Best practice guidelines on genetic diagnostics of FSHD now available!

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Best practice guidelines on genetic diagnostics of Facioscapulohumeral muscular dystrophy are now available online in the journal *Neuromuscular Disorders*. The FSH Society is kindly acknowledged as one of the sponsors of this necessary and valuable workshop held June 9, 2010, at the Leiden University Medical Center in Leiden, The Netherlands.

Workshop report

Best practice guidelines on genetic diagnostics of Facioscapulohumeral muscular dystrophy: Workshop 9th June 2010, LUMC, Leiden, The Netherlands

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Selected abstracts and section headings [in bold] follow:

1. Introduction
"During the 171st European Neuromuscular Centre international workshop Standards of care and management of facioscapulohumeral muscular dystrophy (FSHD) in January 2010 [1], it was concluded that there was a need for further discussion to better define the "gold standard" for diagnostic procedures for FSHD. With the increasing complexity of the genetics of FSHD, it is important to reach an international consensus on the molecular testing methods. To this end, a meeting was held with 39 scientists from around the world at the Leiden University Medical Center on June 9, 2010 to establish consensus Best Practice Guidelines on Genetic Diagnosis of FSHD."

2. The clinical perspective
3. General description of the genetics of FSHD
4. Diagnostic techniques
5. Southern blotting
6. Identification of complex D4Z4 rearrangements by Southern blotting: complicating D4Z4 rearrangements
7. Other diagnostic methods
8. Types of Laboratory referral and their analysis

9. Experience and techniques of different diagnostic labs

"There were 19 laboratories who offer molecular testing for FSHD on a service basis who provided data and were represented at the meeting. The activity for each lab varies with five labs testing 20–50 samples per year, five testing 80–150, and eight testing 150–400 per year. The electrophoretic method used is LGE alone in 10/19 labs (53%), PFGE as the primary method in 6/19 (31%), and both techniques in 3/19 (16%), including long rang PCR in one of these. Interestingly, mosaic FSHD cases were as expected mainly recognized by labs performing PFGE analysis on high quality plug DNA. In routine service testing (in 16 labs) the mean of the percentages of positive results on the index case is: 50% (range 27–95%)…. Only 11/19 labs currently use 4qA/B telomeric polymorphism typing, and only in response to a request by the referring clinician for additional testing, and on an individual case basis. The indication is usually in order to check for a proximal (p13E-11 site) deletion in cases believed clinically to have FSHD, or alternatively in prenatal diagnosis where two shortened 4-type fragments are seen in the parents, in order to check if one of these can be discounted from being of relevance if it is of 4qB-type. No lab was yet offering the SSLP 161/163/166 polymorphism, although some may have plans to introduce this on an individual case basis. Similarly, no lab was yet offering any methylation assay to identify cases of FSHD2, as this is not yet felt to be sufficiently discriminatory for service use, although it is hoped that the technical difficulties will be resolved."

10. Consensus genetic testing

"At the end of the meeting all participants together discussed the consensus for the molecular diagnosis of FSHD. It was concluded that for know the most suitable method would be the conventional Southern blot based method. For this genomic DNA is digested with EcoRI (or EcoRI/HindIII), EcoRI/BlnI and XapI and the DNA is separated by either LGE or PFGE. After Southern blotting the hybridization is performed with probe p13E-11. Because of the complex diagnostic results that can be encountered, all participants agreed that it would be helpful to know at the time of referral of DNA to the lab, what the clinician's expectation would be for the likelihood of the patient having true FSHD. Based on this short clinical description the geneticist can decide whether to perform additional genetic analysis, or to forward on the sample to a more specialist lab for further DNA tests. In the flowchart presented in Fig. 3, additional analysis are suggested in case the genetic analysis based on the minimum recommended consensus experiments shows an unexpected outcome based on the clinical description."

11. Workshop Participants

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