



Editorial

NEW BIOCHIP TO ATTACK TUBERCULOSIS

A jointly developed biochip technology to help identify and eradicate drug-resistant strains of tuberculosis will be used by researchers at the U.S. Department of Energy's Argonne National Laboratory and the Russian Academy of Science's Engelhardt Institute of Molecular Biology. The project was undertaken by American and Russian scientists trying to stem outbreaks of a disease that is currently infecting thousands of prisoners in Russian jails, and is making an alarming comeback in the United States. At the Argonne National Lab, researchers want to put the bioarray-type biochip technology they co-designed with the Engelhardt Institute through its paces to head off a worldwide outbreak of tuberculosis.

While TB, a disease caused by the bacteria *mycobacterium tuberculosis*, was nearly eradicated in the United States in the 1940s, it has since returned with a vengeance. New drug-resistant strains have emerged, especially among indigent people living in crowded conditions where hygiene and nutrition are poor. Doctors must prescribe several drugs because it takes weeks or months to identify specific TB strains. Because of the length of time involved, people often die before the correct strain is identified.

Andrei Mirzabekov, a biologist at the Engelhardt Institute of Microbiology in Moscow, suggested testing the technology to help stem an epidemic of tuberculosis that's occurring in hundreds of thousands of prisoners in Russian Jails. Both the U.S. and Russian governments want to stop a further spread of the disease from Russia to Western Europe and the United States. By using biochips, researchers at Argonne and Engelhardt hope to be able to identify new strains of TB and determine which antibiotic is best equipped to combat each. Harvey Drucker, Argonne's associate director, said the work on TB will be the first test of the Argonne / Engelhardt biochip in "the realm of real-world medical diagnosis".

The biochip features a glass slide with up to 10,000 gel pads that act as tiny wells to hold samples. Each gel pad has a short strand of DNA attached to it. Samples are deposited onto the wells so that DNA from the sample can pair up with known DNA.

To identify a particular strain of TB, samples of single-strand TB DNA will be spread on a chip and be allowed to pair up with TB DNA strands whose drug resistance is known. The test will be done using harmless segments of genetic material removed from tuberculosis bacteria. Research with patients will begin only after the method has proved successful. If the tests succeed, the initial studies will be used to make similar evaluations of other bacterial and viral diseases.

"Our biochip design can be adapted to read DNA of every material including virus strains," said Argonne's spokeswoman. Both organizations are also collaborating to develop mass-produced biochips. They are working with Packard Instrument Co. (Meriden, Conn.), a developer of sample-dispensing instruments for biochips, and Motorola Inc. (Schaumburg, Ill.), which is commercializing biochip technology and manufacturing. And Motorola, Arizona State University and CFD Research Corp. are embarking on a three-year project to produce a single disposable plastic microfluidic biochip that can carry out all the preparation and genetic-analysis functions required to diagnose infections. The devices will cut the time required to do traditional diagnostic tests by using a single device that can be employed in doctor's offices and hospitals. NIST's Advanced Technology Program awarded the group \$ 9 billion to develop the devices, which could spur a \$

1.3 billion industry by 2000. Researchers at Motorola will design and fabricate the device and build a test station. CFD Research will develop modeling tools for device optimization and prototype development, and Arizona State researchers will contribute expertise immunology and biology.

Motorola has also made equity investments in biotech companies Genometrix (The Woodlands, Texas) and Clinical Microsensors (Pasadena, Calif.), which aim to incorporate electronics into biochip systems. And it has joined SNP Consortium Ltd., a nonprofit organization dedicated to the identification and analysis of the genetic markers known as single nucleotide polymorphisms, or SNPs (pronounced “snips”). Scientists believe that the study of SNPs, which are common variations that occur in human DNA, can help them pinpoint the subtle genetic differences that predispose some people to such diseases as arthritis, Alzheimer’s, cancer, diabetes and depression. SNPs are also behind the variations in individual responses to given drugs.

Earlier this year, Packard Instruments introduced the first biochip instruments, which deposit samples onto biochips and analyze the reactions. The Biochip Arrayer, based on ink-jet printing, dispenses droplets of a sample onto the wells on the surface of a biochip. The Biochip Imager, a laser optic imaging device, analyzes thousands of reactions on the chip simultaneously. It’s based on technology from GSI Lumonics (Toronto), which produces laser-based automatic advanced manufacturing systems.

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