CRANIOFRONTONASAL SYNDROME (CFNS) – HSS Service
OMIM 304110

INTRODUCTION
CFNS (also known as craniofrontonasal dysplasia or craniofrontonasal dysostosis) is an X linked disorder with paradoxical sex reversal in phenotypic severity (i.e. females are more severely affected than males). It affects about 1 in 120,000 of the general population, with all ethnic groups being equally affected.

The characteristic manifestations of CFNS in females are craniofacial asymmetry, severe hypertelorism, coronal synostosis, strabismus, bifid nasal tip, grooved nails, abnormalities of the thoracic skeleton and wiry, curly hair. Obligate carrier males may be unaffected, or show only mild features such as hypertelorism and rarely cleft lip and/or palate. There are also some cases of affected males having congenital diaphragmatic hernia. Somatic mosaicism occurs in approximately 18.5% of new cases, and these have a wide variety of clinical presentation.

The main benefit of molecular testing is confirmation of the diagnosis, which then enables family testing or prenatal diagnosis to be carried out.

TESTING AND REFERRALS
All diagnostic samples should be accompanied by a completed clinical questionnaire & consent form (click here)
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, Dysmorphologists. Prenatal testing is only accepted from Clinical Genetics and / or Prenatal Diagnosis.

STRATEGY
Family tests: When a mutation has been identified in a family the individual is tested only for the familial mutation.
For new cases: About 85% are due to mutations of EFNB1, and 5% are due to deletions of EFNB1.

TECHNICAL INFORMATION
Mutation analysis: Bidirectional fluorescent sequencing of EFNB1 exons 1-5.
MLPA: dosage across all exons of the craniofacial genes TWIST1, ALX1, ALX3, MSX2, RUNX2 and EFNB1 and at 3 exons of ALX4. CFNS has been reported in association with deletions and duplications of the EFNB1 gene.

TARGET REPORTING TIMES: Supraregionally funded by HSS for referrals from the UK
Diagnostic: 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