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315-321 Lockhart Road,  
Wan Chai, Hong Kong, China

## ESPS Peer-review Report

**Name of Journal:** World Journal of Otorhinolaryngology

**Ms:** 1586

**Title:** SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct

**Reviewer code:** 00503663

**Science editor:** h.h.zhai@wjgnet.com

**Date sent for review:** 2012-12-22 16:43

**Date reviewed:** 2012-12-27 16:35

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS

### CONFIDENTIAL COMMENTS TO EDITOR:

This review article was sent to WJO after I, editor-in-Chief, asked professor Griffith to write it. I expected him as a first author of the review article, but he was a corresponding author. I asked professor Griffith to send photo and biography. The photo was sent to the Editorial office ? If so, who's photo?

### COMMENTS TO AUTHORS:

This is a review article regarding SLC26A4 mutation testing for hearing loss. To publish this review article in WJO, addition of several points of view is recommended. #1 Relationships between hearing loss and MRI findings. Cambell et al described that MRI findings of endolymphatic duct and sac were associated with the degree of hearing loss. Campbell, A. P., O. F. Adunka, et al. (2011). "Large Vestibular Aqueduct Syndrome: Anatomic and Functional Parameters." Laryngoscope 121(2): 352-357. #2 Air-bone gap in large vestibular aqueduct. Air-bone gap is occasionally important to suspect large vestibular aqueduct syndrome from a pure tone audiogram. Merchant, S. N. and J. J. Rosowski (2008). "Conductive hearing loss caused by third-window lesions of the inner ear." Otology & Neurotology 29(3): 282-289. I recommend description about #1 and #2 in PATHOGENESIS OF HEARING LOSS ASSOCIATED WITH EVA or in new sections adding relevant references. #3 This is a review article in FRONTIERS. Future problems or future studies should be added. For example, is a next generation sequencer useful to elucidate MO mutant EVA? If so, how ? I could not find a reference below. Cell Physiol Biochem. 2011;28(3):545-52. SLC26A4 genotypes and phenotypes associated with enlargement of the vestibular aqueduct. Ito T, Choi BY, King KA, Zalewski CK, Muskett J, Chattaraj P, Shawker T, Reynolds JC, Butman JA, Brewer CC, Wangemann P, Alper SL, Griffith AJ. Please add this in the



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Reference list and proceed so as to fit to be published in Frontiers. Delete figures already published or obtain permission from the publisher.



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## ESPS Peer-review Report

**Name of Journal:** World Journal of Otorhinolaryngology

**Ms:** 1586

**Title:** SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct

**Reviewer code:** 00503898

**Science editor:** h.h.zhai@wjgnet.com

**Date sent for review:** 2012-12-22 16:43

**Date reviewed:** 2013-02-22 22:05

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of language polishing	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	<input type="checkbox"/> Grade D: rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

## COMMENTS

### CONFIDENTIAL COMMENTS TO EDITOR:

Dear Editor, Comments to Authors - manuscript: 1586 Title: "SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct". The authors have provided an excellent and detailed review on SLC26A4 mutation in enlargement of the vestibular aqueduct.

### COMMENTS TO AUTHORS:

Dear Editor, Comments to Authors - manuscript: 1586 Title: "SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct". The authors have provided an excellent and detailed review on SLC26A4 mutation in enlargement of the vestibular aqueduct.

**ESPS Peer-review Report**

**Name of Journal:** World Journal of Otorhinolaryngology

**Ms:** 1586

**Title:** SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct

**Reviewer code:** 00503805

**Science editor:** h.h.zhai@wjgnet.com

**Date sent for review:** 2012-12-22 16:43

**Date reviewed:** 2013-03-05 00:13

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ Y] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ] Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

**COMMENTS**

**CONFIDENTIAL COMMENTS TO EDITOR:**

The review entitled “SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct” by Ito, et al. is a very well written synopsis of the current understanding of pathologies associated with enlarged vestibular aqueducts. The authors provide a useful historical perspective in several instances, give information suggesting directions for the search for additional mutations and clearly point out the values and limitations of genetic testing. My recommendation is publication after minor revision attending to the comments listed below.

**COMMENTS TO AUTHORS:**

The review entitled “SLC26A4 mutation testing for hearing loss associated with enlargement of the vestibular aqueduct” by Ito, et al. is a very well written synopsis of the current understanding of pathologies associated with enlarged vestibular aqueducts. The authors provide a useful historical perspective in several instances, give information suggesting directions for the search for additional mutations and clearly point out the values and limitations of genetic testing. My recommendation is publication after minor revision attending to the comments listed below. **ABSTRACT 1.** Abstract: The introduction of the the terms M2, M1 and M0 is confusing. The presence of zero mutant alleles implies all normal alleles and no mutant phenotype, yet the M0 phenotype stated is still has hearing loss and aqueduct enlargement. Are the authors saying that mutations of SLC26A4 account for some but not all of the symptoms of Pendred syndrome? And that no mutant alleles of the solute carrier gene have been found for patients in the M0 group? **2.** To say something does not have an independent effect is also confusing. What is the purpose of the word “independent” ? Is there an effect or not? **PENDRED SYNDROME (PS) AND NONSYNDROMIC EVA (NSEVA) 3.** Figure 1: The panel



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with normal anatomy shows a cochlea with about two and a half turns which agrees with the literature. The lower left panel showing the EVA and enlarged endolymphatic sac also depicts an enlargement of the scala media, but the number of turns changed from two and a half to one and a half. CORRELATION OF SLC26A4 GENOTYPE WITH THYROID PHENOTYPE 4. The words “or both” seems out of place in the sentence beginning “Goiter, an abnormal ...” 5. In the sentence beginning “Furthermore...”, consider using the words “...early adulthood...” 6. As in the abstract, the introduction of the M0 group of patients is awkward. CORRELATION OF SLC26A4 GENOTYPE WITH AUDITORY PHENOTYPE 7. The sentence “This developmental arrest model was refined by Sennaroglu [39].” leaves the reader hanging. The text would be improved by telling how it was refined. 8. Figure 2: It is not clear what feature of the images the arrows are pointing to. 9. As in points 1 and 6, the correlation of unilateral EVA with zero mutations of the solute carrier gene is awkward. PATHOGENESIS OF HEARING LOSS ASSOCIATED WITH EVA 10. The second paragraph in this section introduces the Foxi1 null mouse. It would be helpful to the reader to state here that FOXI1 is a transcription factor for SLC26A4 citing Yang et al [69].