Annual LSB retreat caps another successful year

By Raj Gosavi

The NIEHS Laboratory of Structural Biology (LSB) held its annual retreat Sept. 12-13 at the North Carolina Botanical Garden, part of the University of North Carolina at Chapel Hill (UNC-CH). More than 50 attended the event.

This year's event featured talks by academic speakers, and was structured to facilitate an exchange of ideas between the new and established investigators, and LSB trainees aspiring to become young investigators.

The speakers were selected to represent universities, rather than government organizations, which allowed them to share valuable insights into the role of lead researchers at academic institutions. The major contribution to the success of the retreat was that the speakers were some of the most outstanding structural biologists in the field of DNA repair and crystallography (see text box).

The structural biologists speaking at the retreat discussed a wide range of techniques of interest to NIEHS scientists, including X-ray crystallography, nuclear magnetic resonance, mass spectrometry, and small-angle X-ray scattering (SAXS). Additionally, several of the talks went beyond these techniques and highlighted exciting new findings in structural biology.

NIEHS senior researcher Samuel Wilson, M.D., who headed up the retreat organizing committee, was generous in thanking the entire committee for the retreat's success. "LSB retreats provide an intense scientific experience for all the attendees every year," he said. (Photo courtesy of Steve McCaw)

From single molecule studies to ultra-rapid nanocrystallography

With the breathtaking pace of technological advances in the field, the possibility of looking at single molecules was bound to happen in a matter of time. Stephen Kowalczykowski, Ph.D., from the University of California, Davis (UCD), presented his work on the single molecular visualization studies of RecBCD, a processive DNA helicase that unwinds and degrades DNA. Kowalczykowski's team engineered a system that allows them to track the movement and activity of a single molecule of RecBCD on a single DNA molecule.

"I didn't think that, in my lifetime, not only would it be possible to watch a single DNA, but also to watch a single enzyme on DNA," Kowalczykowski said.

In the discussion of another single molecule study, Dorothy Erie, Ph.D., from UNC-CH, described the use of atomic force microscopy, as well as single molecule fluorescence studies, to show the interaction between DNA and the mismatch repair protein MutS.

New work that has the potential to change the way people think about X-ray crystallography was presented by Petra Fromme, Ph.D., from Arizona State University (ASU). Fromme talked about recent developments in the new area of femtosecond, or one-quadrillionth of a second, X-ray diffraction nanocrystallography, to obtain structures of challenging proteins, such as membrane proteins. With 12 times more intense X-rays, as compared to standard X-ray crystallography, she explained, there is no longer a need to grow large protein crystals, which had been a bottleneck in structural studies.

Eichman's talk discussed his study on "Structural studies of replication fork regression by DNA damage response protein SMARCAL1," which utilized a combination of X-ray crystallography and SAXS to obtain important insights into the process. (Photo courtesy of Steve McCaw)

Poster flashes and ask the experts

LSB retreat organizers used certain activities to vary the pace of the meeting. One of them, the poster flash slide exercise, was introduced at last year's LSB retreat. The exercise involves talking for one minute on a single slide, in a way that captures the essence of the poster and stimulates some playful banter among participants. This activity not only encourages creativity on the part of the presenter, but also provides a perfect platform for interaction at the poster.

Something new in the retreat was the Ask the Experts session. This activity took advantage of the speakers' background experiences and involved them in discussions with the retreat attendees on topics ranging from how to formulate a good research project to getting the work published and the role of collaborators - topics that aren't usually a part of a research presentation.

Emphasizing the importance of keeping an open mind on the use of a variety of techniques and collaboration, Brandt Eichman, Ph.D., from Vanderbilt University, said, "It is important to utilize whatever technique is possible to get the required answer, and use a combination of structural biology techniques, as required."

Similarly, Lorena Beese, Ph.D., from Duke University, encouraged better cross-communication between structural biologists and other disciplines, to formulate stronger and more meaningful collaborations.

(Raj Gosavi, Ph.D., is a research fellow in the NIEHS Structure and Function Research Group.)

Fromme, who had proteins crystallized in a space shuttle, said she thinks this is an exciting time for structural biology. She remarked that, with future advances in instrumentation, femtosecond nanocrystallography can even eradicate the phase problem, which often slows crystallographers. (Photo courtesy of Steve McCaw)

Beese's talk on "Conformational changes that drive the human DNA mismatch repair machinery" highlighted the application of structural biology to her challenging projects. (Photo courtesy of Steve McCaw)

Ramsden provided a great example of efficient collaborative research from his several successful collaborations at the NIEHS. (Photo courtesy of Steve McCaw)

Both Erie, left, and Ellenberger stressed the importance of communication in collaborative projects, and shared their thoughts on how to initiate and complete research projects. (Photo courtesy of Steve McCaw)

Speakers at the LSB retreat

Dale Ramsden, Ph.D.
(http://www.med.unc.edu/biochem/ramsden)
- Professor of biochemistry and biophysics at UNC-CH. Research interests: V(D)J recombination and double strand break repair.

Stephen Kowalczykowski, Ph.D.
(http://microbiology.ucdavis.edu/kowalczykowski/kowalczy.htm)
- Distinguished professor of microbiology and molecular genetics, and of molecular and cellular biology at UCD. Research interests: Molecular mechanism of genetic recombination
(http://microbiology.ucdavis.edu/kowalczykowski/genetic%20recomb.htm)
and biochemistry of DNA helicases.
(http://microbiology.ucdavis.edu/kowalczykowski/DNA%20helicase.htm)

Brandt Eichman, Ph.D.
(https://medschool.mc.vanderbilt.edu/biosci/bio_fac.php?id3=11799)
- Associate professor of biological sciences, and of biochemistry in the Department of Biological Sciences at Vanderbilt. Research interests: Structural biology of DNA repair and replication machinery.

Lorena Beese, Ph.D.
(http://www.biochem.duke.edu/modules/biochem_beese_lab/index.php?id=1)
- James B. Duke Professor of Biochemistry in the Duke University School of Medicine. Research interests: Structural biology of DNA replication and mismatch repair systems, as well as signal transduction proteins.

Tom Ellenberger, Ph.D.
(http://biochem.wustl.edu/faculty/faculty/tome)
- Professor of biochemistry and molecular biophysics at the Washington University School of Medicine. Research interests: Investigating the molecular structures and cellular functions of proteins that replicate DNA, repair chemical damage, and regulate chromatin structure.

Petra Fromme, Ph.D.
(http://www.public.asu.edu/~pfromme/fromme/index.html)
- Professor in the Department of Chemistry and Biochemistry at ASU. Research interests: Structural biochemistry and biophysics of membrane proteins.

Dorothy Erie, Ph.D.
(http://www.chem.unc.edu/people/faculty/erie/)
- Professor in the Department of Chemistry at UNC-CH. Research interests: Atomic force microscopy and fluorescence studies of protein-protein and protein-nucleic acid interactions in DNA mismatch repair.

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