INTRODUCTION

- The outcomes of cochlear implantation (CI) vary and the selection of the appropriate subjects is important through the evaluation of prognostic factors after CI.
- With development of molecular genetics, the genetic testing has become an important component of the diagnostic work-up for hearing loss (HL) from an etiologic perspective.
- Expect successful result from CI in some cases of hereditary deafness.
  - GJB2, SLC26A4, mitochondrial mutations, OTOF, COCH, MYH9
- Next generation sequencing (NGS): Greatly influenced strategy to make a molecular genetic diagnosis of deafness.
  - Targeted resequencing (TRS) of known deafness genes (panel sequencing): number of samples, cost, time
  - New genes for non-syndromic and syndromic HL have been successfully discovered.
- Heuristic influence in mass-screening of sporadic or potentially autosomal recessive (AR) congenital severe to profound HL, a main indication of CI, has not been extensively studied yet.

Aims

- To refine our phenotype-driven candidate gene approach and combined it with a targeted NGS approach in a hierarchical manner to comprehensively understand a genetic etiologic spectrum of our cochlear implantee.
- To provide a clue to the etiology of cases that still remained unanswerd after targeted NGS approach by calculation of recurrence risk of HL.

METHODS AND MATERIALS

- 93 patients who had CI (N=236) between May 2010 and Aug. 2012 in SNUH and SNUBH, consented to molecular genetic test and went through at least one molecular genetic test
  - M: F = 54 : 39, Mean age 8.9 years (10 mo ~ 72 years)

RESULTS

- Calculation of recurrence risk of HL
  - Undiagnosed group: Families with an unknown etiology after TRS-200.
  - Control group: Probands with a definitive AR genotype.
  - Recurrence risk
    - The segregation ratio of HL among siblings of probands
    - Calculated from the remaining member of the sibship.
    - $P = \frac{r}{s}$
    - r: the number of affected offspring
    - s: the total number of offspring in each family
    - Monzygotic twin pairs were treated as a single observation in the analysis

CONCLUSIONS

1. At least 55% of hearing loss in CI candidates can be accounted for by Mendelian genetic etiology.
2. Phenotype-driven candidate gene approach alone, if appropriately applied, enables molecular genetic diagnosis in about 30% of total implantees.
3. A substantial portion of subjects who still remain undiagnosed after going through our hierarchical genetic test pipeline are likely to have other etiology than a simple Mendelian genetic etiology. This is helpful for counseling these families.