BLUTSPENDE SRK
ZÜRICH

Hauptnummer DLZ: +41 58 272 52 52
Direkt +41 58 272 52 20 / s.meyer@zhbsd.ch
www.blutspendezurich.ch

Guideline

Sample submission and explanation of the analysis for «McLeod Neuroacanthocytosis Syndrome (MLS)»

Sample material
2 times 10 mL of EDTA-anticoagulated blood are sufficient for all the analysis described below. Samples need to be shipped at room temperature (maximum) and must not be frozen. Samples should arrive latest 3 days after collection (please check with your carrier) and need to be accompanied by an appropriate <informed consent> of the patient.

Prices
All prices given are provided in Swiss Francs (CHF) and do not include taxes. Current daily exchange rates will be used for final cost calculation (current price list applies, see www.zhbsd.ch).

Shipping address

Blutspende Zürich
Attn: McLeod sample
Molecular Diagnostic and Cytometry
Rütistrasse 19
8952-Schlieren
Switzerland

contact laboratory personal: Eduardo Meyer, Tel. +41-58-272-5176, e.meyer@zhbsd.ch
contact laboratory director: Stefan Meyer, Tel. +41-58-272-5220, s.meyer@zhbsd.ch

Analysis

The diagnosis of MLS is based on findings on clinical examination, immunohematologic testing, and flow cytometry. *XK* is the only gene in which mutations are known to cause MLS. Contiguous gene deletions involving *XK* may also include *CYBB* (causing X-linked chronic granulomatous disease), *DMD* (Duchenne muscular dystrophy) and *RPGR* (X-linked retinitis pigmentosa).

Laboratory tests
Our analysis starts with an **immunohematological test** for the presence or absence of at least 2 antithetical Kell-antigens (usually K/k and Kp^a/Kp^b) and are followed by an immunohematological test for the **Kx erythrocyte antigen as well as direct antiglobulin test (DAT)**, to assess for weakly or unexpressed Kell antigens and to prove Kx negativity.

(Price for the above described testing is approx. 179.00 CHF (current price list applies)).

If Kx erythrocyte antigen is negative, a genetic analysis of the *XK*-Locus on the X-Chromosome is highly recommended (see below). **If the Kx erythrocyte antigen is positive**, MLS may be excluded. However, a very small rest of probability for a mutated *XK* gene (e.g. presence of MLS) cannot be excluded completely. In female cases potential MLS carrier status might be excluded by FACS analysis. Therefore, further testing (see below) is recommended.

For more information regarding the analysis process you may also consult:
"Neurodegeneration in the Elderly – when the blood type matters. An overview of the McLeod Syndrome with focus on hematological features" by B.M Frey, C. Gassner and H.H. Jung, *Transfusion and Apheresis Science, 2015, p.277-84.*

Genetic analysis
Our genetic analysis always follows a clear order of tests: (1) "rough deletion analysis" by positional PCRs in potentially affected males covering a X-chromosomal region of 8 Mb from the Ornithine Carbomyltransferase gene (OTC) to the Dystrophine gene (DMD) (Xp11.4 to Xp21.2), (2) depending on the outcome of (1), identification of the deletional breakpoint with consequent sequence-analysis, or, if there is no evidence for a deletion, sequencing of the coding region (3 exons plus flanking sequences) of the *XK* gene. **Currently, proof of an unmutated *XK* gene offers highest available laboratory evidence for absence of McLeod.**

(Price for the above described testing is CHF 61.00 (DNA-preparation) plus CHF 268.00 (rough deletion analysis). Deletional breakpoint analysis and sequencing (CHF 672.00) or *XK* gene sequencing (CHF 504.00) are further detailed analysis offers).

In the case of a mutation of the *XK* gene or presence of a large X-chromosomal deletion, specific sequences may be used for **detection of carrier/affected status** in males ("homozygous") and **potential carrier-females** ("heterozygous"). Prices for these services are available upon request.

FACS-analysis on Kell antigens is a supplementary investigation provided by our laboratory in this context (CHF 392.00). Mutations of the *XK* gene may be inconclusive with respect to their effect on the development of MLS, when observed for the first time (no comparability to other cases possible) or when encoding (synonymous or highly homologous) amino-acid exchanges only. Currently, no further analysis can be provided in these cases.

Please consider serious implications of Kx negativity in case of need for blood transfusions!
Respective analysis may be performed by our laboratory, but may better be organized by contacting your local blood bank.