National Research Program for Genomic Medicine

Core Facility Project：**D4**

Operation and Upgrade of the Synchrotron Radiation Protein Crystallography Facility (SPXF)

Progress Report (2005.11.01~2006.10.30)

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- Statistics of User Service:

The SPXF operates 2 beamlines at the National Synchrotron Radiation Research Center (NSRRC) for genomic medicine and structural biology users. These include BL13B1 and BL13C1. BL13B1 is a MAD PX beamline with energy tunability from 6.5 keV to 19 keV for unknown structure determinations. BL13C1 is a monochromatic (Mono) beamline with energy selection from 12.4 keV to 13.5 keV for fast crystal screening and high-resolution structure study**.** Each of these beamlines has a beamline manager and 3 support staffs to assist and train users.

Over the last year the number of users accommodated at the SPXF has grown significantly from 10 groups to 18 groups. The number of experiments performed and users trained also grow significantly. A table listed below documents this data by beamline, with the number of user groups, experiments, trained users, beamtime delivered hours, and percentage of beamtime used in user service.

	# of User Groups	# of Experiments	# of Trained Users	# of Beamtime Hours Delivered	% of Beamtime Used for Service
BL13B1 MAD-PX	18	65	475	3760	78.7%
BL13C1 Mono-PX	15	45	322	2776	67.0%

- Geographical Distribution of User Groups

Nation	State	Affiliation
Taiwan, ROC	Taipei	Institute of Chemistry, Academia Sinica

		Institute of Molecular Biology, Academia Sinica Institute of Biological Chemistry, Academia Sinica Genomics Research Center, Academia Sinica Institute of Genome Sciences, National Yang-Ming University Institute of Biochemistry, National Defense Medical Center
	Hsin-Chu	Institute of Life Science, National Tsing-Hua University Research Division, National Synchrotron Radiation Research Center Division of Biotechnology and Pharmaceutical Research, National Health Research Institutes
	Tai-Chung	Institute of Biochemistry, National Chung-Hsing University
Singapore		Institute of Molecular and Cell Biology, A member of A*STAR's Biomedical Sciences Institutes
Thailand		Schools of Biochemistry and Chemistry, Institute of Science, Suranaree University of Technology Department of Chemistry, Faculty of Science, Mahidol University

- Statistics of User Publications:

The publication summary for 2205-2006 shows 55 SCI papers published, and 19 Conference abstract published for 74 total publications. All 74 publications represent service research where the SPXF provided facility and support only. Since the facility PI's major research interests are in solid-state physics and magnetism, there isn't any activity in R&D and Collaboration Research. Total 36 protein structures have been deposit to the Protein Data Bank (PDB) from SPXF beamlines. A table listed below provides a breakdown of the SCI papers in terms of total number and different Impact Factor (I.F.), conference abstracts, and PDB depositions.

	SCI Papers			Conference Abstracts	PDB Depositions
	Total	I.F. > 2	I.F. > 6		
2005	30	19	8	14	22
2006	22	16	4	5	14
Sum	55	35	12	19	36

- Science Highlights

#1 Structure-Based Drug Design of a Novel Family of PPARγ Partial Agonists: Prof. S.-W. Wu presents a successful example of employing structure-based virtual screening, a method that combines shape-based database search with a docking study and analogue search, to discover a novel family of PPAR γ agonists based upon pyrazol-5-ylbenzenesulfonamide.

#2 Crystal Structures of Human Glutaminyl Cyclase, an Enzyme Possibly Involved in Alzheimer's Disease and Osteoporosis: N-terminal pyroglutamate (pGlu) formation from its glutaminyl (or glutamyl) precursor is required in the maturation of numerous bioactive peptides. The aberrant formation of pGlu may be related to several pathological processes, such as osteoporosis and amyloidotic diseases. This N-terminal cyclization reaction, once thought to proceed spontaneously, is greatly facilitated by the enzyme glutaminyl cyclase (QC). To probe this important but poorly understood modification, Prof. Andrew H.-J. Wang has solved the crystal structures of human QC in free form and bound to a substrate and three imidazole-derived inhibitors. Their results provide a structural basis for the rational design of inhibitors against QC-associated disorders.

#3 Crystal Structure of A Bifunctional Deaminase and Reductase Involved in Riboflavin Biosynthesis: Bacterial RibG is an attractive candidate for development of antimicrobial drugs because of its involvement in the riboflavin biosynthesis. Professor S.-W. Liaw has solved the crystal structure of Bacillus subtilis RibG at 2.41-Å resolution, and the structure reveals that the deaminase and the reductase are separate functional domains, and that domain fusion is crucial for the enzyme activities through formation of a stable tetrameric structure.

- User Training and Support:

The best hardware and software are inefficient if well-trained support staffs are not available to assist the user. To assemble a user support team is one of the most important issues to keep this facility running in the most efficient way. Each of the SPXF beamlines has a beamline manager and 3 support staffs to assist and train users. There will be a 4 hours on-site training tutorials for each visiting research group to help how to condition the X-ray beam, get in/out the experimental hutch, mount and center the crystal, collect diffraction data, process diffraction data, and backup data. The support staffs also provide 12 hours a day, 6 days a week on-site user supports to help user collecting high-throughput data.

- Facility Dissemination:

To promote the facility activity, a five-day Protein Crystallography Training Course is held on August 28th. The Protein Crystallography Training Course provides lecture programs and hands-on training. The goal of this training course is to disseminate experimental techniques of macromolecular crystallography to researchers or graduate student with an interest in using this specific method to further the scope of their research. This course covers broad spectrum of topics on synchrotron-based protein crystallography, ranging from crystallization of proteins, data collection strategy, phasing techniques, radiation damage on protein crystals, to structure determination of proteins. It consists of two and half days of lectures focusing on the theory and applications of the methods, and two and half days of interactive hands-on sessions on practicing the techniques. More than 100 scientists and students have submitted their applications, 50 people have been selected to participate the lecture, and 15 lecture trainees are selected for hands-on practice. A table summarized more information about this activity is listed below:

Activity Title	2006 Protein Crystallography Training Course 2006 年蛋白質結晶學訓練課程		
Venue	Two and half days at National Synchrotron Radiation Research Center Two and half days at Institute of Biological Chemistry, Academia Sinica		
Associated Organization	Institute of Biological Chemistry, Academia Sinica		
Date	2006/08/28 to 2006/09/01		
# of Tutors	10	# of Applicants	> 100
# of Lecture Students	50	# of Hands-On Students	15

A new facility web site (http://bionsrrc.nsrrc.org.tw) has been established around Sep. 2006. This web site is modified frequently and includes expanded user information. The user training and dissemination are also included on this web site. This web site is currently experiencing about

600 hits per month and the user guide page is especially popular.

- Committee Activities:

The 2006-1st User's Committee Meeting is held at Institute of Biological Chemistry, Academia Sinica on April 27th 2006, 8 of the 10-committee members attended this meeting. The committee recommended that the priority of future performance upgrade of the facility should be (I) Substantial user support (II) Automation of experimental steps. (III) Provide mail-in crystallography capability. (IV) Develop remote access crystallography capability.

The 2006-2nd User's Committee Meeting is held at National Synchrotron Radiation Research Center on Oct. 4th 2006, 8 of the 10-committee members attended this meeting. The committee recommended that (I) The effective period of the beamtime application proposal should extend from one year to two year. (II) It is not necessary that a user has to prove he/she has crystals in hand already before he/she submit the proposal. (III) Judging from the average MAD beamtime per user per year, it is clear that the NSRRC should start to construct a new MAD beamline as earlier as possible. (IV) The Spring-8 BL12B2 should keep operating until the new beamline construction is completed.

- Future Plans:

With strong synchrotron sources and modern detectors, the data collection time is nill compared to routine processes such as sample mounting, crystal centering, and data collection parameters determination. To make best use of the beam time, these routine processes should be fully automated. By automation we mean that the software and hardware should complete the assigned jobs automatically without human intervention. Automation is an essential part of the high-throughput structural genomics programs. After the SPXF core facility is open to outside users at Sep. 20th 2005, several automation procedures is scheduled to be implemented with this core facility in the next following years, including automatic intensity monitoring and optimization, automatic sample mounting and centering, automatic crystals screening, automatic data collection, and automatic structure determination. The most recently activities about these automation works will be reported in the progress report of next year.