IRF6 mutations may not be a major cause of Van der Woude syndrome in India

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We read with interest the article by GB Ferrero et al. on Van der Woude syndrome (VWS) reporting a novel mutation [2] in the *IRF6* gene coding region. Nearly 100 mutations in the coding region of the gene have been reported from several populations in different geographical regions of the globe. So far, *IRF6* is the only gene shown to be associated with VWS as a dominant trait with variable penetrance and expressivity. However, direct sequencing of all coding regions and exon–intron boundaries of the *IRF6* gene have not shown any mutation in an Indian cohort ($n=13$) [1]. Another Indian study of a VWS pedigree conducted by the authors also corroborates the findings that critical region of the 1q32–q41 may not be causal for VWS in multi-ethnic and diverse Indian populations [3]. As VWS is the most common form of syndromic clefting, the possibility of stochastic factors modifying the expression of the syndrome cannot be denied. However, the tendency towards a publication bias and the “file drawer effect” may sometimes result in inadequate outcome reporting. Published studies may not be truly representative of all valid studies undertaken, and this bias may distort meta-analyses and systematic reviews of large numbers of studies—on which evidence-based medicine increasingly relies. This further compounds the genetic complexity of the one of the most common orofacial clefting syndromes, which needs to be

studied in greater depth before any conclusion can be drawn. Therefore the authors are of the opinion that it is too premature to use only *IRF6* mutations as diagnostic/predictive tests which are being offered by some companies with vested interests.

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