LACRIMOauriculodentodigital Syndrome (LADD) – OMIM 149730, and Aplasia of the Lacrimal and Salivary Glands (ALSD) – OMIM 180920

INTRODUCTION
LADD (also known as Levy-Hollister syndrome) is an autosomal dominant disorder. Although ALSG has been described as a distinct disorder, it is actually an allelic disorder of LADD syndrome. No prevalence information is available but it is thought to be very rare as in 2005 only 35 cases had been reported worldwide.

The characteristic manifestations of LADD are multiple congenital anomalies, mainly affecting the lacrimal glands and ducts, salivary glands and ducts, ears, teeth and distal limb segments. There may also be some facial dysmorphism, malformation of the kidney and respiratory syndrome, and abnormal genitalia. The clinical phenotype is variable both between and within families ranging from congenital renal disease causing death in the neonatal period to aplasia of the lacrimal and salivary glands (ALSG) only.

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.

The types of mutations that have been reported in LADD have been mainly missense and nonsense mutations, and small deletions in FGF10, FGFR3 and FGFR2. A large deletion encompassing exons 2-3 of FGF10 has also been reported previously in a family with LADD syndrome. The current screening strategy is predicted to pick up ~100% of all reported mutations in FGF10.

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, 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: Patients with LADD or ALSG have been found to have mutations in the FGF10 gene, FGFR2 exon 13 & 16 and FGFR3 exon 13.

TECHNICAL INFORMATION
Mutation analysis: Bidirectional fluorescent sequencing of FGFR3 exon 13, FGFR2 exon 13 & 16, and the coding regions (exons 1-3) of FGF10.
MLPA: dosage across all exons of FGF10.

TARGET REPORTING TIMES
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