Bristol Genetics Laboratory

North Bristol NHS Trust

Non-Syndromic Sensorineural Hearing Loss (DFNB1) analysis

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Sample Required
Adult: 5mls blood in EDTA
Paediatric: at least 1ml EDTA (preferably >2ml)

Samples should be accompanied by a FULLY completed request form available to download at www.nbt.nhs.uk/genetics or from the laboratory.

Please include details of test, family history, address and POSTCODE, NHS number, referring clinician and unit/hospital.

Consent and DNA Storage
All genetic testing requires consent. It is the responsibility of the referring clinician to ensure that appropriate consent has been obtained.

DNA is stored from **all** patients unless consent for this is specifically denied.

Stored samples may be used for quality assurance purposes and may be used anonymously for the development of new tests for the disorder in question.

Clinical Background and Genetics

- Non-syndromic sensorineural hearing loss (NSHL) is a common disorder affecting approximately 1 in 1000 newborns. In approximately 50% of children with congenital deafness the hearing loss is due to inherited causes.
- The most common form of inherited hearing loss is autosomal recessive non-syndromic hearing loss (AR-NSHL), which affects approximately 1 in every 2500 children. The autosomal recessive forms are generally more severe and are almost exclusively due to cochlear defects (sensorineural deafness).
- Although highly heterogenous, the most common locus described for AR-NSHL is *DFNB1* (OMIM#220290) on chromosome 13 (13q11-q12) containing the *GJB2* and *GJB6* genes.
- The *GJB2* gene (OMIM121011) encodes a gap junction protein called connexin 26, which is important in the development of the inner ear. Mutations in the in the *GJB2* gene have been implicated in >50% of AR-NSHL cases, making this the most common cause of AR-NSHL. The c.35delG *GJB2* mutation is the most common mutation in the Caucasian population.
- A second gap junction protein, connexin 30 encoded by the *GJB6* gene (OMIM604418), can also cause AR-NSHL. Two deletions involving *GJB6* have been described in association with DFNB1 AR-NSHL. The del*GJB6*-D13S1830 deletion has been reported to cause AR-NSHL in approximately 30% of patients who also have one *GJB2* gene mutation in the UK. The del*GJB6*-D13S1854 deletion is also reported to cause AR-NSHL in approximately 22% of UK patients who have one *GJB2* gene mutation.
- A database of *DFNB1* mutations plus other relevant information for professionals can be found at http://davinci.crg.es/deafness/index.php

Quality

BGL participates in the external quality assurance EMQN sequencing QA scheme for Hereditary Deafness.

Referrals

- **Diagnostic Testing**: The *GJB2* gene is analysed by Sanger sequencing of the coding exon 2 plus the splice site mutation c.-23+1G>A in intron 1. Touchdown PCR analysis is undertaken to detect the *GJB6*-D13S1830 and *GJB6*-D13S1854 deletions. This screen has a sensitivity of approximately 99%.

  Referrals are accepted nationally from all clinicians from patients clinically suspected of being affected with non-syndromic hearing loss.
- **Carrier Testing:** Testing of parental samples is recommended once the mutations have been identified in the affected patient.
- **Cascade testing** for familial mutations in *GJB2* or *GJB6* can be undertaken on close adult relatives.
- **Prenatal Testing**: Prenatal diagnosis is not routinely offered; please contact the laboratory for discussion on a case-by-case basis.

Target Reporting Time

Diagnostic screen of *GJB2* & *GJB6*:	56 days
Known Mutation:	14 days
Urgent:	3 days

For up-to-date prices please contact the laboratory

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