**Author's response to reviews**

**Title:** XLMR in MRX families 29, 32, 33 and 38 results from the dup24 mutation in the ARX (Aristaless related homeobox) gene

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February 25, 2005

Dear Editor:

I am posting a revised version of our manuscript [MS 1114946187526415 - "XLMR in MRX families 29, 32, 33 and 38 results from the dup24 mutation in the ARX (Aristaless related homeobox) gene," by Stepp et al]. We have addressed the concerns of Reviewer 1 (PC) as follows:

1. We toned down the strong statement in the Abstract by eliminating the reference to "73% of nonsyndromic families..." and used "most common" instead. However, in the Discussion section, we have maintained this phrase since we refer to a figure at the website that listed all published linked families not just those studied by us for this paper. The same is true for our statement regarding linked syndromic XLMR families. Furthermore the Discussion does contain a caveat that although many linked families have an ARX mutation, especially the 24dup, expanded studies of males with MR have failed to detect mutations at this high level. Thus, we provide some explanation for this "disconnect" as we call it.

2. We understand the point the reviewer makes about "specific" and "nonspecific" versus "syndromic" and "nonsyndromic". However, the latter we feel is more appropriate as syndromic has long been defined as the presence of some somatic alteration, neurological or metabolic finding which can clearly and quickly distinguishes an affected male from his normal male sibling. The opposite of "syndromic" would be "nonsyndromic". Thus, we have left this wording in the paper. Nonetheless, we certainly recognize that a nonsyndromic family can become a syndromic family if an abnormality, such as a metabolic defect, is later identified.

3. We have made the correction asked for: MRX54 has replaced MRX56. We have also altered the references and added references as suggested.

We hope that these changes adequately address the concerns of Reviewer 1 (Reviewer 2 expressed no concerns) and that you deem the revised paper acceptable for publication.

Sincerely,

Charles E. Schwartz, Ph. D  
Director, JC Self Research Institute  
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CES/jwd