Bristol Genetics Laboratory

North Bristol NHS Trust

Thrombocytopenia-Absent Radius Syndrome (TAR)

Contact details:
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Sample Required:
Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml). Given possible difficulties in obtaining blood samples from these patients a buccal or saliva sample is an alternative primary sample for DNA extraction.

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

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 Advice

If clinical discussion is required we would recommend contact with Dr Ruth Newbury-Ecob, Clinical Genetics, St. Michael's Hospital, Bristol (Tel: 0117 342 5652).

Clinical Background and Genetics

- Thrombocytopenia-absent radius (TAR) syndrome is characterised by hypomegakaryocytic thrombocytopenia and bilateral radial aplasia in the presence of both thumbs.
- These characteristic patterns differentiate TAR syndrome from other conditions with involvement of the radius, namely Holt-Oram syndrome, Roberts syndrome and Fanconi Anaemia in which the thumb is usually absent or severely hypoplastic.
- Additional skeletal features associated with TAR syndrome include shortening and, less commonly, aplasia of the ulna and/or humerus.
- The hands may show limited extension of the fingers, radial deviation and hypoplasia of the carpal and phalangeal bones.
- The majority of TAR syndrome cases develop when an individual has a deletion of the *RBM8A* gene (chromosome 1q21.1) on one chromosome and a *RBM8A* hypomorphic SNP on the other allele.Two *RBM8A* hypomorphic SNPs have been identified, that when in *trans* with an *RBM8A* deletion account for approximately 96% of TAR syndrome cases (Nat Genet. 2012 Feb 26;44(4):435-9).
- A minority of TAR syndrome cases are explained by a null mutation in the *RBM8A* gene in *trans* with a *RBM8A* hypomorphic SNP on the other allele. In deletion negative cases point mutation analysis of the entire coding region of *RBM8A* gene can be completed.
- There are believed to be other, as yet unknown, hypomorphic alleles in the *RBM8A* gene.

Testing for TAR Syndrome

- MLPA analysis of the *RBM8A* gene (1q21.1 region).
- Analysis of the known *RBM8A* regulatory variants and point mutation analysis of the entire coding region of *RBM8A* by DNA sequencing.
- Bristol Genetics Laboratory also offers a gene panel for limb anomaly disorders including TAR syndrome, Holt-Oram Syndrome, Fanconi Anaemia, Robert Syndrome, Ulnar-Mammary Syndrome and Duane-Radial Ray Syndrome (please contact the laboratory for further details).

Target reporting Time and Indicative Cost

RBM8A MLPA *(*1q21.1 region)	28 days
RBM8A hypomorphic SNP analysis	28 days
RBM8A point mutation analysis	56 days

Please contact the laboratory for up to date prices.

Quality

- This is a UKGTN approved service. There are no specific EQA schemes for this service. BGL participates in the EMQN scheme for DNA sequencing.

Referrals

Referrals are only accepted from Clinical Geneticists.

- Diagnostic referrals.
- Carrier testing for the *RBM8A* deletion.
- Carrier testing for the *RBM8A* hypomorphic SNPs for the partner of an individual with a confirmed *RBM8A* deletion.
- Prenatal testing is available when an *RBM8A* null mutation and a *RBM8A* hypomorphic SNP have been confirmed in parents.

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