LETTER TO THE EDITOR

Reply to Benito-Sanz et al.

To the Editor: We applaud the thorough characterization by Benito-Sanz et al. (in this issue)[1] of deletions encompassing the *SHOX* gene (MIM 312865) in patients with Léri-Weill dyschondrosteosis (MIM 127300). Benito-Sanz et al. suggest a founder effect to explain the apparent recombination hotspot we observed among our probands with *SHOX* deletions.[2] Indeed, four of our five probands who shared both 5′ and 3′ breakpoints were Hispanic. However, the same 3′ breakpoint was present in four non-Hispanic white probands, only one of whom had the common 5′ breakpoint. Additional studies will be required to determine whether the common *SHOX* deletion we observed was recurrent or arose only once. Benito-Sanz et al.[1] also propose that diagnosis of *SHOX* disorders should include testing for deletion of downstream Xp-Yp pseudoautosomal region 1 (PAR1) markers. It will be important to determine whether any of the SNP or microsatellite markers used in their study show deletion polymorphisms among unaffected individuals, since such variations could cause false-positive results in clinical testing. We agree with the statement by Benito-Sanz et al. that Xp deletions extending beyond PAR1 have important genetic counseling implications. Of the 49 deletions they mapped, 5 or 6 were large enough to be visible cytogenetically; our results were similar, but we excluded such deletions from our study. We suggest a low threshold for karyotyping patients with *SHOX* deletions, which may result not only from simple deletions but also from complex chromosomal rearrangements, such as unbalanced translocations or isodicentric chromosomes.[3,4]

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Web Resource

The URL for data presented herein is as follows:

Online Mendelian Inheritance in Man (OMIM), http://www.ncbi.nlm.nih.gov/Omim/ (for Léri-Weill dyschondrosteosis and *SHOX*)

References

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