

Dear Prof. Ma and dear reviewers,

Re: Manuscript ID:61508 and Title: **Hb Fukuoka caused unexpected HbA<sub>1c</sub> results: A case report.**

Thank you for your letter and the reviewers' comment concerning our manuscript entitled "**Hb Fukuoka caused unexpected HbA<sub>1c</sub> results: A case report**"(ID:61508).Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have read the comments carefully and have made correction which we hope to get your approval. The revised part will be shown below, and the revised article will be re-uploaded. The main corrections in the paper and the responds to the reviewers' comments are as follows:

Responds to the reviewers' comments:

Reviewer#1:

1. Responds to comments: page 5, line 2: the b2 gene should be as b-globin gene, what is the codon on b-globin gene that the C>T was identified.

Responds: The mutation site was on the 7<sup>th</sup>ammino acid, C>T. The codon on b-globin gene that the C>T was identified as CAC>TAC. "the β2 gene possessed a histidine >tyrosine (C >T) mutation" was changed to "the β-globin gene possessed a histidine > tyrosine (CAC >TAC)"(Page 6, line 2).

2. Responds to comments: Figure 3, the arrow presented in HA-8160 indicate? please provide information

Responds: The arrow in figure of HA-8160 program indicate that the HbA<sub>1c</sub> peak did not appear, and there was an abnormal protruding peak on the left of peak A<sub>0</sub>. We have marked the position of the arrow to the peak of the abnormal protrusion, and added a note on the legend note.

**Before the change**

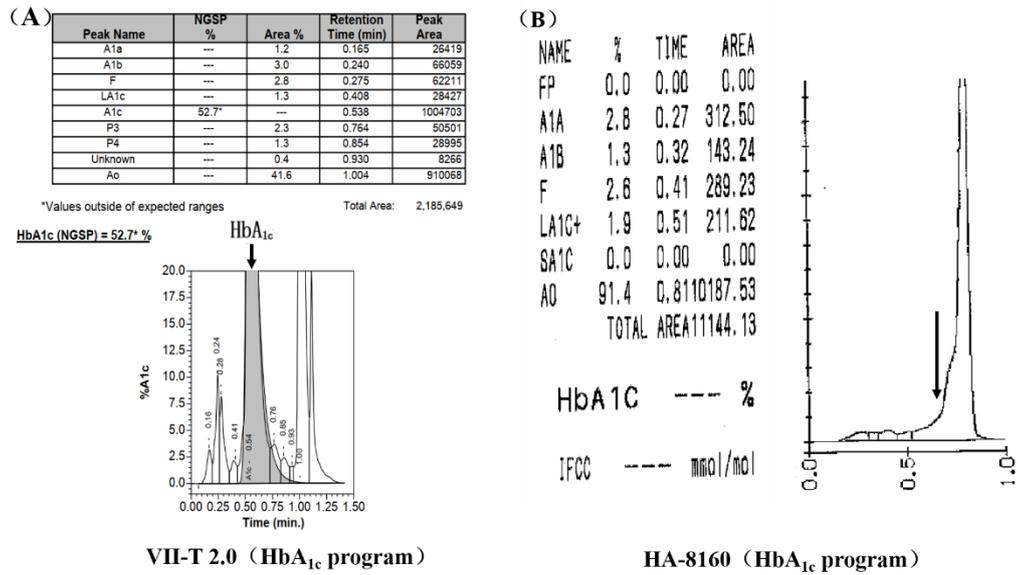


Figure1. The detection of HbA<sub>1c</sub> by a Variant II Turbo 2.0 system(A) and an Arkray HA-8160 system(B).

After the change

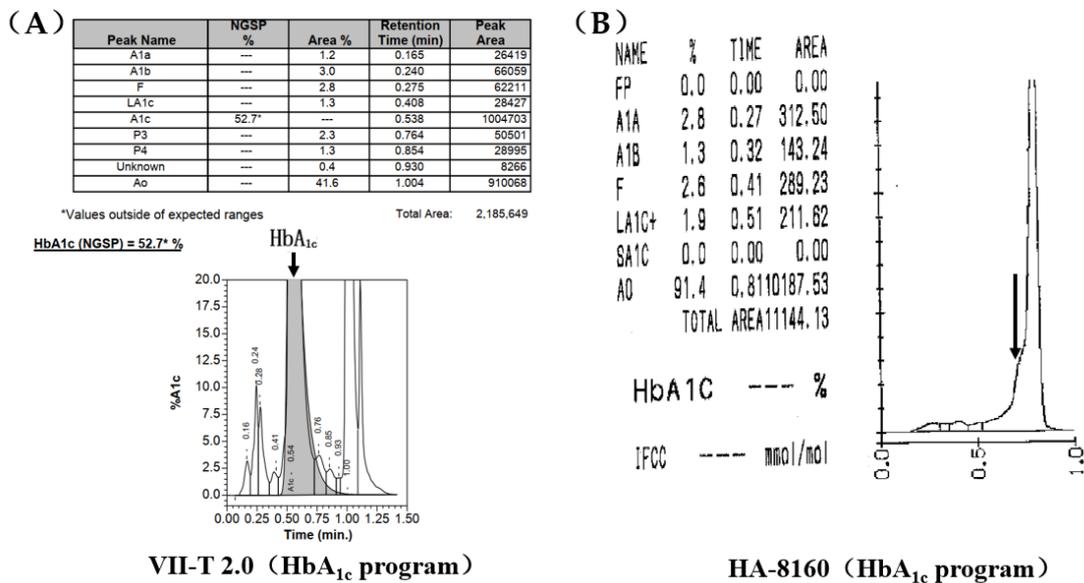


Figure1. The detection of HbA<sub>1c</sub> by a Variant II Turbo 2.0 system(A) and an Arkray HA-8160 system(B). A: The peak of HbA<sub>1c</sub> was abnormally elevated (black arrow). B: The HbA<sub>1c</sub> peak did not appear, and there was an abnormal protruding peak on the left of peak A<sub>0</sub> (black arrow).

3. Responds to comments: Please specifies the HGVS name of Hb Fukuoka in the text.

Responds: The HGVS name of Hb Fukuoka is *HBB:c.7C>T*. We add the HGVS

name to the page6 line 5, and “Hb Fukuoka” was changed to “Hb Fukuoka (HBB:c.7C>T)”.

4. When revising the manuscript, we found that the description of result of the Arkray HA-8160 system in the part of “*Further investigations for hemoglobin variants*” was not very appropriate, we have modified as follows :“The Arkray HA-8160 system returned no result; the instrument reported that A<sub>1c</sub> and A<sub>0</sub> could not be distinguished, although A<sub>0</sub> appeared earlier (Figure1(B))” was changed to “The Arkray HA-8160 system returned no result; the instrument showed that the HbA<sub>1c</sub> peak did not appear, and there was an abnormal protruding peak on the left of peak A<sub>0</sub>. (Figure1(B)).”(Page5, line 15-18).

The above is our reply to the reviewer’s comments.

Special thanks for your comments.

Sincerely,

Xue-Ping Lin