**ROR2 SKELETAL DISORDERS – OMIM 602337**

(Brachydactyly type B1 - OMIM 11300; Recessive Robinow syndrome – OMIM 268310)

**INTRODUCTION**

*ROR2* encodes a 943 amino acid tyrosine kinase receptor localised to chromosome 9q22 and is an essential component of a signalling pathway in mammalian skeletogenesis. There are 2 skeletal dysplasias associated with mutations in *ROR2*:

1) **Autosomal dominant Brachydactyly type B1 (BDB1)** is caused by gain-of-function truncating mutations localised to 2 hotspots within *ROR2* and is characterised by absence or hypoplasia of the terminal portions of the digits.

2) **Recessive Robinow syndrome (RRS)** is a more generalised skeletal dysplasia with mesomelic limb bone shortening, defects of the ribs and spine, brachydactyly, hypoplastic genitalia and a characteristic facial appearance, and is caused by homozygous or compound heterozygous loss-of-function mutations located throughout the gene. Penetrance is considered to be very high for both disorders.

There is a dominant form of Robinow syndrome which has a similar phenotype to RRS but with less severe rib and spine abnormalities and in sporadic cases these conditions can be difficult to differentiate. Molecular analysis of *WNT5A* associated with one form of this disorder is available (see separate information sheet).

**TESTING**

- **Diagnostic:** Clinically affected patients
- **Carrier/Familial mutation test:** Relatives of clinically affected patients (known mutation(s))
- **Prenatal:** At risk of having an affected child (known mutation(s))

**REFERRALS**

- From Geneticists, Paediatricians, Antenatal Services, Neurologists, Endocrinologists or Dysmorphologists
- Prenatal referrals must be discussed with the laboratory and, where possible, arranged in advance.

**STRATEGY AND TECHNICAL INFORMATION**

- **For new diagnostic cases:**
  - **BDB1** - bi-directional sequencing analysis of exons 8 and part of exon 9 of *ROR2*
  - if negative, screening of the rest of the gene as described below for RRS can be undertaken.
  - **RRS** - bi-directional sequencing analysis of the 9 coding exons (12 amplicons) of *ROR2*
    - Multiplex Ligation-dependent Probe Amplification (MLPA) to detect deletions/duplications.

**TARGET REPORTING TIMES**

- **BDB1 Diagnostic test:** 40 days
- **RRS Diagnostic test:** 40 days
- **Familial mutation test:** 10 days
- **Prenatal test (includes maternal contamination check):** 3 days

N.B. Details are correct for the date of printing only – last updated 18/08/2015