voluntarily disclosing information about your family member, without their consent in incidents such as child abuse, and intent to harm oneself 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 proxy for 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

LEGAL AUTHORIZED REPRESENTATIVE STATEMENT

This study has been explained to me. 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. I will receive a copy of this consent form.

Printed name of subject

Relationship of legal authorized representative

Printed name of legal authorized representative
Date

Signature of legal authorized representative

ADDENDUM:

APPROVED

MAR 0 1 2012

UW Human Subjects
Review Committee

If you agree to any of the following, we would contact you for permission to release your family member your family member's 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 your family member 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 for your family member? ☐ 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 for your family member that would require contact and a separate consent form, would you wish to be notified? ☐ YES ☐ NO

Copies to: Subjects
Investigator's File