**HOXD13 SKELETAL DISORDERS – OMIM 142989**

**Synpolydactyly (186000) and Brachydactyly types D / E – (113200 / 113300)**

**INTRODUCTION**

*HOXD13* is the most 5’ gene of the *HOXD* gene cluster on chromosome 2q31 and encodes a homeodomain transcription factor with important functions in limb patterning and growth. Three distinct classes of heterozygous mutations are found: polyalanine tract expansion associated with **synpolydactyly type 1 (SPD1)**, truncating mutations resulting in loss of the homeodomain and haploinsufficiency associated with SPD1 with reduced penetrance, and missense mutations within the homeodomain associated with **brachydactyly types D and E (BDD and BDE1)**. Penetrance is considered to be very high but there is marked phenotypic variability, both between family members and in opposite limbs of the same individual.

**TESTING**

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

**REFERRALS**

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

**STRATEGY AND TECHNICAL INFORMATION**

- For new diagnostic cases:
  - Bi-directional sequencing analysis of the 2 coding exons (3 amplicons) of *HOXD13*
  - Multiplex Ligation-dependent Probe Amplification (MLPA) to detect deletions/duplications.

**CLINICAL SENSITIVITY**

There are at least three distinct genetic entities showing similar synpolydactyly features. *HOXD13* mutations account for the majority of these cases (Grzeschik et al 2008 Clin Genet 73: 113-120). The proportion of cases of brachydactyly types D and E due to *HOXD13* mutations is unknown.

**TARGET REPORTING TIMES**

- 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