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genetic  
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news

Your biotech insider from bench to business

Volume 26, Number 12, June 15, 2006

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# Progress Report on the NIH Roadmap Initiative

## The New Way of Doing Business at the NIH Draws Accolades from Industry

*Bridget Coila*

At its inception in 2002, the NIH Roadmap initiative ([nihroadmap.nih.gov](http://nihroadmap.nih.gov)) was created to “identify major opportunities and gaps in biomedical research that no single institute at the NIH could tackle alone but that the agency as a whole must address.” Put into effect in the 2004 budget year, the program has developed into not only a way of operating for the NIH but also as a model for other organizations to follow.

As the first step in creating the NIH Roadmap, NIH director Elias A. Zerhouni, M.D., consulted with stakeholders, including over 300 scientists from both academia and industry, to address the issues the NIH faced. The result was a novel program aimed at providing organizations and companies with the tools to promote high-risk, high-reward research and enabling them to focus on

emerging areas of science and creative ways to move research from lab to clinic more quickly.

Dr. Zerhouni points out that while some people think the Roadmap refers to a single initiative, it is actually a strategy of doing business for the NIH, a way of coordinating the organizations involved and acting as an incubator for projects and ideas. Of 96 initiatives originally proposed to be a part of the Roadmap, 28 were ultimately selected. These initiatives have been staggered in implementation, and the project itself is now in the third year of its first five-year plan.

The initiatives making up Roadmap are divided into three main themes: New Pathways to Discovery, Research Teams of the Future, and Re-engineering the Clinical Research Enterprise. Some of the initiatives within

these themes focus on issues like providing better interdisciplinary training for graduate students and postdocs, awarding grants to scientists who propose innovative and high-risk research, and fostering collaboration between researchers in



NIH recently launched the Office of Portfolio Analysis and Strategic Initiatives to improve the way the Institutes find and fund research and to increase trans-NIH dialogue, decision-making, and priority-setting.

different fields. Others involve the cooperation of public industry and private organizations, including the development of a network of biological and chemical repositories and public databases.

### Small Molecule Centers

One of the most ambitious goals of the Roadmap has been the establishment of small molecule centers, which operate with cooperation between public organizations and private industry. These centers are the result of the New Pathways to Discovery theme and its Molecular Libraries initiative and are collectively called the NIH Molecular Libraries Screening Center Network.

In 2004, at the start of the practical application of the Roadmap initiatives, **Discovery Partners International** (DPI; [www.discoverypartners.com](http://www.discoverypartners.com)) was looking at ways to move from being a producer of chemical libraries into a chemical library manager and saw involvement with the NIH Roadmap's Molecular Libraries initiative as a way to demonstrate its abilities.

The NIH awarded DPI a \$24-million, five-year contract to develop and maintain the NIH Molecular Libraries Small Molecule Repository ([mlsmr.discoverypartners.com](http://mlsmr.discoverypartners.com)) and its associated website.

The repository was created to provide a public collection of organic chemicals for use in multiple NIH Screening Centers and to deposit the structures of these compounds into PubChem ([pubchem.ncbi.nlm.nih.gov](http://pubchem.ncbi.nlm.nih.gov)), the NCBI's publicly accessible cheminformatics database of small organic molecules and their biological activity. The chemicals in the database are derived from public and private sources and include FDA-approved drugs, known compounds,

compounds derived from natural templates, and new compounds generated by centers in the program.

One of the centers within the network is the New Mexico Molecular Libraries Screening Center (NMMLSC; [screening.health.unm.edu](http://screening.health.unm.edu)). This center focuses on developing high-throughput flow cytometry assays, screening small molecules identified as targets by NIH partner institutions with this technology, and providing access to the screening data to both the public and private sectors.

According to Alexander Kiselyov, Ph.D., executive vp of R&D at **ChemDiv** ([www.chemdiv.com](http://www.chemdiv.com)), NMMLSC is the only public center capable of doing parallel FACS assays and committing to a pharma-like robust approach of reading up to 20 parameters at once.

As a result of previous collaboration with the University of New Mexico, Chemdiv was chosen to provide the chemicals used by the NMMLSC for screening biological targets.

Another center, the NIH Chemical Genomics Center (NCGC; [www.ncgc.nih.gov](http://www.ncgc.nih.gov)) recently began collaborations with **Invitrogen** ([www.invitrogen.com](http://www.invitrogen.com)) and **Genedata** ([www.genedata.com](http://www.genedata.com)). Invitrogen provides cell-based assays for high-throughput screening at the center, and Genedata's Screener® software is used to compare and analyze high-throughput screening data across different assays.

"Our involvement with Roadmap stemmed from a conference Invitrogen held in April 2005 focused on the chemical genomics initiative," notes John Printen, R&D director of Invitrogen's drug discovery solutions. "We saw a group of academicians looking for the same screening that

pharmaceutical companies have, and we looked into collaborating based on a new screening paradigm and how our cell-based tools could help the NCGC look at whole pathways of interaction."

According to Printen there was a high degree of interaction between Invitrogen and the screening center during this collaboration. "We provided access to cell-based assay sensors that were not yet on the market, giving NCGC the first look. They screened their chemicals with these assays, which demonstrated how useful these technologies are for various approaches. It has been a good intellectual exchange."

Invitrogen is also looking into the future for possible means of expanding its collaboration with the NCGC. "A lot depends on how this collaboration ends up," explains Printen. "We might apply some of our other technologies in the future, such as RNAi screening. We see a nice flow from the development of biological tools for screening of cell-based assays into labeling and visualization technology of molecular probes."

### Industry Reaction

Overall, the response from both industry and academia to the NIH Roadmap has been enthusiastic, and the program is seen as an effective way for companies to get involved with academic and government organizations.

Dr. Kiselyov explains, "We used to work with a variety of neighborhood universities, and that was a nightmare. Universities surround themselves with mysterious technology transfer offices which insist on following the book to get maximum profits for their university, not understanding that this has to be a two-way road. We entered into working with



**The NIH Patient-Reported Outcomes Measurement Information System Network will host a conference in September to examine conceptual, clinical, and methodological aspects of assessing and using patient-reported outcomes in clinical research and practice.**

Roadmap and the University of New Mexico very cautiously, but it has been a very rewarding experience thus far. Everyone has gotten what they wanted.”

While there have been setbacks—in the first set of 100,000 compounds sourced by DPI, many had to be removed from the database—the NIH has proven willing to work with industry to resolve any potential problems. “The relationship we have had with the NIH has been fantastic. They have been extra helpful, and nothing has gone unresolved,” reports Douglas Livingston, Ph.D., senior vp of chemistry at DPI.

One of the problems noted by Dr. Kiselyov was that in the beginning, there was no clear guidance with regard to hit followup. “If organization X found a really good hit against target Y, we wanted to be able to make a chemical against that target. Chemdiv proactively suggested doing follow up on tangible hits and committed to doing just that, working on multiple probe designs and actual follow up of molecules from hit to lead.”

Another concern noted by Printen was the need for education about the differences between academic benchwork and high-throughput applications. “Individual investigators sometimes don’t have the knowledge to know what technology they should be using for high-throughput applications verses traditional benchwork.”

Printen explained that the NIH is promoting education programs to deal with this concern, working with industry to sponsor meetings and workshops for investigators to increase their knowledge on high-throughput processes.

Overall, the prospects for the future of the Roadmap look good. “Any initiative as massive as the Roadmap will have surprises. It is important to develop a crystal-clear road to follow, but it is also possible to learn as you go and develop more clear and tangible strategies with input from the scientists, pharmaceutical companies, and organizations involved,” says Dr. Kiselyov.

For future public-private collaborations within Roadmap to work as well as these current ones have, Dr. Liv-

ingston recommends that companies considering such a collaboration anticipate the difference in working with government contracts compared to dealing with others in industry.

“If they take that into account and are willing to have an infrastructure to support the various regulations government organizations require, then they should have a positive experience,” Dr. Livingston adds.

Dr. Kiselyov agrees, “Before entering into a collaboration of this type, make sure all sides clearly understand what will happen in one year, five years, and ten years. Successes need to be published and publicized.”

### **Adaptation—The Future of the Roadmap**

“This is something that hasn’t been done before, so flexibility is required,” explains Dr. Livingston. Thankfully, flexibility was built into the program from the beginning. According to Dr. Zerhouni, one of the best features of Roadmap is that it adapts as those involved learn more about the process. The plan is to bring scientists together

every 2–3 years to see how Roadmap is progressing and adjust the focus based on what those involved have learned. It's a process of doing science on science, notes Dr. Zerhouni, a way of changing the program based on empirical evidence as to what is and isn't working.

One example of Roadmap's ability to adapt is that its original conception,

multiple translational research centers were included. Once the organizers realized that these wouldn't work, they cancelled the competition for grants and applied the money to the Clinical Trials Institute Awards instead.

According to Dr. Zerhouni, changing course so dramatically would not have been possible under the previous organizational structure of the NIH, but

with the Roadmap, they were able to make the best use of available funding and expertise.

“The real message is that it is a factor of change across all institutes. We want this to be a feature of how the NIH does business on a regular basis,” concludes Dr. Zerhouni. “The future of Roadmap is running organizations not by anecdote but by science.” **GEN**