Distal Arthrogryposis Service

Clinical Background and Genetics:
- Distal Arthrogryposis (DA) is a group of disorders characterised by congenital contractures in the distal limbs without an obvious neurogenic or myopathic cause. Ten different clinical forms (DA1 to DA10) have been described, with DA1 and DA2B as the most common forms; some other forms are very rare. Features shared amongst all distal arthrogryposes include consistent patterns of hand and foot involvement, limited involvement of proximal joints, and variable expressivity within families.
- Utility: Molecular genetic analysis reduces the requirement for other invasive tests such as nerve conduction studies and muscle biopsy. Testing also enables a precise diagnosis in this difficult group where there is clinical overlap and a wide variety of conditions presenting with contractures, allowing clinicians to decide on appropriate management.

Service offered: See table below for details.
- Ten genes associated with Distal Arthrogryposis are screened using Agilent’s ‘Focussed Exome’ custom target enrichment system (SureSelectXT2) and Next Generation Sequencing. Please contact the lab for further details.
- If required for specific phenotype: Mutations in the TPM2 gene are identified by bidirectional direct sequence analysis. Screen sensitivity approx 99%.

Sample Required:
- Adult: 5mls blood in EDTA
- Paediatric: at least 1ml EDTA (preferably >2ml)

Consent and DNA Storage:
- All genetic testing requires consent. It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.
- DNA is stored from all patients unless consent for this is specifically denied.
- Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Referrals:
- Diagnostic referrals are accepted from Consultant Clinical Geneticists or specialist clinicians with liaison, from probands with suspected or confirmed diagnosis of Distal Arthrogryposis.
- Familial referrals are accepted from Consultant Clinical Geneticists with appropriate clinical information.

Quality:
- BGL participates in the following external quality assurance schemes: EMQN sequencing QA scheme (since the pilot scheme was introduced in 2002) and UKNEQAS Unclassified Variant interpretation scheme (pilot scheme in 2012).


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