

In the “Materials and methods” section, the authors declare the use of the *CYP21A2* nucleotides numbering according to Higashi et al [3]. This reference, like the one we used (M13936), reports at –9 position of *CYP21A2* intron 9 a “C” as wild-type base.

For this reason, the mutation described by Katsumata et al should be identified as IVS-9C>A and not as IVS-9A>C. In fact, the wild-type sequencing of the last nucleotides of intron 9 is accgcccgc**ag** AT CGC TTC... (the original acceptor site splicing is in boldface); and the substitution of –9 “c” with an “a” can create a new “ag” acceptor splice site (underlined bases): accagcccgc**ag** AT CGC TTC....

Finally, we concord with the authors regarding the importance of reporting the discovery of novel *CYP21A2* mutations and performing their functional in vitro characterization. This can help to predict the correlation genotype/phenotype and may offer an appropriate genetic and prenatal counseling.

In addition, we want to underline the necessity to update the actual *CYP21A2* mutations databases [4] (unfortunately, the last update of the most accurate database, <http://www.imm.Ki.se/CYPalleles/cyp21.htm>, dates back to 2006.) and to correctly report the newly identified mutations, always indicating the sequencing reference number used (*CYP21A2* being a widely polymorphic gene, many errors can occur).

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References

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Reply: IVS9-9C>A, not IVS9-9A>C, mutation in *CYP21A2* causes classic salt-wasting steroid 21-hydroxylase deficiency

To the Editor:

We thank Dr Concolino et al for their interest and comments regarding our recent publication on a *CYP21A2* mutation in *Metabolism* [1]. Just after online publication of this article, Dr Gonçalves (Centro de Genética Humana, Instituto Nacional de Saúde Dr Ricardo Jorge, Lisboa, Portugal) kindly pointed out our error in designating the mutation. As seen in Fig. 1A, the patient has a homozygous A at the IVS9-9 position [1]; thus, the mutation should have been designated IVS9-9C>A, not IVS9-9A>C. We already asked the Editor to add an “Erratum” section to correct the designation error, which has come out in the latest version of the article [1]. As discussed by Dr Concolino et al and demonstrated by our in vitro expression study [1], the IVS9-9C>A, not IVS9-9A>C, mutation creates a novel splice acceptor site and results in classic salt-wasting steroid 21-hydroxylase deficiency.

We concur with Dr Concolino et al in the necessity to update the *CYP21A2* databases and to discuss *CYP21A2* mutations always with the sequence references because the *CYP21A2* gene is highly polymorphic. We also emphasize the necessity to report new *CYP21A2* mutations with their functional consequences.

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Reference

- [1] Katsumata N, Shinagawa T, Horikawa R, Fujikura K. Novel intronic *CYP21A2* mutation in a Japanese patient with classic salt-wasting steroid 21-hydroxylase deficiency. *Metabolism* 2010 [Epub ahead of print].