

DNA testing for Lowe Syndrome (OCRL syndrome)

Direct molecular diagnosis performed routinely in the OCRL1 gene :

Mutation detection : Screening of mutations by SSCA/DHPLC and sequencing of exonic DNA. When fibroblasts are available, mutations are screened using cDNA obtained by RT-PCR.

Efficiency : We have tested so far 81 unrelated families or patients suspected to be affected by Lowe syndrome. We have identified more than 55 different mutations (Am J Human Genet (1999) 65, 68-76; Human Mutation (2000) 16, 157-165) with a few of them being recurrent in 2 or 3 unrelated families. According to our experience, almost 30% of the mutations identified in our patients were neo-mutations. No mutation was found in 12 cases. In at least 4 cases the Lowe syndrome diagnostic was clearly questionable (lack of any kidney symptoms for example). In 3 others cases, we had only access to the mothers' DNA and considering the rate of neomutation observed in Lowe's syndrome patients, it was not surprising to not identify a mutation in the mothers's OCRL1 gene.

These mutations are tested on DNA extracted from a 10 ml blood sample obtained using EDTA as anti-coagulant. Delay is 3 weeks for unknown mutations, cost is 350 € (325 USD). Blood can be directly sent if the sample can be shipped directly to the laboratory in less than 2-3 days (Fedex, UPS...). Otherwise, extracted DNA (PCR quality) has to be sent and this can be alternatively sent by air mail. Alternatively, cultured fibroblasts can also be analyzed. Once a mutation has been identified in a family, molecular testing of additional individuals for this mutation is charged 120 € (100 USD) per patient. In that case, delay is less than a week. Prenatal diagnosis using trophoblast cells or amniocytes can be proposed.

Biochemical testing of the PiP2-5 phosphatase activity (OCRL1 activity) can also be performed if fibroblasts or amniocytes are available. Cost of the biochemical test is 450 € (400 USD).

Special Requirements:

- an informed consent signed by the patient or his parents (special form can be provided)
- a medical prescription for genetic testing established by a physician or a genetic counselor
- a formal order to Laboratoire de Biochimie de l'ADN – CHU Grenoble and indicating to whom invoice has to be sent

Payment has to be addressed to CHU Grenoble as International Money Order or by Bank Transfer

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Informed consent for a molecular diagnosis

I undersigned,, having received sufficient information from Dr..... concerning the following disease : agrees that a molecular diagnosis may be performed on myself / my child his study is performed for a diagnostic purpose.

I want I don't want to be informed of the results of the study

I agree I don't agree to the collection and processing of data included in my medical file solely by authorized people who are bound by professional confidentiality. All the data will remain strictly confidential. Only authorized people will be allowed to consult the data. I could ask, at any time, to be excluded from the study. In this case, all the data of my medical and genetic files will be eliminated. I can have access to my medical and genetic files at any time through a medical doctor of my choice.

Date :/...../.....,

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CHU Grenoble 217X. 38043 Grenoble Cedex. France
phone: 33+ 4 76 76 55 73 fax: 33+ 4 76 76 58 37 e-mail : jlunardi@chu-grenoble.fr

Molecular Diagnosis

Name : **First name** :

Date of birth : **For a child (< 18)** **father's name** :
mother's name :

Pathology investigated :

Name and signature of the physician requesting the molecular diagnosis :

.....

Nature of the biological sample : **Date of sampling** : .../...../.....

Proposant : affected patient family related patient

Pregnancy : yes no **date of the last period** :

Medical information (*An informed consent of the proposant and/or his parents is required and in the case of a family study, a genetic pedigree of the family should be enclosed*)

Clinical information :

Biological information :

In the case of a prenatal diagnosis, the following part must be filled :

I undersigned, Dr, certifies that a genetic counseling in agreement with the ethical regulation of my country has been delivered to Mrs..... in view of a molecular prenatal diagnosis for the following pathology :

Date :/...../..... ,

signature