FRONTORHINY/FRONTONASAL DYSPLASIA TYPE ONE (FND1)
OMIM 606014, 136760

INTRODUCTION
Frontorhiny/frontonasal dysplasia type 1 (FND1) is an autosomal recessive disorder caused by mutations in the ALX3 gene. No prevalence information is currently available, and currently only 8 cases have been reported where homozygous ALX3 variants were identified.

It is characterised by a distinctive facial appearance with hypertelorism, wide nasal bridge, short nasal ridge, bifid nasal tip, broad collumella, widely separated slit-like nares, long philtrum with prominent bilateral swellings, and midline notch in the upper lip and alveolus. Additional recurrent features that may present in a minority of individuals include upper eyelid ptosis and midline dermoid cysts of craniofacial sutures.

Although growth and development have been normal in the affected individuals, most have required surgical procedures for improved appearance and function. These may include; multiple nasal reconstructions, ptosis correction, strabismus collection, excision of dermoid cysts, cleft-lip repair, advancement of the maxilla, advancement and medialisation of orbits, repair of the anterior cranial-base defect and reconstruction of nasal airway.

The main benefit of molecular testing is confirmation of the diagnosis, which then enables family testing and if appropriate prenatal diagnosis to be carried out. In addition a positive diagnosis will enable surgical intervention.

TESTING AND REFERRALS
The aim is to provide a joint Molecular and Clinical service, and Professor Andrew Wilkie (+44 (0)1865 222619) is available for advice. We test:
- Clinically affected patients
- Relatives of clinically affected patients in whom a mutation has been identified
- Prenatal testing is available in cases where a mutation has been identified. These must be discussed with the laboratory and arranged in advance.

REFERRALS
- From Clinical Genetics, Paediatrics, Craniofacial clinics and Dysmorphologists.
- Prenatal testing is only accepted from Clinical Genetics and / or Prenatal Diagnosis.

STRATEGY & TECHNICAL INFORMATION
- Mutation screening in new diagnostic cases is undertaken by:
  - Bidirectional fluorescent sequencing of ALX3 exons 1-4.
  - Dosage analysis by MLPA across all exons of the craniofacial genes TWIST1, ALX1, ALX3, ALX4, MSX2, RUNX2 and EFNB1. Although no whole gene rearrangements have been reported in the literature in association with FND1, it is probable that these mutations could be present.
- Family tests: When a mutation has been identified in a family the individual is tested only for the familial mutation.

TARGET REPORTING TIMES
Diagnostic test (Sequencing & MLPA): 8 weeks
Familial Mutation test: 10 days
Prenatal testing (includes maternal contamination check): 3 days

N.B. Details are correct for the date of printing only – last updated 11/06/2015