Cartilage hair hypoplasia (CHH)

Contact details
Molecular Genetics Service
Level 6, Barclay House
37 Queen Square
London, WC1N 3BH
T +44 (0) 20 7762 6888
F +44 (0) 20 7813 8578

Samples required
• 5ml venous blood in plastic EDTA bottles (>1ml from neonates)
• Prenatal testing must be arranged in advance, through a Clinical Genetics department if possible.
• Amniotic fluid or CV samples should be sent to Cytogenetics for dissecting and culturing, with instructions to forward the sample to the Regional Molecular Genetics laboratory for analysis
• A completed DNA request card should accompany all samples

Patient details
To facilitate accurate testing and reporting please provide patient demographic details (full name, date of birth, address and ethnic origin), details of any relevant family history and full contact details for the referring clinician

Introduction
Mutations in the untranslated \textit{RMRP} gene on chromosome 9p13-p12 (encoding the RNA component of RNase MRP endoribonuclease) lead to a wide spectrum of autosomal recessive skeletal dysplasias, ranging from the milder phenotypes metaphyseal dysplasia without hypotrichosis (MDWH) and cartilage hair hypoplasia (CHH) to the severe anauxetic dysplasia (AD). This clinical spectrum includes different degrees of short stature, hair hypoplasia, defective erythrogenesis, and immunodeficiency.

Mutations in \textit{RMRP} are found in both the transcribed region and the promoter region (from the TATA box to the transcription initiation site). A founder mutation, 70A>G, is present in 92% of Finnish and 48% of non-Finnish patients with CHH (Thiel et al (2007) Am. J. Hum. Genet 81: 519-529).

Nomenclature: Please note, although HGVS recommendations for the description of DNA sequence variants (den Dunnen JT and Antonarakis SE (2000). Hum.Mutat. 15: 7-12) state that numbering should start with 1 at the first nucleotide of the database reference file (genomic Reference Sequence M29916.1), it is common practice in the literature for \textit{RMRP} numbering to start with 1 at the transcription start site.

Referrals
• Patients with suspected \textit{RMRP}-related disorder for mutation screening of \textit{RMRP}.
• Adult relatives of patients with \textit{RMRP} mutations for carrier status.
• Testing is available for minor siblings to establish carrier status prior to bone marrow/stem cell donation.

Prenatal testing
Prenatal testing is available for families in whom specific mutations have been identified or in whom appropriate family studies have been undertaken- please contact the laboratory to discuss.

Service offered
Mutation screening of the \textit{RMRP} gene. Detection of known mutations in relatives of patients with confirmed \textit{RMRP} mutations.

Technical
Direct sequencing analysis of the \textit{RMRP} gene - promoter region and the transcribed region.

Target reporting time
8 weeks for routine mutation screen in index case.
2 weeks for routine testing of specific mutations.
For urgent samples please contact the laboratory.