Molecular diagnostic testing

To the Editor: I read with interest the article by Xue et al. in the June 2015 issue of *Genetics in Medicine*.[1] I am concerned about an omission in the molecular genetic testing algorithm (Figure 1 in the article).

The authors mention performing chromosomal microarray testing and fragile X testing in cases of autism and intellectual disability before proceeding to exome sequencing. Fragile X testing is not shown in the algorithm for testing—this is a significant omission. Because algorithms are often used after articles have been published and have a life of their own in the hands of clinicians and third-party payers, I would ask that the algorithm be amended to correct this error. I further submit that autism and intellectual disability should not be "coupled" as a precondition for this testing. Microarray testing and fragile X analysis are appropriate in the presence of autism *or* intellectual disability. Intellectual disability is difficult to diagnose early in life, so significant (global) developmental delay should be used as a standard for this genetic testing in the pediatric population.[2]

DISCLOSURE

The author declares no conflict of interest.

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2. Moeschler JB, Shevell M; Committee on Genetics. Comprehensive evaluation of the child with intellectual disability or global developmental delays. *Pediatrics* 2014;134:e903–e918.

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Response to Saul

To the Editor: We understand the concern raised by Dr Saul[1] that a fragile X analysis is not included along with a microarray in the testing algorithm for the categories of "multiple nonspecific concerns," "autism and intellectual disability," and "no gene panel available" (Figure 1) of our recent publication.[2] The algorithm refers to clinical problems in addition to intellectual disability and autism. Fragile X testing is discussed twice in the text as first-tier molecular testing for autism and intellectual disability. Furthermore, in Figure 1, suspicion of a triplet-repeat disorder (such as fragile X) should prompt a triplet-repeat analysis. Our article was intended to inform clinicians on how to select from among the often confusing variety of available molecular testing options. The algorithm is not presented as a formal guideline. Other papers, including a guideline from the American College of Medical Genetics and Genomics, are more comprehensive and appropriate for specific clinic problems such as intellectual disability and autism.[3,4]

DISCLOSURE

Y.X., A.A., and M.R.H. work for a nonprofit diagnostic laboratory. W.R.W. declares no conflict of interest.

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