香港中文大學　婦產科學系

Department of Obstetrics and Gynaecology
The Chinese University of Hong Kong

# Genetic Testing for Hearing Impairment
# 遺傳性聽力障礙基因檢測

## 什麼是遺傳性聽力障礙？

研究統計約每五百個新生兒當中，就有一個患有聽力障礙，是新生兒出生缺陷最常見的原因之一。在中國，聽力語言殘疾患者超過2700萬，其中超過60%是由遺傳因素引起的，這些稱之為遺傳性聽力障礙。導致遺傳性聽力障礙的基因突變類型繁多，而其中以*GJB2*, *SLC26A4*基因及線粒體DNA的突變最為常見，其他類型比例較少。

香港中文大學婦產科現在提供SNaPshot®遺傳性聽力障礙基因檢測。 SNaPshot®是一種快速有效的基因檢測技術，對*GJB2*, *SLC26A4*基因編碼區及線粒體DNA中14個常見已知的突變位點進行一次性檢測（表1, 背面）。

通過聽力障礙基因檢測能及早發現患者攜帶的導致聽力障礙的基因突變，確定其遺傳方式，便能夠及早提供干預及治療建議，預估疾病風險。結果能對患者家庭成員的攜帶者風險及子代的遺傳風險作出準確評估（圖1）。

## 如果我被診斷為聽力障礙基因的攜帶者怎麼辦？

耳聾基因突變的攜帶者一般不會表現聽力障礙， 但是存在將該突變等位基因遺傳給後代的風險，及其他健康問題，應進行遺傳諮詢（圖1）。我科可提供相關遺傳諮詢和產前診斷等服務。

## 檢測方法

血液、唾液或組織樣本將會用來提取基因組DNA。利用SNaPshot®技術，針對*GJB2*基因, *SLC26A4*基因及線粒體DNA上共14個突變位點進行多重PCR(*Chen et al.2015*)。利用單鹼基螢光延伸標記測試樣本，再採用毛細管電泳分析儀器進行基因分型。其檢測效能高，檢測的特異性和敏感性均>99%。

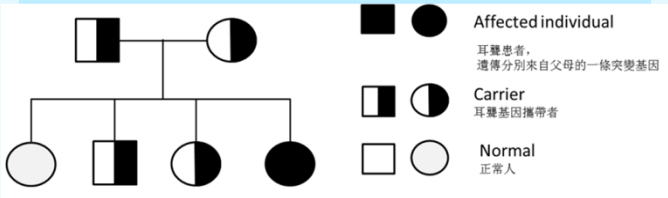


**Figure 1: Carriers are at risk of transmitting the defected gene to their offspring**
**圖1:耳聾基因的攜帶者存在將突變基因遺傳給後代的風險**

## 誰應該做遺傳性聽力障礙基因檢測？

- 新生兒聽力篩查陽性者
- 患有聽力損失，但原因未明的患者（已排除感染外傷等因素，任何年紀均可）
- 耳聾家庭的聽力正常家庭成員希望檢測自身是否為突變攜帶者（先證者致病突變已明確， 涵蓋與該檢測的十四個突變之內）

## 用於做攜帶者篩查的樣本及報告

**所需樣本：**從血液、唾液或組織中提取的DNA均可做該篩查。

**報告：7**個工作天內可取

**Enquiries 查詢電話及電郵：**

**(852) 2632 6412 (general enquiries 一般查詢)**

**(852) 2636 0008 (appointments 預約診症)**

**obsgyn@cuhk.edu.hk**

**For more details, please refer to your clinician or visit our website 如欲知道更多資料，可向您的專科醫生查詢，或請瀏覽我們的網頁:**

**http://www.fetalmedicine.hk/en/mainmenu.asp**

Last updated on 31.07.2015

## What is hearing impairment?

Hearing impairment is one of the most common birth defects worldwide with the incidence of 1 in 500. In China, it has been estimated that over 27 million people are with hearing and speech disabilities. Of which more than 60% of these hearing impairment is caused by genetic factors. The most frequent mutations in non-syndromic hearing loss patients occur in *GJB2*, *SLC26A4* and mitochondrial genome. Department of Obstetrics and Gynaecology, The Chinese University of Hong Kong offers hearing loss SNaPshot® genetic testing for screening of hearing impairment. This test is a robust and efficient test that targets 14 common mutations on *GJB2*, *SLC26A4* and mitochondrial DNA that are known to cause hearing loss, with carrier rate up to one in 6.3 babies(Table 1) .

Early diagnosis of hearing impairment would clarify the etiology, which aid early and effective interventions and treatment and make accurate risk assessment of other family members (Figure 1,back ).

**REGISTRATION FORM 預約表格 (Fill in block letters)**

**Name**
**姓名**

**HK ID Number**
**香港身分證號碼**

**Telephone Number & Contact Email**
**聯絡電話 及 電郵**

**Referring Doctor**
**轉介醫生**

**Reason of Referring**
**轉介原因**

## What can I do if I diagnosed as carrier?

Carriers of hearing loss mutations normally would not present hearing loss, but are at risk of transmitting the defected gene to their offspring, and having other health problems. Considering these, genetic counseling for carriers should be warranted. Genetic counseling and prenatal diagnostic services are now available in our department.

## Who should consider hearing impairment genetic testing?

- Universal Neonatal Hearing Screening positive
- Nonsyndromic hearing loss patients with unknown causes, excluding traumatic or infection reasons
- Normal individuals with family history of hearing impairment caused by these 14 mutations

## Specimen Requirement & Reporting

This screening test involves the testing of DNA sample. It could be isolated from blood, saliva or other tissues.

**Reporting time**: seven working days

## Methodology

DNA will be extracted from blood, saliva or other tissues. In the hearing loss SNaPshot® Multiplex system, 14 common hearing loss mutations of *GJB2*, *SLC26A4* and mitochondrial DNA will be detected *(Chen et al.2015*). After multiplex PCR, the product will be followed by the sequence-specific probe interrogation and labeling of targeted DNA fragment. The resulting products will be separated electrophoretically in capillary Genetic Analyzer ABI 3130 for genotype of each mutation. The specificity and sensitivity of the SNaPshot® technology have been proven to be >99%.

**Table 1: Carrier frequency of 14 common hearing loss mutations**
**表1: 14個常見的遺傳性耳聾攜帶機率**

| Mutations 突變位點 | Genomic Coordinate 基因組坐標(GRCh38) | Carrier frequency 攜帶頻率 |
|---|---|---|
| *GJB2* c.35delG | Chr13:20189547 | 0.02% |
| *GJB2* c.109G>A | Chr13:20189473 | 10.29% |
| *GJB2* c.176-191del16bp GCTGCAAGAACGTGTG | chr13:20189391-20189406 | 0.19% |
| *GJB2* c.235delC | Chr13:20189347 | 1.88% |
| *GJB2* c.299-300delAT | Chr13:20189282 - 20189283 | 0.29% |
| *SLC26A4* c.919-2A>G | Chr7:107683453 | 1.62% |
| *SLC26A4* c.1174A>T | chr7:107690148 | 0.16% |
| *SLC26A4* c.1229C>T | Chr7:107690203 | 0.02% |
| *SLC26A4* c.2027T>A | Chr7:107702050 | 0.03% |
| *SLC26A4* c.2168A>G | Chr7:107710132 | 0.35% |
| mt1494C>T | ChrMT:1494 | 0.02% |
| mt1555A>G | ChrMT:1555 | 0.14% |
| mt3243A>G | ChrMT:3243 | 0.16% |
| mt-7444G>A | ChrMT:7444 | 0.71% |
| Total | | 15.90% |

**Reference 參考資料:**

Chen et al. SNaPshot reveals high mutation and carrier frequencies of 15 common hearing loss mutants in a Chinese newborn cohort. Clin Genet. 2015 87(5): 467-72. [PMID:24989646]