Thrombocytopenia-Absent Radius Syndrome (TAR)

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.