



The University of Michigan  
Health System

Ann Arbor, Michigan, 48109-0646, USA

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18 May 2007

Dear Colleagues,

Thank you for your interest in the mutational screening of patients with Branchio-Oto-Renal (BOR) syndrome. We are performing linkage analysis for the urinary tract malformation loci on chromosomes 1p13, 6p21, 10q26, and mutational analysis in the *AGRT2*, *BMP4* (both identified in monogenetic mouse models), *KALI* (Kallmann's syndrome), *EYAI* (Branchio-Oto-Renal syndrome), *PAX2* (renal coloboma syndrome), *SALL1* (Townes-Brocks syndrome), *OFDI* (Oro-Facio-Digital syndrome) genes, and further genes for BOR syndrome, which are identified from our group, but not published so far. This genetic analysis is investigational and is performed in the setting of a research laboratory and there are no universal standards for the performance of these studies. The investigators endeavor to attain the highest standards in their analysis, but these analyses should not be considered diagnostic tests, rather investigational genetic tests not intended to replace other clinical or laboratory evaluations or treatments that would otherwise be considered the standard of care.

As these genetic tests are presently considered investigational and are part of a research protocol there should be no cost for the blood draw, shipping or processing of the samples to the patients or family members of the patients who agree to participate in the study. If the participant family or their insurance company is billed for the office visit or blood draw, this is an error and should be brought to our attention as it jeopardizes the insurability of the participant and/or their family. Furthermore, this billing error compromises the privacy of the participant and their family, and could potentially affect the employability of the participant and/or the participant's family. Should this error occur, please contact either myself or the study coordinator using the information provided in section 10 of the Informed Consent Document. We will then take steps to either pay for the office visit and/or blood draw, or remove the participant or participating family from the study. However, due to the prohibitive costs of office visits for the withdrawal of blood and the high volume of participants that we expect for this study, our laboratory cannot reimburse physicians for the withdrawal of blood, or the office visit for the withdrawal for this study. Office visits for 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. 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**

**urinary tract malformation at the time of enrollment.** If an individual is found to have urinary tract malformation after enrolling in the study a local physician may contact the investigators at which time results of any genetic testing, which has been performed, can then be released to the local physician. Local physicians or their representatives are expected to review the consent document with prospective participants and indicate that they feel the participant understands the nature of the study by signing the consent document before the participant signs the consent document. In addition to the copy that is returned to the investigators, the participant and the local physician should also keep a signed copy of the consent.

Please return the following items to the investigators:

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

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

As in the past, we are happy to provide free shipping of your samples (blood or extracted DNA). However, there has been abuse of our customer numbers recently. Therefore, we would like to kindly ask you to contact our laboratory for information on free shipping. Bethan Hoskins will be happy to help you and can be contacted by e-mail at [bhoskins@med.umich.edu](mailto:bhoskins@med.umich.edu).

Please e-mail us at the time of shipping with the shipping number so that 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,

A handwritten signature in blue ink, appearing to read "F. Hildebrandt".

Friedhelm Hildebrandt, M.D.

Professor of Pediatrics and of Human Genetics  
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## **BLOOD SAMPLE COLLECTION FOR MUTATIONAL ANALYSIS**

### **Instructions for blood collection and shipping:**

1. Review and sign consent document with each patient from whom blood is to be drawn.
2. A single 3ml EDTA or Na-Heparin tube of blood is required from each individual. Use sterile technique to obtain blood sample, invert several times after drawing to prevent coagulation and **always store blood at room temperature do not freeze.**
3. As in the past, we are happy to provide free shipping of your samples (blood or extracted DNA). However, there has been abuse of our customer numbers recently. Therefore, we would like to kindly ask you to contact our laboratory for information on free shipping. Bethan Hoskins will be happy to help you and can be contacted by e-mail at [bhoskins@med.umich.edu](mailto:bhoskins@med.umich.edu). Please indicate contents as blood or DNA, non-hazardous, non-toxic and non-infectious. The value is \$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 return these items to the following address:

The shipping address is:

**Prof. Dr. F. Hildebrandt**  
**University of Michigan**  
**Department of Pediatrics**  
**8240 MSRB III**  
**1150 West Medical Center Drive**  
**Ann Arbor, MI 48109-0646, USA**

6. Once you are ready to ship samples please let us know at this e-mail address: [fhilde@umich.edu](mailto:fhilde@umich.edu) with the shipping number so that we can track the package and ensure its safe delivery.
7. Results of the genetic analysis are generally available in 4-6 months and a report will be sent to you when they are available.

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

# Identification of new genes for Branchio-oto-Renal syndrome and congenital urinary tract malformations

Date \_\_\_\_ (mm)/ \_\_\_\_ (dd)/ \_\_\_\_ (yy)

## Health Questionnaire

Dr. Friedhelm Hildebrandt

This form is to be completed by the participant's physician.  
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: \_\_\_\_\_ kg on date: \_\_\_\_\_  
consanguineous\* parents?  yes  no  
*\*consanguineous: related by blood or share a common ancestor*  
relatives with urinary tract malformations:  mother  sister  
 father  others \_\_\_\_\_  
 brother

**Ethnicity:**  African  African American  American Indian or Alaskan Native  Arabic  Asian  Caucasian  
 Central Slavic  Chinese  European  Finnish  Hispanic  Indian subcontinent  Japanese  
 Pacific Islander  Turkish  Other \_\_\_\_\_

### I. Initial Clinical Examination \_\_\_\_ (mm)/ \_\_\_\_ (dd)/ \_\_\_\_ (yy)

#### 1. Symptoms (initial)

- |   |  |
|---|--|
| <input type="checkbox"/> acute event                | <input type="checkbox"/> fever                               |
| <input type="checkbox"/> during regular examination | <input type="checkbox"/> urinary tract infection             |
|   | <input type="checkbox"/> diminished/increased urinary output |
|   | <input type="checkbox"/> pyelonephritis                      |
|   | <input type="checkbox"/> hypertension                        |
|   | <input type="checkbox"/> others: _____                       |

#### 2. Laboratory findings (initial)

<b>Blood:</b> <input type="checkbox"/> creatinine: _____ mg/dl	<b>Urine:</b> <input type="checkbox"/> proteinuria: _____ g/d or g/g Krea
<input type="checkbox"/> GFR: _____ ml/min/1.73m <sup>2</sup>	<input type="checkbox"/> hematuria
<input type="checkbox"/> serum protein: _____ g/dl	<input type="checkbox"/> bacteriuria: _____ CFU/ml
<input type="checkbox"/> albumin: _____ g/dl	
<input type="checkbox"/> CRP: _____ mg/l	

3. Imaging techniques (initial)

- ultrasound                       voiding cystourethrography     renal scintigraphy  
 intravenous pyelogram         cystoscopy  
 others: \_\_\_\_\_

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                       others: \_\_\_\_\_

**II. Treatment**

- dialysis     ureterocystostomy  
 Tenckhoff catheter                               anti-reflux operation  
 pyelocystostomy                                 Anderson-Hynes pyeloplasty  
 others: \_\_\_\_\_

**III. Extrarenal Manifestations**

- face dysmorphism                               skeletal deformity  
 microcephaly                                       polydactyly/syndactyly  
 mental retardation                               pulmonary hypoplasia  
 deafness     heart anomalies  
 blindness     allergy  
 growth retardation                               others: \_\_\_\_\_

**IV. Remarks**

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**Thank you very much for your assistance. Please provide us with the following information in order to facilitate further correspondence.**

**Name:**

**Phone:**

**Address:**

**Fax:**

**E-mail:**

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