NEWS FROM THE ADVANCED TECHNOLOGY PROGRAM

ATP Update

FEBRUARY 13, 2009

VOLUME 3 NO.1
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Director's Point of View

On Providing Science *and* Value

Tim Harris, Ph.D., Chief Technology Officer

We are about a third of the way through the first year of the new contract. In these days of flat budgets and reduced spending for the Advanced Technology Program (ATP) and other parts of the Technology and Research Group, we need to work harder to increase the amount of money we bring in from our NCI customers.

The paradigm provided to us by the NCI Office of the Director (OD), in which they give us money to develop technology for NCI to then pay us to use, is actually a perfectly reasonable one. The use of the technology by NCI principal investigators (PIs) is called "cost recovery." In commercial parlance, this concept would be called "sales," and it is not a bad thing to think of it as such. This does not mean that we do not collaborate with our NCI customers: it means that we get them to pay what it takes to get the work done or at least contribute to it.

It will not be possible to maintain the ATP in its current form unless we increase our ability to bring in money from the NCI PIs and other government sources. The ATP directors will be taking a critical look at the work we do for our customers, and will examine very carefully the costs of doing the work. There is actually no question that we provide a very high value "service" to NCI, both in the quality and quantity of the work we do. Some of it indeed is *in*valuable in the sense that it would be impossible to get elsewhere.

We need to become better at explaining the value proposition to NCI so that they understand what a good deal they are getting by working with us. First and foremost, the science has to be the very best, but secondly, we must provide value for the money and always be thinking of both aspects as we do the work.

In This Issue

Congratulations to Our Outstanding Contributors

The following people were recognized as outstanding contributors for their respective groups in the fourth quarter, 2008:

Genetics and Genomics Group
Casey Dagnall, Quality Control Analyst II

Casey Dagnall has been a member of the Core Genotyping Facility's (CGF's) Quality Assurance/Quality Control team since its inception and is critical to the success of multiple process improvements and cost savings initiatives. Ms. Dagnall developed, documented, and implemented the inventory control system at the CGF. Her efforts, which included extensive collaborations, have eliminated the use or disposal of expired reagents due to excess ordering, and have ensured that required stock levels are maintained to minimize work stoppages and avoid excess shipping charges.

Ms. Dagnall recently implemented a new assay service offering. Gene copy number assays detect gene deletion and duplication variants and represent a critical addition

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Congratulations continued

to the CGF toolbox. With two initial gene targets, Ms. Dagnall determined the best platform to use and worked with the CGF Laboratory Information Management System team to design, test, and implement the new assay workflow. As a result, the CGF can quickly develop and validate copy number variation assays for other interesting targets.

Ms. Dagnall continues to supply staff with expert service in automation, internal controls, and equipment management. When necessary, she also assists with production overload and coverage for other quality staff. Her dedication to improving CGF, her willingness to help others, and her proactive approach make her a valuable contributor.

Imaging and Nanotechnology Group
Prabhakar Gudla, Ph.D., Scientist II

Since March 2008, Prabhakar "Reddy" Gudla, Ph.D., has taken on significant additional duties to support the infrastructure of the Optical Microscopy Analysis Laboratory (OMAL) and the Electron Microscopy Laboratory (EML). At the Advanced Biomedical Computing Center (ABCC), Dr. Gudla transferred image data from old snap servers to a new file server that is compatible with the Federal Desktop Core Configuration. Dr. Gudla also set up a new image analysis server at the ABCC and collaborated with the group to develop protocols for user access to BlueArc®. Dr. Gudla continues to collaborate with the ABCC in developing and distributing new image analysis software. While doing all of this, Dr. Gudla maintains his level of confocal microscopy support and continues to conduct outstanding research. In May 2008, he was the first author of a major publication about a conceptually new method to automatically segment cell nuclei in microscope images, which was published in *Cytometry*. The publication was cited by the journal's "In This Issue" section, and Dr. Gudla was invited to present the work at the International Society for Advancement of Cytometry (ISAC) Conference in Budapest that same month. ISAC is the society that publishes *Cytometry*.

Information Technology Group
Michael Loss, Web Developer II

Michael Loss, a web developer at the Advanced Biomedical Computing Center, is responsible for developing the Reagent Data Portal for the Clinical Proteomic Technologies for Cancer (CPTC) group. The portal is a new service that allows researchers to access information and acquire antibodies for cancer-related targets. Although Mr. Loss has been at SAIC-Frederick for only seven months, he has designed, developed, and implemented multiple phases of the data portal for CPTC from the ground up. He has shown a consistently positive attitude in working with the Office of the Director for NCI to ensure a timely and successful rollout of the initial phase of the project. As multiple phases are developed and placed into production, Mr. Loss continues to demonstrate the kind of customer interaction and innovation that leads to a positive outcome for NCI and the rest of the cancer community.

Proteins and Proteomics Group
Jennifer Mehalko, Research Technician

Jennifer Mehalko has been a technician in the Protein Expression Laboratory (PEL) for two years, starting as an intern during her last semester at Hood College, and continuing with a permanent position after graduation.

She demonstrates a great deal of patience in the lab while working on her own projects and supervising a Werner H. Kirsten student intern. In particular, she carried out two recent tasks that surpassed her expected duties.

Ms. Mehalko archived more than 10,000 samples of DNA and cells in the PEL. This project involved labeling tubes and transferring materials, which required 100 percent accuracy, and entailed a significant amount of searching through notebooks and printed materials for

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Congratulations continued

information to enter into a database. This work created a system that modernized operations in the Clone Optimization Group and has allowed members to have nearly instant access to samples that previously required hours (or days) of freezer diving to locate.

Ms. Mehalko has also been responsible for populating a database of manuscripts relevant to PEL personnel. This task required her to retrieve PDF files for more than 600 journal articles and enter the information in a database. The database, which lab personnel can access at work or remotely, has streamlined access to manuscripts that are frequently used for core service and technology development projects.

Visual Communications and Support Services Group
Annie Chaltain, SPGM Coordinator

Do you need help with a poster? Have a site visit report or manuscript that needs editing? Need a passport? Want to turn your data into graphs, charts or other illustrations? Then you'll probably make your way to Building 362, Scientific Publications, Graphics & Media (SPGM), where Annie Chaltain will help you solve your problem.

As SPGM Coordinator, Ms. Chaltain finds ways to make every project work, whether it's for a customer who needs a unique service, one who's reached the limit on his or her budget, or a co-worker who needs help with a project. She treats every customer like a personal friend and every job as if it were her own. Besides offering exceptional customer service, Ms. Chaltain has helped refine numerous processes in the office to make projects run more smoothly for SPGM staff and customers alike.

Ms. Chaltain has redefined "customer-friendly." With her gentle approach and reassuring smile, she puts you at ease and ensures that your job request is handled efficiently and quickly. She is truly the "face" of SPGM.

Bruce Crise To Play Key Role in Business Development

By Tim Harris, Ph.D.

Last November, it was my pleasure to announce the appointment of Bruce Crise, Ph.D., to Director, Business Development, Scientific and Technical Operations, Advanced Technology Partnerships Initiative (ATPI). Dr. Crise reports to David Hoekzema, Director, Strategic Business Development, ATPI.

This appointment is a reflection of the momentum building in the ATPI, with new research and development (R&D) partnerships forming and numerous opportunities for collaborative R&D under consideration. Strategic business development through the ATPI Business Development Office (BDO) includes coordinated activities of in-reach to NCI programs and investigators, as well as outreach to industry to align on areas of mutual interest for potential translational R&D partnerships.

In his new role, Dr. Crise supports business development activities as the lead scientific and technical liaison in the assessment of R&D partnerships through the ATPI BDO. He also plays a key role in developing a formal approach to enhancing in-reach activity to NCI programs and investigators, to advance strategic alignment between SAIC-Frederick and NCI on opportunities for collaborations related to cancer and AIDS research, and to help accelerate partnership activity accordingly. Dr. Crise will continue as coordinator of the Non-government-Sponsored Work Program, overseeing processes and project continuum for the Advanced Technology Program, Biopharmaceutical Development Program, Laboratory Animal Science Program, and the AIDS and Cancer Virus Program.

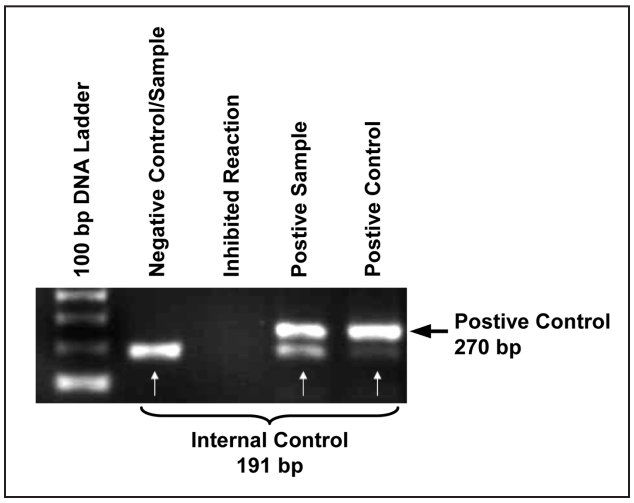
Dr. Crise comes to this position with an excellent scientific background and a broad knowledge of technologies and applications in cancer and AIDS research. He has more than nine years of institutional knowledge with SAIC-Frederick and an extensive internal network, with a long history of effective internal collaborations in SAIC-Frederick and NCI.

You may contact Dr. Crise on 301-846-5739 or criseb@mail.nih.gov.

Viral Technology Laboratory Offers New Service

By Rachel Bagni, Ph.D.

The Viral Technology Laboratory (VTL) of the Advanced Technology Program offers two kinds of services to the NCI and NIH communities: (1) production of recombinant animal viruses (adenovirus and lentivirus) and (2) testing of cells and samples for viruses (by PCR), antibodies (by ELISA and Luminex), and other analytes. The Molecular Detection Group within the VTL recently introduced testing for mycoplasmas, a class of contaminants of cultured cells. Mycoplasma testing



Mycoplasma test PCR products resolved by gel electrophoresis. PCR reactions include an internal control (IC) which appears as a 191 bp band. IC bands may fade in the presence of mycoplasma loads >5x106 copies/mL (~270 bp band). If the PCR is negative for both mycoplasma amplification and the IC, the sample contains inhibitors, which can be removed by either dilution or DNA extraction.

of cell lines is an important quality control measure. These common tissue culture contaminants can cause aberrant cell growth and performance, and may lead to experimental artifacts. Additionally, mycoplasma testing is routinely required for cells and cell products that are used in animal experiments at NCI-Frederick facilities. The VTL test for mycoplasmas is fast, inexpensive, detects 25 mycoplasma species as well as *Acholeplasma laidlawii* and *Ureaplasma*, and is performed on antibiotic-free supernatants from cultures that are two to three days old. The test is extremely sensitive (detects fewer than 5 organisms by PCR), but it should be noted that the volume assayed is relatively small and that slower, more costly assays may be required to detect extremely low-level contamination.

For more information on mycoplasma testing and control, contact Dr. Rachel Bagni at 301-846-5469, or bagnir@ncifcrf.gov.

"Next-Next-Generation" DNA Sequencing: The Future Is Here!

by David Munroe, Ph.D.

Although still in its infancy, next-generation (next-gen) sequencing technology has the potential to revolutionize biomedical research, allowing the sequencing of nucleic acids at levels that were unimaginable as recently as a few years ago. Compared to capillary DNA sequencers, with a single-run capacity of ~100 kilobases, next-gen DNA sequencers have a capacity of more than 40 gigabases per 2- to 5-day run, at an accuracy of 99.94%. This unparalleled throughput has opened up a vast array of new opportunities in biotechnology, biological research, and medicine.

However, as fast as next-gen sequencing platforms have come on the scene, they will soon face significant competition (and perhaps elimination) from the so-called next-next-generation (next-next-gen) DNA sequencing technologies. Currently there are three commercial next-next-gen sequencing platforms either on, or slated to be on, the market by 2010. These platforms are all single-molecule DNA sequencers, requiring no template amplification. They boast of read lengths between 25 and 25 kilobases, multiplex run formats, accuracy rates averaging 99.3%, and throughput in excess of 50 megabases per hour.

Overview of Three Next-Next-Generation Platforms

Helicos Biosciences (Helicos). The only next-next-gen DNA sequencing platform currently available, the Helicos platform utilizes a flow-cell format onto which DNA template molecules are anchored and incubated in the presence of DNA polymerase and a fluorescently labeled nucleotide. With each cycle, a single-labeled nucleotide is added (A, T, C, or G), an image is captured and its position recorded, and the fluorescent group cleaved. Subsequent cycles are repeated with a differently labeled nucleotide achieving read lengths of 25 to 50 bases. Helicos instruments are currently available for ~$1M per unit. Despite previous financial trouble,

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Next-Next-Generation continued

Helicos received an infusion of cash in early January and now appears more stable.[1]

Pacific Biosciences (PacBio). Perhaps the most intriguing and promising of the next-next-gen DNA sequencing platforms, PacBio is scheduled to become commercially available in early 2010. In this technology, single DNA polymerase molecules are anchored to a solid support within a zero-mode waveguide nanostructure (ZMW). Each ZMW is a "hole" tens of nanometers in diameter and 20 zeptoliters in volume. Unlike Helicos, which utilizes base-labeled nucleotides, the PacBio platform incorporates phosphate-labeled fluorescent nucleotides (see figure below) allowing for considerably longer read lengths (up to 25 kilobases). Current plans call for PacBio instruments to be sold at $0.3M to $0.5M per unit. PacBio remains financially strong, with current cash reserves in excess of $100M.[2]

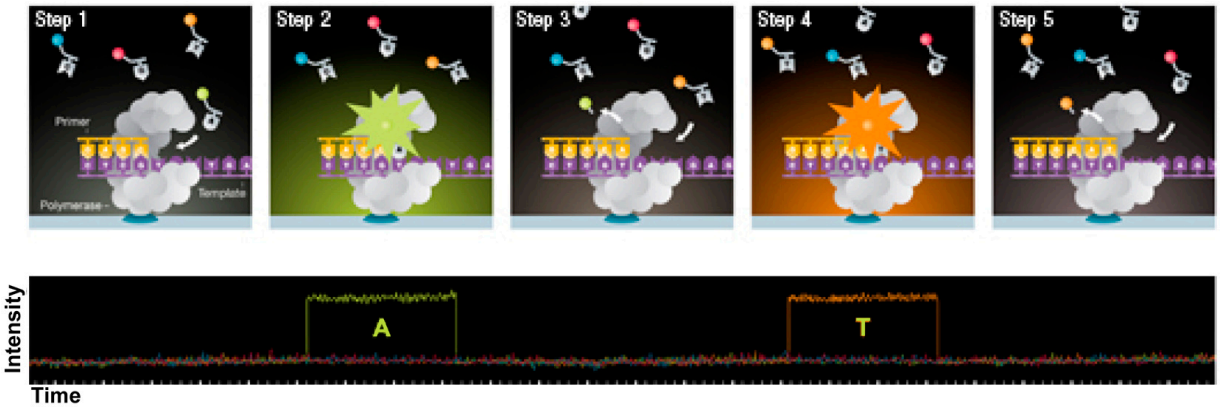
VisiGen Biotechnologies, Inc. (VisiGen). Also intriguing, yet less further along, is the VisiGen platform, which, like PacBio, relies upon a modified DNA polymerase immobilized onto a solid surface. What makes this platform unique is its use of fluorescent resonance energy transfer labeling technology, whereby a fluorescent donor molecule is transferred from DNA polymerase to a phosphate-labeled nucleotide during incorporation. Currently, VisiGen has not announced a specific commercial release date or a projected instrument sale price. VisiGen was recently acquired by InVitrogen, which has made firm financial commitments to both next-gen and next-next-gen DNA sequencing.[3]

Also noteworthy is a fourth company, Oxford Nanopore, which raised $21.1M in January from Illumina for development of its next-next-gen sequencing platform.[4]

New Challenges To Be Addressed

The exciting potential of next-next-gen sequencing technologies, however, comes with significant challenges, particularly with respect to data storage, transfer, and analysis. These platforms can sequence at a rate of more than 50 megabases per hour, with a single run file occupying up to 14 terabytes. Next-next-gen sequencing will require equally large advances in accompanying data management and bioinformatics. Stay tuned to see what develops in this rapidly evolving and exciting field.

[1]GenomeWeb staff, Helicos to raise $18.6M from private financing, *GenomeWeb Daily News*, December 19, 2008 (http://www.genomeweb.com).
[2]Karow, J., Pacific Bio raises $100M in Series E; says cash will last through first shipments, *GenomeWeb Daily News*, July 15, 2008 (http://www.genomeweb.com).
[3]Karow, J., With VisiGen in hand, Invitrogen hopes to bolster its own third-gen platform, *GenomeWeb Daily News*, October 28, 2008 (http://www.genomeweb.com).
[4]Karow, J., With Oxford Nanopore stake, Illumina makes another claim in third-generation sequencing, *GenomeWeb Daily News*, January 13, 2009 (http://www.genomeweb.com).
[5]Pacific Biosciences *Technology Backgrounder*, November 24, 2008, page 11 (http://www.pacificbiosciences.com).



In the Pacific Biosciences platform, "an optimized set of algorithms is used to translate the information that is captured by the optics system. In the figure above, "enzymatic incorporation of the labeled nucleotide creates a flash of light, which is converted into a base call using optimized algorithms."[5]

$5,000 of Services To Be Awarded at the ATP Expo

By Ken Michaels

ATP is hosting its first-ever Technology Expo on March 27 from 11:30 AM to 1:30 PM. Attendees will have an opportunity to receive $5,000 worth of ATP services by filling out a simple form describing what services they would use and how they would use them. A panel of judges will award the "mini-grant" based on scientific merit.

By showcasing the various technologies and services offered by ATP labs, the Expo is designed to attract potential clients and collaborators from NCI-Frederick and Bethesda, as well as generate new projects from current clients. Attendees will have an opportunity to browse posters and other materials describing the services offered by ATP labs as well as those offered by the Laboratory Animal Sciences Program.

The Expo opens 30 minutes after the Distinguished Scientist Lecture by George Vande Woude, Ph.D. Dr. Vande Woude is Director of the Van Andel Research Institute, Grand Rapids, Michigan, where he is a Distinguished Scientific Investigator and head of the Laboratory of Molecular Oncology. His laboratory focuses on the role of the Met protein in a variety of cancers and whether Met expression or anti-Met antibodies may be used as detection or prognostic tools in the treatment of cancer.

ATP Technology Expo

March 27, 2009
11:30 A.M. – 1:30 P.M.
Building 549

For information, contact:

Ken Michaels
301-846-1057
michaelskv@mail.nih.gov

On Effective Communication

We've Got To Stop Meeting Like This

By Ken Michaels

Have you ever been to a meeting when there was no discernable agenda?

Perhaps the person who called the meeting had a checklist of items to cover, but simply didn't think to share it with the others attending. Or perhaps the person who called the meeting really hadn't thought out what the meeting was intended to cover. In any case, if you were there, you had no idea what was coming next, or what the scope of topics to be discussed was going to be. How did that feel?

I've been to meetings like this. And I hate them. Having no idea what all is coming makes a lot of us—people like me, anyway—nuts.

Bear in mind that any time several people are called together to meet, all of them are contributing time that they would otherwise be spending doing productive things. If ten people are there and five minutes are wasted, fifty minutes are wasted. It's important to the efficiency and productivity of any organization for people to optimize the time they spend in meetings.

There are several guidelines for conducting effective meetings, and at the top of the list is: have an agenda and share it with the participants. An agenda not only clues the participants in, but it also gives direction to the meeting.

Another important guideline is to meet no longer than necessary. It's interesting how often meetings expand in duration to consume a full hour when the business could have been concluded in less time. When you have an agenda, once you've covered all the topics listed, your meeting is over.

Ideally, the agenda should be provided in advance to all who attend, so attendees know what topics will be discussed and they will be prepared to participate. The

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We've continued

broader the scope of the meeting and the greater the number of participants, the more important this rule is.

In the case of meetings involving only a few people, or recurring meetings that follow a regular and predictable course, alternatives to a written agenda provided in advance may suffice. Those alternatives include a written agenda provided at the opening of the meeting, a list of topics to be discussed written on a white board or easel pad, or, at very least, an oral rundown at the beginning of the meeting of what the meeting is about and what topics are on the docket. But in all cases, everyone present in a meeting should have some idea of what will be under discussion.

When organizing a meeting, always make the agenda known to those who will attend. You'll have a more productive meeting, and everyone in attendance will leave with a sense of accomplishment. I (almost) guarantee it.

Working with the Advanced Technology Program

The expertise of the Advanced Technology Program may be accessed through a variety of funding, contractual, and partnership mechanisms. For further information, please contact:

Timothy Harris, Ph.D.
Executive Vice President of Research and Technology
SAIC-Frederick, Inc.
301-846-1144; harristjr@mail.nih.gov

Public–Private Partnerships
Advanced Technology Partnerships Initiative (ATPI)
David Hoekzema, M.B.A.
Director of Strategic Business Development
SAIC-Frederick, Inc.
301-846-5895; hoekzemadt@mail.nih.gov

Intramural/NIH Institutional Programs
Bruce Crise, Ph.D.
Director, Business Development
SAIC-Frederick, Inc.
301-846-5739; criseb@mail.nih.gov

On-line requests for services from ATP may be made through the ATP/LASP Accession System (CSAS), at: http://web.ncifcrf.gov/rtp/csas/requestor/help.asp.

ATP Mission
To partner with NCI-Frederick to provide highly specialized support in a complex biomedical research environment, using a broad spectrum of advanced technologies.

ATP Update is an electronic publication published quarterly by the Scientific Publications, Graphics & Media department for the Advanced Technology Program of SAIC-Frederick, Inc., Operations and Technical Support Contractor for the National Cancer Institute at Frederick in Frederick, Maryland. The content of this publication does not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

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