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Automated Mass Spectrometry in Personalized Medicine

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Personalized medicine is a laudable goal but it is realistic only if, simultaneously, it allows a reduction in the overall cost of health care. There may be several ways to achieve this. By profiling individual disease risk susceptibility, the frequency of testing for disease onset can be tuned to individual needs. By replacing invasive tests for disease risk or progression with non-invasive tests, considerable cost savings can be realized. By using inexpensive biomarkers as indicators of disease progression, more expensive testing of people who are actually well may be avoidable. In addition, a great deal of individual responsiveness to particular therapies such as pharmaceuticals may be predictable before these medications or procedures are implemented.

SEQUENOM approaches individualized medicine in two ways. Its automated mass spectrometry platform for the analysis of nucleic acids provides a uniquely sensitive and quantitative way to detect both genetic risk markers and disease onset and progression markers. The system is totally flexible and allows many tests to be multiplexed and run simultaneously on a single sample. During 2005 the first diagnostics tests using the SEQUENOM platform will be launched commercially. These are likely to include such tests as noninvasive fetal sex determination, by detecting Y-chromosomal markers in the maternal circulation, and highly multiplexed tests of common genetic variations that predispose to cystic fibrosis.

Because automated mass spectrometry coupled to PCR provides sensitivity down to single molecules, it promises improvements in such tests as viral load, infectious disease agent typing, and markers in blood, urine, or the mouth that reflect disease progression. While RNA profiles can be studied in this way, our experience thus far suggests that corresponding methylated DNA markers may be more powerful and more easily utilized.

SEQUENOM's second contribution to the prospects of individualized medicine comes as a result of the large program of human genetic studies that has been executed over the past few years. More than 11 whole genome single nucleotide polymorphism scans have been carried out to measure disease association in the general population. Included are studies of breast cancer, lung cancer, prostate cancer, type II diabetes, and schizophrenia. In every study multiple disease predisposing genes have been discovered that can be replicated in multiple independent populations and thus present true positive associations and not false positive type I errors. A number of these gene discoveries will be described. What is intriguing is that many of them, while discovered purely as disease risk markers, also appear to have predictive or monitoring value in

disease progression. Some genes are found that play a role in multiple disease indications such as breast cancer and prostate cancer.

In diagnostic testing a major source of error is sample mix up. Because of the high multiplexing power of SEQUENOM's analytical platform, it may become cost effective to carry out a personal identity test on every diagnostic sample under examination for a particular purpose. If this aspect of personalized medicine can be realized, it promises to improve the overall standard and reduce the cost of medical care in a simple but direct way.