

## Two Days of Experiments in Vietnam: Asian Chemical Biology Initiative, Hanoi Meeting

Takashii Morii\* and Motonari Uesugi

Kyoto University, Kyoto 611-0011, Japan

The bus arrived at the Hanoi Daewoo Hotel amid the clamor of honking cars and clouds of exhaust billowing from motorcycles. Unlike the surrounding traditional Vietnamese structures, the hotel is an ultramodern high-rise like those customarily seen in Tokyo or Seoul—a fitting site, we thought, for the 2012 Annual Meeting of the Asian Chemical Biology Initiative (ACBI). We were eager to join our colleagues who traveled from across Asia and the South Pacific to attend the meeting: 7 from Korea, 5 from China (Mainland and Hong Kong), 2 from Singapore, 1 from New Zealand, and 15 from Japan.



Held on February 25 and 26, the meeting was convened to continue the mission of ACBI to promote the field of chemical biology throughout Asia, to accelerate international collaborations in the region, and to foster young chemical biologists in emerging Asian countries. The initiative is funded by the Japan Society for the Promotion of Science to build a partnership between Japan, Korea, China, Hong Kong, Singapore, and other Asian countries over the next 5 years.



Prof. Motonari Uesugi of Kyoto University, the chief organizer of the Hanoi event, opened the meeting, calling it a “2-day experiment”. The first aim of this experiment was to

develop a Far East version of the Gordon Research Conference, 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 as roughly summarized in the latter half of this report. Participants engaged in lively discussions throughout the meeting, whether during sessions, coffee breaks sponsored by the publishers of *ACS Chemical Biology* and *Chemistry & Biology*, or meals. Participants also engaged in dialogues with vice presidents of the Vietnam National University, other Vietnamese professors, and a minister from the Embassy of Japan in Vietnam. Some took the opportunity to visit the chemistry department at VNU.



### SCIENTIFIC MEETING OVERVIEW

**Biologically Active Small Molecules.** Prof. Uesugi of Kyoto University described the discovery and mechanistic analysis of small molecules that enhance cell adhesion or distinguish human stem cells.<sup>1</sup> Prof. Midori Arai of Chiba University talked about the characteristics of flavonoid molecule libraries and how they are being used to study molecules that affect DNA-binding proteins.<sup>2</sup> Prof. Ho Jeong Kwon of Yonsei University in Korea presented the discovery of small molecules targeting angiogenesis and their target proteins identification using phage display biopanning.<sup>3</sup> Prof. Kyeong Lee of Dongguk University explained small molecules that target MDR1 and HIF-1 $\alpha$  discovered in focused libraries.<sup>4</sup> Prof. Ming-Wei Wang of Shanghai Institute of Materia Medica, the Chinese Academy of Sciences, discussed drugs discovered through screening of China's largest public compound library.<sup>5</sup>

Published: April 20, 2012

Prof. Youngjoo Kwon, Ewha Women's University, Korea gave a presentation on the use of structural biology and molecular modeling to design a molecule to target topoisomerase II.<sup>6</sup> Dr. Mikiko Sodeoka, RIKEN in Japan, described the discovery of a molecule that targets protein phosphatases and the use of Raman microscopy to visualize alkyne-tagged small molecules in cells.<sup>7</sup> Prof. Hiroki Oguri of Hokkaido University in Japan explained how his lab compiles a highly diverse compound library efficiently.<sup>8</sup> Prof. Gyoonee Han of Yonsei University in Korea presented a rational methodology for drug discovery that employs *in silico* screening.<sup>9</sup> Dr. Hiroyuki Osada of RIKEN talked about studying the physiological activity, target identification, and mechanisms of antibiotics derived from microorganisms.<sup>10</sup>

**Molecular Imaging and Tools.** Prof. Seung Bum Park of Seoul National University presented an approach to rational design of fluorescent molecules and how this strategy is being applied to develop fluorescent glucose probes.<sup>11</sup> Prof. Shiroh Futaki of Kyoto University explained the cell-penetrating properties of arginine-rich peptides.<sup>12</sup> Prof. Takashi Morii of Kyoto University described the use of multiple fluorescent sensors to visualize cellular events and the use of DNA origami to assemble proteins.<sup>13</sup> Prof. Kazuya Kikuchi of Osaka University discussed his lab's efforts to employ theoretical molecular modeling to synthesize turn-on fluorescent probes and selective labeling of intracellular proteins.<sup>14</sup> Dr. Minoru Yoshida of RIKEN introduced a bioprobe that enables real-time visualization of histone modifications and epigenetic regulation.<sup>15</sup> Prof. Takeaki Ozawa of the University of Tokyo talked about a method to visualize *in vivo* protein interactions and mRNA localization in real time using split fluorescent proteins and split luciferase.<sup>16</sup> Prof. Dan Yang of the University of Hong Kong discussed compounds that form ion channels and fluorescent probes for reactive oxygen species.<sup>17</sup> Prof. Itaru Hamachi of Kyoto University explained how his group used a chemical reaction of tosyl compounds to selectively tag intracellular proteins.<sup>18</sup> Prof. Young-Tae Chang of the National University of Singapore presented selective imaging of cells and biological macromolecules through the systematic use of an independently compiled fluorescent molecule library.<sup>19</sup> Prof. Yoshie Harada of Kyoto University introduced a method for single-molecule detection of DNA–protein interaction using TIRF microscopy.<sup>20</sup>

**Biological Macromolecules.** Prof. Brendan Orner of Nanyang Technological University in Singapore reported the use of ferritin protein cages to create nanomaterials.<sup>21</sup> Prof. Jiang Xia of the Chinese University of Hong Kong explained a methodology for coating nanoparticles and quantum dots with polyhistidine peptide dendrimer ligands.<sup>22</sup> Prof. Yao Zhongping of the Hong Kong Polytechnic University described how adopting paraffin oil in MALDI-MS and wooden tips in ESI-MS and other techniques could facilitate analysis of biomolecules.<sup>23</sup> Prof. Xuechen Li of the University of Hong Kong introduced a new chemical ligation method without thioester formation.<sup>24</sup> Prof. Fumi Nagatsugi of Tohoku University discussed oligonucleotides that promote cross-linking reactions.<sup>25</sup> Prof. Yongseok Choi of Korea University explained how peroxiredoxin and sulfiredoxin can be potential targets for cancer therapy.<sup>26</sup> Prof. Hiroshi Sugiyama of Kyoto University presented a new DNA nanotechnology for monitoring nucleic acid structures and enzymatic reactions.<sup>27</sup>

**Chemical Understanding and Modulation of Biology.** Prof. Yasuo Mori of Kyoto University talked about the

discovery of the TRP calcium channel and how this ion channel may act as a sensor for reactive oxygen species and temperature.<sup>28</sup> Prof. Sunghoon Kim of Seoul National University reported the newly discovered functions of t-RNA synthases and their potentials as cancer drug targets.<sup>29</sup> Prof. Peter Shepherd of the University of Auckland described the role phosphoinositide 3-kinase in intracellular signal transduction.<sup>30</sup>

## ■ NEXT GENERATION CHEMICAL BIOLOGISTS IN VIETNAM

The second aim of the 2-day experiment was to identify talented students who could become the next generation of chemical biologists in Vietnam. Before the meeting, Vietnamese students majoring in chemistry or biology were invited to visit the ACBI Web site ([www.asianchembio.jp](http://www.asianchembio.jp)) to browse the member database and identify laboratories they wished to join. A total of 41 qualified students came to the meeting to be interviewed by meeting attendees during a half-day session. After Prof. Uesugi gave a general overview of chemical biology, the meeting participants screened about 10 students each, describing their research and educational background and explaining in detail how the students could apply for scholarships for overseas Ph.D. programs in individual countries or at specific institutions. Even though these students had not been exposed to state-of-the-art chemical biology research, we all were impressed by their competence and eagerness to learn.



## ■ IN CONCLUSION

The spirit of the 2-day event was captured at the dinner held for the student attendees at a local Vietnamese restaurant. The festive occasion began with a toast by Prof. Seung Bum Park of Seoul National University. Although science dominated the evening's conversation, the blending of Asian cultures was evident, even during a heated discussion of Vietnamese cuisine. As the festivities came to a close, Prof. Young-Tae Chang of the National University of Singapore reminded all that science is our common language and that we represent the whole of Asia as well as our individual countries.

Content with the success of the meeting, we boarded the bus to the airport. Watching the neon lights and the motorcycle lamps colorfully illuminating the streets of Hanoi, we recalled the faces of every Vietnamese student we interviewed and wondered what future is waiting for them. The bus seat that felt rigid when we first arrived now felt oddly pleasant. We left

Vietnam with expectations of next year's meeting in Bangkok, Thailand.

## AUTHOR INFORMATION

### Corresponding Author

\*E-mail: t-morii@iae.kyoto-u.ac.jp.

## REFERENCES

- (1) Yamazoe, S., Shimogawa, H., Sato, S., Esko, J. D., and Uesugi, M. (2009) A dumbbell-shaped small molecule that promotes cell adhesion and growth. *Chem. Biol.* 16, 773–782.
- (2) Arai, M. A., Tateno, C., Koyano, T., Kowithayakorn, T., Kawabe, S., and Ishibashi, M. (2011) New Hedgehog/GLI-signaling inhibitors from *Adenium obesum*. *Org. Biomol. Chem.* 9, 1133–1139.
- (3) Lee, Y. J., Choi, I.-K., Sheen, Y. Y., Park, S. N., and Kwon, H. J. (2012) Moesin is a biomarker for the assessment of genotoxic carcinogens in mouse lymphoma. *Mol. Cells* 33, 203–210.
- (4) Xia, Y., Jin, Y., Kaur, N., Choi, Y., and Lee, K. (2011) HIF-1 $\alpha$  inhibitors: Synthesis and biological evaluation of novel moracin O and P analogues. *Eur. J. Med. Chem.* 46, 2386–2396.
- (5) He, M., Su, H., Gao, W., Johansson, S. M., Liu, Q., Wu, X., Liao, J., Young, A. A., and Wang, M.-W. (2010) Reversal of obesity and insulin resistance by a non-peptidic glucagon-like peptide-1 receptor agonist in diet-induced obese mice. *PLoS ONE* 5, e14205.
- (6) Jun, K. Y., Lee, E. Y., Jung, M. J., Lee, O. H., Lee, E. S., Park Choo, H. Y., NA, Y., and Kwon, Y. (2011) Synthesis, biological evaluation, and molecular docking study of 3-(3'-heteroatom substituted-2'-hydroxy-1'-propyloxy) xanthone analogues as novel topoisomerase II $\alpha$  catalytic inhibitor. *Eur. J. Med. Chem.* 46, 1964–1971.
- (7) Yamakoshi, H., Dodo, K., Okada, M., Ando, J., Palonpon, A., Fujita, K., Kawata, S., and Sodeoka, M. (2011) Imaging of EdU, an alkyne-tagged cell proliferation probe, by Raman microscopy. *J. Am. Chem. Soc.* 133, 6102–6105.
- (8) Oguri, H., Hiruma, T., Yamagishi, Y., Oikawa, H., Ishiyama, A., Otoguro, K., Yamada, H., and Omura, S. (2011) Generation of anti-trypanosomal agents through concise synthesis and structural diversification of sesquiterpene analogs. *J. Am. Chem. Soc.* 133, 7096–7105.
- (9) Yang, J. S., Song, D., Lee, B., Ko, W. J., Park, S.-K., Won, M., Lee, K., Kim, H. M., and Han, G. (2011) Synthesis and biological evaluation of novel aliphatic amido-quaternary ammonium salts for anticancer chemotherapy: Part I. *Med. Chem.* 46, 2861–2866.
- (10) Takahashi, S., Toyoda, A., Sekiyama, T., Takagi, H., Nogawa, T., Uramoto, M., Suzuki, R., Koshino, H., Kumano, T., Panthee, S., Daiiri, T., Ishikawa, J., Ikeda, H., Sakai, Y., and Osada, H. (2011) Reveromycin A biosynthesis uses RevG and RevJ for stereospecific spiroacetal formation. *Nat. Chem. Biol.* 7, 461–468.
- (11) (a) Oh, S., and Park, S. B. (2011) Privileged-substructure-based diversity-oriented synthesis (pDOS) for designing drug-like polyheterocycles in chemical biology. *Chem. Commun.* 12754–12761. (b) Kim, E., Koh, M., Lim, B. J., and Park, S. B. (2011) Emission wavelength prediction of a full-color-tunable fluorescent core skeleton, 9-aryl-1,2-dihydropyrrolo[3,4,b]indolizin-3-one. *J. Am. Chem. Soc.* 133, 6642–6649.
- (12) Nakase, I., Akita, H., Kogure, K., Gräslund, A., Langel, U., Harashima, H., and Futaki, S. (2012) Efficient intracellular delivery of nucleic acid pharmaceuticals using cell-penetrating peptides. *Acc. Chem. Res.* Published ASAP ahead of print, DOI: 10.1021/ar200256e.
- (13) Nakata, E., Liew, F.-F., Uwatoko, C., Kiyonaka, S., Mori, Y., Katsuda, Y., Endo, M., Sugiyama, H., and Morii, T. (2012) Zinc-finger proteins for site-specific protein positioning on DNA origami structures. *Angew. Chem., Int. Ed.* 51, 2412–2424.
- (14) Mizykami, S., Yamamoto, T., Yoshimura, A., Watanabe, S., and Kikuchi, K. (2011) Covalent protein labeling with a lanthanide complex and its application to photoluminescence lifetime-based multicolor bioimaging. *Angew. Chem., Int. Ed.* 50, 8750–8752.
- (15) Ito, T., Umehara, T., Sasaki, K., Nakamura, Y., Nishino, N., Terada, T., Shirouzu, M., Padmanabhan, B., Yokoyama, S., Ito, A., and Yoshida, M. (2011) Real-time imaging of histone H4K12-specific acetylation determines the modes of action of histone deacetylase and bromodomain inhibitors. *Chem. Biol.* 18, 495–507.
- (16) Ozawa, T., and Umezawa, Y. (2011) Genetically-encoded fluorescent probes for imaging endogenous mRNA in living cells. *Methods Mol. Biol.* 714, 175–188.
- (17) Jiao, Z.-G., Chang, X.-W., Ding, W., Liu, G.-J., Song, K.-S., Zhu, N.-Y., Zhang, D.-W., and Yang, D. (2011) 2-Aminoxy peptides: Synthesis and conformational studies. *Chem. Asian J.* 6, 1791–1799.
- (18) Tsukiji, S., Miyagawa, M., Takaoka, Y., Tamura, T., and Hamachi, I. (2009) Ligand-directed tosyl chemistry for protein labeling in vivo. *Nat. Chem. Biol.* 5, 341–343.
- (19) Kang, N. Y., HA, H. H., Yun, S. W., Yu, Y. H., and Chang, Y. T. (2011) Diversity-driven chemical probe development for biomolecules: beyond hypothesis-driven approach. *Chem. Soc. Rev.* 40, 3613–3626.
- (20) Sasuga, Y., Iwasawa, T., terada, K., Oe, Y., Sorimachi, H., Ohara, O., and Harada, Y. (2008) A simple single-cell chemical lysis method for analyses of intracellular molecules using an array of picoliter-scale microwells. *Anal. Chem.* 80, 9141–9149.
- (21) Zhang, Y., Fu, J., Chee, S. Y., Ang, E. X. W., and Orner, B. P. (2011) Rational disruption of the oligomerization of the mini-ferritin E. coli DPS through protein-protein interface mutation. *Protein Sci.* 20, 1907–1917.
- (22) Wang, J., and Xia, J. (2011) Preferential binding of a novel polyhistidine peptide dendrimer ligand on quantum dots probed by capillary electrophoresis. *Anal. Chem.* 83, 6323–6329.
- (23) So, P. K., and Yao, Z. P. (2011) Oil-assisted sample preparation: A simple method for analysis of solid samples using matrix-assisted laser desorption/ionization mass spectrometry. *Anal. Chem.* 83, 5175–5181.
- (24) Li, X. (2011) Click to join peptides/proteins together. *Chem. Asian J.* 6, 2606–2616.
- (25) Nagatsugi, F., and Imoto, S. (2011) Induced cross-linking reactions to target genes using modified oligonucleotides. *Org. Biomol. Chem.* 9, 2579–2585.
- (26) Min, H. S., Kang, E., Koo, H., Lee, J., Kim, K., Park, R. W., Kim, I.-S., Choi, Y., Kwon, I. C., and Han, M. (2012) Gas-generating polymeric microspheres for long-term and continuous in vivo ultrasound imaging. *Biomaterials* 33, 936–944.
- (27) Wickham, S. F. J., Bath, J., Katsuda, Y., Endo, M., Hidaka, K., Sugiyama, H., and Tuberfield, A. J. (2012) A DNA-based molecular motor that can navigate a network of tracks. *Nat. Nanotechnol.* 7, 169–173.
- (28) Takahashi, N., Kuwaki, K., Kiyonaka, S., Numata, T., Kozai, D., Mizuno, Y., Yamamoto, S., Naito, S., Knevels, E., Carmeliet, P., Oga, T., Kaneko, S., Suga, S., Nokami, T., Yoshida, J., and Mori, Y. (2011) TRPA1 underlies a sensing mechanism for O<sub>2</sub>. *Nat. Chem. Biol.* 7, 701–711.
- (29) Han, J. M., Jeong, S. J., Park, M. C., Kim, G., Kwon, N. H., Kim, H. K., Ha, S. H., Ryu, S. H., and Kim, S. (2012) Leucyl-tRNA synthetase is an intracellular leucine sensor for the mTORC1-signaling pathway. *Cell* 149, 1–15.
- (30) Jamieson, S., Flanagan, J. U., Kolekar, S., Buchanan, C., Kendall, J. D., Lee, W. J., Rewcastle, G. W., Denny, W. A., Singh, R., Dickson, J., Baguley, B. C., and Shepherd, P. R. (2011) A drug targeting only p110 $\alpha$  can block phosphoinositide 3-kinase signalling and tumour growth in certain cell types. *Biochem. J.* 438, 53–62.