NEWS FROM THE ADVANCED TECHNOLOGY PROGRAM

ATP Update

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Director's Point of View

New Technology and Research Group Formed

Tim Harris, Ph.D., Chief Technology Officer

As part of the new contract, SAIC-Frederick was reorganized, and the Advanced Technology Program (ATP) is now part of a larger technology group known as the Technology and Research Group. In addition to the ATP, this newly formed group consists of the Basic Science Program (AIDS and Cancer Virus Program [ACVP], and the Basic Research Program [BRP]); the Laboratory Animal Sciences Program (LASP); and a new Information Systems group consisting of the Advanced Biomedical Computing Center (ABCC) and the cancer Bioinformatics Grid (CaBIG) support. A new executive position, Chief Technology Officer, has been created to direct the Technology and Research Group, and I am proud to have been appointed to this new role. Owing to the diversity of the work going on in each area, a different management style will be required for each one. What works for the ATP may not work for the BRP, and vice versa. The ATP is primarily a technology-focused organization, with a heavy accent on core service provision and cost recovery. The LASP delivers an even bigger core service footprint, by providing animals and veterinary support to NCI. The ACVP and the BRP are focused on basic research and do not need the same type of management oversight as the technology programs. For the time being, I will continue to act as director of the Advanced Technology Program in addition to taking on the new role of Chief Technology Officer, and I really look forward to the opportunities for further integration presented by our new structure. If we work together in a cohesive way, we can be a very powerful ally for the NCI in the fight against cancer..

In This Issue

ATP Managers Recognize Employees

The Employee Recognition Program was launched this fall, with an outstanding contributor named from each of the five Supergroups. ATP managers recognized the following employees for the third quarter:

Genetics and Genomics Group
Nicole Lum, Research Associate III

Nicole Lum has been with the Laboratory of Molecular Technology (LMT) since it was established in January 2000. Ms. Lum started as a senior research technician and now works under Dr. Xiaolin Wu in the Affymetrix Microarray Services Group. The Affymetrix service offers both low- and high-throughput sample processing. LMT has a robotic Caliper GeneChip Array Station called a high-throughput arrayer (HTA), which allows a large number of samples (24 to 96 at a time) to be simultaneously processed using Affymetrix PEG arrays. This versatile system can accommodate large projects involving thousands of RNA samples, as well as consolidate smaller projects into one HTA run. Given the large number of NCI projects performed involving thousands of samples, it is critical

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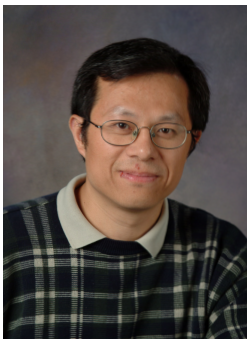
to properly coordinate and closely follow up on each run in the HTA robot. Ms. Lum is very proficient in managing the HTA system and will often come to the lab in the evenings, especially during the first day of a run, to make sure the whole process is working properly. With her excellent work, Ms. Lum significantly contributes to the success of this high-demand LMT service.

Imaging and Nanotechnology Group
David Parmiter, Research Associate I

David Parmiter has been with the Electron Microscopy Laboratory for nearly two years, where he performs nanoparticle characterization using both transmission (TEM) and scanning (SEM) electron microscopes. He developed a standard protocol to detect the atomic element of nanoparticles in both bulk samples and epoxy resin–embedded tissue samples using X-ray energy dispersed spectroscopy (EDS). Mr. Parmiter also provided an excellent TEM analysis of nanoparticles in tissue samples for the U.S. Food and Drug Administration (FDA). This work is part of NCL's collaborative research with FDA to visualize and localize the titanium oxide nanoparticles in skin tissue samples. Mr. Parmiter not only identified, but also confirmed the elemental make-up of the nanoparticles using EDS; elemental analysis is the only method to positively identify such small materials in a thin-sliced (~80 nm) TEM sample. Mr. Parmiter's support extends to investigators in both private and intergovernment agencies, such as the National Institute of Standards and Technology.

Information Technology Group
Ming Yi, Programmer Analyst IV

Ming Yi provides bioinformatics support for all forms of high-throughput biology, including microarray and proteomics analysis, for the scientific community in Frederick and in Bethesda. He has demonstrated his expertise in a variety of projects that have resulted in several publications. At the same time, he has continued to develop his WholePathwayScope (WPS) software, which enables microarray data to be visualized in the context of biological pathways as well as other biologically relevant gene annotation families. This software is now licensed at many academic sites worldwide. Most recently, he added the capability to detect cellular perturbations at the pathway level, even in the absence of common gene perturbations, which has significantly increased the ability to detect alterations between cancer and normal cellular states. This analysis method, termed Sample-Level Enrichment-Based Pathway Ranking (SLEPR), has also recently been published and presented at several meetings, where it was well received. Dr. Yi's continued hard work in an environment of essentially unlimited demand has contributed substantially to the continued success of the ABCC and its bioinformatics support group.



Proteins and Proteomics Group
John R. Klose, Associate Scientist

John Klose, of the Laboratory of Proteomics and Analytical Technologies (LPAT), has been with NCI-Frederick for 27 years, working in nuclear magnetic resonance (NMR) spectroscopy for the last 21 years. Over the last year, much of Mr. Klose's service was dedicated to supporting the NMR center of the Chemical and Structural Biology Faculty (CSBF). He has been responsible for user training and maintenance of a 400 MHz NMR spectrometer, and for running samples for CSBF scientists. Last November, the Developmental Therapeutics Program (DTP) asked LPAT to analyze 1,000 compounds using NMR and MS. Mr. Klose analyzed 50 of the compounds each week, in addition to maintaining his commitments to CSBF and LPAT.

Mr. Klose has always willingly handled emergency requests from NCI investigators. In one instance, Dr. Glenn Merlino, Chief of the Laboratory of Cancer Biology and Genetics, needed a compound's structure verified immediately because it was about to enter clinical trials. The request came on a Friday morning; Mr. Klose verified the compound's structure and delivered the results the same afternoon. Dr. Merlino was enthusiastic in his relief and praise for LPAT.

Although Mr. Klose has an enormous workload, he is a pleasure to work with and has the skills to solve any problem he faces.

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Visual Communication and Support Services Group
Susan Skidmore, Assistant Manager, Conference Center

Susan Skidmore is extremely dedicated to providing exceptional customer service to Conference Center users. She was specifically cited in the most recent Coordinator's Report for Technical Management support by the NCI. She was noted for being very accommodating and attentive to community needs. Her efforts and teamwork were key factors in the "Outstanding" rating.

During the past three months, she has helped schedule more than 922 meetings and 50 video teleconferences attended by 13,514 participants. She makes every effort to anticipate the requirements of conference center users and accommodates them in any way possible. Her attention to detail and dedication to serving customers are instrumental in the success of the NCI-Frederick Conference Center.

Ms. Skidmore was also instrumental in providing exceptional audiovisual support at Hood College for the Chemical Insights Symposium held August 15–16. As a result of her efforts, the symposium was successful and productive for all attendees. She also received positive comments from the meeting organizer on the outstanding support she provided.

The increase in room usage, along with limited available meeting spaces, makes scheduling increasingly difficult. Ms. Skidmore continually finds creative ways to accommodate users' needs. Her creativity and professional manner ensure meetings in the conference center run flawlessly and the high standards of the conference center are maintained.

ATP Retreat Focuses on Scientific Exchange

By Timothy Veenstra, Ph.D.

The Advanced Technology Program (ATP) held its second annual retreat on October 23 at the Clarion Hotel in Shepherdstown, WV. The day kicked off with an introduction by ATP Director Dr. Tim Harris, followed by the keynote address from Dr. Patricia Steeg, Center for Cancer Research, NCI. Dr. Steeg provided an insightful treatise on how primary tumors evolve into metastatic lesions, while highlighting many of the challenges that scientists face in detecting these lesions.

Other invited NCI speakers included Dr. Olga Aprelikova, Cell and Cancer Biology Branch, who spoke about the analysis of gene expression, microRNA, and proteins in endometrial tumors, and Dr. Eric Freed, HIV Drug Resistance Program, who shared recent findings on HIV-1 assembly, release, and maturation. All three presentations highlighted the synergy gained when research efforts are conducted in partnership with ATP laboratories.

The objective of the retreat was to provide a forum for information exchange, and presentations from ATP scientists focused on current technologies and research directions. Speakers included Dr. Oleg Chertov and Dr. Andrew Stephen, both of the Protein Chemistry Laboratory; Dr. Stephen Lockett, Optical Microscopy and Analysis Laboratory; Amy Hutchinson, Core Genotyping Facility; Butch Hopkins, Protein Expression Laboratory; Dr. Ester Rozenblum, Laboratory of Molecular Technologies; Dr. Betty Conde, Viral Technology Laboratory; and Drs. Jack Collins and Robert Stephens, Advanced Biomedical Computing Center. David Hoekzema, Director of Strategic Business Development, wrapped up with an update on the Advanced Technology Partnerships Initiative.

The keynote address by Dr. Patricia Steeg, Center for Cancer Research, NCI, provided insights into tumor metastasis.

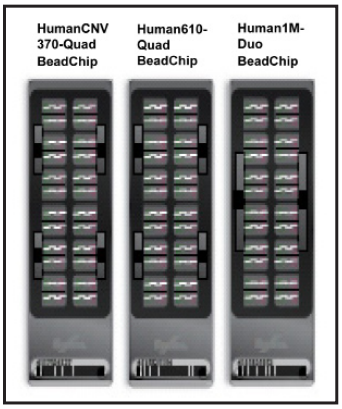
The retreat drew 120 attendees, including 7 people from programs outside the ATP. Dr. Tim Veenstra organized the event, with assistance from Barbara McElroy and Sandi Walker. Plans are already underway for next year's retreat; planners will focus on increasing participation by NCI scientists, whose presence will strengthen the scientific exchange as the ATP strives to support their research.

CGF Provides Specialized Support

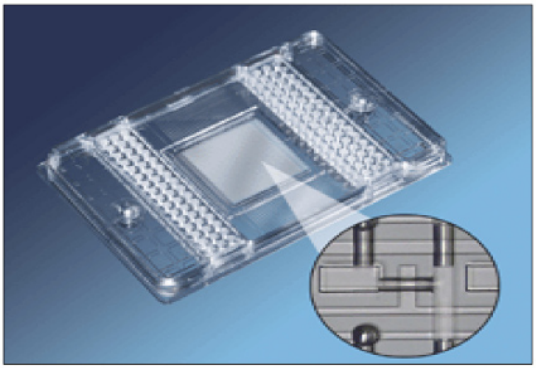
By Amy Ann Hutchinson

The Core Genotyping Facility (CGF), located at the Advanced Technology Center in Gaithersburg, functions as a high-throughput genotyping laboratory that supports NCI's Division of Cancer Epidemiology and Genetics (DCEG) and Center for Cancer Research (CCR). The CGF works closely with investigators to design specific genotyping projects for genome-wide association studies (GWAS), and replication and candidate gene studies.

Liquid-handling robotics, like the BioMek FX shown, are the cornerstones of the high-throughput lab.



Lineup of new, high-density SNP chips by Illumina and utilized for GWAS at CGF. Left to right: HumanCNV370-Quad BeadChip; Human610-Quad BeadChip; Human1M-Duo BeadChip.



Fluidigm's BioMark Dynamic Array in the 48.48 format. This variety is capable of over 2300 TaqMan reactions per chip.

A major focus of CGF has been conducting GWAS under the Cancer Genetics Markers of Susceptibility (CGEMS) initiative. While the CGEMS program ended this year, the CGF will continue to follow up on studies related to breast and prostate cancers. CGF's success with GWAS and replication studies has led to the exploration of other cancers using this methodology, including lung, renal, pancreatic, non-Hodgkin lymphoma, and bladder cancers.

The laboratory is equipped with advanced automated robotic systems, and all processes are tracked using a highly integrated and customized Laboratory Information Management System (LIMS). In addition, a sample-handling pipeline ensures proper quantification and identification of donor samples. With these tools, the laboratory is capable of fast-paced genotyping of either single SNPs or large, multi-SNP panels and chips.

Recently, the CGF acquired a Roche 454 GS FLX next-generation sequencer. This exciting new platform will be integral to the follow-up of GWAS due to the technology's capabilities of deep re-sequencing and SNP discovery in regions of interest. Steps are underway to optimize the process and add functionality into the LIMS to facilitate detailed tracking of samples, processes, and projects.

In addition to providing high-quality data to our customers, the CGF also has developed, designed, implemented, and launched the following informatics tools for the entire scientific community: Genewindow (http://genewindow.nci.nih.gov/); SNP500Cancer Database (http://snp500cancer.nci.nih.gov); GLU (Genotype Library and Utilities) (http://code.google.com/p/glu-genetics/).

CGF's staff of 40 employees is divided into seven functional groups, from project management to data analysis, each dedicated to a specific part of the genotyping process. All seven groups are integral to CGF's workflow and have made the idea of a high-quality, high-throughput genotyping and analysis facility a reality.

For more information on the CGF pipeline, details on processes and requirements, and contact information, please visit the web site: http://cgf.nci.nih.gov.

NCL and ABCC Move to Develop Nanotechnology Standards

By Jennifer Hall, Ph.D.

SAIC-Frederick's Nanotechnology Characterization Laboratory (NCL) and Advanced Biomedical Computing Center (ABCC) are collaborating with the National Institute of Standards and Technology (NIST) and the National Nanotechnology Initiative (NNI) to develop an international, on-line collaboration to speed up creation of critically needed nanotechnology standards, including reference materials and tests, to support the development of nanotechnology-based products.

This new, Internet-linked "community of interest" will combine efforts of materials scientists with those of biological and medical researchers and will use Web 2.0–style social networking technologies for creating and sharing information, and deliberating over technical details. The initial focus will be on preliminary-stage development of standards for characterizing the structure and properties of engineered nanoscale materials—those with at least one feature measuring between 1 nanometer (nm) and 100 nm.

The concept for the web-based collaboration was endorsed during a recent international workshop on Enabling Standards for Nanomaterial Characterization, hosted at NIST. A prototype wiki—or collaborative web site—was demonstrated by representatives of the ABCC.

There is increasing recognition of the need to facilitate the development of standard protocols and standard research materials for nanotechnology. Voluntary consensus standards and reference material standards contribute to making the development, manufacturing, and supply of products and services efficient, safer, and cleaner. Standards developing organizations (SDOs), like ASTM International and the International Organization for Standardization (ISO), create standard protocols that are used for regulatory evaluation and quality control. For example, the pharmaceutical industry has long used ISO and ASTM standards to assess such material characteristics as biocompatibility, hemolytic properties, immunotoxicity, purity, and sterility. Nanoparticle developers leverage these well-established methodologies whenever possible; however, the unique properties of nanomaterials frequently complicate this seemingly straightforward process.

Representatives from ABCC and NCL participated in an international workshop on web-based collaboration at the National Institute of Standards and Technology on October 8–9 .

The new on-line community of interest will concentrate on streamlining the many back-and-forth technical deliberations that take place during the drafting of a standard before it is submitted for formal approval by an SDO. Now under further development at NCI, the nanotechnology standards wiki will enable instantaneous dissemination (as well as archiving) of drafts, discussions, votes, and supporting materials.

For more information on the NIST workshop, go to http://www.ceramics.nist.gov/nanomaterial_workshop.htm. For more information on the development of nanotechnology-based cancer therapies, visit the NCL at http://www.ncl.cancer.gov.

PCL Beta Tests New Technology in ATPI Agreement

By Andrew Stephen, Ph.D. and David Hoekzema

As part of a partnership agreement signed last month between SAIC-Frederick and Silicon Kinetics (SKi), the Protein Chemistry Laboratory (PCL) has begun an evaluation of the SKi Pro™, a new biosensor from SKi. This new technology platform uses a process known as optical interferometry, in which molecules are attached within pores in a nanoporous silicon surface and an interacting molecule is flowed over the surface. If the two molecules interact, there will be a change in the interference pattern of light reflected back from the surface. This technology offers the potential to improve the sensitivity over traditional biosensors that characterize molecular interactions by measuring changes in the surface plasmon resonance (SPR) signal.

Highly sensitive and specific protein–protein interaction/binding technologies are critical to understanding biomolecular processes in cancer and infectious disease, and enable insights into drug

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intervention/binding properties that can guide rational drug design strategies. The PCL plans to test antibody–antigen, protein–DNA, and protein–small molecule interactions.

SKi is an ideal partner for this leading-edge research and development (R&D) in the PCL, with the first-of-kind, label-free 3D biomolecular analysis platform. SKi granted PCL "early access" to the technology platform through the partnership agreement.

This partnership agreement is part of the Advanced Technology Partnerships Initiative (ATPI), launched this year by NCI to accelerate the flow of new discoveries and technologies to clinical development and commercialization. The ultimate goal of the ATPI is to improve diagnostics and therapeutics for cancer and AIDS patients.

Technology development is a critical aspect of the initiative, and the agreement with SKi represents a seminal partnership in support of proteomics, with three high-level objectives: (1) to continue to build leading biomolecular interaction R&D capabilities for NCI; (2) to gain new insights into tumor cell receptor biology and application of drug-binding properties; and (3) to gain new insights into HIV cellular binding properties.

Methods and applications development are expected in the coming months and will benefit both companies in the collaboration.

New Facility: Progress Report

By Hoyt Matthai

The Advanced Technology Research Facility (ATRF) has become a reality. The groundbreaking occurred on November 12, with federal, state, and local dignitaries in attendance (see photograph below).

Activity leading to the groundbreaking occurred at a brisk pace throughout the fall. A major milestone was reached in September, when the Environmental Protection Agency issued a Finding of No Significant Impact for the proposed ATRF construction site. This finding means that the proposed action (construction/placement of the ATRF on the site) will not have a significant effect on the quality of the human environment and is based on the environmental assessment of the site. The release of this document was critical to moving forward with the lease negotiation and signing.

Throughout October, we focused on the IT needs of the facility in identifying a fiber provider and designing the ATRF data center. Various routes were proposed for the fiber run in an effort to create redundancy of service for the ATRF and other local, off-campus NCI-Frederick facilities. For the data center, we continue to investigate the latest technology that places servers in enclosed, liquid-cooled racks, eliminating the need for a traditional raised floor. This technology would allow

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ATRF Groundbreaking November 12 at Riverside Research Park

Left to right: Mark Matan, Principal, Matan Companies; Jan Gardner, President, Frederick Board of County Commissioners; Roscoe Bartlett, U.S. Congressman; Dr. John Niederhuber, Director, National Cancer Institute; David Edgerley, Secretary, Maryland Department of Business and Economic Development; Craig Reynolds, Associate Director, NCI-Frederick; Larry Arthur, President, SAIC-Frederick, Inc.; Jeff Holtzinger, Mayor, City of Frederick.

New continued

future expansion of servers/racks in the data center without affecting the air-cooling capacity of the system(s) servicing that area.

Looking forward, we will start working with our architecture and engineering firm on the design and layout of the research laboratories for the ATP. We anticipate beginning this process before the end of the year.

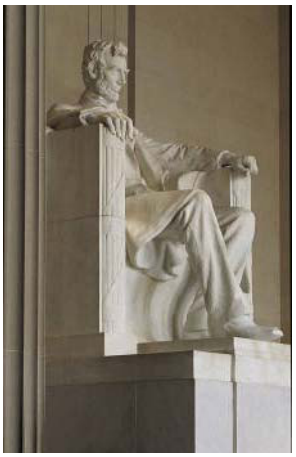
More information will follow in future issues of the ATP Update as we continue to move ahead on the ATRF project.

The Scientific Publications, Graphics & Media staff take a moment to pause for a group photo during their all-day retreat at ThorpeWood October 22. The crisp autumn day in the Catoctin mountains was spent in celebration of recent accomplishments and exercises in effective communication and team building. Front row, left to right: Tammy Schroyer; Ashley Hartman; Debbie Shores; Jennifer Klabansky; Kathy Green; Jiro Wada; Jon Summers. Back row, left to right: Christina Sealander; Jennifer Brown; Nancy Parrish; Colin Celaya, Manager, Conference Center; Maritta Grau; Anne Chaltain; Marti Welch; Allen Kane; Richard Frederickson; Ken Michaels.

On Effective Communication

How Abe Lincoln Got It Right… and Wrong!

By Ken Michaels



On November 19, 1863, President Abraham Lincoln gave an oral presentation at the dedication of the Soldiers National Cemetery a few miles north of here. The Gettysburg Address, as we now know it, is an elegant example of oratorical excellence; arguably the most famous speech in American history. On that crisp November day in southern Pennsylvania, Honest Abe got it right.

He got it right by being brief. Lincoln was not the featured speaker, and not a particular favorite of Pennsylvania Governor Andrew Curtain, who sponsored the event. Edward Everett, one of the nation's foremost orators, was the principal speaker, and he held forth nonstop for two hours. When it came time for Lincoln's turn at the lectern, he delivered his message in less than two minutes. It's hardly a wonder that his speech was more appreciatively received than Everett's, which is long forgotten. As someone once said, if you want your speech to go over well, always remember the "Three Bs" … be sincere, be brief, and be seated.

He got it right by using language that the audience understood. Seventy-six percent of the 267 words in Lincoln's short speech are of five letters or less. Plain talk, in my view, is an underrated tool for effective communication. Jargon, technospeak, and (especially in government) acronyms can act as "speed bumps" on the pathway to understanding, particularly when overused. True, in a gathering of scientists, it makes more sense to say "DNA" than "deoxyribonucleic acid," because it's a virtual certainty that all present recognize that very common acronym. Caution, however, is advised in the use of less well-known abbreviations.

He got it right by situating his main message between an interesting opening and a powerful conclusion. "Four score and seven" is infinitely more interesting to the ear,

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and the brain, than "eighty seven." And his concluding line packed one heckuva punch: "… government of the people, by the people, for the people shall not perish from the earth." Wow.

But he also got one thing wrong, when he said, "The world will little note nor long remember what we say here …" As senator Charles Sumner commented a year-and-a-half later, "The world noted at once what he said, and will never cease to remember it."

All things considered, that November day, Abe Lincoln really got it right.

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:

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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.

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