



# The SER-CAT SPECTRUM

A Biannual Newsletter of the Southeast Regional Collaborative Access Team • Summer 2005

## Director's Message

Bi-Cheng Wang

Welcome to the Summer 2005 issue of *The SER-CAT Spectrum*. Although we have just reached the half way mark in the year, I am pleased to report we have already made great strides in several aspects of the SER-CAT program. The last six months have been filled with activities and accomplishments that we will share with you in this issue, including our second annual scientific symposium, a TV segment featuring the SER-CAT facility, increases in scientific productivity and participation in the APS General Users' program, to name a few.



Dr. B.C. Wang with Ohio State University President Dr. Karen Holbrook

While I feel a great sense of pride about the things accomplished this year and our plans for moving forward, it is interesting to look back once in a while at how our program developed. Recently, I had the opportunity to visit Dr. Karen Holbrook, President of Ohio State University. Before accepting the position at Ohio State, Dr. Holbrook served as Provost for the University of Georgia. She was instrumental in supporting the SER-CAT program by helping to establish the trust account needed for our future operations. We now have a strong financial structure for our future growth.

It is amazing how we have come from a small group of southeastern crystallographers selling a plan to our administrators to such a large consortium with a facility that is now deemed "one of the best in the world." It was a pleasure to look back and to update Dr. Holbrook on all we have achieved. As a small token of our gratitude for her visionary leadership and understanding, I thanked

her once again and presented her with an official SER-CAT coffee mug.

Indeed, we have come a long way together over the past several years, thanks to SER-CAT's outstanding membership and hard-working staff. Also, we have recently introduced new ways to recognize accomplishments of SER-CAT users, such as the SER-CAT Young Investigator and Outstanding Science Awards. These awards were presented for the first time at our symposium at St. Jude Children's Research Hospital in March and will continue in the same fashion at our 2006 symposium, which will be held at Georgia State University. Congratulations to our first award recipients, Dr. Nicole LaRonde-LeBlanc of NCI-Frederick and Dr. Lorena Beese of Duke University, who received the Young Investigator and Outstanding Science awards, respectively.

I hope you will read on to discover more details behind all of these and other activities. We are striving to make the SER-CAT beamlines the best possible beamlines for protein crystallography in terms of data quality and user-friendliness. If you have any suggestions for improving our program or if you have an achievement you would like to have highlighted in our next issue, please let us know. Thank you for your interest and have a great summer!



## SER-CAT Featured on World Business Review

SER-CAT was recently featured in a segment on *World Business Review with General Alexander Haig*, a television program developed to highlight new and interesting technologies and activities around the world. Although synchrotron research is not new, the *World Business Review* felt that SER-CAT was a unique program because of the number of institutions involved and the state-of-the-art research facility available to its members. The staff at *World Business Review* first

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learned about the SER-CAT program at the 2003 American Crystallographic Association Meeting in Cincinnati, Ohio, the second time that a SER-CAT booth was presented at the ACA meeting.

The program featuring SER-CAT originally aired on the Bravo Network on Tuesday, February 1, 2005 and will air again on Thursday, June 2, 2005 at 7:30 AM Eastern Standard Time. A streaming video of our segment can now be viewed at [www.ser-cat.org](http://www.ser-cat.org) and is also available in CD-ROM and DVD-R format. In addition, the segment will be broadcast on all United Airlines international flights during the entire month of August 2005.

We are excited about this new addition to our outreach efforts and hope you will have a chance to view the segment. For more information on *World Business Review*, please visit [www.wbrtv.com](http://www.wbrtv.com).

## 2<sup>nd</sup> Annual SER-CAT Symposium at St. Jude Children's Research Hospital

The second annual Southeast Regional Collaborative Access Team (SER-CAT) symposium, "Practical Aspects of Structure Determination Using Synchrotron Radiation," was held at St. Jude Children's Research Hospital in Memphis, Tennessee, on March 18, 2005. This year's symposium brought in a diverse group of approximately 50 participants from both SER-CAT member and outside institutions, including senior scientists and graduate students. In addition to the scientific program, attendees had the opportunity to tour the facilities and learn more about the research and history behind St. Jude Children's Research Hospital.



Symposium participants gather for a group picture in front of the main entrance of St. Jude Children's Research Hospital

The scientific program began with a presentation by Irene Weber (Georgia State University) who presented atomic resolution crystal structures of HIV protease mutants and described how these findings will be used in the development of new antiviral inhibitors.

John Chrzas (SER-CAT) followed with a talk entitled, "Did I collect the data I need to solve my problem?" which highlighted practical solutions for making the most efficient use of the SER-CAT facility. Participants were also given an overview of new beamline features that will be provided by the SER-CAT Operations Team, including automated tools for data processing, structure solution and refinement.

Andy Mesecar (UIC) continued the discussions on practical applications but focused on the technique of time-resolved X-ray diffraction studies. His lab is currently studying the structure and function of enzymes and receptors involved in cancer chemoprevention, cancer cell proliferation, cell longevity (aging), bacterial and viral pathogenesis, and bioremediation. Time-resolved X-ray crystallography is one of many tools from the fields of chemistry, biology and physics that are used in these studies.

Pappannan Thiyagarajan (IPNS, ANL) and Dean Myles (ORNL) gave an overview of neutron macromolecular crystallography (NMC) at the Spallation Neutron Source (SNS) being developed at Oak Ridge National Laboratory. NMC can be used to provide accurate information on positions of protons and water molecules in the active sites of enzymes that will enable the elucidation of the mechanistic details involved in their function. Participants also learned of proposed plans to develop a dedicated high intensity macromolecular neutron diffractometer (MaNDi) beamline at the SNS.

Joanne Yeh (Brown University) illustrated methodologies used by her lab in protein crystallization and diffraction of macromolecular crystals. Yeh first described an easily adaptable, manual nanoscale method for protein crystallization currently used in her laboratory, which allows screening of up to 100 conditions while using a minimum amount of protein. Participants also learned how *in-situ* annealing, or "flash-annealing," has been implemented at a synchrotron site to improve the diffraction qualities of macromolecular crystals.

K.R. Rajashankar (MSKCC) offered practical advice to participants in his presentation appropriately entitled, "Getting the best data and getting the best out of your data." This talk summarized his experiences and general community knowledge on ways of collecting good data sets and means of making the best use of it. Rajashankar is currently a scientist at the Memorial Sloan-Kettering Cancer Center in New York City, but has previously worked at both Brookhaven and Argonne synchrotron facilities.

Brenda Schulman (SJCRH) presented an interesting story on working around the problem of poor electron density in several crystals that diffracted moderately at the SER-CAT facility. Schulman gave an overview of a selenomethionine-scanning

## 2nd Annual SER-CAT Symposium, from Page 2

mutagenesis technique and described how it was used to help solve the structure of the 110 kDa ternary complex between human SPPBP1-UBA3 and a 26-residue peptide corresponding to the N-terminal region of Ubc12.

Continuing on the topic of practical aspects, participants took part in a workshop, entitled "A New Approach to Structure Determination Applicable to SER-CAT and In-house Operations." The workshop was led by University of Georgia researchers Zhi-Jie Liu, Zheng-Qing Fu and Wolfram Tempel. An overview was given on techniques recently used to solve five structures in 23 hours during a visit to the SER-CAT facility. Attendees learned the techniques used in preparation, data collection and structure determination as well as the combination of technologies used behind the scenes.

## SER-CAT Science Awards

The symposium included the introduction of two awards new to the SER-CAT program for 2005, designed to recognize important scientific accomplishments at or of benefit to SER-CAT. The SER-CAT Outstanding Science Award was presented to Lorena Beese of Duke University, recognizing the scientific impact of her work in DNA polymerase studies related to the understanding of cancers and aging, as published in *Nature* and *Cell*. The SER-CAT Young Investigator Award, open to researchers within two years of a Ph.D. degree, was presented to Nicole LaRonde-LeBlanc of the National Cancer Institute recognizing her work on RIO serine kinases, which was recently published in *Structure*. Both award recipients gave an overview of their research at the symposium.



B.C. Wang presents the Outstanding Science Award to Lorena Beese



B.C. Wang presents the Young Investigator Award to Nicole LaRonde-LeBlanc

We would like to acknowledge Stephen White, Dayna Baker and others at St. Jude Children's Research Hospital for hosting the symposium at their outstanding facility and also the wonderful speakers who made the event possible.

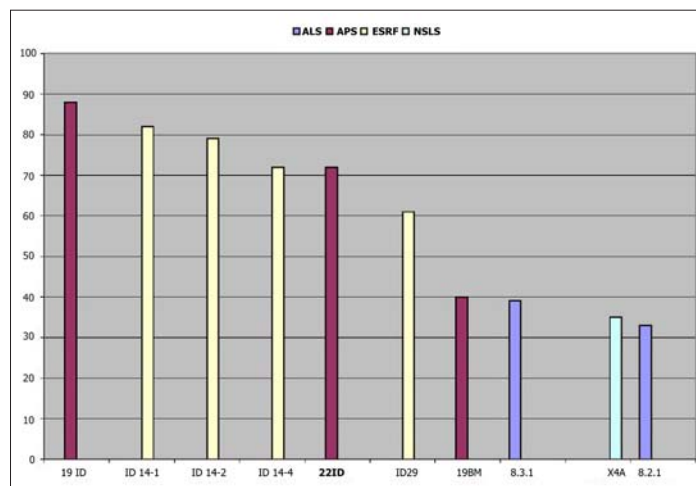
In addition, we would like to thank Irene Weber, who has graciously volunteered to host the next

symposium in March 2006 at Georgia State University in Atlanta, Georgia. The next SER-CAT Board meeting will be held in conjunction with the symposium. Details will be posted at [www.ser-cat.org](http://www.ser-cat.org) and distributed to our members when available.

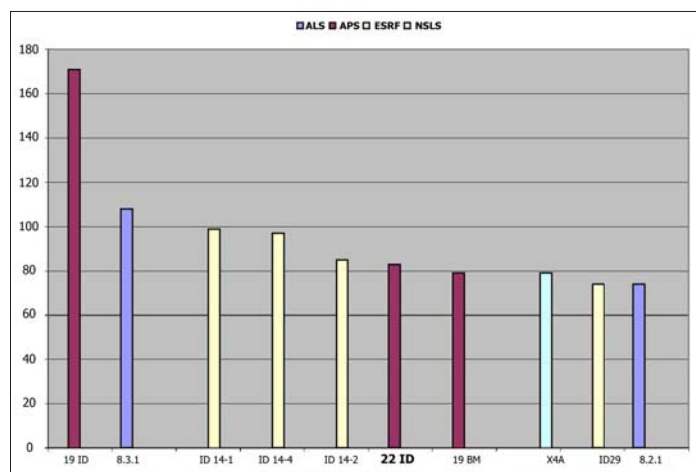
■ The preceding was a revision of an article submitted for the Summer 2005 newsletter of the American Crystallographic Association.

## Scientific Productivity in 2004

The results are in, and we are pleased to announce that our 22-ID beamline is not only among the top beamlines at the APS in publications and PDB submissions but is also among the top ten beamlines in the world! The graphs below show how 22-ID stacks up against other beamlines in the number of publications as reported on each facility's website and the number of PDB submissions for 2004 as reported by PDB Statistics.



Top Ten Beamlines in Number of Publications for 2004



Top Ten Beamlines in Number of PDB Submissions for 2004

The numbers for 2005 are steadily increasing and will likely surpass those reported in 2004. Several factors have contributed to this increase in productivity. The SER-CAT facility has become more robust, allowing our members to make the most effective use of their beamtime. Structures and publications submitted by general users collecting data at SER-CAT have also enhanced productivity.

Please be sure to give SER-CAT credit where it is due when depositing structures in the PDB and in publications. The proper wording of acknowledgements is available at [www.ser-cat.org](http://www.ser-cat.org).

## SER-CAT's 100<sup>th</sup> Publication

In April 2005, SER-CAT reached a new milestone in productivity. We now have over 100 publications in the APS database. As of May 23, 2005, there were 113 publications credited to SER-CAT.



Dr. Carla Mattos

The 100<sup>th</sup> publication - "Structural Mechanism of Oxidative Regulation of the Phosphatase Cdc25B via an Intramolecular Disulfide Bond," *Biochemistry-US* 44, 5307-5316 (2005) - was submitted by principal investigator, Carla Mattos, of North Carolina State University. *The SER-CAT Spectrum* asked Dr.

Mattos to comment on the background behind the article and her experiences at the SER-CAT beamlines. Her story is not only a testament to the strengths of our facility but also a great example of how SER-CAT members are working together to produce outstanding science in the crystallographic community.

"The research published in the 100<sup>th</sup> article is fruit of a collaborative project between my group and that of Johannes Rudolph's group at Duke University," explained Mattos. "Johannes and I met at the Enzymes, Co-enzymes and Metabolic Pathways Gordon Research Conference a few years ago and discovered that we not only had some common interests but we worked at neighboring universities in the Triangle. Johannes was studying the enzymology of the phosphatase Cdc25B and had several inhibitors in hand. He asked if I would like to collaborate with him on determining the structure of Cdc25B in complex with some of the inhibitors. Johannes and his people gave us lots of protein, and my graduate student Greg Buhrman took the phosphatase on as a side project.

"Although we were not able to see the bound inhibitor," she continued, "Greg worked out a protocol to remove sulfate from the active site and to capture the various oxidation states of the phosphatase as it is reversibly deactivated in the presence of reactive oxygen species. He actually took a tray full of crystals to the APS and did the experiments 'on the fly' at SER-CAT in order to find conditions that optimized the presence of the disulfide form of the phosphatase. The five resulting structures allowed us to couple the mechanistic steps studied by Johannes and his group (Sohn and Rudolph (2003) 'Catalytic and chemical competence of regulation of cdc25 phosphatase by oxidation/reduction,' *Biochemistry* 42, 10060-10070) with the structural transitions that occur during the reaction."

Dr. Mattos described how her membership in SER-CAT has benefited the research behind this latest publication and other ongoing projects in her group. "Being a member of SER-CAT has allowed us a steady and reliable beamline for high quality data collection," Mattos proclaims. "The phosphatase work, for example, would not have been possible without the synchrotron because the crystals diffract very poorly at home. The SER-CAT facility not only provides a lab for us to do experiments there, but

we are able to look at electron density maps within minutes of data collection. In the case of the phosphatase project, this was essential to determine whether we had captured the disulfide form. We had to collect several data sets before confirming that we had 'hit the jack pot.' The availability of SER-CAT is also critical to our main project on the GTPases and to a project aimed at studying protein binding surfaces using Multiple Solvent Crystal Structures. These projects require a huge amount of data collection that would probably not be feasible for us through the normal venues available in the general user program."

After earning her Ph.D. in Chemistry at the Massachusetts Institute of Technology and postdoctoral training at Harvard University and Brandeis University, Dr. Mattos joined North Carolina State University, where she is currently Assistant Professor in the Department of Molecular and Structural Biochemistry. Mattos was recently the recipient of the Presidential Early Career Award for Scientists and Engineers (PECASE), the highest national honor for researchers in the early stages of their careers, in which she was recognized at being at the "forefront of research in structural biology, using a novel method of multiple solvent crystal structures to identify functional parts within proteins." Her research is supported by grants from the NIH (R01 CA096867) and the NSF (0237297). More information on her research is available at her lab website, <http://biochem.ncsu.edu/faculty/mattos/lab/index.html>.

## Technical Update

In addition to assisting users, the SER-CAT Operations Team is steadily working behind the scenes to improve both beamlines and make the facility as user-friendly as possible. This approach has allowed our users to maintain control of their experiments without extensive staff support, which in turn has helped ease the transition of operating two beamlines with the same number of staff members.

Both the 22-ID and BM beamlines have experimental envelopes that define the beamline capabilities and experiments that users can perform without staff participation, such as changing the wavelength, optimizing beamline optics, collecting, processing and backing up data, to name a few. The "Beamline Usage Guide" at the SER-CAT website ([www.ser-cat.org](http://www.ser-cat.org)) is constantly being updated as the experimental envelopes are expanded, so users should check out the latest capabilities before data collection. Printable tutorials are now available in PDF format with detailed instructions on all user-controlled experiments.

The staff has also made headway on several interactive elements at the SER-CAT facility, including several software and hardware enhancements. A new version of SERGUI is being commissioned on both beamlines and has already been used to collect several data sets. The program remains in a tab-notebook format for easy access to user options, and the updated functions are similar to those in the old version. Work is currently being performed to integrate SERGUI control of the ALS robot. Users are encouraged to give the staff feedback on the look and feel of the new GUI, which will eventually replace a number of

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different software programs to simplify beamline control. The robot program will begin commissioning by members on the 22-BM beamline in June. Members should be checking it out and getting the proper tools in place. Details are available at [www.ser-cat.org](http://www.ser-cat.org).



Sample Changer at 22-BM Beamline

Plans for remote access via Access Grid are also underway, and our members have been eager to test this capability. The staff is currently testing several elements to streamline the process of remote access, using the 22-BM beamline as a test bed. The Access Grid set up is ready to go at APS, pending some fine tuning on the audio element, and an alpha

test site is set up at the administrative offices at the University of Georgia. Interactive elements such as SERGUI and the sample changer are operating and undergoing commissioning at the beamlines, and the next step will be integrated commissioning with the UGA test site. The objective behind each step is to make certain the technology is mature enough to be easily transferred before expanding the program. The end result should be a user-friendly software environment mirroring the SERGUI control of the beamlines at member institutions.

## Update on General User Program

After having operational status from the APS for one year, SER-CAT began accepting General Users through the APS in January 2005. General Users now account for 25% of beamtime on the 22-ID beamline. The Operations Team has done a great job in making the transition as smooth as possible for all involved.

Our General Users have been impressed with our facility and it is now in high demand. *The SER-CAT Spectrum* contacted a few of the principal investigators and asked them to comment on their experience and the reasons that they chose 22-ID for their research. Here's what they had to say:

Dr. Frank Whitby of University of Utah School of Medicine chose SER-CAT because he "wanted an intense beam with a large CCD detector." Whitby explained, "We felt that SER-CAT would offer us the best chance of getting good data and extending the resolution limit of our data from weakly diffracting, small crystals with 500+ angstrom cell edge." He rates the 22-ID beamline as "one of the best in the world" and looks forward to using the facility in the future.

Dr. Alfonso Mondragón of Northwestern University was also looking for "a beamline with a very bright beam to collect data from weakly diffracting crystals," and SER-CAT fit those characteristics. When asked about his experience, Mondragón remarked, "We were very happy with SER-CAT. Overall, our experience was outstanding. We would like to continue visiting SER-CAT in the future to help us with our synchrotron needs."

The General User program has also introduced our facility to potential members, such as Dr. Mavis McKenna of the University of Florida, who had an "excellent" experience at SER-CAT. "The staff was extremely helpful and the set-up was great. The beamline was designed with a crystallographer in mind!" proclaimed McKenna. Her group determined the structure for a virus capsid (Adeno-associated virus serotype 8) for which they collected data at SER-CAT in February, and they are currently working on a second virus capsid structure. "We are hoping to try to purchase a user share at SER-CAT and the General User program provided us the opportunity to 'check out' the beamline," McKenna explained.



## SER-CAT at 2005 ACA Meeting

This will be the fourth consecutive year that SER-CAT will host a booth at the annual ACA meeting. This has proven to be a great outreach effort for our program, not to mention a nice spot for our users to stop by and visit. This year's meeting will be held at the Walt Disney Swan and Dolphin Hotel in sunny Orlando, Florida, May 28 – June 2, 2005. We will be highlighting activities and progress at the beamlines since last year's meeting and will also be promoting new elements such as Access Grid and the new look of SERGUI, which is now being commissioned on both beamlines. Nomination information on the SER-CAT Science Awards and other informative SER-CAT materials will be available. Please come see us at **Booth # 605** and let us know what you think!

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*The SER-CAT Spectrum* is the biannual newsletter of the SER-CAT group. Additional information about SER-CAT and the Advanced Photon Source at Argonne National Laboratory can be found at our website [www.ser-cat.org](http://www.ser-cat.org) or by contacting the SER-CAT Administrative Office at 706-583-8243.

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