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Implementation of DNA Technology

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The implementation of DNA technology for the support of newborn screening or any other large, population-based programs will require two key components: improved automation to reduce the personnel expenses for critical but repetitive and tedious technical tasks and individuals who can relate to both the laboratory and the clinical setting.

There are a number of technical aspects of molecular genetics which are amenable to automation. Equipment exists at present for routine extraction of DNA from liquid blood specimens. This equipment would need to be scaled down to meet the requirements for microextraction of the dried blood specimens used in newborn screening. Our group has shown that microextracted DNA from these dried blood specimens can be used for automated direct sequencing of the A, S, and C alleles of β-globin after polymerase chain reaction (PCR) amplification[1]. This approach would be useful for detection of several allelic point mutations with a defined genomic region. Undoubtedly it will become more feasible economically as the cost of automated sequencing decreases in the course of the Human Genome Initiative, and if dedicated diagnostic instrumentation is developed. Chehab and Kan have demonstrated an elegant diagnostic approach for the A and S alleles, utilizing competitive oligonucleotide priming (COP) and allele-specific primers labeled with two different fluorescent dyes[2]. The products could be analyzed by an automated sequencer of the single-lane, laser-based type or by similar automated gel-scanning equipment which is currently under development for gel analysis of PCR products. This latter equipment could also be utilized for detection of alleles using a variety of PCR-based methods targeting point mutations, insertions, and deletions, e.g., direct digestion[3], heteroduplex formation[4], and multiplex PCR[5]. Robotic applications for laboratory automation are also being designed[7].

The second important component which will foster broad implementation of this technology will be people who will function at the clinic-laboratory interface and will be able to serve as facilitators and interpreters. With knowledge of both the clinical and laboratory areas, these individuals will assure that appropriate specimens are received by the laboratory and they will be able to interpret the results from the DNA laboratory for the primary health care providers and the families. If this technology is to be accepted, information must be given to the providers and the families in a manner that is meaningful and not intimidating. At the Institute for Molecular Genetics at Baylor College of Medicine, we have found that genetics associates and nurses are extremely capable in fulfilling this role. In order to meet the needs of this expanding diagnostic technology, training programs must develop the requisite skills in their trainees.

In summary, DNA technology is beginning to be utilized by newborn screening programs for diagnostic confirmation. Broader implementation of this strategy will require improved automation to increase its cost effectiveness and trained individu-

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als who can assure clear and effective information transfer back to the primary health care providers and the families.

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