Letters

Phillip A. Isotalo¹ Donald C. Greenway^{1,2,4} James G. Donnelly^{1,3,4*}

¹ Department of Pathology and Laboratory Medicine University of Ottawa Ottawa, Ontario, Canada K1H 8M5

² Division of Biochemistry Department of Pathology and Laboratory Medicine Ottawa Hospital–General Campus Ottawa, Ontario, Canada K1H 8L6

³ Division of Biochemistry Department of Pathology and Laboratory Medicine Ottawa Hospital–Civic Campus Ottawa, Ontario, Canada K1Y 4E9

⁴ Department of Biochemistry, Microbiology, and Immunology Faculty of Medicine University of Ottawa, Ottawa, Ontario, Canada K1H 8M5

*Address correspondence to this author at: Division of Biochemistry, Department of Laboratory Medicine, Ottawa Hospital–Civic Campus, 1053 Carling Ave., Ottawa, Ontario, Canada K1Y 4E9. Fax 613-761-5361; e-mail jdonnelly@ civich.ottawa.on.ca.

Mass Spectrometry of Nucleic Acids

To the Editor:

We read with interest the review by Kricka (1) on nucleic acid detection technologies, in which he mentioned that nucleic acids do not have any intrinsic properties for direct detection. In response to this, we would like to point out the determination of intrinsic molecular weights of nucleic acids using mass spectrometry (MS) has been widely accepted as one of the most accurate methods to detect nucleic acids (2). Using matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) MS, a mass resolution of 1 per 1000 and the detection of low femtomole quantities of DNA can be achieved routinely (3). Nucleic acids ranging from 2 to 2000 nucleotides can be

detected by using MALDI-TOF MS (4). Because of the mass differences of the nucleobases, MS can also be used to analyze mixtures of different nucleic acid fragments without the use of any label (5). Furthermore, in most cases, the separation of the fragments before MS measurements is not required. The minimum sample volume required for MALDI-TOF MS is only a few nanoliters (3). MS can, therefore, be easily linked to any miniaturization of sample processing. Typically, each mass spectroscopic measurement including acquisition and interpretation of mass spectrum takes <10 s. With the availability of automatic high-throughput MS systems that include sample preparation (6), the cost-effectiveness of using MS to analyze nucleic acids has become comparable to other analytical techniques. Currently, the size of a MALDI-TOF mass spectrometer is similar to an immunoassay analyzer. However, as stated in a recent report (7), the size of mass spectrometers can be substantially reduced. Together with the continued development of software for automated interpretation of mass spectra, MS has a great potential to become one of the most important analytical tools for clinical laboratories. Some of the current clinical applications of MS are (a) DNA sequencing (8); (b) detection of genetic variations such as single-nucleotide polymorphisms (9), microsatellites (10), short tandem repeats (11), and small insertions/deletions; and (c) gene expression.

References

- Kricka LJ. Nucleic acid detection technologies—labels, strategies, and formats [Review]. Clin Chem 1999;45:453–8.
- Crain PF, McCloskey JA. Applications of mass spectrometry to the characterization of oligonucleotides and nucleic acids [Review]. Curr Opin Biotechnol 1998;9:25–34.
- Little DJ, Cornish TJ, O'Donnell MJ, Braun A, Cotter RJ, Koster H. MALDI on a chip: analysis of arrays of low-femtomole to subfemtomole quantities of synthetic oligonucleotides and DNA diagnostic products dispensed by a piezoelectric pipet. Anal Chem 1997;69:4540–6.
- Berkenkamp S, Kirpekar F, Hillenkamp F. Infrared MALDI mass spectrometry of large nucleic acids. Science 1998;281:260–2.
- Ross P, Hall L, Smirnov I, Haff L. High level multiplex genotyping by MALDI-TOF mass spectrometry. Nat Biotechnol 1998;16:1347–51.
- 6. O'Donnell MJ, Little DP, Braun A. MassArray as

an enabling technology for the industrial-scale analysis of DNA. Genet Eng News 1997;17:39.

- Henry CM. The incredible shrinking mass spectrometers. Anal Chem 1999;71:264A–8A.
- Fu DJ, Tang K, Braun A, Reuter D, Darnhofer-Demar B, Little DP, et al. Sequencing exons 5 to 8 of the *p53* gene by MALDI-TOF mass spectrometry. Nat Biotechnol 1998;16:381–4.
- Braun A, Little DP, Koster H. Detecting *CFTR* gene mutations by using primer oligo base extension and mass spectrometry. Clin Chem 1997;43:1151–8.
- Braun A, Little DP, Reuter D, Muller-Mysok B, Koster H. Improved analysis of microsatellites using mass spectrometry. Genomics 1997;46: 18–23.
- Ross P, Belgrader P. Analysis of short tandem repeat polymorphisms in human DNA by matrixassisted laser desorption/ionization mass spectrometry. Anal Chem 1997;69:3966–72.

Norman H.L. Chiu^{1,2*} Charles R. Cantor^{1,2}

¹ Sequenom Inc. 11555 Sorrento Valley Rd. San Diego, CA 92121

² Boston University Center for Advanced Biotechnology 36 Cummington St. Boston, MA 02215

*Author for correspondence. Fax 619-350-9237; e-mail nchiu@sequenom.com.

Application of the MediSense Precision-G Blood Glucose Testing System in a Neonatal Intensive Care Unit

To the Editor:

The ability to perform stat glucose testing in support of a neonatal intensive care unit has traditionally depended on transporting the sample to the central laboratory because most point-of-care glucose analyzers cannot accurately test glucose below 2.22 mmol/L (40 mg/dL). In addition, the high hematocrits commonly encountered in newborns and the high bilirubin concentrations often seen in the neonate can cause major problems with glucose measurements in whole blood. Most glucose meters are used for monitoring the diabetic; thus, their accuracy at low glucose concentrations has not been a prime consideration in their design.

The acute management of glucose

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