so complete confidential personal and family health profiles. If a profile matches research needs, the person is asked to participate. The method "for the first time enables us to conduct studies with large sample sizes that would otherwise have been too time-consuming and costly to conduct," Rienhoff says. Voluntary participation does not excuse the company from avidly protecting confidentiality, he says. "If we say we're going to keep things private, we have to keep them private." The information is encrypted and stored off-line.

What keeps companies and academic researchers struggling to assemble the mass of data needed to pursue annotation of the genome is the potential payoff in biomedical understanding.

While diagnostics to deal with major complex diseases will take some time, for some single-gene diseases, genome understanding already has led to diagnostics that help patients, says Craig Basson, MD, a molecular cardiologist at the Cornell Medical School. For the past four years Basson's research group has studied a benign recurring and proliferating cardiac tumor that is inherited in some families but also occurs as a nonheritable condition. Their "progress over the past year has been greatly accelerated by the human genome project (HGP)," he says.

Currently, the disease is treatable only with surgery; if left untreated, it causes major strokes. With screening, people who don't have the gene can skip the expensive long-term monitoring they got in the past. Meanwhile, those with the gene can get annual electrocardiograms to determine when surgery is needed to prevent strokes. The cost of monitoring people with the gene is high, but likely is offset by the even higher financial and health burdens of stroke, Basson explains.

Farther down the line, genome-based understanding of the condition will provide clues to understanding not only the nonfamilial version of the tumors but other diseases of the heart. "Clinicians will need to learn about genetic medicine" because the day will come when genome-based understandings can inform practice for many diseases, says Basson. But he says it's important "not to get caught up in the hoopla" or "lose sight of what we can do today." Given the current early stages of genetic knowledge, "as a cardiologist, I can make a far bigger impact today by telling a patient not to smoke."

Chapel Hill-based BioSignia is one of many companies putting its eggs in the diagnostics basket. The company is betting on the proposition that growing knowledge about genetic contributions to disease risk — along with improving bioinformatics tools that can calculate risk more precisely — will begin to shift the medical paradigm toward prevention. In BioSignia's case, however, it's with a difference. Rather than relying only on gene-based diagnostic tools, the company's risk-forecasting model will focus on both an individual's genotype and phenotype — how the genetic profile has expressed in response to environment, says CEO Tim Smith.

Using a patented computational "synthesis technology," the company will maintain and update a disease risk-prediction algorithm based on the wealth of currently available clinical, epidemiological, and, ultimately, genome-based peer-reviewed studies. The result: an increasingly refined evidence-based prediction database, says Smith. Feed an individual's data in; get back a computer print-out outlining both the relative and absolute risk of developing numerous major conditions.

"I have yet to see a doctor who really doesn't want evidence-based tools that can help make decisions about what to target with prevention," says Smith. Doctors "know all these risk factors but can't go through the entire complex decision-making process on their own." The potential for developing better risk forecasting means that "every person in the world could benefit" from the HGP, he says.

How Many Ounces of Prevention Will We Buy?

It will be necessary to be on guard against irresponsible marketing of genetic tests by some companies and irresponsible use by some physicians, and patients, analysts agree.

Two things are needed for diagnostic testing to be useful, says Rienhoff. The test must produce "a meaningful piece of information," that is, "a series of decisions you could make" about managing your health. "A test for Huntington's, for example, would not be very useful." A test that indicated increased risk for breast cancer at an early age would be because patients could get regular screenings.

The other necessity: "Getting somebody to help interpret the data."

Who'll get that job?

U.S. geneticists and counselors see a median of six genetic patients a week, compared to the 100-150-per-week median patient load for primary care doctors, according to a multi-year 37-nation survey conducted by genetics analyst Dorothy Wertz of the Shriver Center. "This means that in effect most genetic information, and probably most genetic tests, will be provided to patients by their primary care physicians," she concludes. "Although inevitable, this is worrisome in view of the gaps in knowledge — even about relatively common genetic disorders— among the primary care physicians in our sample.".

Although "some physicians got most things right on a knowledge quiz...some gave incorrect answers to questions of considerable importance to patients. For example, 11 percent thought that most children with Down syndrome could complete regular (not special) high school; the majority thought that males with cystic fibrosis could father biological children (they are actually sterile)."

Getting up to speed on gene science won't be the only challenge providers face.

For one thing, part of physicians' new job will be to cool some of the ardor for gene testing, the University of Alberta's Timothy Caulfield wrote in the *Canadian Medical Assn. Journal* in 1999. "The recommended approach to genetic testing is generally one of caution and restraint," he wrote. "Concerns include the effect of test results on the insurability of patients, on family relationships and on self-image." But "there is concern that pressure from the growing biotechnology industry, coupled with understandable public excitement, will induce premature implementation and inappropriate use of some testing." As evidence Caulfield cites recent Canadian and U.S. surveys