Correspondence

Whole-Genome Array Comparative Genome Hybridization

The Preferred Diagnostic Choice in Postnatal Clinical Cytogenetics

In the November issue of *The Journal of Molecular Diagnostics*, we published a Commentary to a Review by Drs. Bejjani and Shaffer regarding the use of genomic microarrays in diagnosis.^{1,2} We appreciated the open discussion and felt it would be appropriate to respond to the section that Drs. Bejjani and Shaffer wrote in response to our Commentary.³ The primary difference between our approach and that of Drs. Bejjani and Shaffer concerns the type of microarray to use. They opt for a small genomic microarray targeting chromosomal regions of known clinical significance, whereas we have implemented whole-genome copy-number profiling in the diagnostic screening of patients with unexplained mental retardation and/or congenital abnormalities. In their response, it is argued that the differences are chronological rather than conceptual. We can only agree with this; however, we feel that their arguments should also be seen within the context of their commercial setting. In comparison with a targeted array, the whole-genome approach is more expensive and requires more laboratory expertise, and the molecular and clinical interpretation is more complex and time-consuming. These notions, however, do not argue against a whole-genome approach; they just point out that this approach is difficult to implement in a commercial setting without direct access to patients and their families. Aided by proper clinical interpretation, counseling, and parental analyses, completely normal procedures in routine cytogenetics, the application of whole-genome arrays will result in a significantly higher diagnostic yield compared with targeted arrays. This yield is likely to increase even further with the recent availability of ultra-high density genome-wide oligonucleotide-based microarrays, which will soon allow the detection of all genomic copy number variations larger than 1 to 10 kb in the human genome. Drs. Bejjani

and Shaffer state that “diagnostic laboratories should always remain at least one step behind the cutting edge of research.”³ In contrast, it is our strong conviction that research technologies should be implemented in diagnostics as soon as they have demonstrated their added value, thus providing the best patient care available. In the early 1970s, implementation of chromosome banding techniques in clinical medicine dramatically enhanced the diagnostic yield for many disorders.^{4,5} Also through this technology, observations with unknown clinical relevance were initially made, ie, differences in the length of chromosome bands, small marker chromosomes, and inversion chromosomes. This did not keep the medical world from implementing banding techniques then, nor should it do so now for the microarray-based whole-genome approach.

Joris A. Veltman
Bert B.A. de Vries

*Radboud University Nijmegen Medical Centre
Nijmegen, The Netherlands*

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