

Bangkok Meeting Report

“Merging Chemistry and Biology in Emerging Countries”

(Asian Chemical Biology Initiative, Bangkok Meeting)

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Chemical biology is not a new discipline, as research at the interface of chemistry and biology has been growing for decades. However, the field still needs regional and global support in emerging countries. The meeting organized by Asian Chemical Biology Initiative in Bangkok, Thailand in January 2013, brought together regional communities of young and established researchers to nurture chemical biology research programs and highlight some of the newer developments. Here, we report on the meeting and some of the key research topics discussed.

Newly emerging countries are like clocks. The fast-paced development of cities with new subway lines, skyscrapers, and bridges enhances our perception of elapsed time. Such dynamic changes can no longer be seen in more developed parts of the world. But, the five major Southeast Asian countries—Thailand, Vietnam, Indonesia, the Philippines, and Malaysia — are all experiencing record-breaking economic growth; the total of their gross domestic products (GDPs) are expected to rise 12% in 2014 to \$2,436 billion, surpassing the combined GDPs of South Korea, Taiwan, Singapore, and Hong Kong. This emerging region will undoubtedly play a central role in the growth of both the Asian and global economies. This exciting economic growth is partly fueled by steady investment into science education and research. The missions of the Asian Chemical Biology Initiative (ACBI) are two-fold: to promote the field of chemical biology throughout Asia, including emerging countries in Southeast Asia, and to accelerate international collaborations in the region. This bold initiative is a joint project supported by a number of Asian funding agencies and institutions such as the Japan Society for the Promotion of Science. Each year, a regional meeting is held to showcase the progress of the ACBI and the ongoing research activities of Asian scientists. The 2013 ACBI meeting was held in Bangkok, where attendees experienced subtropical temperatures while Seoul and Beijing battled sub-zero weather and Tokyo was buried in heavy snow.

The Bangkok Meeting

Forty-four principal investigators conducting chemical biology research throughout Asia gave lectures at the Bangkok meeting, which was held on January 26th–28th, 2013 (Figure 1). Like the 2012 gathering in Hanoi, Vietnam, the Bangkok meeting was convened to continue pursuing two experimental approaches to fostering collaboration, education, and innovation on which ACBI aims its focus. The first aim is to develop a strong regional, Far East conference built on a model similar to a well-established conference series, the Gordon Research Conferences. The idea is to hold a closed meeting of principal investigators organized to promote rapid decision making on international collaborations, to share research resources, and to streamline chemical biology research in the region. Over a day and a half, participants not only presented results from their ongoing research but also created opportunities for collaborative projects. The presentations covered a wide range of topics and are briefly summarized in the latter half of this report. The second goal was to identify graduate students who could become the next generation of chemical biologists in Southeast Asia. Members of the ACBI think that one of the most effective ways to promote chemical biology in emerging countries is proactive recruitment of the brightest students to the field of chemical biology. Before the meeting, Thai students majoring in chemistry or biology were invited to visit the ACBI Web site (<http://www.asianchembio.jp>) to browse the member database and identify laboratories they wished to join. A total of 36 qualified students came to the meeting to be interviewed by meeting attendees during a half-day session (Figure 2). The meeting participants had an opportunity to meet one-on-one with about seven students each and talk with the students about their research, educational background, and scholarship opportunities for overseas PhD programs in individual countries or at specific institutions. Participants engaged in lively discussions throughout the meeting, during both the scientific sessions and social events.

Newcomers to the ACBI Kick Off the Meeting

The Bangkok meeting started with lectures by new members and participants who were unable to attend the 2012 meeting. Prof. Yan-Mei Li of Tsinghua University introduced the discovery of a novel conjugate of mucine 1-glycopeptide and bovine serum albumin as a vaccine for cancer immunotherapy (Huang et al., 2012). Prof. Margaret Brimble of the University of Auckland described the synthesis and medical applications of bioactive natural products and she showcased her peptide, glycopeptide and peptidomimetic synthesis capabilities used for the development of drugs to treat traumatic brain injury and osteoporosis (Hung et al., 2012). Prof. Ikuo Fujii of the Osaka Prefecture University explained a directed evolution of conformationally constrained peptides, discovering “microantibodies” against Aurora-A kinase and granulocyte colony-stimulating factor receptor, which possess high affinity, nonantigenicity, membrane permeability, and stability (Fujiwara et al., 2010). Prof. Kazuhiko Nakatani of Osaka University discussed the design and synthesis of small heterocyclic molecules that bind and regulate RNA (Murata et al., 2013). Using

oxygen-sensitive drugs as examples, Prof. Hideko Nagasawa of Gifu Pharmaceutical University talked about the development of drug candidates targeting metabolic stress in tumor microenvironments (Okuda et al., 2012). Prof. Jianhua Qi of Zhejiang University elaborated on the isolation, structural determination, and biological activities of hormones a1 and a2 which induce sexual reproduction in *Phytophthora* spp., as well as on the characteristics of the neuritogenic gentiside derivative tetradecyl 2,3-dihydroxybenzoate as a potential treatment for Alzheimer's disease (Ojika et al., 2011). Prof. Munetaka Kunishima of Kanazawa University reported on the development of a novel modular strategy for affinity labeling that employs a 1,3,5-triazines-based reagent (Kunishima et al., 2009). Prof. Juyoung Yoon of Ewha Womans University explained the development of a cyanine-based fluorescent chemosensor for zinc ions and a near-infrared fluorescent chemosensor that can recognize cysteines and homocysteines (Guo et al., 2012). Prof. Yoich Nakao of Waseda University discussed the isolation, structural determination, and antiprotozoal properties of the marine natural product cristaxenicin A (Ishigami et al., 2012). Prof. Timothy Dore of New York University Abu Dhabi introduced research to develop applications for compounds that induce the release of neuromodulators, such as ATP and serotonin, when subject to two-photon excitation and efforts to identify inhibitors of Ras converting enzyme (Rce1p) that can assist in revealing Rce1p's role in regulating CaaX proteins (Ma et al., 2012). Prof. Xing Chen of Peking University presented a cell-specific and tissue-specific method of metabolic glycan labeling that takes advantage of the azidealkyne cycloaddition reaction that follows intracellular delivery of azidosugars encapsulated in ligand-targeted liposomes (Xie et al., 2012). Dr. Peng Chen, also of Peking University, discussed the discovery and analysis of protein-protein interactions within living cells via genetic and site-specific incorporation of a diazirine-based photo-crosslinking probe (Zhang et al., 2011). Prof. Takayoshi Suzuki of the Kyoto Prefectural University of Medicine introduced the discovery and chemical genetics study of a lysine-specific demethylase 1-selective inhibitor (Ueda et al., 2009). Prof. Yasuteru Urano of the University of Tokyo presented the development of a fluorescent probe that enables imaging of γ -glutamyltranspeptidase, a compound that exhibits elevated activity in many types of cancer cells. Prof. Takaki Koide of Waseda University talked about the applications of laboratory-created collagen-like triple-helical supramolecules that can be used to elucidate unexplored biological properties of collagen and about the drug-delivery systems for such compounds and formation of the supramolecular triple-helical peptide (Yasui et al., 2013).

Focusing on the Signal Transduction

Prof. Dan Yang of the University of Hong Kong described the identification of the intracellular target and binding site of triptolide, a natural substance toxic to cancer cells, and proposed a mechanism of action for this molecule. Dr. Mikiko Sodeoka of RIKEN explained the total synthesis of the naturally occurring molecule (+)-chaetocin and its ability to inhibit

histone methyltransferase G9a (Iwasa et al., 2010). Prof. Fumi Nagatsugi of Tohoku University discussed the regulation of genetic expression with rationally designed synthetic oligonucleotides and presented details about a molecular motor that can recognize and regulate the structures of duplex DNA (Nagatsugi et al., 2013). Prof. Gyoonhee Han of Yonsei University explained the process of screening compounds that can both inhibit histone deacetylases (HDACs) and stabilize the acetylation of the tumorsuppressive runt-related transcription factor 3 and how such compounds can shrink tumors in in vivo assays (Choi et al., 2012). Associate Prof. Midori Arai of Chiba University described how protein-immobilized beads can be used to quickly isolate natural products and promote neural stem-cell differentiation (Arai et al., 2013). Prof. Kazuya Kikuchi of Osaka University discussed the development of a novel fluorogenic probe whose fluorescence is turned on when it binds to photoactive yellow protein, which is used as a tag protein for imaging target protein in live-cells (Hori et al., 2012). Prof. Hiroshi Sugiyama of Kyoto University described how a DNA-binding conjugate of suberoylanilide hydroxamic acid, pyrrole, and imidazole polyamide can be used for cell reprogramming and the production of induced pluripotent stem cells (Pandian et al., 2012).

Tackling Cancer

Prof. Sunghoon Kim of Seoul National University elaborated on the intracellular events triggered by structural changes in lysyltRNA synthetase and on the identification of a compound that can prevent metastases by specifically inhibiting interaction between this enzyme and 67 kDa laminin receptor (Ofir-Birin et al., 2013). Prof. Ho Jeong Kwon of Yonsei University talked about identifying and elucidating the mechanism of molecules that regulate angiogenesis and small-molecule compounds that promote autophagy (Cho and Kwon, 2012). Prof. Peter Shepherd of the University of Auckland demonstrated how a selective inhibitor of the p110 α isoform of the phosphoinositide 3-kinase is effective in treating cancer types that express mutated P110 α (Jamieson et al., 2011). Associate Prof. Hiroki Oguri of Hokkaido University reported on a divergent synthetic process that installs multiple fragments on naturally occurring and skeletally diverse scaffolds through modular assembly and divergent cyclizations (Mahendar et al., 2013). Prof. Young-Tae Chang of the National University of Singapore talked about the screening of fluorescent molecule libraries to identify probes that can stain specific cells and biomolecules and about how these probes recognize their molecular targets (Yun et al., 2012). Associate Prof. Youngjoo Kwon of Ewha Womans University reported on how calpain inhibitors prevent the Ca²⁺ influx-mediated cleavage processing of the DNA repair protein Ku86 and how such compounds can act as anticancer agents (Lee et al., 2013). Dr. Minoru Yoshida of RIKEN described how the combination of CREB-binding protein (CBP) and sirtuin-2 protein (SIRT2) catalyzes the acetylation and deacetylation of cortactin and how the acetylation of cortactin regulates cancer cell motility. Assistant Prof. Zhongping Yao of the Hong Kong Polytechnic University

introduced solid-substrate electrospray ionization mass spectrometry and its further development for in vivo studies of living organisms (Hu et al., 2013). Dr. Hiroyuki Osada of RIKEN explained the discovery of the anti-osteoclastic compound, reveromycin A (RM-A), isolated from an actinomycetes, and presented its anti-osteoporosis activity and antibone metastasis activity in vivo (Takahashi et al., 2011a).

Zooming In on the Intracellular Events

Associate Prof. Kyeong Lee of Dongguk University reported on the establishment of the Open Translational Research Center for Innovative Drug (OTRCID) at the university and how this organization has already discovered a number of drug leads (Naik et al., 2012). Prof. Takeaki Ozawa of the University of Tokyo explained an mRNA-imaging method that employs protein chemistry to reconstitute split fragments of green fluorescent protein (Yamada et al., 2011). Prof. Motonari Uesugi of Kyoto University introduced new findings on fatostatin, a molecule that blocks intracellular lipid synthesis, and its derivatives (Kamisuki et al., 2011). Prof. Yoshie Harada of Kyoto University described the development of a novel single-molecule imaging technique that exploits nitrogen-vacancy centers in fluorescent diamond nanoparticles and discussed its application in detecting biomolecules (Igarashi et al., 2012).

Cell Surface Events

Prof. Itaru Hamachi of Kyoto University presented a method of using tosyl and acyl imidazole chemistry to selectively label intracellular and cell surface proteins (Fujishima et al., 2012). Prof. Shiroh Futaki, also of Kyoto University, described how binding of artificial ligands to the epidermal growth factor receptor leads to its dimerization (Nakase et al., 2012). Introducing covalent binding in the PDZ-peptide complex as an actual example, Assistant Prof. Jiang Xia of the Chinese University of Hong Kong explained how the development of orthogonal protein conjugation reactions inspired by proximity-induced reactivity and PDZ-peptide binding interactions benefits efforts to design artificial models of multienzyme complexes. Prof. Yasuo Mori of Kyoto University described how oxidation of cysteine residues in TRPA1, a transient receptor potential channel with six transmembrane domains, can be used to recognize molecular oxygen in the environment (Takahashi et al., 2011b).

Emerging Chemical Biology in Thailand

In Thailand, the field of chemical biology is emerging and is expected to expand rapidly in the near future. The session, “Emerging Chemical Biology in Thailand,” was devoted to presentations from five young Thai researchers. Associate Prof. Palangpon Kongsaree of Mahidol University introduced the apoptosis-inducing compound gambogic acid and discussed the identification of the target molecule of the antimalarial compound artemisinin. Dr. Chutima Jiarpinittun, also of Mahidol University, talked about the molecular design,

synthesis, and bioactivity of heterodimeric sulfonamide antibiotics with the goal of developing treatments for multidrug-resistant *Staphylococcus aureus* (Phetsang et al., 2013). Dr. Thanit Praneenararat of Chulalongkorn University discussed his doctorate study about the molecular design, synthesis, and biological evaluation of synthetic N-acyl-L-homoserine lactones, a class of compounds known to regulate bacterial quorum sensing (Praneenararat et al., 2009). Associate Prof. Supason Wanichwecharungruang, also of Chulalongkorn University, reported on ultraviolet-absorbing carriers for photolabile drugs and on drug carriers that can synergistically enhance therapeutic efficacy (Amornwachirabodee et al., 2012). Dr. Supakarn Chamni, also of Chulalongkorn University, described the development of a diazo reagent with fluorine footprint and tethered alkyne for tag attachment that can be used to identify molecular targets of alcohol-containing natural products via O-H insertion (Chamni et al., 2011).

Conclusion

The three-day meeting was intense but enjoyable. A particularly memorable event was the vibrant session that lasted until 11 p.m. on the 36th-floor venue overlooking the neonilluminated nightscape of Bangkok. Just before this scientific session, the banquet dinner was attended by the former Minister of Science in Thailand, the Vice President of Mahidol University, and officials from the Embassies of South Korea and Japan, indicating the high expectation for chemical biology in the country. On the last day, after visiting the chemistry departments of both Chulalongkorn University and Mahidol University, we savored the spicy Thai lunch of pu pat pong kari (curried crab claws) and tom yum kung soup before heading to Suvarnabhumi Airport. Watching the colorful neon lights through taxi windows, we wondered how the city streets and university campuses would change in coming years. Although the three-wheeled scooter taxis roaring and backfiring on traffic-jammed Silom Road may disappear, we hope to again see chemical biology research bloom in Thailand and the region. As other attendees said good-bye and headed to boarding gates one after another, we were left alone in the airport lobby waiting for red-eye flights to Japan. In the midnight airport lobby, we found ourselves rubbing our short-sleeved arms. We left Bangkok with winter jackets in-hand and with expectations of next year's meeting in Manila in our hearts.

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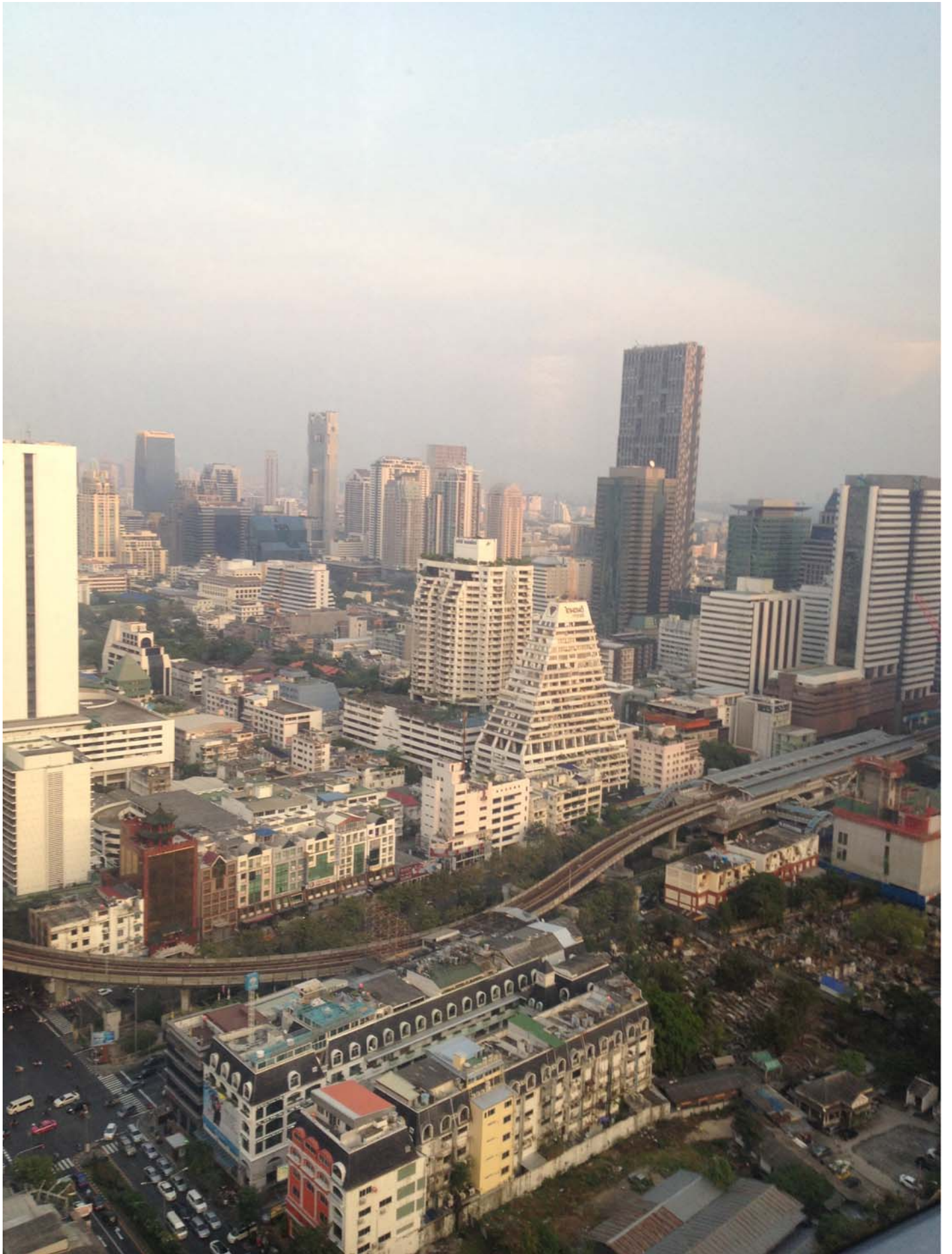


Figure 1. A view from the Meeting venue Overlooking Bangkok City



Figure 2. 36 ACBI Professors interviewing 36 Thai Students