The United Kingdom Haemophilia Centre Doctors' Organisation Genetic Laboratory Network – a valuable resource for the development and standardisation of genetic testing in individuals with hereditary disorders of haemostasis

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http://www.ukhcdo.org/genetics_nw.htm

The United Kingdom Haemophilia Centre Doctors' Organisation (UKHCDO) Genetic Laboratory Network (GLN) was established in 2002 with the remit of creating a professional collaborative body to ensure quality and equity in the provision of molecular diagnostic services for patients with heritable bleeding disorders in the UK. The GLN represents a valuable resource, with a wealth of expertise and knowledge provided by members representing the 12 National Health Service (NHS) funded laboratories that provide all such testing in the UK and an affiliated laboratory in Dublin, Ireland. Membership is restricted to accredited laboratories that are associated with Haemophilia Comprehensive Care Centres and can demonstrate provision of a robust genetic service through their active participation in external quality assurance (EQA).

The location of member laboratories and a brief description of some of the current activities of the GLN are shown below.

United Kingdom National External Quality Assurance Scheme – Molecular Genetics of Heritable Bleeding Disorders

Since its inception, the network has been actively involved in advocating for quality improvement and standardisation and has developed close links with the UK NEQAS external quality assurance scheme for Molecular Genetics of Heritable Bleeding Disorders.

This EQA scheme was first established in 1998 and now comprises 27 participants, including a number of international laboratories. Material for testing is derived from whole blood samples or immortalised cell lines, with specimens distributed twice yearly for analysis and interpretation.

Participants receive an individual performance report, as well as an overall summary of the exercise. The individual laboratory 'score' for each exercise includes points awarded for correct identification of the genotype, clerical accuracy of reporting and interpretation of the genetic findings in the context of the supplied patient information.

www.ukneqasbc.org

The triennial audit programme

In addition to external audits carried out by the national accreditation body in the UK (United Kingdom Accreditation Service, UKAS), members of the GLN participate in a triennial audit scheme comprising part of the UKHCDO Haemophilia Centre clinical audit programme. Audit of the laboratory in the context of the comprehensive haemophilia service focuses on issues such as integration of the molecular diagnostic laboratory within the clinical service, communication links, robustness of the service and quality outcomes related to patient care and experience.

Audit tools including a pre-visit questionnaire, formal inspection visit and vertical audits are used in the current national programme and support improvements at the local level while also providing an overview of the equity of provision and quality of molecular diagnostic services for heritable bleeding disorders across the UK as a whole.

The GLN represents an integral component of the triennial audit scheme with input to the design of audit tools and members of the network participating as auditors. The network has also collated data from these audit activities for publication, providing valuable information relating to; laboratory profiles, service provision, quality, sample processing, results, reporting, service links, service development and continuity.

Locus Reference Genomic Sequence [1]

It has long been recognised that there is a requirement for standardisation in nomenclature of sequence variants used for clinical reporting. To this end, standardised systems, such as the Human Genome Variation Society (HGVS) recommendations, have now been widely adopted, with all members participating in the UK NEQAS EQA scheme using these guidelines for annotation of changes at the DNA and protein level.

Despite these advances, the consistency of reporting can only be ensured where a stable and fixed reference sequence is available. In line with the GLNs remit in advocating for quality improvement and standardisation, the network has recently embarked on the preparation of *F8* and *F9* Locus Reference Genomic (LRG) files to create stable reference sequences for these genes.

These manually curated files will provide a universal reference sequence that can be used in combination with HGVS guidelines[2] to eliminate ambiguity in the reporting of variants, ensuring consistency of reporting, regardless of the laboratory in which testing is performed.

Best practice guidelines

The network provides an exemplar model of the benefits afforded through collaborative working, with the compilation and publication of best practice guidelines for genetic testing in inherited haemostatic disorders such as Haemophilia A and B.

These guidelines represent a set of recommendations based on the combined scientific, technical and interpretative experience of experts working in the field; thus providing a comprehensive overview of best practice in the analysis and interpretation of genetic data to provide informative, concise and clear reports. These articles are submitted for publication in peer-reviewed journals and are accessible via the link below;

www.ukhcdo.org/UKHCDOguidelines.htm

Bi-annual meetings of senior members of scientific staff from laboratories within the GLN and active interim communication provides access to an extensive knowledge base for expert consultation on unusual cases, stimulates debate on applicability of state-of-the art techniques for advancing service provision and allows the network to address current challenges facing the diagnostic laboratory; gaining consensus opinion on the appropriate approach for delivering high quality molecular diagnostic strategies for the advancement of patient care in this challenging era of rapid technological advance.

A directory of laboratories involved in the network is available at www.ukhcdo.org/GeneticsNetworkNW/directory.htm

1. MacArthur, J.A.L., et al (2013). Locus Reference Genomic: reference sequences for the reporting of clinically relevant sequence variants. *Nucleic Acids Research*, 42; D873-D878
2. www.hgvs.org

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