

Search

cals.wisc.edu



Above ↑ Graduate student Jill Hershleb and undergraduate Austin Ramme use an automated microscopy system, developed by researchers in David Schwartz's lab, to scan single DNA molecules many thousands at a time. The system enables them to analyze DNA from individuals in order to detect genetic variations, or errors, that may be linked to various medical conditions. The human genetic "blueprint" is represented by six feet of DNA. This scanning system scans all six feet to pinpoint errors in an individual's genome..

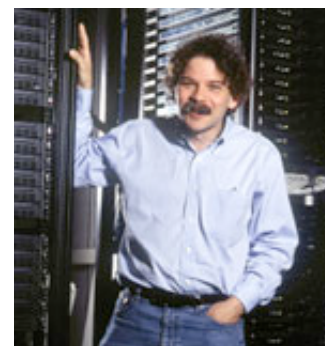
Your Body's Bar Code

[Home](#) >> Your body's bar code

A scan of your genome will reveal health problems and help doctors tailor treatments

Scientists, like all inventors, are recyclers. They don't reinvent the wheel – they apply it to their specific needs. In the burgeoning field of nanogenomics, bar codes are the 21st century wheel, assuming a whole new purpose in the skilled hands of College genomicist **David Schwartz**. Bar codes are serving as maps of human DNA molecules, providing key information quickly, efficiently and cost effectively – just like the universal product codes that served as their models.

Instead of ringing up price and quantity, these molecular bar codes convey information about an individual's DNA. "This is going to provide



Analyzing vast amounts of DNA data takes a lot of computing muscle. David Schwartz has an array of 200 computers in his lab and

the basis for everyone to have their genome scanned, if that's what they want," says Schwartz. He predicts that within five years, a patient may be able to walk into a doctor's office, give a blood sample and get a whole genome scan for about \$100.

The benefit of the scan is its predictive value, Schwartz says. Once a database of 100,000 individuals is established, researchers will catalog variations in the genome and then conduct broad-based association studies to look for apparent links between genetic variations and physical conditions such as the presence of a disease.

Smart medicines

Schwartz believes that an individual's genome scan can be used to predict whether he or she will develop diseases such as hypertension, heart disease and leukemia. They will also facilitate the use of "smart medicines" – drugs targeted to individuals to increase effectiveness and reduce toxicity, he says.

"Such new therapies will be especially useful in chemotherapies, where toxicity and cures often hang in balance due to horrible side-effects," he explains. "Here, the exact genetic composition of tumor genomes will enable individualized targeting.

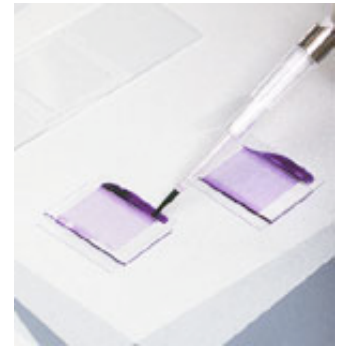
"Few diseases are cured, [most are] just managed," Schwartz says. "With this technology, we may have the tools and insights to finally deliver on the promise of gene therapy."

One of the main challenges in working with DNA has been that the molecules are unwieldy. If stretched out, the DNA in the nucleus of a single cell would measure about six feet. The DNA from one chromosome would be about an inch long – quite large in the world of genomicists.

The solution, says Schwartz, was to narrow the focus and revamp the process. He has helped make genome scans a reality by inventing a novel approach to single-molecule DNA analysis: optical mapping. The process involves extracting DNA molecules and using microfluidic devices to deposit the negatively charged DNA molecules in channels on positively charged glass surfaces. The devices work quickly, guiding the deposition of thousands of DNA molecules. They're also efficient: The amounts of sample and reagent they use are measured in billionths of a liter.

Once the DNA molecules are deposited, restriction enzymes cut them at specific base pairs. The cutting yields a unique pattern, resembling a bar code's array of thick and thin stripes. The DNA is then stained with a fluorescent dye and scanned by a fluorescent microscope, which detects genetic variations. To develop the process, researchers had to come up with new systems that could handle the large volumes of information. Schwartz's team developed not only automation to analyze the images, but also a type

access to another 1,000 across campus



From genetic code to bar code. DNA molecules are deposited via microfluidic channels onto glass surfaces, then cut (by enzymes) into fragments and stained with fluorescent dye. The bar-code-like patterns that result can be scanned by an automated fluorescence microscopy system to reveal genetic variations.

Related Links

- [Laboratory for Molecular and Computational Genomics](#)

of image processing. While Schwartz calls the images “entertaining,” he admits that looking at hundreds of thousands of them would be tedious, as well as time-consuming.

Spotting genetic gaps or add-ons

“What we’ve perfected is a high-throughput way of presenting the DNA, taking the bar codes and doing this hundreds of thousands of times,” Schwartz says. “We’ve gotten this platform to the stage where we are starting to analyze human populations, and we are starting to make some very interesting discoveries.”

Those discoveries include insertions and deletions in the chromosomes that no other system can discern. Schwartz believes these structural variants, or indels, are responsible for a variety of cancers and congenital abnormalities.

“These events are really important not only as markers for the disease, but in actually causing the disease,” says Schwartz. “The discoveries that we’re making are absolutely breathtaking.” So far, researchers in Schwartz’s lab have used the optical mapping system to detect chromosomal lesions in tumor cell lines and tumors themselves, including gliomas, a deadly brain tumor, a colon carcinoma, breast carcinomas, and a nonmalignant tumor called hydatidiform mole. They have also mapped the genome for *Plasmodium falciparum*, a uni-cellular parasite that causes malaria and kills millions every year. In a project funded by the National Cancer Institute, Schwartz’s team will collaborate with researchers at the M.D. Anderson Cancer Center and Yale University to map the genomes of tumors from cancer patients.

Navigating a sea of data

The accomplishments of the genome center that Schwartz has helped build required a multidisciplinary approach. Schwartz has collaborated with chemical engineers, geneticists, physicists, materials scientists and computational biologists both on and off campus.

“Nobody ever considered data like this before, so we’ve worked very closely with computer scientists and mathematicians, most notably Michael Waterman, one of the fathers of bioinformatics.”

These collaborations helped Schwartz’s team acquire the processing heft to sort through 20,000-25,000 genes and hundreds of millions of base pairs. With 200 computers in his lab and another 1,000 at his disposal, Schwartz and his team have been able to collect and analyze huge data sets.

“One of the things we’ve been able to do is integrate this whole thing. We are the only university in the world doing single-molecule genome analysis. “What is before us is the genomics era, being able to analyze complex data sets from a very large number of individuals. Ultimately, we will be able to know every base, every message, every peptide, every interaction, in every cell, under every stress,” says Schwartz. “We are revolutionizing the way we do science.”