

Molecular diagnosis of fragile X syndrome: An exploration of current practices and future directions

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Molecular diagnosis for fragile X syndrome (FXS) and *FMR1* related disorders is generally performed with a combination of PCR and Southern blot. New testing methods that have become available in recent years can now detect larger expansions and methylation status, previously only identifiable via Southern blot. These newer methods lack some of the disadvantages of Southern blot including the necessity for a large amount of DNA, laborious protocol, and a longer turn-around-time.

With the increasing availability of these methods we aimed to explore which methodologies were currently being utilized in laboratories and to discover if there is a transition in the field away from Southern blot. To do this, lab directors and managers from genetic testing laboratories in the United States and Canada were invited to participate in an online survey. The survey assessed what methods each lab had recently used, or were currently using, their satisfaction with those methods, and their opinions on transitioning.

Twenty-three individuals responded to our survey, 21 from academic and two from commercial laboratories. We found that 65.2% of the respondents primarily utilized Southern blot, 26.0% used a kit and the remaining 8.6% utilized another method. Overall satisfaction was highest with the kits, followed by the other methods, and those using Southern blot reported the lowest satisfaction. Labs currently employing Southern blot cited the prohibitive expense of purchasing new equipment, and the current ability to determine methylation status as reasons not to transition. Users of other methods weighed the benefits of reduced turn-around-time with cost and the inability, in some cases, to determine methylation status. The majority of labs using alternative methods reported transitioning to those methods in the past two years and being very satisfied with them. Future research may discover if an increasing trend towards the use of alternative methods develops.