Correspondence

Targeted versus Whole-Genome Array Comparative Genome Hybridization

The Atlantic Divide

To the Editor-in-Chief:

It has been only 30 years since the first clinical molecular diagnostic was performed.¹ In the interim, we have seen many different technologies at the forefront of molecular diagnostics, ranging from linkage analysis using Southern-based, two-allele single nucleotide polymorphisms in the 1980s to the current myriad applications of the polymerase chain reaction. We are amazed and impressed by the clinical utility of comparative genome hybridization (CGH) as described in the recent reviews and associated commentary,^{2–5} and we wish to comment on the impact of the health care system on the choice of clinical array.

We are clinical laboratory directors working in two very different environments, one in Europe (D.B.) and the other in the United States (J.A.W.). In our opinion, the advantage of targeted versus whole-genome CGH arrays is embedded in the economic and regulatory differences between the health care systems in Europe and the United States.

Although each country in Europe has its own independent health care system, we can generally state that each system is publicly funded, either directly as in the United Kingdom and Ireland or by social insurance payments in most other countries. Moreover, European genetic services, for the most part, are delivered through medical genetics centers that serve the local or regional population, incorporating clinical genetics, cytogenetics, and molecular genetics services. Thus, the laboratory director in Europe has the combined and coordinated testing facilities, regulatory and economic flexibility, as well as the relative lack of patient-specific economic constraints, to order and perform a cascade of assays, each reflexed from the previous result.⁶ It makes sense that a European laboratory director, as a decision-maker, can first choose to perform subtelomeric screening or other relevant screening assays before whole-genome CGH.

In the United States, laboratories are regulated by Clinical Laboratory Improvement Amendments and operate largely within a private insurance system. Unlike their European counterparts, U.S. laboratory directors act as clinical consultants to the ordering physician and function far less as decision makers. Array-based CGH is performed in only a few U.S. laboratories; thus, this assay is separated spatially and temporally from routine chromo-

some analysis and other related testing for the patient. The U.S. physician ordering CGH, often an M.D. from a major children's hospital (B. Bejjani, personal communication), drives the choice and timing of testing orders and coordinates the integrated interpretation of tests. In the interest of time to diagnose, it makes sense that a U.S. physician would order a targeted array, rather than a cascade of arrays or specific fluorescence in situ hybridization assays, based on ease of interpretation and clinical sensitivity.

Drs. Bejjani and Shaffer state in their commentary that the difference between the U.S. and European outlook "may reflect an historic, regulatory, and perhaps cultural difference in the adoption of new medical technologies and newly developed drugs between Europe and the United States."⁵ Although it is certain that other factors also contribute to the choice of array type, we find it interesting to speculate that the prevailing health care system may have a profound effect on the decisions made by laboratory directors when developing novel assays.

Jean Amos Wilson

Focus Diagnostics Inc.
Cypress, California

David Barton

National Centre for Medical Genetics,
Our Lady's Children's Hospital
Dublin, Ireland

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