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BLUTSPENDE ZÜRICH

Blutspende Zürich, DLZ Schlieren, Rütistrasse 19, 8952 Schlieren ZH, Switzerland

Guideline for sample submission of samples and explanation of the analysis for <<McLeod Neuroacanthocytosis Syndrome (MLS)>>

All prices given are denoted in Swiss Francs (CHF) and do not include taxes. Current exchange rates as of April 17th 2015 are: 1 CHF = 1.04 USD, 0.97 EUR. Current daily exchange rates will be used for final cost calculation (current price list applies, see our homepage at www.zhbsd.ch).

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. Send samples to:

Blutspende Zürich
Attention: MOC-laboratory, McLeod sample
Rütistrasse 19
8952-Schlieren
Switzerland

contact laboratory personal: Eduardo Meyer, Tel. +41-58-272-5170, e.meyer@zhbsd.ch
contact laboratory director: Christoph Gassner, Tel. +41-58-272-5195, c.gassner@zhbsd.ch

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).

Our analysis starts with an **immunhematologic 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 immunhematologic 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. **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, published in *Transfusion and Apheresis Science, 2015, available online 14. April 2015*

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Our genetic testing always follows a clear order of tests: (1) "rough deletion analysis" by positional PCRs around XK in potentially affected males covering a genetic region from 8 mbp telomer - XK - 0.7 mbp centromer, (2) depending on the outcome of (1), identification of the deletional break-point 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 a wildtype (unmutated) XK gene offers highest available laboratory evidence for absence of McLeod.**

Price for the above described testing including DNA-preparation and rough deletion analysis is carried out in any case (costs are CHF 61.00 plus 268.00). Deletional breakpoint analysis and its' sequence (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 comparancy 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.

Blood Transfusion Service Zurich - Swiss Red Cross
Molecular Diagnostics and Cytometry
Zurich, Switzerland
Dr Christoph Gassner, PhD
Apr. 17th, 2015