Bristol Genetics Laboratory is a UKAS accredited medical laboratory No.9307.

Distal Arthrogryposis Service

NHS North Bristol NHS Trust

Contact details:
Bristol Genetics Laboratory
Pathology Sciences
Southmead Hospital
Bristol, BS10 5NB
Enquiries: 0117 414 6168
FAX: 0117 414 6464

Head of Department:
Professor Rachel Butler, FRCPath
Consultant Clinical Scientist

Consultant Lead for Rare Disease:
Maggie Williams, FRCPath

Consultant Lead for Oncology:
Christopher Wragg, FRCPath

Service Lead: Julie Honeychurch
julie.honeychurch@nbt.nhs.uk or
juliehoneychurch@nhs.net

Sample Required
See Sample requirements page at www.nbt.nhs.uk/genetics **for full details**

Adult: 5mls of blood in EDTA.
Paediatric: at least 1ml EDTA (preferably >2ml)

Samples should be accompanied by a FULLY completed request form (available as download at www.nbt.nhs.uk/genetics or from the laboratory).

Please include details of the test required, family history, address and POSTCODE, NHS number, referring clinician and centre.

Consent and 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 undergoing DNA testing, unless consent for this is specifically denied.

Stored material from all referrals may be retained for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

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 a custom clinical exome target enrichment Next Generation Sequencing approach. Please contact the lab for further details.
- If required for specific phenotype: Pathogenic variants in the *TPM2* gene are identified by bidirectional direct sequence analysis. Screen sensitivity approx. 99%

Assay	Gene (MIM)	Phenotype	Reporting Time
Level 1 Distal Arthrogryposis Clinical Exome NGS panel	***TPM2*** (190990) 9p13.3	DA1, DA2B	42 days (routine) 21 days (urgent i.e prenatal diagnosis)
	TNNI2 (191043) 11p15.5	DA2B	
	TNNT3 (600692) 11p15.5	DA2B	
	MYBPC3 (160794) 12q23.2	DA1B, Lethal congenital Contacture Syndrome 4	
	MYH3 (160720) 17p13.1	DA2A, DA2B, DA type 8	
	MYH8 (160741) 17p13.1	Carney Complex (associated with DA), Trismus-pseudocamptodactyly Syndrome	
	FBN2 (612570) 5q23.3	Congenital Contractual Arachnodactyly	
	PIEZ02 (613629) 18p11.22-p11.21	DA Type 3, DA type 5, MArden-Walker Syndrome	
	CHST14 (608429) 15q15.1	Ehlers-Danlos Syndrome Musculocontractual Type I	
	ECEL1 (605896) 2q37.1	Arthrogryposis Distal Type 5	
Level 2 Sanger sequencing of all 9 exons of *TPM2* (both isoforms covered)	***TPM2***	DA1, DA2B	42 days
Level 3 Familial (Cascade or segregation).	As required	As required	42 days (routine) 3 days (prenatal diagnosis)

Please contact the laboratory for current test prices.

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 (since the pilot scheme in 2012).

Reference

Bamshad M *et. al* (2009) **Arthrogryposis: A review and Update**. *J Bone Joint Surg Am*; 91 Suppl 4: 40-6

Information document No.74 Version 5
Active date of this version: 16/07/2019
DETAILS CORRECT AT DATE OF PRINTING ONLY
Approved by: Rebecca Whittington