Mutations in SLC26A4 can cause both DFNB4 and Pendred syndrome. However, a certain percentage of EVA or Pendred syndrome patients carried only one or no mutation in SLC26A4. In 2007 and 2009, Yang et al. reported that digenic mutations in both SLC26A4 and either FOXI1 or KCNJ10 may cause Enlarged Vestibular Aqueducts (EVA) or Pendred syndrome. Then whether there is association between mutations of KCNJ10 or FOXI1 and SLC26A4 mutations in Pendred syndrome/EVA is concerned by many researchers worldwide.

The data in the study is sound. But the reviewer think screening FOXI1 and KCNJ10 in a number of ethic-matched normal hearing controls are necessary to support the opinion that variants found in FOXI1 and KCNJ10 in the present study are only polymorphisms but not disease causing mutations. Another thing is, for the patients carried FOXI1 or KCNJ10 variant, did the genes including SLC26A4, FOXI1 and KCNJ10 were screened in the family? Results from the pedigrees will contribute to the judgement of the pathogenity of variants.


The writing is acceptable.

The reviewer suggest Major Compulsory Revisions for the supplement of FOXI1 and KCNJ10 variant data in ethic-matched normal hearing controls and/or pedigree members.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.