NEWS FROM THE ADVANCED TECHNOLOGY PROGRAM

ATP Update

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Director's Point of View

Tim Harris, Ph.D., Director, ATP

Welcome to the fourth edition of *ATP Update*, the newsletter of the Advanced Technology Program (ATP). As many of you know, one of our responsibilities is to help NCI in its mission to translate basic research into clinical practice. We call this translational research, or bringing research from "bench to bedside."

The Advanced Technology Partnerships Initiative represents the means that SAIC-Frederick, Inc. (and the ATP and the Biopharmaceutical Development Program [BDP], in particular) is using to encourage collaborations and partnerships with industry on behalf of NCI. We already have mechanisms to do that (e.g., the Work for Others program), but this new initiative is designed to encourage larger and more strategic relationships. We have recently had good meetings with several potential industrial partners, including GE Healthcare and MedImmune (Astra-Zeneca). It is early, but the signs are encouraging. We believe that, with the right business structure, we should be able to deal with intellectual property (IP) and other issues that sometimes get in the way of fruitful collaborations. The construction of the new research building at the new campus near Frederick will certainly help to foster these interactions, but the idea is to have some partnerships formed before the ATP and BDP move to the new site. Incidentally, the most suitable site has been identified, and we are in negotiations with that developer. The other developer has not been dismissed in case we are unable to complete negotiations on the most suitable site, and pending the National Environmental Policy Act (NEPA) evaluation. So it appears that the new building is now a lot more than just wishful thinking. We should thank the vision and foresight of the NCI Director for this to be happening in the way that it is.

Inside This Issue

Timothy M. Lohman, Ph.D., Guest Lecturer in January

By Andrew Stephen, Ph.D.

Dr. Timothy Lohman, guest lecturer at January ATP seminar.

On January 7, the ATP was pleased to host Timothy Lohman, Ph.D., the Marvin A. Brennecke Professor of Biological Chemistry from Washington University in St. Louis School of Medicine, for the second lecture in the 2008 ATP guest seminar series. In his seminar, entitled "Multiple Activities of *E. coli* SSB Protein," Dr. Lohman reviewed over 20 years of work in detailing the complex interactions of the single-stranded binding protein (SSB) with single-stranded DNA. He described how he and his colleagues had used stopped-flow fluorescence experiments and single-molecule fluorescence resonance energy transfer (FRET) approaches to understand the kinetics of SSB-DNA interactions. During the rest of his stay, he toured the Protein Expression Laboratory and the Laboratory of Proteomics and Analytical Technologies. In addition, Dr. Lohman met with members of the Protein Chemistry Laboratory, and Dr. Donald Court and laboratory members to discuss the role of SSBs in bacterial recombineering.

The Role of NMR and HPLC/MS in Clinical Metabolomics

By Gary Muschik, Ph.D.

Metabolomics, or alternately, metabonomics, is an emerging field of biochemical research that complements genomics, transcriptomics, and proteomics. Direct quantitative measurements of metabolite expressions in urine, serum, plasma, and tissue are essential to the study of biological processes in normal and disease states.

Because metabolic networks in living organisms are firmly connected, any change in the concentration of a single enzyme can lead to large concentration differences in many metabolites. The complexity and concentration range of the metabolites that constitute the metabolome make the separation, detection, and quantitation of each metabolite extremely challenging. The expertise of the Laboratory of Proteomics and Analytical Technologies (LPAT) staff in separation sciences, mass spectrometry (MS), and nuclear magnetic resonance spectroscopy (NMR) enables NCI and contractor scientists to perform complex studies on the metabolome of living organisms.

Metabolite profiling using NMR has been accomplished primarily by using one-dimensional (1D) NMR, which detects the most abundant metabolites. In a recent publication, Dr. Que N. Van of LPAT explains a two-dimensional (2D) NMR method she developed for analyzing low-abundance metabolites in urine.[1]

While acquiring 2D NMR data requires more time, the data obtained results in a more meaningful and comprehensive metabolite profile, aids in identifying metabolites, and minimizes ambiguities in peak assignments (See Figure 1).

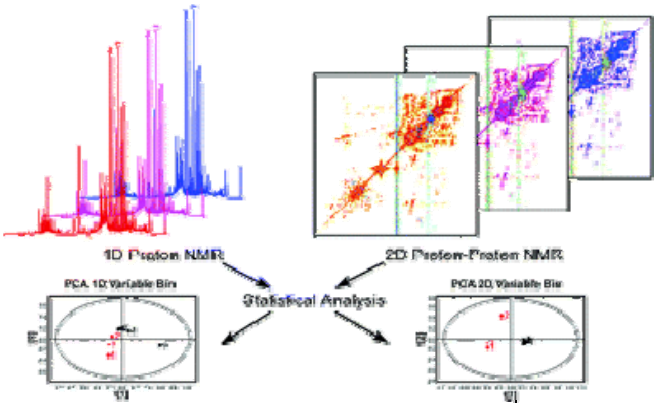

Figure 1. Metabolic profiling by NMR and statistical analyses.

In another metabolic study recently accepted for publication, Dr. Haleem J. Issaq, also of LPAT, demonstrates that metabolite variations can be used to discriminate between urines obtained from healthy individuals and bladder cancer patients.[2] HPLC metabolite separations and MS data collection, along with statistical analyses of the data, were used to identify metabolite variations between the normal and diseased individuals. The HPLC/MS procedure used is depicted in Figure 2.

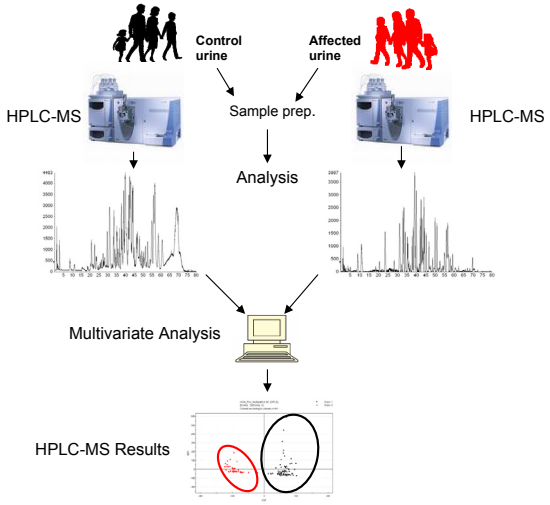

Figure 2. HPLC/MS-statistical analysis scheme for metabolite profiling.

Dr. Issaq's study included 41 urine samples from transitional cell carcinoma patients and 48 control urine samples. OPLS-DA and PCA analyses of the data resulted in two separate groups corresponding to normal and cancer urine samples. The OPLS-DA analysis correctly predicted 41 of 41 bladder cancer subjects (100% sensitivity) and 48 of 48 healthy (100% specificity). PCA analysis resulted in predicting 40 of 41 cancer urines (98% sensitivity) and 46 of 48 (96% specificity) control subjects.

These metabolomic projects represent the kind of activity currently taking place in LPAT. The utilization of available expertise, hardware, and statistical analysis within LPAT, and also within the whole of ATP, enables NCI and contractor investigators to apply the latest technologies to their research challenges and results in new capabilities for understanding human diseases.

References

1. Van et al., Comparison of 1D and 2D NMR spectrometry for metabolic profiling, J. Proteome Res., In press.
2. Issaq et al., Detection of bladder cancer in human urine by metabolic profiling using HPLC/MS, J. Urol., In press.

First ATP Lab Directors' Retreat

By Ken Michaels

Thorpewood Conference Center in the Catoctin mountains near Thurmont was the site for the Advanced Technology Program's first offsite directors' retreat, held February 6. The morning was spent with a study of Myers-Briggs personality type indicators, facilitated by Sukanya Bora, Training and Development Manager. MBTI, as the tool is known, is an instrument that can be useful in understanding the differing preferences among individuals in communication style, information processing, decision making, and human interaction. The afternoon session was devoted to developing SMART goals and objectives. SMART is an acronym that reminds us that workable objectives should be Specific, Measureable, Attainable, Realistic, and Time-limited. Working in teams, time was spent actually re-working some goals in order to SMARTen them up. The day wrapped up with an overview from Tim Harris about a major strategic goal of the entire program: coming together as a program as plans for the design of a new research facility move forward.

On Effective Communication

It's About Time!

by Ken Michaels

Back in high school, a history teacher told us of the railroad system in Italy being notorious in the mid-twentieth century for the lack of reliability of its daily schedules. This was a time of political turmoil as well, and a certain Benito Mussolini bolstered his rise to power by promising to end the country's transportation troubles. After seizing control, he touted his authority and leadership effectiveness with the claim that it was he who made Italy's trains run on time. (Many consider this an urban myth, finding it impossible to believe that trains in Italy have ever run on time, but he claimed it as a personal accomplishment all the same.)

Aside from trains, wouldn't it be nice if scientific meetings and symposia, too, also ran on time, especially when concurrent sessions are involved?

Meetings that don't run on time are annoying. In my own communications utopia, the meetings I attend begin on time, each speaker sticks scrupulously to his

Lab Directors pause for a few minutes from the day's business for a group photo on the porch at Thorpewood. Front row, L to R: Jim Hartley; Jeff Lake; Betty Conde; Bob Welch; Meredith Yeager; Stephen Lockett. Back row, L to R: Scott McNeill; Sukanya Bora, Training and Development Manager; Tim Harris; Bruce Crise; Bob Fisher; Deb Chaterjee; Gordon Whitely; Bob Stephens; Barbara McElroy, ATP Program Coordinator; Ken Michaels.

or her allotted time slot, and the event concludes either on time or a little early. Because when that happens, I'm able to more fully concentrate on what I'm there for—the content.

Speakers who drone on past their allotted time show disrespect for both the audience and for the speakers who follow. More than once I've heard the last speakers on the docket having to rush their presentations because of prodding by the emcee to end the session on time. In such situations, those last few speakers were shortchanged. Running over one's allocated time slot is poor form for a presenter.

Even when prompted by the emcee to finish up, the "overtime" speaker has few options available if there's still more material. I've seen speakers speed talk and fast-flip through a dozen slides or more, sometimes skipping some altogether—which prompts the question: if the material was unimportant enough to skip, why was it in the talk to begin with? It mainly demonstrates to the audience that the speaker was not well prepared.

Here's a suggestion that, if followed, will endear you to your colleagues: If you're invited to give a 30-minute presentation, do it in 25. Nobody minds when you finish early; the worst it can do is provide a few extra minutes for Q&A. And how do you know if you can do it in 25 minutes? *Practice it.*

I understand that the idea of practicing a presentation is considered unnecessary by many experienced public speakers. But if there's only one good reason for practicing a presentation in advance, regardless of experience, it would be to ensure that you can get your important messages across in the time frame allotted.

The importance of being on time cannot be overemphasized. Just ask anyone who has ever traveled to Italy.

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