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21 May, 2010

Dear Colleagues,

Thank you for your interest in the mutational screening of nephronophthisis (NPH) patients; patients with nephrotic syndrome (NS), branchio-oto-renal syndrome (BOR); or patients that have a congenital or developmental abnormality of the urinary tract (UTM).

We are performing deletional analysis in the *NPHP1* gene (nephrocystin) and may perform mutational analysis in other genes known to cause similar genetic kidney diseases, if the clinical situation strongly suggests it. We are also performing mutational analysis in the *NPHS2*-gene (podocin) and *WT-1*-gene. Our aim is to find out whether there is any correlation between the occurrence of mutations in the *NPHS2*-gene and the clinical outcome of these patients (e.g. response to steroids and cytotoxic drugs, relapse after transplantation) (Karle et al. *J Am Soc Nephrol* 13:388, 2002). This genetic analysis is investigational and is performed in the setting of a research laboratory and there is no universal standard for the performance of these studies. The investigators endeavor to attain the highest standards in their analysis, but this analysis should not be considered a diagnostic test, rather an investigational genetic test not intended to replace other clinical or laboratory evaluations or treatments that would otherwise be considered the standard of care. Samples are kept indefinitely and may be used to identify new genes which cause NPH, NS, or UTM or examined for mutations in new genes found to cause any of these genetic kidney diseases, as this information becomes available.

As these genetic tests are presently considered investigational, and are part of a research protocol, there are no costs to the patient(s), or family members of the patient(s) who agree to participate in the study, for the blood draw or buccal swab shipping or for the processing of samples. Office visits to physicians or genetic counselors are not paid for by this study, nor are any other laboratory tests. Results of genetic analysis are generally available 4-6 months following the receipt of a sample. At that time we will report the presence or absence of a mutation in a gene. If no deletion is present these results will not provide a definitive diagnosis for the cause of the individual's disease. We will continue to perform mutational analysis on these samples, but results defining the genetic mutation responsible for a particular patient's disease are likely to take a much longer time (e.g. months to years), and in some cases a genetic cause for disease may never be found. All results are transmitted directly to the corresponding physician and not to individual participants. Participants will, therefore, need to depend upon their local physician to communicate and explain the results of the genetic tests. The investigators would be happy to discuss the results of the genetic testing with any local physician who wishes to do so. **No results will be reported for individual participants who do not have evidence of genetic kidney disease at the time of enrollment.** If an individual develops evidence of kidney disease, after enrolling in the study, a local physician may contact the investigators to release results of any genetic testing. Local physicians or their representatives are expected to review the consent document with prospective participants. By signing the consent document, before the prospective participant signs the consent document, the local physician will indicate that they feel the participant understands the nature of the study. The local physician and the

participant should keep a signed copy of the consent, and a signed copy should be sent to the investigators (see below).

Please ship the following items to the investigators:

1. Signed consent document
2. Health questionnaire
3. Blood sample: 3-10 ml EDTA or Na-Heparin blood for each participant, or two buccal swabs

Blood samples or buccal swabs without a signed consent document cannot be processed or analyzed.

If you like, you may use our courier account to ship the items. For information on the account number please contact Susan Allen at sjallen@umich.edu.

When you ship the items, please e-mail us the tracking number of the shipment immediately, so we can track the package and ensure safe delivery. Thank you again for your participation. Please do not hesitate to contact us with any questions or concerns.

Best Regards,



Friedhelm Hildebrandt, M.D.
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Cure and Prevention of Birth Defects
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BLOOD SAMPLE COLLECTION FOR MUTATIONAL ANALYSIS

Instructions for blood collection and shipping:

1. Review and sign the consent document with each patient from whom blood is drawn.
2. A single 3-10 ml EDTA or Na-Heparin tube of blood is required from each individual. Use sterile technique to obtain blood sample. Invert tube several times after drawing to prevent coagulation. **Always store blood at room temperature -- do not freeze.**
3. Use FedEx for the shipment of blood.
Please indicate shipping contents as: Blood or DNA, non-hazardous, non-toxic, non-infectious.
Value \$1.00
4. When returning blood sample please include:
 - a. Blood sample
 - b. Signed consent documents
 - c. Health questionnaire
 - d. Any available renal imaging or biopsy reports
5. Please ship the above items to the following shipping address:

Dr. F. Hildebrandt
University of Michigan, Department of Pediatrics
8220 MSRB 3, 1150 W. Medical Center Drive
Ann Arbor, Michigan 48109-5646, USA
6. When you ship the items, please e-mail sjallen@umich.edu with the tracking number of the shipment immediately, so we can track the package and ensure safe delivery.
7. Results for deletion analysis are generally available in 4-6 months and a report will be sent to your physician when it is available.

Thank you for your interest. Please do not hesitate to contact us with any questions or concerns.

BUCCAL SWAB SAMPLE COLLECTION FOR MUTATIONAL ANALYSIS

Instructions for buccal swab collection and shipping:

In order to collect good DNA it is best to collect the cells first thing in the morning before eating, drinking, and brushing teeth. It is especially important that no tea, coffee, or soda pop is consumed before the sample is taken.

Instructions for collection:

1. Review and sign the consent document with each patient from whom blood is drawn.
2. Two buccal swabs are required from each individual. Gently run the brush firmly backwards and forwards along the inside cheek, and in between the cheek and gum. This should be done for 30 seconds. **Please time it.** It is longer than you think! **There is no need for force, do not brush so hard that the patient bleeds.**
3. When you have finished, place the brush back in the package (**the used end goes in first**).
4. When returning buccal swab samples please include:
 - a. 2 buccal swabs
 - b. Signed consent documents
 - c. Health questionnaire
 - d. Any available renal imaging or biopsy reports
5. Please ship the above items to the following shipping address:

Dr. F. Hildebrandt
University of Michigan, Department of Pediatrics
8220 MSRB 3, 1150 W. Medical Center Drive
Ann Arbor, Michigan 48109-5646, USA

6. When you ship the items, please e-mail sjallen@umich.edu with the tracking number of the shipment immediately, so we can track the package and ensure safe delivery.
7. Results for deletion analysis are generally available in 4-6 months and a report will be sent to your physician when it is available.

Thank you for your interest. Please do not hesitate to contact us with any questions or concerns.

Juvenile Nephronophthisis (Questionnaire)

Prof. F. Hildebrandt, M.D.

Thank you very much for taking the time to fill out this form.

General Patient Information

Last name: _____ First name: _____

DOB: ___(mm)/___(dd)/___(yy)

m f

height: ___ cm

weight before illness: ___ kg

Consanguineous parents

yes no

Relatives with renal diseases

mother

sister

father

others: _____

brother

I. Initial Clinical Examination: ___(mm)/___(dd)/___(yy)

1. Symptoms (initial)

acute event

oedema

during regular examination

high blood pressure

polyuria

need of treatment

polydypsia

others:

2. Laboratory Findings (initial)

Blood studies:

hemoglobin ___ g/l

HCO₃ ___ mEq/l

hematocrit ___ %

GFR ___ ml/min

Na ___ mmol/l

creatinine ___ mg/dl

K ___ mmol/l

uric acid ___ mg/dl

Ca ___ mg

serum protein ___ g/l

P ___ mg

albumin ___ g/l

SGOT ___ IU

immunologic abnormalities

SGPT ___ IU

(immunoglobulins/complement

pH ___

components) following: _____

Urine analysis:

urine concentration
___ mosm/kg H₂O

aminoaciduria

hematuria

proteinuria ___ g/day

or ___ g/g crea

selective

nonselective

3. Imaging Techniques

bone age _____
ultrasonography

medullary cysts

increased echogenity

4. Renal Biopsy

1st biopsy

2nd biopsy

(mm/yy)

(mm/yy)

Nephronophthisis (NPH)

others: _____

Patient Name: _____

II. Treatment

Dialysis / renal transplantation

date of end stage renal failure: ___/___/___
1st transplantation: ___/___/___
2nd transplantation: ___/___/___
(mm/yy)

- unsuccessful transplantation because of:
 - recurrence
 - graft loss because of:
 - recurrence
 - rejection

III. Extrarenal Association

The patient suffers / suffered from one of the following diseases:

- | | | |
|---|--|--|
| <input type="checkbox"/> deafness | <input type="checkbox"/> short stature | <input type="checkbox"/> urinary/genital tract anomalies |
| <input type="checkbox"/> blindness/retinitis pigmentosa | <input type="checkbox"/> newborn's tachypnea | <input type="checkbox"/> heart anomalies |
| <input type="checkbox"/> microcephaly | <input type="checkbox"/> hexadactylia | <input type="checkbox"/> allergy |
| <input type="checkbox"/> mental retardation | <input type="checkbox"/> vermisaplasia | <input type="checkbox"/> others: _____ |

IV. Possible Gene Involvement

- _____ Infantile NPHP (NPHP2/inversin)
- _____ Leber amaurosis (NPHP5)
- _____ Liver fibrosis (NPHP11/MKS3)

V. Remarks

Thank you very much for your assistance. Please provide us with the following information in order to facilitate further correspondence. Results of genetic analyses will be sent to the physician at the address below:

Name: _____	Phone: _____
Address: _____	Fax: _____
Address: _____	eMail: _____

Idiopathic Nephrotic Syndrome Questionnaire, version January 25, 2008

Prof. F. Hildebrandt, M.D.

Thank you very much for taking the time to fill out this form.

General Patient Information

Last name: _____ First name: _____ DOB: ____ / ____ / ____
MM DD YYYY

M F Height: ____ cm Weight before illness: ____ kg

Consanguineous parents Yes No
 Relatives with nephrotic syndrome Mother Brother
 Father Sister
 Others: _____

Ethnicity: African African American American Indian Arabic Asian Caucasian Central Slavic
 Chinese European Finnish Hispanic Indian Subcontinent Japanese Pacific Islander
 Turkish Other: _____

I. Initial Clinical Examination: ____MM/____DD/____YYYY

1. Symptoms (initial)

- Acute event Edema
 During regular examination High blood pressure (before steroid therapy)
 need of treatment
 Other: _____

2. Laboratory Findings (initial)

Blood studies: Creatine: ____mg/dl Urinalysis: Proteinuria ____g/day or
 GFR: ____ml/min ____g/g crea
 Serum protein: ____g/l selective non-selective
 Albumin: ____g/l
 Immunologic abnormalities Hematuria
 (immunoglobulins / complement Yes No
 components) following:

3. Renal Biopsy

	1 st Biopsy	2 nd Biopsy	Institution
	____/____	____/____	
	MM / YYYY	MM / YYYY	
MCNS (minimal change nephrotic syndrome)	<input type="checkbox"/>	<input type="checkbox"/>	
FSGS (focal segmental glomerulosclerosis)	<input type="checkbox"/>	<input type="checkbox"/>	
Other: _____	<input type="checkbox"/>	<input type="checkbox"/>	

Patient Name: _____

II. Treatment

1. Corticosteroids Yes No

- Steroid sensitive
 - Complete response
 - Relapse Yes No
 - Partial response
 - Relapse Yes No
- Steroid resistant

2. Cytotoxic drugs Yes No Cyclosporine Yes No

Name of drug: _____ Clinical response: _____
 Clinical response: _____

3. Dialysis / Renal Transplantation MM / YYYY

Date of end stage renal failure: ____ / ____
 1st transplantation: ____ / ____
 2nd transplantation: ____ / ____

- Unsuccessful transplantation because of:
 - Recurrence
 - Graft loss because of:
 - Recurrence
 - Rejection
- Date of transplant failure: ____MM/____YYYY

III. Extrarenal Association

The patient suffers / suffered from one of the following diseases:

- Deafness
- Blindness
- Microcephaly
- Mental retardation
- Short stature
- Facial dysmorpby
- Hexadactylia
- Spondyloepiphyseal dysplasia (Schminke-disease)
- Urinary/genital tract anomalies
- Heart anomalies
- Allergies
- Other: _____

IV. Remarks

*Thank you very much for your assistance.
 Please provide us with the following information in order to facilitate further correspondence. Results of genetic analyses will be sent to the physician at the address below:*

Name: _____ Phone: _____
 Address: _____ Fax: _____
 Address: _____ eMail: _____

Branchio-oto-Renal Syndrome and Congenital Urinary Tract Malformations Questionnaire, version January 4, 2009

Prof. F. Hildebrandt, M.D.

Thank you very much for taking the time to fill out this form.

This form is to be completed by the participant's physician.

General Patient Information _____MM/____DD/____YYYY

Last name: _____ First name: _____ DOB: _____ / _____ / _____
MM DD YYYY

M F Height: _____ cm Weight: _____ kg

Consanguineous parents Yes No

Relatives with urinary tract malformations Mother Brother

Father Sister

Others: _____

Ethnicity: African African American American Indian Arabic Asian Caucasian Central Slavic
 Chinese European Finnish Hispanic Indian Subcontinent Japanese Pacific Islander
 Turkish Other: _____

I. Initial Clinical Examination: _____MM/____DD/____YYYY

1. Symptoms (initial)

- Acute event Fever
 During regular examination Urinary tract infection
 Diminished/increased urinary output
 Pyelonephritis
 Hypertension
 Other: _____

2. Laboratory Findings (initial)

Blood studies: Creatine: _____mg/dl GFR: _____ml/min/1.73m²
 Serum protein: _____g/dl Albumin: _____g/dl
 CRP: _____mg/l

Urinalysis: Proteinuria _____g/day or g/g crea
 Hematuria
 Bacteriuria: _____CFU/ml

3. Imaging Techniques (initial)

- Ultrasound Voiding cystourethrography Renal scintigraphy
 Intravenous pyelogram Cystoscopy Other: _____

4. Diagnosis (initial)

- Renal agenesis right left Prevesical ureter stenosis right left
 Hydronephrosis right left Vesico-ureteral reflux right left
 Ureteral stenosis right left Bladder exstrophy
 Ureteropelvic junction obstruction right left Other: _____

Patient Name: _____

II. Treatment

- Dialysis
- Tenckhoff catheter
- Pyelocystostomy
- Ureterocystostomy
- Anti-reflux operation
- Anderson-Hynes pyeloplasty
- Other: _____

III. Extrarenal Association

The patient suffers / suffered from one of the following diseases:

- Face dysmorphism
- Microcephaly
- Mental retardation
- Deafness
- Blindness
- Growth retardation
- Skeletal deformity
- Polydactyly/syndactyly
- Pulmonary hypoplasia
- Heart anomalies
- Allergy
- Other: _____

IV. Remarks

Thank you very much for your assistance. Please provide us with the following information in order to facilitate further correspondence. Results of genetic analyses will be sent to the physician at the address below:

Name: _____ Phone: _____
Address: _____ Fax: _____
Address: _____ eMail: _____

University of Michigan

Consent To Be Part Of A Research Study

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.' *NOTE: Items with an "*" asterisk are for the child's understanding and assent.

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.*

(This document was prepared in April, 2010.)

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title:

Genetics of Kidney Disease

1.2 Company or agency sponsoring the study:

National Institutes of Health
Doris Duke Charitable Foundation
Howard Hughes Medical Institute

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

Friedhelm Hildebrandt, MD	Principal Investigator	U of M Pediatric Nephrology
Edgar Otto, PhD	Co-Investigator	U of M Pediatric Nephrology
Rannar Airik, PhD	Co-Investigator	U of M Pediatric Nephrology
Susan Allen, MS	Co-Investigator	U of M Pediatric Nephrology
Shazia Ashraf, MS	Co-Investigator	U of M Pediatric Nephrology
Massimo Attanasio, MD	Co-Investigator	U of M Pediatric Nephrology
Hassan Chaib, PhD	Co-Investigator	U of M Pediatric Nephrology
Moumita Chaki, PhD	Co-Investigator	U of M Pediatric Nephrology
Gil Chernin, MD	Co-Investigator	U of M Pediatric Nephrology
Amiya Ghosh, PhD	Co-Investigator	U of M Pediatric Nephrology
Saskia Heeringa, MD	Co-Investigator	U of M Pediatric Nephrology
Julia Hoefele, MD	Co-Investigator	Ludwig-Maximilians University
Toby Hurd, PhD	Co-Investigator	U of M Pediatric Nephrology
Jeffrey Innis, MD	Co-Investigator	U of M Pediatric Genetics
Sabine Janssen, BS	Co-Investigator	U of M Pediatric Nephrology
Sivakumar Natarajan, MS	Bioinformatician	U of M Pediatric Nephrology
Bugsu Ovunc, MD	Co-Investigator	U of M Pediatric Nephrology
Pawaree Saisawat, MD	Co-Investigator	U of M Pediatric Nephrology
Dominik Schoeb, BS	Co-Investigator	U of M Pediatric Nephrology
Virginia Vega-Warner, PhD	Co-Investigator	U of M Pediatric Nephrology
Weibin Zhou, PhD	Co-Investigator	U of M Pediatric Nephrology

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of this study is to find genes that cause nephronophthisis, nephrotic syndrome, BOR, and congenital or developmental abnormality of the urinary tract. *This means that the kidneys are not doing what they should. We are trying to find out why.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. 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. You do not have to participate if you do not want to.

*You do not have to be in the study if you don't want to. Your parent (or guardian) can make sure that this study will be okay for you. Both you and your parent have to agree to you being in the study, but it is still up to you if you *want* to do it.

You will not be penalized and will not lose any non-research benefits to which you otherwise may be entitled if you refuse to participate in the study or if you leave the study early. No aspect of your treatment (except the experimental procedures described below), or non-research benefits depends on your enrollment or continued participation in this or any other study. The results of the genetic testing in this study should not be considered a diagnostic test, as it is performed by a research laboratory and is not performed as a CLIA standardized test. Therefore, the results of this study should not replace any care or treatment that would otherwise be considered the standard of care. No results will be reported for participants without a diagnosis of nephronophthisis. Results will only be reported to the local physician, and only if approved by the participant. Results cannot be directly reported to participants.

3.1 Who can take part in this study?

Individuals who may have nephronophthisis, nephrotic syndrome, or any individual that has been diagnosed with Branchio-oto-renal (BOR) syndrome, or a congenital or developmental abnormality of the urinary tract, as determined by a kidney specialist; and any first degree family members (i.e. siblings, parents or children) of these individuals are eligible to participate in this study. In cases in which the parents of the affected individual are consanguineous (ie. they share a blood relationship) more distantly related family members may be considered eligible for the study. *If your doctor has told you that your kidneys have nephronophthisis, NS, BOR, or UTM, you can be in the study.

*Note: It is very **important** for you to give the researchers **accurate** and **complete** information about your medical history and condition.*

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

Over 1,000 families have enrolled in the study over the last ten years. Based upon this experience we would expect to enroll about 1 new family a week.

4. INFORMATION ABOUT STUDY PROCEDURES

4.1 What exactly will be done to me in this study? What kinds of research procedures will I receive if I agree to take part in this study?

In order to enroll in this study you must review this document with your doctor, give a blood sample or buccal swab sample, and return a signed copy of this document and a signed copy of a health questionnaire with the blood sample or buccal swab sample to the investigators. The health questionnaire will contain your age, current laboratory values and imaging studies or biopsy results that you may have had done already as a part of your health care to this point. If you are known to have kidney disease, as determined by your doctor, a report of the results of genetic testing for nephronophthisis can be sent to your doctor if you wish. Results cannot be reported directly to participants, but will be returned to each participant's primary physician. No results will be reported for individuals who do not have a diagnosis of kidney disease. All samples received will be saved indefinitely, unless the participant withdraws from the study. This type of research can take years. If you develop kidney disease after enrolling in the study your doctor is encouraged to inform the investigators of this change and you would be eligible to receive results of genetic testing if you desired them.

A portion of the white blood cells obtained from the initial blood draw may be isolated from the blood sample and infected with a virus so they can be grown indefinitely in culture as a source for further DNA or RNA isolations. The DNA or RNA obtained from these isolations will only be used for mutational analysis.

*If you want to be in the study a doctor or nurse will take some blood from your arm (it might hurt a little), or use a little brush that you put in your mouth for about 30 seconds (it will not hurt). The blood, or spit on the brush, is what we will use to do our tests to find out why the kidneys leak. That is all you have to do to help us. There is currently no treatment for nephronophthisis, and this study does not offer any treatments. The cost of office visits to local physicians or genetic counsellors are not covered by this study, nor is any testing for the DNA sample requested by this study.

If the researchers develop or learn of significant new findings during the study that may affect your willingness to continue to participate, they will contact your physician. If new information is provided to you after you join the study, you may be asked to sign a new consent document to continue participating. Results can be made available to the local physician of individuals who have the disease prior to testing. Individuals who have no evidence of kidney disease will not be eligible to receive results. If an individual, who was healthy at the time of enrollment, and blood collection, subsequently develops kidney disease, they are encouraged to contact the investigators. At that time results from any genetic testing which has been done can be made available to their physician.

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

*To participate in this study a single visit to your doctor is required to complete this consent form and to draw blood. Enrollment in the study will consist of the review of the consent document with your doctor and a routine venous blood draw or buccal swab sample. The researchers will then analyze the blood sample or buccal swab for mutations in the known genetic causes of nephronophthisis, NS or UTM. These results are generally available in 4-6 months. At that time we will report the presence or absence of a mutation in a gene. If no deletion is present, these results will not provide a definitive diagnosis for the cause of this individual's disease. We will continue to perform mutational analysis on these samples, but results defining the genetic mutation responsible for your particular disease is likely to take a much longer time (e.g. months to years), and in some cases a genetic cause for the disease may never be found. Results will be communicated to your doctor at that time, if you request it and you are eligible to receive results. The DNA taken from the blood sample or buccal swab will be stored indefinitely for the evaluation of the genetic causes of genetic kidney diseases exclusively as described in this document.

4.3 When will my participation in the study be over?

If you withdraw from the study any existing samples will be destroyed. Existing data will not be destroyed, but will be anonymized by removing all personally identifying information such that the data could never be traced back to the participant. *We will keep your samples until we are done studying them.

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 for people participating in the study include:

- The risks for routine venous blood draw which include discomfort, bruising, faintness or lightheadedness, and very rarely infection.
- The risk for identifying a genetic cause of disease can include difficulty in obtaining insurance or increased cost of insurance. However, since insurance companies do not cover the costs for genetic testing, blood draws for genetic testing or shipping and handling of the blood for genetic testing in this study, they are not entitled to the results of this study. The investigators will not disclose any findings of this study to anyone other than the participant's private physician. If desired, the researchers will not report any results to the participant's private physician.
- The risk for learning of a genetic cause of disease may cause the participant emotional distress which could result in depression or anxiety. We hope to minimize distress caused by this information as we report only for individuals who are already aware that they have kidney disease, and therefore this information will only provide a definitive diagnosis for people who are already known to have kidney disease. Costs for genetic counseling or office visits related to the discussion or review of genetic testing performed in this study may generate costs that are not reimbursed by this study.

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

- The blood draw will be performed in a controlled environment using antiseptic technique. Your insurability will not be jeopardized by the investigators, as no information from this study is shared with anyone other than the participant's private physician, if so desired.
- Please consider the emotional impact that receiving the results of this study will have for you. Your participation in this study does not require that the results of the study be reported to your physician. If you do not understand potential ramifications of learning the results of this study you are encouraged to discuss these with your local physician, the investigators, or obtain genetic counseling prior to signing this consent and enrolling in the study. This study does not cover the costs of genetic counseling or physician visits to review or discuss results of this study before or after results become available.

5.2 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. If necessary, first aid will be provided.

*Please note: It is **important** that you tell both the **researchers** and your **regular doctor** about any injuries or side effects you experience while participating in the study.*

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

Yes. *Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies.* You should not take part in more than one study without approval from the researchers involved in each study.

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

You may not receive any personal benefits from being in this study.

We cannot promise that you personally will receive any benefits from being in this study. However, your participation in this study will help us to move the general understanding of this disease forward with the hope that effective treatments will be developed in the future.

5.5 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 of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

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

If you do not want to participate in this study, there will be no penalty. In this case, we cannot offer you genetic testing for nephronophthisis, or any other genetic kidney disease described above. Ask your doctor about other options you may have. We cannot offer genetic testing to those who do not enroll in the study.

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 want to withdraw, you may do so by notifying the study representative listed in the "Contact Information" section below at the e-mail mutation@renalgenes.org.

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.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Will taking part in this study cost me anything? Will I or my insurance company be billed for any costs of the study? If so, which costs? What happens if my insurance does not cover these costs?

There are no costs or billing for this 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?

No person or organization has a financial interest in the outcome of this study.

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

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

University of Michigan policies and certain federal and state laws require that personal health information be kept confidential, but allow disclosures in specific situations. You are not required to sign this document, but if you do not, you will not be able to participate in this study.

9.1 How will the researchers protect my privacy?

Upon receipt of blood samples or buccal swab samples for DNA analysis, signed consent and baseline health information, all information will be given a unique code without personal identifiers and is secured in locked cabinets available only to the researchers. DNA samples are labeled with the unique code only, without personal identifiers. When results are shared with other scientists no names or other information which could be used to identify the participant will be shared. No results will be disclosed except at the request of the participant.

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
- Submission of data to the gdGAP data repository as outlined in the NIH GWAS Policy

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.
- Researchers may share anonymized large-scale sequencing data and phenotype data with the dbGAP database (<http://grants.nih.gov/grants/gwas/>).

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. Your health information may be shared with another investigator in collaboration with the investigators of this study. However, if this were to occur no information would be shared which could identify you personally, nor will personally identifying information be used in publications or presentations.

If you agree to participate in this study and sign your name on the last page, you will be giving the University of Michigan, including its Health System (hospitals, health centers, clinics and health care providers), or your local health care provider and other providers involved in your care, permission to disclose your medical information (doctors' notes, lab results, x-rays, hospital charts, biopsy tissues obtained for non-research purposes, etc.) to the researchers. Personally identifying information will be kept confidential by the researchers and will not be shared, published, or made available to others in any way.

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?

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

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

For more information about the study, or the study procedures or treatments, or to withdraw from the study, contact:

Principal Investigator: Friedhelm Hildebrandt, MD
 Professor of Pediatrics and of Human Genetics
 Investigator, Howard Hughes Medical Institute
 Frederick G.L. Huetwell Professor for the Cure and Prevention of Birth Defects
 Doris Duke Distinguished Clinical Scientist
 University of Michigan Medical Center, Department of Pediatrics
 1150 W. Medical Center Drive, Room 8220C, MSRB 3
 Ann Arbor, Michigan, 48109-5646 USA
 e-mail: mutation@renalgenes.org

Study Coordinator:
 University of Michigan Medical Center, Department of Pediatrics
 1150 W. Medical Center Drive, Room 8220, MSRB 3
 Ann Arbor, MI 48109-5646
 e-mail: mutation@renalgenes.org

To report any illness or injury you experience during the study, contact the researchers listed above *and your regular doctor*.

For more information about your rights and responsibilities as a research subject, or to express a concern about the study, contact:

University of Michigan Medical School Institutional Review Board (IRBMED)
 2800 Plymouth Rd, Rm 2086, Bldg 200
 Ann Arbor, MI 48109-2800
 Telephone: 734-763-4768
 Fax: 734-615-1622
 e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy, contact the University of Michigan Health System Privacy Officer at 1-888-296-2481.

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): _____

**The following should be completed by the study member conducting the assent process. If the child agrees to be in the study, check all that apply:*

- The child is capable of reading and understanding the assent form and has signed below as documentation of assent to take part in this study.
- The child is not capable of reading the assent form, but the information was verbally explained to him/her. The child signed below as documentation of assent to take part in this study.
- The child had ample opportunity to have his or her questions answered.

**I have read this form or someone has read it to me. If I did not understand something, I asked the doctor or the assistant to explain it to me. I can always ask the doctor or the assistant a question about the study if I don't understand something.*

12. SIGNATURES

Option to Receive Results: (please check only one of the following choices)

If a **result** is obtained by the research:

- I may have nephronophthisis and I would like results to be sent to the counseling physician as noted above.

Yes, I want to know the result _____ (Please initial)

- I may have nephronophthisis and I do NOT want results of the genetic testing sent to me or my doctor.

No, I do NOT want to know the result _____ (Please initial)

- I do not have any evidence of kidney disease at this time and understand that I am not eligible to receive results of this testing.

I am not eligible to receive results _____ (Please initial)

Research Subject:

I understand the information printed on this form and in the attached materials. I have been given copies of all of these. My questions so far have been answered. I have discussed this study, its risks and potential benefits with _____ (Counseling Physician or Designee).

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: _____

Name (Print legal name): _____ Phone: _____

Address: _____

Check Relationship to Subject:

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: _____

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: _____

Witness (optional):

I observed the above subject (or his/her legally authorized representative, if applicable) sign this consent document.

Name: _____ Title: _____

Signature: _____ Date of Signature: _____