

ATP's Investment in DNA Chip Technologies Accelerates Personalized Medicine

Background

In the 1990s the technology path to using genomic information for personalized medicine and other applications was unclear, fraught with risk, and under funded.

From 1994 through 2001, the Advanced Technology Program's Tools for DNA Diagnostics focused program provided nearly \$140 million in cost-share funds to 42 projects for research and development to biotechnology firms that could not otherwise secure funding for their high-risk technology ventures. Most were small start-up companies.

These firms developed much of the technology infrastructure for the genomics revolution.

The study of an organism's entire set of genetic information holds enormous potential for our understanding of diseases and our ability to treat them. ATP funding supported a broad platform of knowledge with which to study genetic variations among people, how diseases affect people differently, and which course of treatment would be most effective for a patient based on his or her genetic makeup.

In-depth case studies by RTI International of two ATP- funded projects involving DNA-chip technologies and qualitative studies of three related projects will quantify early impacts of ATP funding on the genomic revolution for a subset of ATP-funded projects. Preliminary results indicate the following significant areas of impact.

ATP advanced the state of the art of DNA Chips

DNA chips now enable medical research that previously would take months, years, or possibly would not have occurred at all. These chips work on the front line in the fight against diseases like cancer and cystic fibrosis and help identify the presence of deadly pathogens like SARS.

- Created by building genetic sequences onto wafers using techniques similar to those in the semiconductor industry, DNA chips are used to analyze tissue samples for diseases and drug efficacy, among many possible applications. They document the responses of cells to diseases and the effects of drug treatments.
- Until the introduction of DNA chips by ATP awardee Affymetrix in 1994, scientists used \$100 blood tests and other diagnostic procedures to identify individual genes.
- Affymetrix's DNA chip, in contrast, permits thousands of those experiments to run simultaneously, significantly reducing costs and analysis time.

Affymetrix, a small company at the launch of its ATP award, built technology infrastructure supporting generations of improvements in DNA chips. As a result of ATP funding:

- DNA chips became a robust method of molecular analysis by supporting the development of innovative testing, measurement, and production techniques that increased the quality and analytic capability of the Affymetrix' chips.
- Affymetrix chips that medical researchers use are more efficient and effective than they otherwise would have been.

- A software industry dedicated to managing and analyzing the data output from DNA chips was born (thus enabling the data to be used for robust analysis). Affymetrix used ATP's cost-share funds to develop the first software tools for use with DNA chips and encouraged the software industry to further that work. An entire ecosystem of firms has since emerged to fill the data analysis and management needs that ATP co-funded research validated.

ATP accelerated completion of the Human Genome Project

Molecular Dynamics, a small engineering company when it received a joint venture award with Affymetrix, developed and integrated new DNA sequencing technologies for determining the order of the 3 billion paired building blocks of human DNA. This ATP-funded sequencer technology:

- Lowered per-unit operating costs, increased efficiency by eliminating many time-consuming manual processes, and enhanced the quality of data output. Instrument run times decreased from an average of about 5 to 6 hours to just 2 to 3 hours.
- Spurred competing R&D at other instrument manufacturers.
- Enabled researchers to dramatically accelerate the completion of the Human Genome Project:
 - Producing 30 percent of the finished Human Genome Project using Molecular Dynamics instrumentation.
 - Putting revolutionary data in the hands of researchers, saving federal tax dollars, and helping deliver the final draft of the human genome 2 years ahead of schedule.
 - Providing an enabling mechanism for other technology programs and revolutionizing our understanding of molecular biology.

ATP advanced the analysis of human genetic variation

Analysis of single nucleotide polymorphisms (SNPs) – small variations in the sequence of bases that make up the human genome – allows researchers to understand how genetic differences among people relate to their susceptibility to ailments and the efficacy of possible treatments. For instance, common ailments such as diabetes, cardiovascular disease, obesity, psychiatric illnesses and inflammatory diseases may stem from both genetic and environmental factors. The study of SNPs has already provided fundamental insights into the diagnosis and treatment of these and other ailments.

While DNA chips produced by Affymetrix and other companies are being used for SNP analysis as well as gene expression, techniques developed developed by Molecular Tool and Orchid Cellmark with ATP funding offer more specific analysis and a lower per sample cost. This technology:

- Enabled significant decreases in SNP analysis costs and provided one of the first automated products on the market.
- Is being used in academia, biotech firms, and pharmaceutical firms as a cost-effective way to analyze SNP.
- Has been licensed widely, covering 90 percent of DNA sequencers in use in the year 2000.

Without the ATP award, Molecular Tool would not have been able to develop this technology.

Third Wave Technologies' ATP-supported technology enabled a 90 percent reduction in DNA experiment preparation time and was used to map 25 percent of known SNPs.

ATP deepened scientific knowledge of molecular diagnostic tools and broadened their availability

ATP funded projects led to open architecture technologies and diagnostic tools that moved health care to the brink of “personalized medicine” – in which every person will receive clinical treatment and drug therapies based on their individual genetic structure.

- Curagen developed an open architecture process for gene expression sample preparation that had smaller sample requirements than its competitors and faster turn around for gene confirmation. This technology is licensed extensively to drug discovery firms.
- Nanogen was recently granted the first patent for a complete point-of-care diagnostic device. Research begun under the award was credited as providing the foundation for their new technology.
- Third Wave’s technology enables a new point-of-care device that will test patients for the likelihood of adverse drug reactions.

Doctors will soon be able to use these tools to quickly identify which course of treatment is best for a patient, avoiding adverse drug reactions and identifying the most appropriate treatment regimen.

Source: Preliminary results from *Benefit-Cost Analysis of a Cluster of ATP-funded DNA Chip Technologies* by RTI International. NIST GCR. Forthcoming late 2006.

Factsheet 1.B14 (April 2006 by Jeanne Powell)