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ICBS2012 Catalyzes Robust Response from Global Chemical Biology Community

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World-renowned chemical biologists along with promising young investigators gathered for the first official conference of the International Chemical Biology Society (ICBS), held in Cambridge, MA, on October 3−4, 2012. Rathnam Chaguturu (SRI), Founding President, opened the meeting by noting that few opportunities have existed for scientists with a mutual interest in the vastly unexplored chemical biology space to assemble. Now, the ICBS provides a home to chemical biologists. Through conferences and innovative initiatives, this home will expand to the four corners of the globe and to the broad scientific areas in chemical biology. The ICBS mission is "to provide an important international forum that brings together cross-disciplinary scientists from academia, nonprofit organizations, government, and industry to communicate new research and help translate the power of chemical biology to advance human health." With industry-wide representation and cutting edge scientific presentations from the chemical biology field, ICBS2012 took a decisive step toward fulfillment of this mission.

ICBS2012, organized by Haian Fu (Emory University), Doug Auld (Novartis), and a dynamic organizing committee,[1] convened chemical biologists from around the globe and from all sectors of the research community. The agenda was anchored by keynote presentations from pioneers and entrepreneurs in the chemical biology field: Stuart Schreiber (Broad Institute and Harvard University), Paul Workman (The Institute of Cancer Research, London), Lewis Cantley (Harvard Medical School), and Leonard Zon (Harvard Medical School). Building on these outstanding lectures were nine scientific sessions with more than 30 research presentations, including an excellent representation of young investigators in the field. Although speakers were from different sectors, all were aimed at discovering and utilizing small molecules to gain biological insight and advance human health.

"Explore New Frontiers, Foster Global Collaborations" was the theme of ICBS2012. Meeting participants explored new frontiers of chemical biology space by probing "chemi-omics" data sets, targeting biology with chemistry, and catalyzing research with innovative technologies and techniques. The international group fostered global collaborations with an emphasis on data and resource sharing, and a final meeting session titled "Emerging policies and initiatives to promote global collaborations." Overall, ICBS2012 provided participants an important glimpse of current chemical biology research from around the world, and formed a promising foundation to catalyze future growth of the society.

PROBING "CHEMI-OMICS" DATA

The strong desire to translate the vast amounts of available genomic information into therapeutic benefit for patients has driven open a new frontier in the chemical biology field. In the past, use of small molecules was mostly limited to traditional high throughput screening as part of drug discovery research in pharmaceutical companies. The advancement of omics has fueled the spread of high throughput technologies into government and academic sectors. As well, expanded collaboration among private and public sectors has increased the availability of small molecule libraries. In combination with new genomic data, these changes have made feasible large-scale systematic experiments with small molecules to define and target gene and protein functions. Multiple presentations during ICBS2012 utilized large-scale chemi-omics data sets to increase understanding of normal and disease-related cellular biology.

Stuart Schreiber's keynote presentation, a highlight of ICBS2012, included thought-provoking analyses of large chemi-omics data sets leading to a wide-range of new biological insights and therapeutic potential. Schreiber's work was aimed to link cancer genomic alterations to small molecule sensitivity (Figure 1). His team utilized chemi-omics data sets derived from systematically profiling the sensitivity of ∼900 well-characterized cell lines, part of the Broad/Novartis Cancer Cell Line Encylopedia,[2] to individual and combinations of small molecules in a defined informer set comprising ∼480 compounds. Access to this data set will be made available through an interactive Cancer Genetic Dependency Resource. Schreiber presented multiple illustrations for use of this resource, with an overall focus on the prediction of drug combinations for more effective therapeutics by identifying coordinated oncogenic changes within the cell lines. He defined these changes as the direct driver genetic events (oncogenic dependencies) and indirect nononcogenic genetic events, which are required for the driver gene phenotype (non-oncogenic dependencies). Identification and targeting of these coordinated changes might lead to more effective therapeutics. An example presented by Schreiber was the β-catenin signaling pathway (Figure 1), which is commonly activated in tumors. Regression analysis of the chemi-omics data correlating sensitivity with genomic alterations resulted in a predictive model of β-catenin signaling that is defined by 203 genetic/epigenetic features. Thus, the cancer-related β-catenin circuitry includes multiple subpathways important for oncogenic signaling. Schreiber noted that the predictive model for β-catenin signaling implicated the Bcl-2/BAX pathway as an important downstream effector in certain tumor subtypes. These findings have suggested a targeted clinical study of navitoclax (a Bcl-2 inhibitor) in a subset of patients with activating mutations in β-catenin. This example captures the concept of nononcogene

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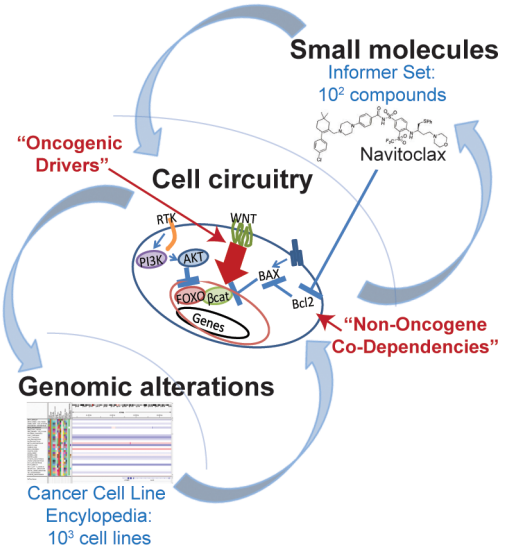

Figure 1. Large-scale, systematic experiments linking the effects of cancer genomic alterations and small molecules on cell circuitry lead to new biological insights and therapeutic potential. As described by Schreiber, an informer set consisting of 100s of compounds with known selectivity profiles are used to generate sensitivity data sets for the ~1000 cell lines in the Cancer Cell Line Encyclopedia (CCLE). Regression analysis of this chemi-omics dataset, linking sensitivity data to genetic data, generated predictive models. This included a predictive model defining 203 features enriched in the β-catenin signaling pathway. The β-catenin signaling pathway is frequently activated by mutations in cancer (oncogenic drivers). The predictive model identified other downstream effectors linked to β-catenin signaling, including Bcl-2 (nononcogenic codependencies). Thus, a combination therapy targeting both the oncogenic driver and its nononcogenic codependencies (e.g., navitoclax) might prove more effective therapeutically.

codependencies, whereby downstream effectors required for oncogene function determine sensitivity to small molecules.

Joseph Lehar (Novartis) presented collaborative efforts among industry and academic partners to comprehensively describe cancer with large-scale, systematic chemical biology experiments. He described the Cancer Cell Line Encyclopedia, a catalog of mutations, copy number alterations, gene expression data, and extensive chemosensitivity data for ~1000 cancer cell lines.[2] Lehar also highlighted an ongoing comprehensive combinatorial screen measuring cellular responses with pairs of 70 chemicals across 140 high priority CCLE cell lines, which are then analyzed for synergy and antagonism. To date, 4505 synergistic interactions have been identified out of a possible 151730 combinations, or a 3% hit rate for synergies. Lehar presented novel algorithms to analyze compound profiling data, including a machine learning algorithm trained with known features and compound responses to predict effective inhibitors. He discussed the use of isobologram response surfaces to map synergy and measure the combinatorial index (CI). Current efforts by his group are aimed at tackling drug resistance, or adaptive resistance, in selected Novartis clinical trials by analysis of DNA/RNA from tumor and blood samples at different treatment stages in order to identify response mechanisms.

Talks by Krister Wennerberg and György Dormán also delved into the new area of chemi-omics. Wennerberg presented an update of efforts by the Institute for Molecular Medicine in Finland. This group is focused on systematic profiling of primary AML tumors with a functional screening collection of 300 active compounds to identify specific sensitivities for patient subgroups, thus generating chemi-omics data for primary tumors. The results of these analyses are directly translated into treatment regimens for patients and further provide insight into the underlying mechanism of disease. György Dormán (Targetex) discussed forward chemical genomics efforts underway by the European ChemoGrid consortium. As part of this effort, a large-scale differential cell-based screening was undertaken to document the viability of the HCT116 colon cancer cell line and the MRC-5 fibroblast cell line following exposure to a library of 30 000 compounds, selected based on the drug-like index (DLI). Following screening, they found 225 compounds with differential selectivity representing 85 chemotypes.[3] Current efforts are focused on systematic methods to identify the cellular targets of the selective compounds, using assays such as kinase panel screening, pull down assays, and *in silico* target annotation. Overall, these large-scale, systematic studies are generating new chemi-omics data sets, which are expanding the frontiers of chemical biology.

TARGETING BIOLOGY WITH CHEMISTRY

A major theme of ICBS2012 was targeting biology with chemistry. Consistent with the ICBS mission, many ICBS2012 talks focused on development of chemical probes to interrogate biology with small molecules. Keynote speakers Paul Workman and Lewis Cantley highlighted how chemical probes can lead to novel biological insights, while work presented by James Bradner (Harvard) demonstrated the widespread impact a single high quality chemical probe can have on scientific research. Speakers targeted different aspects of biology, including signaling pathways, cellular metabolism, and epigenetics. These pathways were linked to various diseases, ranging from rare and neglected diseases to cancer.

The opening keynote talk for ICBS2012 was Paul Workman's "The continuum of chemical biology probes and drugs for novel biological mechanisms and disease targets." With an overall focus on targeting cancer with small molecules, Workman's information-dense talk ranged from general guidelines for defining chemical probes to specific examples of target-directed probe development. "Probes need to be more selective than drugs if the purpose is to understand biology," noted Workman. He suggested an objective set of guidelines, or fitness factors, for development of useful chemical probes.[4] The suggested fitness factors included attributes related to chemistry, potency, selectivity, and context (Figure 2). However, Workman noted that suboptimal probes "are useful pathfinders on the journey." Workman also highlighted multiple successful examples in developing chemical probes for specific targets including PI3K and HSP90, and then translating these discoveries into the clinic. This included the use of various combined chemical and siRNA screening approaches to improve understanding of chaperone and stress pathways and to identify new drug targets. In addition, he highlighted a new method for systematic, unbiased, interdisciplinary computational assessment for chemical probe and drug discovery, revealing cancer genes that have been unexplored chemically to date.[5] He noted, "Smart science and technology accelerate discovery of targeted drugs, and shorten the lab to clinic cycle."

Lewis Cantley, a pioneer in cell signaling, presented his keynote lecture on using chemical biology approaches to target

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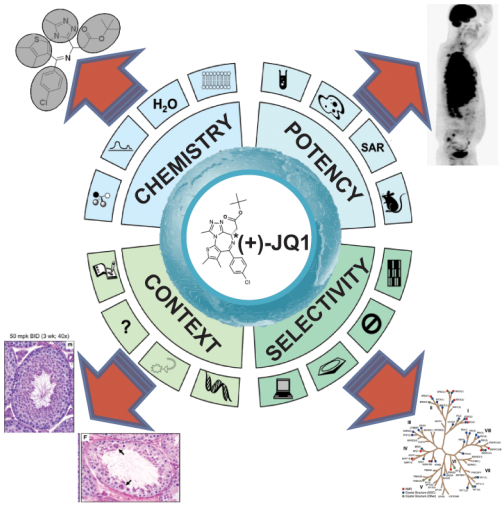

Figure 2. Scientific impact of a tractable chemical biology probe. When chemical probes are identified with sufficient fitness factors, such as selectivity, context, chemistry, and potency, they can have widespread impact on scientific research and human health. Generation of the JQ1 chemical probe with selectivity for BRD4 has identified a potential new therapeutic, opened new target space for epigenetic protein−protein interactions and for bromodomain family members, and demonstrated the impact of open collaboration by a new indication as a male contraceptive. Adapted with permission from refs 10, 27, and 4. Copyright 2010 Elsevier.

cancer metabolism. Cantley focused on the M2 isoform of the pyruvate kinase enzyme, a critical enzyme in the metabolic switch allowing increased proliferation of cancer cells. Cantley described the identification of small molecules, such as TEPP-46, that selectively activate the PKM2 isoform. These small molecule activators bind to the subunit interface and promote the formation of stable, active tetramers, increasing PKM2 activity to the level of PKM1.[6] In mice, treatment with TEPP-46 promotes the formation of tetramers and decreases the development of human cancer cell xenografts, suggesting that increased pyruvate kinase activity inhibits tumorigenesis. Further, Cantley presented a novel post-translational regulatory mechanism of PKM2 by reactive oxygen species through oxidation of Cys358.[7] This inhibition of PKM2 diverts glucose flux to the pentose phosphate pathways generating reducing potential for detoxification of ROS. Interestingly, in the presence of activators, PKM2 is resistant to inhibition by ROS. In an unexpected twist, Cantley's group also found that activation of PKM2 with small molecules results in a strict dependency on serine for continued proliferation.[8] Overall, Cantley's data suggested that regulation of PKM2 may allow cancer cells to adapt to oxidative and nutrient stress. Since treatment of tumors with PKM2 activators alone would only slow growth, Cantley hypothesized that therapeutic advantage would be achieved by drug combinations. In particular, by combining PKM2 activators with ROS-inducing drugs. Cantley's work highlighted the use of small molecules to specifically probe the function of the PKM2 protein isoform and the ability to utilize small molecules to discover novel and therapeutically relevant, biological insights.

Investigators also targeted the biology of gene regulation. This was captured in the session "Targeting epigenetic mechanisms with small molecules," chaired by Masatoshi Hagiwara (University of Kyoto). In this session, James Bradner's presentation highlighted the significant impact that a single, tractable chemical biology probe and a collaborative environment can have on scientific research (Figure 2). Bradner's presentation focused on the chemical probe JQ1, an inhibitor of the epigenetic-related protein BRD4. Utilizing SAR, JQ1 was designed to bind acetyl-lysine recognition motifs, or bromodomains, with specificity toward BRD4.[9] The JQ1 target, BRD4, is involved in a recurrent translocation in a rare subtype of human squamous carcinoma, and Bradner described how JQ1 exhibits specific antiproliferative effects in BRD4-dependent cell lines and patient-derived xenograft models. Following distribution of JQ1 to collaborators around the world, an unexpected use for JQ1 was revealed. A collaborator found JQ1 inhibits a testis-specific and bromo-domain-containing protein, BRDT. Biochemical studies confirmed binding of JQ1 to BRDT, and treatment of mice with JQ1 resulted in reversible reduction of seminiferous tubule area, testis size, and spermatozoa number and motility without affecting hormone levels or mating activity. Thus, JQ1 has become a lead compound for development as a male contraceptive.[10] The identification of JQ1 as a chemical probe was significant in multiple ways. First, these studies served as a proof of concept for targeting a protein−protein interaction domain in an epigenetic reader. Second, the studies have opened up a new family of bromodomain targets, including DOT1L and EZH2, which are frequent participants in oncogenic translocations. Third, although the chemical probe JQ1 has not been optimized for *in vivo* use, it is a promising therapeutic candidate for AML. Fourth, JQ1 is an important chemical scaffold to identify additional related compounds for development as potential chemotherapeutics. Finally, emphasizing the importance of open collaborative research, Bradner's distribution of JQ1 to collaborators around the world led to a completely unexpected and novel line of work.

Other highlights of this session included work by Zaneta Nikolovska-Coleska (University of Michigan) aimed at validating the recruitment of DOT1L (histone methyltransferase) as a potential therapeutic target and by David Bates (University of Bristol) targeting alternative splicing for development of antiangiogenesis therapeutics. In her talk, Nikolovska-Coleska focused on detailed biochemical, structural, and functional characterization of protein−protein interactions (PPI) between DOT1L and MLL oncogenic fusion proteins. She described a 10-mer peptide in DOT1L, which is a minimal interaction region with MLL-fusion proteins, AF9 and ENL. Nikolovska-Coleska has shown that deletion of this fragment in DOT1L abolished interaction with AF9 and eliminated MLL-AF9-mediated immortalization, indicating an essential function for this interaction in leukemogenesis and validating the PPI as a novel therapeutic target for mixed lineage leukemia (MLL).[11] David Bates began his talk by noting that 83% of everyone in the room would die from a disorder related to alterations in VEGF, ranging from blindness and heart disease to cancer. VEGF alternative splicing is altered in many diseases and is dependent on the SRSF1 splicing factor, which is active when phosphorylated by SRPK1. SPRK1 is in turn regulated by WT1. Bates has shown that inhibitors of SRPK1, such as SRPIN340,[12] normalize VEGF splicing as measured by re-expression of the antiangiogenic b isoforms. Functionally, treatment with SRPIN340 demonstrates dose-dependent inhibition of neovascularization in mouse and rat CNV models. Further, Bates found that SRPIN340 demonstrates significant CNV suppression without any adverse effects to the cornea, when administered daily as a topical eye drop. Thus, SRPIN340

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may be an alternative treatment for exudative AMD and possibly other proliferative retinopathies [for review, see ref 13]. Overall, Bates' work provides a proof of concept for the feasibility of therapeutic regulation of splicing.

The session "Approaches to understanding and treating rare and neglected diseases", chaired by Doug Auld, featured efforts at targeting Trypanosoma disease. Malcolm Walkinshaw (University of Edinburgh) highlighted work focused on taking advantage of unexpected differences in allosteric regulation of human and trypanosome glycolytic enzymes and leveraging these differences for therapeutic benefit. Focusing on pyruvate kinase, a high throughput screen identified saccharin derivatives that inhibit LmPYK (*Leishmania mexicana* PYK) activity in a time- and dose-dependent manner. The crystal structure demonstrated that an active-site lysine residue in LmPYK formed a covalent bond with the positive compound, sterically hindering the binding of ADP/ATP.[14] Walkinshaw also described a screen of 100 cellular metabolites and identified metabolites that differentially regulated the Tb and human PYK isoforms, M1 and M2. Jonathan Baell described a HTS strategy with 90K compounds against *T. brucei* whole cells.[15] Cautioning against progressing compounds, which are of limited potential, Baell applied PAINS analysis to positive hits,[16] leaving 11 distinct chemical classes for hit-to-lead optimization with a selectivity index (SI) > 10 and IC_{50} < 10 μM. Young investigator Brad Haubrich (Texas Tech), a graduate student with W. David Nes, furthered the session with a discussion of validation of the C-24 methyltransferase enzyme, part of a novel sterol biosynthetic pathway in *T. brucei*.

Leonard Zon (Harvard) presented the closing lecture for ICBS2012, demonstrating the power of zebrafish as a model organism with his fishtank to bedside approach. In his talk titled "Discovering therapeutics using the zebrafish: applications for stem cells and cancer," Zon described multiple phenotypic screens in zebrafish leading to the advancement of human health. In one example, a zebrafish-based phenotypic screen led to the discovery of compounds that improve engraftment of hematopoietic cells following bone marrow transplant.[17] For this study, a screen of 2498 compounds identified 35 chemicals that increased the frequency of repopulating stem cells, including prostaglandin dmPGE2. After optimization of conditions for clinical engraftment studies, initial clinical results with dmPGE2 are highly promising. In other work, Zon discussed screening for antimelanoma agents. Gene signatures for melanoma revealed upregulation of 123 genes, all of neural crest origin. Zon's lab performed a chemical screen with 3000 compounds and found one that erased the neural crest, a known compound approved by the FDA for treatment of arthritis. Following Zon's work, this compound is now under testing as an antimelanoma drug.

CATALYZING RESEARCH WITH INNOVATIVE TECHNIQUES

"Our perception of selectivity is a reflection of our screening capacity" was a point made by Jordi Mestres (IMIM/UPF) during his talk, "A critical view on the use of chemical probes." Mestres noted that the target profile of chemical probes expands as the concentration is increased. For example, the probe PJ34, well-known as a selective PARP inhibitor, also targets the PIM kinases as the concentration of probe is increased.[18] Thus, perception of PJ34 selectivity is limited by the assay conditions. In a similar way, chemical biology findings are limited by available technologies. Novel techniques and technologies presented during ICBS2012 ranged from computational approaches and inventive methods for target screening and validation, to cutting-edge chemistry-based approaches for generating photoaffinity probes and chemical ubiquitination.

An HTS assay is "an *efficiently-designed* experiment measuring the effect of a substance on a biological process of interest," emphasized James Inglese. Representing the National Center for Advancing Translational Sciences (NCATS), whose mission includes "catalyzing the generation of innovative methods and technologies," Inglese noted that "time spent developing the right assay is worth the investment as the cost of failure increases exponentially, the further it occurs from the start of a program." Inglese focused on innovative assay design. He described development of novel reporter gene technology and applied it to discovery of chemical agents that transcriptionally repress expression of PMP22, the culprit target in the gene-dosage disease Charcot–Marie–Tooth.[19] Inglese's innovative assay design addresses the issue of false positive detection of active compounds due to direct interaction with a reporter gene by utilizing cross-validating orthogonal reporters. These orthogonal reporters are used in an HTS-compatible cell-based assay resulting in a coincidence reporter biocircuit detecting readouts for the two stably stoichiometrically coexpressed reporter genes.[20] However, the suggested coincidence reporter strategy could be easily applied to improve the efficient design of a large number of HTS assays. The coincidence biocircuit plasmids have been made available to the public through the not-for-profit company Addgene (http://www.addgene.org/James_Inglese/).

Innovative computational techniques can significantly enhance the efficiency of chemical biology research. As part of the "Highly innovative cheminformatics and computational approaches" session chaired by Petr Bartůněk (Institute of Molecular Genetics), scientists presented computational efforts to catalyze chemical biology research. Jürgen Bajorath (University of Bonn) presented work focused on computer-assisted molecular probe identification for inhibitors of a multifunctional target, cytohesin. Structurally diverse inhibitors with differential activities were identified. Bajorath also presented a novel computational approach to the analysis of compound profiling data. A kinase inhibitor profiling data set was analyzed using a simple yet highly informative 2D representation termed ligand-target differentiation (LTD) map. These maps reduce the complexity of high-dimensional bioactivity spaces and allow identification of key compounds with high target differentiation potential. Other presentations included Samy Meroueh (Indiana University) on structure-based computational design of small molecules that target protein interactions in cancer. He highlighted novel computational techniques and described development of a novel compound identified through virtual screening, which inhibits the urokinase-type plasminogen activator (uPA) interaction with its receptor (uPAR), inhibits invasion, metastasis, and adhesion *in vitro*, and has promising initial results in mouse *in vivo* tumor models.[21] Eugene Lounkine (Novartis) discussed the large-scale prediction and testing of drug activity on side-effect targets, as adverse drug effects are one of the leading causes for drug attrition. Lounkine described use of a computational similarity ensemble approach (SEA) to generate predictions of the activity of 656 drugs on 73 off-targets based on similarity to known ligands. More than 150 novel predictions were experimentally confirmed. Development of

drug-target-adverse drug reaction networks identified clinical side effects that could be better explained by the novel predictions than by the already known off-targets.[22]

The first place winner of the Young investigator's Award was Devlin Noblin, a Ph.D. candidate in Craig Crews' lab (Yale University). Noblin presented a promising novel platform for target validation studies, the HyT-HALTS system. With this system, the expression levels of a Halo-tagged protein of interest can be regulated upward or downward with small molecules. Previous work in Crew's lab demonstrated that hydrophobic tagging of Halotag fusion proteins allows small-molecule control over a protein of interest by targeting the proteasome, leading to degradation and decreased protein levels.[23] In his talk, Noblin described a small molecule screen leading to the discovery of novel HaloTag2 stabilizer (HALTS) compounds. Noblin showed this stabilization occurred through direct binding and blockage of proteasome-mediated aggregation. With both HyT and HALTS compounds in hand, the HyT-HALTS system can be used to increase or decrease protein expression of Halotag fusion proteins by the addition of HALTS or HyT36, respectively.

In the expanding ubiquitin research area, the generation of reagents is extremely difficult and is often a limiting factor in experimental design. Huib Ovaa (The Netherlands Cancer Institute (NKI), Amsterdam, and founder of UBIQ BV) highlighted a novel approach developed in his lab to chemically synthesize ubiquitinated material with an automated, solid phase synthetic process.[24] Ovaa described use of his approach to generate all possible ubiquitin topoisomers and the synthesis of ubiquitin-based probes to profile the activity of deubiquitinating (DUB) enzymes in functional studies.[25] In addition, Ovaa has shown that chemical ubiquitination can be extended to chemically introduce virtually any ubiquitin-like proteins, such as SUMO and NEDD8, in ubiquitin-like conjugates.

A new azide chemistry-based approach for generating novel tools was described in a lively presentation by Takamitsu Hosoya (Tokyo Medical and Dental University, Japan). Hosoya hoped to inspire "azido-mania" with his presentation of novel chemistry using azido-type selective reactions. Hosoya discussed use of this chemistry to label small molecule probes with a photoreactive tag for target identification, to chemically modify proteins via a double-click reaction, and to synthesize new probes via sequential conjugation. In a surprising finding, Hosoya described increased reactivity of a sterically hindered 2,6-disubstituted phenyl azide compared to an unhindered azide.[26] This discovery was applied to multifunctional probe synthesis allowing sequential triple-click reactions to generate triple-tagged molecules.

FOSTERING GLOBAL COLLABORATIONS

A collaborative spirit pervaded the meeting, evident in presentations and the final session highlighting policies and initiatives fostering global collaborations. For example, Bill Zuercher's (GlaxoSmithKline) talk "Catalyzing chemical biology through strategic compound sets" focused on GSK efforts to define and release an open access set of kinase inhibitors to foster research on orphan kinases through an innovative network of experts. As such, the 367 compound Published Kinase Inhibitor Set (PKIS) is available to any academic investigator with a requirement for public release of the resulting data. To facilitate research on neglected tropical diseases (NTDs), Michael Pollastri (Northeastern University) described development of a hybrid open source discovery initiative consisting of a knowledge store containing targeted product profiles for each pathogen and resources for key tasks. The database contains both public and private data sets deposited by initiative members. Pollastri encouraged any interested scientists to contact him.

Perhaps defining the spirit of global collaboration during ICBS2012 was the final session of the meeting, "Emerging policies and initiatives that promote global collaborations" chaired by Barbara Mroczkowski (NIH). Representatives of chemical biology efforts in the US, EU, and Japan presented updates of current initiatives and highlighted collaboration and open innovation. Mroczkowski discussed USA efforts in the chemical biology field. She presented an overview of the NExT therapeutic pipeline, with a focus on the NCI's Chemical Biology Consortium (CBC). Meant to function as a discovery engine accelerating the development of investigational drugs, the NCI CBC offers a full-range of chemical biology resources open to academia, nonprofit, and private enterprises for promising projects with therapeutic potential but not likely to be advanced by industry. Part of the available resources includes a collection of chemical biology centers with complementary expertise and a CBC small molecule repository. The chemical library contains a highly curated diversity set of 100K compounds and is in the process of expanding to include new scaffolds and natural products. Representing the EU, Ronald Frank (FMP) discussed EU OPENSCREEN, an infrastructure initiative whose mission is to accelerate the discovery of biologically active substances and the development of tools for chemical biology. This mission will be accomplished through shared resources, such as joint compound collections built from commercial and proprietary sources, distributed screening centers, broad bioprofiling of compounds, and data sharing with a centralized management office and database. Currently it is in the final stages of development of the strategic roadmap for the efforts. Representing Japan, Hirotatsu Kojima (University of Tokyo, Japan) discussed the Japanese network for open innovation in drug discovery. Developed by the MEXT (Ministry of Education, Culture, Science, and Technology), the Targeted Protein Research Programs (TPRP) is aimed to reveal the structure and function of proteins that are of great importance. Research teams consisting of biologists, medical scientists, structural scientists, and medicinal chemists are formed around promising targets. An initial HTS hub at the University of Tokyo is now being expanded to six HTS hubs, which collaborate with neighboring researchers. The compound libraries can be freely accessed by Japanese researchers, both profit and nonprofit, with scientists paying only actual expenses of the screen.

CONCLUSIONS

ICBS2012 brought together thought leaders and served as an important forum for young investigators in chemical biology. During the business portions of the meeting, enthusiastic participants suggested broad expansion of the society into the many scientific areas encompassed by the emerging discipline of chemical biology. Haian Fu, the newly elected ICBS president, encouraged continued grassroots efforts to accelerate growth of the society and together to generate a collective impact on the chemical biology field. The robust response from the global chemical biology community indicates that this meeting will be the first of an annual showcase for cutting edge chemical biology research. ICBS2013, to be hosted by President-elect Masatoshi Hagiwara in Kyoto, Japan, promises

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to feature the latest worldwide advances in the fast-paced science occurring at the interface of chemistry and biology.

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