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

North Bristol NHS Trust

Axenfeld-Rieger Syndrome – *PITX2/FOXC1*

Contact details:
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Sample Required:
Adult: 3mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

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

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

Please include details of test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

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.

Clinical Background and Genetics

- Axenfeld-Rieger Syndrome (ARS, OMIM 180500/602482) is a rare autosomal dominant (AD) disorder with an estimated frequency of 1/250,000 in the UK.
- ARS describes a group of genetically and phenotypically heterogeneous disorders that primarily affect the anterior segment of the eye. Affected individuals display a characteristic spectrum of ocular anomalies which can include iris hypoplasia, corectopia, polycoria, iridogoniodysgenesis, and a prominent anteriorly displaced schwalbe's line.
- Systemic features of ARS although more variable in presentation can include microdontia, hypodontia, maxillary hypoplasia and hypertelorism. In addition some patients have cardiac anomalies.
- One of the most serious associations is the increased risk of glaucoma with approximately 50% of affected individuals acquiring this progressively blinding disease. Identifying an "at risk" group allows glaucoma development/progression to be monitored and treated appropriately.
- There are four known genetic loci for ARS, situated on chromosome 4q25 (*PITX2*), 6q25 (*FOXC1*), 13q14 and 16q24 (genes remain unidentified).
- It is estimated that 40% of patients with ARS are due to point mutations or dosage anomalies in either the *FOXC1* or *PITX2* gene.

Strungaru MH *et al*. 2007 Invest Ophthalmol Vis Sci. Jan 48: 228-237
Tümer Z *et al*. 2009 Eur J Hum Genet 17: 1527-1539

Service offered

- First line test is screening *FOXC1* and *PITX2* for dosage anomalies using MLPA.
- Patients without any dosage abnormalities are screened for point mutations in *FOXC1* and *PITX2* by direct sequence analysis.

Referrals

Referrals are accepted from Genetic Ophthalmologists and Clinical Geneticists for patients meeting the UKGTN clinical criteria; please complete the UKGTN proforma found below.

Target reporting Time

MLPA (*FOXC1* + *PITX2*)
FOXC1 Full gene screen
PITX2 Full gene screen
} 42 days

Please contact the laboratory for up to date prices.

Quality

This is a UKGTN approved service. BGL participates in the external quality assurance EMQN Sanger sequencing scheme and the GenQA Pathogenicity of sequence variants scheme.

Clinical Advice

If clinical discussion is required we would recommend contact with Dr Amanda Churchill, Bristol Eye Hospital, Bristol (Tel: 0117 342 4653).

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DETAILS CORRECT AT DATE OF PRINTING ONLY.
Approved by: Natalie Forrester

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NHS North Bristol NHS Trust

Axenfeld-Rieger Syndrome – *PITX2/FOXC1*

UKGTN testing criteria

Please complete as applicable and return to the laboratory with any additional information available.

Patient Name	
Date of Birth	
NHS Number	

OMIM disease reference **180500/**602482

Referrals are only accepted from one of the following:

Tick the relevant box:

Genetic Ophthalmologist ☐

Clinical Geneticist ☐

Minimal referral criteria as stated in the Gene Dossier

Criteria		
Clinical phenotype of Axenfeld-Rieger Syndrome (ARS); individuals should fulfil at least 2 of the following criteria		
	Tick the box if patient meets the criteria	**Comments** i.e. Bilateral
Anterior Segment Dysgenesis		
Posterior embryotoxon	☐	
Iris hypoplasia	☐	
Corectopia	☐	
Polycoria	☐	
Abnormal iris strands	☐	
Childhood glaucoma (but not congenital)	☐	
OR		
Autosomal dominant inheritance with one of the above Ocular features excluding glaucoma	☐	
Additional features		
Cardiac abnormalities	☐	
Hearing loss	☐	
Microdontia	☐	
Hypodontia	☐	
Maxillary hypoplasia	☐	
Hypertelorism	☐	
Telecanthus	☐	
Umbilical hernia	☐	
Further Information:		
If the patient does not fulfil these criteria and you still feel that testing should be performed please contact the Bristol Genetics Laboratory to discuss testing (Tel: 0117 414 6168).		