



CEDARS-SINAI MEDICAL CENTER®

This form contains a description of a research project. Please discuss the content of this form with the investigator before you agree to participate.

CONSENT FORM FOR GENETIC RESEARCH

The Skeletal Dysplasia Registry - Genetics and Pathogenesis of the Skeletal Dysplasias

**(This form will also serve as a Permission Form for your child to participate in this research. In this case, “You” refers to “Your child” and “you”)*

A. Who is conducting this research?

You are being asked to participate in a research study called **GENETICS AND PATHOGENESIS OF THE SKELETAL DYSPLASIAS** which is being conducted by the principal investigator, David L. Rimoin, MD, PhD. Dr. Rimoin’s address is 8700 Beverly Blvd., Los Angeles, CA, 90048 and his phone number is (310) 423-4461.

The Co-investigators on this study are: Ralph Lachman, MD, PhD, John M. Graham, MD, ScD, Rena Falk, MD, Leslie Raffel, MD, Angela Sun, MD, Eyal Reinstein, MD, Grace Noh, MD, Rey Lozano, MD, Tara Funari, MS, Mitchel Pariani, MS, Catherine Quindipan, MS, Claudia Hernandez, MS, Alicia Lelis, MS, Nancy Kramer, MS. Their address is 8700 Beverly Blvd., Los Angeles, CA, 90048 and their phone number is (310) 423-9915. Co-investigators on this study are also: Dan Cohn, PhD, William Wilcox, MD, PhD, Deborah Krakow, MD. Their address is 8723 Gracie Allen Drive, Los Angeles, CA, 90048 and their phone number is (310) 423-6451. Additional Co-investigators are David Eyre, PhD at the University of Washington, Seattle, WA and Brendan Lee, MD, PhD, at the Baylor College of Medicine, Houston, TX.

This Registry (ISDR) is funded by a grant from the National Institutes of Health (NIH) and National Institute for Child Health and Development (NICHD).

B. Why am I invited to participate in this Registry?

You are being asked to take part in this Registry (ISDR) because you or your relative has a problem with bone growth, which results in conditions called skeletal dysplasias or short stature syndromes. This diagnosis has been established outside of this research study. You have expressed an interest in participating in research that seeks to better understand how such a problem presents and to contribute to knowledge that can be used to build upon the clinical opinion you have received.

Research studies include only people who choose to take part. Please take your time to make your decision and discuss it with your friends and family. Remember that your participation is completely voluntary.

C. What is the purpose of this research?

The purpose of this Registry is to collect information about skeletal dysplasias that will be used to better understand the clinical characteristics and genetic basis of these conditions and help doctors in their diagnosis and treatment. It is hoped that this study will help identify new types of skeletal dysplasias, describe their different characteristics, identify their causes and determine how they are inherited. In order to accomplish this, we may ask to review your medical records (including x-rays, measurements and photographs) and you may be asked to provide a blood/tissue sample when available. Research data will be kept in a Registry and used only for ongoing research on skeletal dysplasias, including the study of changes in genes that are associated with skeletal dysplasias.

An invitation to participate in genetic testing does not necessarily indicate that you or other family members suffer from a particular disorder or are genetically at risk for that disorder.

D. Are there potential conflicts of interest?

Cedars-Sinai investigators must satisfy federal requirements for identifying and managing potential conflicts of interest before a research study can be approved. The purpose of these requirements is to ensure that the design, conduct and reporting of the research will not be biased by any conflicting interests. If at any time you have specific questions about the financial arrangements or other potential conflicts for this study, please feel free to contact any of the individuals listed in Section S.

The investigator of this research does not have any financial interest in the sponsor or in the study; this means that the investigator will not be financially affected by the results of the study (positive or negative). However, Cedars-Sinai Medical

Center and the investigators will be reimbursed by the Sponsor for the work that they and the medical staff have to do as part of this study, and for the use of the site's facilities.

The person inviting you to participate in this research may also be your treating doctor. In such cases, the doctor has an interest in both your care and promoting the successful conduct of this research. Sometimes these two interests may cause conflict. You can choose not to participate in the research and still receive treatment from your doctor. If you wish, you may also request to speak to another doctor who is not a member of the research team about your options.

E. How many people will take part in this Registry?

Several hundred families with skeletal dysplasias are added to this Registry each year.

F. What will I be asked to do?

Most of the procedures are part of standard medical care to diagnose and treat your condition. “**Standard Procedures**” would be conducted even if you did not participate in this Registry. Standard procedures include physical measurements, photographs (to assist in describing features of genetic and skeletal dysplasias), x-rays, physical examinations, detailed family history (including a family tree), and possibly the collection of blood/tissue sample. The Registry also involves the collection, storage and distribution of, fetal tissues for research purposes. In some cases where fetal tissues are collected, we will request blood/tissue sample from the parents and possibly other family members.

“**Research Procedures**” are performed solely for research purposes; these procedures would *not* be conducted if you did not participate in this research. Research procedures include:

1. Blood Draw: Up to 12 teaspoons of blood, taking into consideration you or your child’s age, will be drawn from a vein with a small sterile needle. This is the standard method used to obtain blood for routine hospital tests.
2. Skin Biopsy: A small piece of skin (less than 1/8”) may be required for chromosome analysis, culture of skin cells, microscopic study of the skin, or other laboratory tests. The skin will be removed using a local anesthetic (numbing medication) and a special instrument called a “punch”. A separate consent will be required for the skin biopsy.

3. **Other Tissue Biopsies:** The purpose of these procedures is to establish a diagnosis by examining bone, cartilage and other tissues under the microscope or by studying cells grown in the laboratory. Biopsy of a rib, joint or hip to obtain bone or cartilage will only be done when you or your child is already undergoing surgery.

You are being asked for your authorization to allow the research team to review medical records and also to gather or create new health information about you, from any of the following sources:

- laboratory tests to help confirm the diagnosis of your genetic condition
- other laboratory that could rule out the possible causes for your condition
- diagnostic images (Xrays, MRIs, or CT scans) that confirm key findings in your condition
- photographs or videos that demonstrate key features of your clinical evaluation that can be used to compare with published images concerning your condition and its clinical findings
- doctor/clinic records
- hospital/medical records
- pathology reports
- mental health records, or developmental evaluations that document your functional capabilities
- previous genetic, neurological, endocrinological, or craniofacial evaluations
- other types of medical information such as the family history of other similarly affected individuals in your family

You may be asked to sign a release medical records form that will then be sent to the hospital or doctors who have cared for you. In addition, any medical records belonging to The Medical Genetics-Birth Defects Center and/or the International Skeletal Dysplasia Registry may be reviewed and used as part of this research study. Donation of tissue plus health information together helps researchers to discover relationships between health history and specific characteristics of skeletal dysplasias and various other genetic diseases and birth defects.

Paragraph M tells you who would be allowed to share your identifiable health information. That Paragraph also tells you who would be allowed to receive and use it, and why.

G. What will my sample(s) be used for?

DNA is the substance in our cells which contains information we inherited from our parents and other family members. Your DNA contains “genes” which predict things like physical characteristics (eye color, hair color, height, etc.) and may also be a factor in whether you develop or are at risk of developing certain illnesses or disorders. Your DNA will be tested to see if we can find the gene or genes that lead to skeletal dysplasias. Your blood/tissue sample will be used to isolate DNA for genetic analysis.

Part of your blood/tissue sample will also be used to grow a long term cell line. This immortalized cell line, called a lymphoblastoid cell line (or fibroblast cell line) will be stored in a Cell Bank and will be available for research, both now and in the future. This also allows us to perform many tests without having to ask you for additional blood/tissue samples.

H. How long will I be in this research?

In many genetic studies, testing of the DNA may go on for very long periods of time. This is true because we are continually finding new genes that may be involved in skeletal dysplasias. Therefore, while your direct participation in this study will be done once you have completed the procedures/visits described above, the DNA isolated from your blood/tissue sample may continue to be studied for many years. In addition, we may analyze your DNA sample as part of other research activities or share portions of it with other researchers working in other institutions.

Cells, blood, or other specimens removed from you during the course of this study may be valuable for scientific, research or teaching purposes or for the development of a new medical product. By agreeing to participate in this research, you authorize Cedars-Sinai and members of its staff to use your cells, blood or other specimens for these purposes.

Any tissues you have donated which are used in research may result in new tests, discoveries, or products. In some cases, these may be valuable and may be developed and owned by the investigators, Cedars-Sinai Medical Center, or the study sponsor. You no longer own your tissue after it has been donated and therefore you will not share in any revenues from these products, tests, or discoveries should they occur.

Cedars-Sinai will maintain these routine samples indefinitely or until the samples are exhausted. These samples are unavailable for clinical (diagnostic) purposes.

Therefore, any future diagnostic testing as a result of this or other research must be performed using a new sample. In the event this research project results in a product which could be sold commercially, Cedars-Sinai and its collaborators will assert the exclusive right to any revenue from the sale of such a product.

I. Will I receive information about my genetic sample(s)?

Research is a long and complicated process. Obtaining new general information from research may take many years. Even if there is new general information, there may not be information that is specific to you as an individual participant. However, you may request that the results of this research be disclosed to your treating doctor (who will then communicate with you). **You and your doctor should understand that the testing and evaluations completed as part of this research have not been validated (confirmed). The findings are for research purposes only, and should not be relied upon for clinical purposes.** Incidental findings not relevant to this research will not be disclosed.

At the end of this consent form, you will be given an opportunity to indicate whether you wish to have the results of this research disclosed to your treating doctor. The researchers listed on the first page of this consent document will disseminate the information to your treating doctor.

J. What are the risks of this research?

There are some possible risks associated with your participation in this study. They are as follows:

1. Blood Drawing – There may be discomfort, bruising and swelling at the site. There is a rare risk of infection, but precautions will be taken to avoid this.
2. Skin Biopsy – There will be temporary discomfort when the local anesthetic is injected and when its effect wears off. Some slight bleeding may occur after the biopsy. There is a rare risk of infection but precautions will be taken to avoid this. The biopsy will leave a small scar.
3. Other Tissue Biopsies – All risks will be explained by the appropriate specialist, such as the orthopedic surgeon and anesthesiologist, as part of a standard surgery consent. The risks include those involved with bleeding and infection. In addition, to obtain this biopsy, your surgery may take longer than it otherwise would. There may be temporary discomfort when the anesthetic wears off. The biopsy will not be done when the patient has complications, such as a bleeding disorder, low blood count, weakness, jaundice (yellowing of

the skin), inflammation or tumor, which might increase the risks of the procedure, outweighing the potential benefit of the study.

There is a risk for discrimination against individuals who are at-risk for a medical disorder or have a medical disorder/condition in their family. Discrimination may include barriers to obtaining health, life or long-term care insurance, or obtaining employment. Extensive efforts are made to protect all research subjects from prejudice, discrimination, or uses of this information that will adversely affect them. Specifically, clinical and research information specific to this study is maintained in a research file separate from hospital medical records and will not intentionally be placed in the official Cedars-Sinai medical record by research staff. Research data from which you may be identified will not be disclosed to third parties except with your permission or as may be required by law.

If your participation in a genetic study becomes known to persons or agencies outside of the research team, then it is possible that you and your family members could potentially find it difficult to obtain health, life, or disability insurance. It might also effect your ability to obtain certain jobs. While these things could occur, it is important for you to know that very few (if any) individuals who have participated in genetic studies such as this have had any difficulty with either insurance or employment.

An insurance company might consider participation in genetic research as part of a family study an indication that there is a family history of a genetic condition.

It is possible that this study will identify information about you that was previously unknown (such as disease status or risk). Such incidental findings, if any, will not be shared with anyone related to you unless the incidental findings regard an inherited risk for a disease known at the time of testing to be likely to cause premature death if untreated. Should such life-threatening results be uncovered through these genetic research studies and, if they are directly applicable to you or to your minor children, you will be notified via certified mail to contact the International Skeletal Dysplasia Registry and principal investigator David L. Rimoin, MD, PhD at Cedars-Sinai Medical Center (CSMC). Notification will be sent to the last address you provided to us. The CSMC staff will not release these specific research findings over the telephone or in the mail. The International Skeletal Dysplasia Registry and principal investigator David L. Rimoin, MD, PhD will arrange for you to meet with him and/or a genetic counselor or other appropriate health care provider either at CSMC or at another institution.

There may be other risks or discomforts, which are currently not foreseeable.

K. How can this research help society?

The study of your blood/tissue sample may, one day, result in new tests or treatments, or may help to prevent or cure skeletal dysplasias. Scientific knowledge often advances slowly, but it may greatly benefit future generations.

L. What other options are there?

You may choose to not participate in this study. **Evaluation of morphology (review of skeleton and tissue) can only be done as part of this research program. Genetic testing and additional commentary based on our review of skeleton and tissues have not yet been validated as diagnostic tests. If you do not wish to undergo this testing, our team can provide a clinical evaluation based solely on x-rays and evaluation of your clinical course.**

M. How will my information be protected?

What information about me will be used for the research study?

When this information is gathered from your past medical records and/or new medical information about you is created and used for the research study, it may or may not include information that identifies you, such as your name, Social Security Number, medical record number, address, and more. When the medical information includes any of these "identifiers," the medical record information is called "identifiable health information." If all of the identifiers have been removed from the medical information, it is called "de-identified health information." Using or giving other people "de-identified health information" does not affect your privacy. However, this particular research study requires the research team to create, use and disclose "identifiable health information."

Information about you to be recorded for the purposes of this study includes:

- Names;
- Street address (city, county, precinct, zip code, and their equivalent geocodes);
- Birth date;
- Admission date/discharge date;
- Date of death;
- Telephone numbers;
- Fax numbers;
- Electronic mail addresses;
- Medical record numbers;
- Full face photographs and any other comparable image; and
- Any other unique identifying number, characteristic, or code (except one assigned by the research study as long as it is not derived from or related to information about the individual and is not capable of being translated and used

to identify the individual, and only specific researchers have access to the unique code).

You have the right to allow, or to refuse to allow, the research team to create and use and give other people your identifiable health information. At the end of this consent form is a paragraph that asks for your signature, to authorize the research team to create and use and give other people your identifiable health information for purposes of this research study.

The research team will share information among themselves as part of the research study process. In addition, various institutional committees and governmental agencies that oversee research may request or require access to your identifiable health information. These include one or more Institutional Review Boards of Cedars-Sinai Medical Center, in an oversight capacity, the Cedars-Sinai Office for Research Compliance, the Food and Drug Administration, the Department of Health and Human Services, and other agencies that must receive reports about certain diseases. Additionally, the following parties may receive information about you:

- Other non-Cedars Sinai Medical Center researchers who are participating in this study
- These researchers are on file with the IRB in a separate amendment to our protocol. In addition, researchers are listed in a computerized resource used by medical geneticists throughout the world to identify researchers studying various rare genetic conditions. This resource is entitled GeneTests <http://www.genetests.org>.
- Other non-Cedars Sinai Medical Center researchers for future and related research purposes
- Other Cedars-Sinai Medical Center researchers for future and related research purposes
- Medical and other health care professional students who are assisting with research study tasks
- The study Sponsor (in other words the organization that is paying for the costs of the study) for matters related to study oversight, data analysis and use of research results in product development
- Data coordinating center for the study
- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, in conjunction with the Sponsor and/or the FDA.

You should be aware that when you authorize the disclosure of your health information by signing at the end of this form, the person or organization might not be required by federal privacy law to keep it confidential. However, California law explicitly prohibits the recipient of your health information from re-disclosing that information without another signed authorization form from you, unless the recipient is required or allowed by law to make a particular disclosure.

Why would my health information be shared as part of the study?

Research involves the gathering and analysis of information. With medical research, the research team is gathering and analyzing health information about individuals in the hope that they will be able to answer specific questions about a bodily function, disease, or wellness. Those team members who act in a supportive role to the research study use health information when necessary for various administrative tasks, such as tracking data, making reports that are required by government oversight agencies or the study sponsor, and assisting the researchers with other data-related tasks. The Institutional Review Boards act as watchdog groups for the protection of the rights and interests of research subjects. It may be that the study results, including your identifiable health information, will be used by the Sponsor or others to develop or further refine medications, medical devices or medical procedures.

It is important for you to know that if your health information is used for teaching purposes outside the study, or to prepare a medical journal report about the research study, your identifiable health information will not be made public; your identity will be kept confidential in those circumstances.

Each time your identifiable health information is disclosed to any of the individuals listed above, precautions will be taken to minimize the possibility that the information shared could directly identify you. When possible, all identifying information will be coded. This means that the researchers will assign a unique code to represent your identifiable data so that people who see the coded data will not be able to identify you. However, coding is not possible in some cases. For example, a Sponsor may require your Social Security Number (SSN) to process payment for participation. In this situation, it would not be possible to withhold this identifying information. You may choose not to participate in this study and, therefore, not authorize disclosure of your private information to the entities listed above.

You are being asked to authorize the research team to use and disclose your identifiable health information until January 1, 2075.

N. Can I retrieve my sample(s)?

You may change your mind and refuse to participate in this research at any time. If you withdraw from this research your research records and sample(s) will be removed from the Registry. Withdrawal will not have any effect on the medical care you may be receiving for your condition at Cedars-Sinai Medical Center or any other future care or services.

O. What are the costs?

You and your insurance company will not be charged for your participation in this research. However all exams, tests and procedures that are part of standard medical care for your condition will be billed to you or your insurance company.

P. Will I be paid?

You will not be paid for your participation in this Registry.

Q. What happens if I need emergency care?

In the event of injury or illness resulting from this research, you should immediately contact one of the personnel listed in Section S “Whom do I call if I have questions or problems?”

R. What are my rights as a research participant?

Taking part in this study is voluntary. You may choose not to take part or may leave the study at any time. Your decision not to participate or to withdraw from the study means that you will not or will no longer undergo any research-related procedures. You will, however, still be able to receive treatment and services at Cedars-Sinai Medical Center that are not related to this research. If you leave the study:

- We will no longer be able to allow you to participate in the research study; and
- We will stop collecting any additional identifiable health information about you. However, we are allowed by law to continue to use the health information we already have about you, as necessary to maintain the integrity of the research study and make reports that oversight agencies require of us.
- You also have the right to revoke or withdraw your authorization for us to use your identifiable health information. If you wish to revoke or withdraw your authorization, you must do so in writing, and provide that written revocation to the investigator David L. Rimoin, MD, whose mailing address is: 8700 Beverly Blvd., Los Angeles, CA, 90048.
- In addition, if we have provided your identifiable health information to the National Institutes of Health (NIH) and National Institute for Child Health and Development (NICHD) or the Data Coordinating Center, that information cannot be withdrawn.

You normally have the right to access (see or copy) your identifiable health information, including health information that is collected for research. However, in order to protect the integrity of the research study, your right to access your

research records will be postponed while the study is in progress. After the study is over (meaning the end of the whole study, not just your own participation), you will again have the right to access your identifiable health information upon your request, in accordance with the policies and procedures of Cedars-Sinai Medical Center.

During your participation in this study, we will tell you about any new information that may affect your health, welfare, or willingness to stay in this study.

S. Whom do I call if I have questions or problems?

For questions about this Registry or a research-related injury, contact Dr. David L. Rimoin at (310) 423-4461.

For questions about your rights as a research participant, contact the Cedars-Sinai Medical Center Institutional Review Board (CSMC-IRB) office at (310) 423-3783. The IRB is a group of people who review the research to protect your rights and welfare.

T. Consent and Authorization Provisions

Your signature below means that: (1) you have carefully read and understood the information presented in this informed consent form and in the “Experimental Subject’s Bill of Rights”; (2) the information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction; (3) you have received all of the information you desire; (4) you consent to your participation in the research study, and (5) you authorize the use and disclosure of your identifiable health information as described in this form. If you have any additional questions during the course of your involvement in the research, you should contact the investigator(s), the IRB Chair(s) and/or the IRB Office at any time.

Your signature below reflects that, after considering both the potential risks, anticipated benefits and alternatives (and their relative risks and benefits) of participation, you voluntarily agree to participate in this research and authorize the research team to create, obtain, use or disclose your identifiable health information as described in Section M of this document, and in connection with this research study. By consenting to participate in the research, you are not giving up any of your legal rights, except that you have agreed that you will not be granted access to review the health information we generate about you in the course of the research study, until the end of the research study. You will be

given a copy of this signed and dated consent form, in addition to a copy of the Experimental Subject's Bill of Rights.

U. Permission to share my sample(s) with other researchers?

If you agree, your sample(s) may be shared with other researchers performing research on your condition. Please note your preferences below:

I give permission for the research team to share my sample(s) with the individuals noted below:

YES NO Researchers at CSMC studying skeletal dysplasias

YES NO Researchers at other institutions studying skeletal dysplasias

V. Willingness to have results of testing performed as part of research disclosed

YES NO I wish to have information about the testing conducted on my sample(s) disclosed to my treating doctor.

YES NO Should information that may be important to my health become available in the future, I would like to be contacted and given an opportunity to have this information disclosed to my treating doctor. I understand that it is my responsibility to update any changes to my address information.

SIGNATURE BY THE ADULT SUBJECT:

Name of Subject (Print) Signature of Subject Date of Signature

SIGNATURE BY THE ADOLESCENT SUBJECT
My signature below reflects my agreement to participate in this research.

Name of Subject (Print) Signature of Subject Date of Signature

SIGNATURE BY THE SUBJECT'S
PARENT(S)/GUARDIAN(S)/PARENTAL PERMISSION SIGNATURE
By providing my signature below, I consent and give permission for the
participation of my child, _____, in the research study
Name of child
described in this document.

Parent/Guardian Name (Print) Parent/Guardian Signature Date of Signature

SIGNATURE BY THE INVESTIGATOR:
I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the subject. I further attest that all questions asked by the subject were answered to the best of my knowledge. The subject has been provided with the Experimental Subject's Bill of Rights.

Signature of the Investigator Who Obtained Consent Date of Signature

SIGNATURE BY THE WITNESS/TRANSLATOR:

Signature of Witness Date of Signature

Distribution instruction for investigators:

The signed consent form and "Experimental Subject's Bill of Rights" should be distributed to:

- 1) Medical Chart
- 2) Patient/Subject
- 3) Pharmacy (if a drug study)
- 4) Principal Investigator's research records (Original)

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.
2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.
3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.
4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.
5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.
6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.
7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.
8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.
9. Be given a copy of any signed and dated written consent form used in relation to the experiment.
10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

Signature of Experimental Subject

Date