Connexin 26

Introduction

Pre-lingual non-syndromic sensorineural hearing loss (NSSNHL) is predominantly due to recessive mutations. DFNB1 was the first locus described for autosomal recessive NSSNHL and accounts for a high proportion of cases.

The GJB2 gene (located at 13q11-q12) encodes the gap junction protein, beta 2 - also known as connexin 26. GJB2 mutations may account for 10-30% of sporadic non-syndromic deafness. The c.35delG mutation is the most common GJB2 mutation described so far and is found in the majority of families linked to DFNB1. Other common mutations have been detected in specific ethnic groups.

A small proportion of individuals with DFNB1 have one identifiable GJB2 mutation and one of two large deletions (del(GJB6-D13S1830) – 309kb, del(GJB6-D13S1854) – 232kb) that include a part of GJB6 (encoding connexin 30) inherited on the opposite chromosome (del Castillo et al., J Med Genet (2005) 42:588-594).

Specific heterozygous GJB2 mutations have also been described in patients with idiopathic autosomal dominant hearing loss and rare cases of hearing loss associated with skin phenotypes: (Keratoderma ichthyosis and deafness syndrome (KID), Vohwinkel syndrome, and palmoplantar keratoderma (PPK) and deafness.

Referrals

- Patients with hearing loss for mutation screening of connexin 26
- Patients with hearing loss and a relevant skin phenotype for mutation screening of connexin 26.
- Adult relatives of patients with connexin 26 mutations for carrier status.

Service offered

Mutation screening of connexin 26 coding exon 2. Analysis for the 309kb deletion (GJB6-D13S1830) and 232kb deletion (GJB6-D13S1854), connexin 26 intron 1 splice donor site mutation (c.-23+1G>A) and splice acceptor site mutation (c.1-24A>C). Detection of known mutations in relatives of patients with confirmed connexin 26 mutations.

Technical

Direct sequencing analysis of connexin 26 exon 2 which covers the 681bp coding region and the c.-24A>C splice acceptor site mutation. Size separation assay for the 309kb and 232kb deletions and restriction digest assay for the c.-23+1G>A splice donor site mutation.

Target reporting time

Routine mutation screen in index case takes 8 weeks.
Routine testing of specific mutations takes 2 weeks.
Please contact the laboratory for urgent cases.