Introduction and Welcome to the Society of Biomolecular Imaging and Informatics (SBI²)

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INTRODUCTION

As we embark on the first annual conference for the Society of Biomolecular Imaging and Informatics (SBI²), the authors would like to provide the readers of *Assay and Drug Development Technologies* with some insights into the activities that prompted the formation of the society. In the mid-1990s, the commercialization of automated platforms that provided integrated solutions for the acquisition and analysis of digital images of cells arrayed in microtiter plates heralded both the democratization of fluorescence microscopy and dramatic increases in both the throughput and capacity of these important cellular analysis disciplines. Grounded in the technologies of microscopy, computer-assisted image analysis, and informatics, a variety of descriptive terms have been coined for this type of cellular analysis, with high content screening (HCS), high content analysis (HCA), high content imaging (HCI), and image cytometry (IC) being some of the most common. Prior to the launch of SBI², practitioners of HCS/HCA/HCI/IC were typically members of existing scientific societies such as the Society for Biomolecular Sciences (SBS) and the Association for Laboratory Automation (ALA), which merged to become the Society of Laboratory Automation and Screening (SLAS), or the International Society for the Advancement of Cytometry (ISAC). While each of these societies have added HCS/HCA/HCI/IC sessions to the scientific tracks of their annual conferences, biomolecular imaging and informatics represents only a minor subset of the overall charters of these societies. SBI² was founded in 2012 to represent the scientists, engineers, informatics specialists, and vendors that develop and utilize biomolecular imaging and informatics approaches for cellular analysis.

GENESIS OF SBI²: WHAT'S IN A NAME?

The earliest conferences dedicated to biomolecular imaging and informatics were user group meetings, typically hosted by instrument vendors. For example, Cellomics (ThermoFisher Scientific), one of the first companies to commercialize an automated imaging platform, hosted user group meetings in Pittsburgh in 2000 and in Bal Harbour, FL in 2001. Even at these early meetings, Joe Trask was a strong proponent for the formation of a society, stating that "we have a great opportunity to drive this technology where we want to go and we should form a user's group amongst us that would mirror for example ISAC or the Great Lakes International Imaging and Flow Cytometry Association (GLIIFCA) and exchange ideas using email similar to the mailing list at Purdue University." It was several years, however, before these sentiments came to fruition. The emergence and importance of the use of HCS/HCA/HCI/IC technologies for cellular analysis was quickly recognized by the commercial sector, especially by companies that organized scientific meetings and conferences. Although many of these companies added HCS/HCA/HCI/IC-focused meetings to their portfolios, the annual HCA meeting in San Francisco sponsored by Cambridge Health Tech Institutes (CHI) at the Fairmont Hotel arguably became the flagship meeting for HCS/HCA/HCI/IC practitioners. The first CHI HCA meeting was held in 2003, and over the years, these meetings have provided tremendous opportunities for HCS/HCA/HCI/IC scientists to network. It was there that the formation of a society gathered momentum.

In 2008, a high content imaging Google group was created that was intended to provide users of the technology an outlet to exchange information outside of the instrument or software vendor space. Although this Google group provided valuable information about the available HCS commercial available systems and despite having more than 100 users, the volume of information and networking were low. Also in 2008, Facebook and LinkedIn HCS groups were formed, and Joe Trask hosted the first HCI Symposium in conjunction with RTCA at Duke University with more than 75 people in attendance. In his introductory talk at the 2010 HCI HCA meeting, Jeff Haskins of ThermoFisher Scientific announced that "it was time we (the community) started a society." This statement sparked a lot of discussion, and colleagues/experts in the field gathered in the hallways and corridors of Fairmont Hotel to explore strategies for the formation of a society that included Anthony Davies, Roy Edward, J. Paul Robinson, Steve Haney, Paul Johnston, and Joe Trask. Later in 2010, Joe Trask hosted the 2nd HCI Symposium at The Hamner Institutes for Health Sciences with more than 85 people in attendance.

However, it took another two years of discussion and the "magic of twelves" at the 2012 HCA meeting in the Fairmont Hotel, San Francisco, before we decided it was time to "fish or cut bait" and agreed to launch a society. But launching a society required skill sets that neither of us had—what were we thinking? We reached out to

DOI: 10.1089/adt.2014.1506

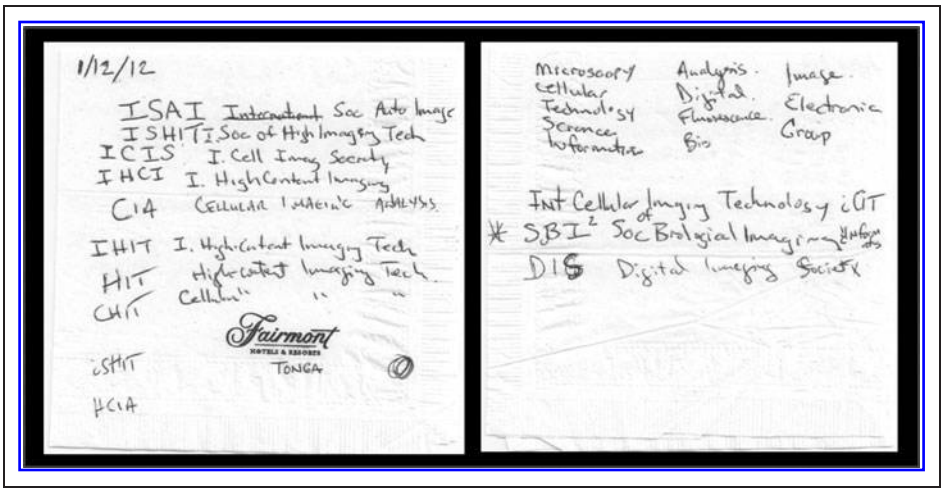

Fig. 1. "So what's in a name?" Image of the napkin with the list of potential names for the Society of Biomolecular Imaging and Informatics discussed in the Tonga room of the Fairmont Hotel in San Francisco on January 12, 2012.

other well-established societies, including SLAS and ISAC, but after due consideration we concluded that the HCS/HCA/HCI/IC community would be better served by a dedicated society rather than a special interest group. The first major challenge was what we should name the society. This should be easy—just call it the High Content Screening Society, right? But what about the Society of High Content Analysis or Society of High Content Imaging or Society of Image Cytometry? Although many terms were already used to describe the technology, we had a bigger picture in mind and wanted the name of the society to be inclusive, bold, and representative of the undertaking. With the creative aid of a few beverages in the Tonga room, we jotted down potential names for the society on a napkin, and being a bit foresighted and nostalgic, we dated and preserved the napkin that will be on display at the Annual Conference (*Fig. 1*). The list of potential society names only contained 13 suggestions (*Fig. 1*), but it was the 12th name on January 12, 2012 (the "magic of twelves") that struck us as being the name we should pursue. The next morning, we modified the name to the Society of Biomolecular Imaging and Informatics, and the rest is history.

THE FOUNDING OF SBI²

Having committed to this endeavor, the days, weeks, and months following would determine whether the society would be formed and succeed. In early February 2012, we met in a Pittsburgh coffee shop to craft an SBI² mission statement. The same mission statement is still used today with one significant modification—the addition of "student," as suggested by Steve Haney. The SBI² mission statement: "The Society of Biomolecular Imaging and Informatics is an international community of leaders, scientists, and students promoting technological advancement, discovery, and education to quantitatively interrogate biological models to provide high context information at the cellular level. SBI² is a non-profit scientific society dedicated to increasing the understanding, utility and rigor of quantitative imaging or high content analysis." Even though we were enthusiastic and optimistic that SBI² was a good idea, we were by no means certain that the scientific community would either embrace and/or sustain a new society dedicated to HCS/HCA/HCI/IC technology. After all, the formation of a society had been bandied around for more than a decade. To address this question, we spent several weeks developing a questionnaire of nine questions that were placed on the SurveyMonkey website and sent to a targeted audience of more than 100 people in the field (*Table 1*). From 87 respondents (>95%), the majority consensus vote was to start a "society," and by June 2012, we began filing the paperwork to establish a domain name, website, and so on. Although the initial expenses came from our own charitable donations, the probability of SBI²'s future was significantly enhanced by funding and support provided by Joe's employer, The Hamner Institutes for Health Sciences, who provided legal advice from Bud Nelson, PhD, JD, for document reviews, filing for trademarks, establishing the domain for the website, submission of the articles of incorporation, and also made a home office available.

Coincident with our efforts, we discovered that several other colleagues in the field were also discussing the possibility of starting an HCA-like society, and we were invited to participate in a teleconference call with Mark Collins, Steve Haney, and Anthony Davies amongst others. We followed up with Mark and Steve, and this group of founding members nominated the first officers of the SBI² Board of Directors (BOD): Mark Collins as Treasurer, Steve Haney as Secretary, Paul Johnston as President Elect, and Joe Trask as President. In the following weeks, we submitted trademark protection for SBI², and began writing the Bylaws for the society. The SBI² website was launched in July 2012 (www.sbi2.org/), but in September 2012, Jonathan "Jonny" Sexton (NCCU-BRITE) joined the society and became Webmaster, and has since orchestrated the implementation of the website. In December 2012, SBI² was incorporated, and the BOD had extended invitations to five colleagues to join the Board, including Anthony Davies, Anne Carpenter, Kaylene Simpson, J. Paul Robinson, and Renate Schnitzer. Their three-year appointments commenced on January 1, 2013, and these founding Board members have undertaken many roles to help direct and mold the Society. The current SBI² BOD are: President—Joe Trask, Head Cellular Imaging Core, The Hamner Institutes for Health Sciences; President elect—Paul A. Johnston, Research Associate Professor, University of Pittsburgh; Secretary—Steven Haney, Senior Research Adviser, Eli Lilly & Co.; Treasurer—Mark Collins, Director of Marketing, BioFortis, Inc. Board members are: Anne Carpenter, Director Imaging Platform, Broad Institute of Harvard and MIT; J. Paul Robinson, Director, Purdue University Cytometry Laboratories, Deputy Director, Bindley Bioscience Center; Kaylene Simpson, Head Victorian Centre for

Table 1. Society for Biomolecular Imaging and Informatics Survey Results

Question	Options	%
1. What is your area of interest and/or participation in the field of HCS/HCA /HCI? (select all that apply)	High content screening	86.2%
	High content analysis	83.9%
	High content imaging	78.2%
	Image cytometry	26.4%
	Flow cytometry	24.1%
	Digital pathology	9.2%
	Computer-assisted image analysis	41.4%
	Data management	44.8%
	Bioinformatics and informatics	33.3%
	All of the above	8.0%
	Currently not involved	0.0%
2. Which of the following categories best describes your job description?	Graduate student/postdoc	8.0%
	Scientist	32.2%
	Technician	1.1%
	Informatics and Information Technology	0.0%
	Vendor	8.0%
	Consultant	1.1%
	Management (Director, Gp Leader, Dept Head)	28.7%
	Academia (Professor)	17.2%
	Executive Position (CEO, President, VP) Other (1)	3.4%
3. Where do you see HCS/ HCA/HCI best meeting your research needs?	Target identification/validation (TI/TV)	55.8%
	Primary HCS/lead generation	59.3%
	Hit characterization/mechanism of action	64.0%
	Lead optimization	38.4%
	Toxicology models	33.7%
	Biomarker discovery	27.9%
	Developmental models	15.1%
	Systems biology	40.7%
	Translational/clinical research	33.7%
	Basic science	45.3%
	All of the above	20.9%
4. Please rank the order of importance of each "High Content" for your area of research: **Extremely Important**,[a] Very Important, Important, Less Important, and Not Important	Assay development and design	62.1%
	Data analysis	55.2%
	Data management	34.5%
	Image analysis	59.8%
	Informatics	21.8%
	Instrumentation	26.4%
	Manufacturing	9.2%
	Standards	10.3%
5. What should an HCS/ HCA/HCI society provide for its members? (select all that apply)	Training/education	72.1%
	Scientific meeting focused on HCS/HCA/HCI	74.4%
	Scientific journal focused on HCS/HCA/HCI	37.2%
	Certification of knowledge and competence	24.4%
	Collaboration to establish industry standards	57.0%
	Website for networking and sharing information	66.3%
	All of the above	23.3%
6. If a scientific society representing the core "High Content" technologies described existed, would you consider becoming a member?	Yes	96.6%
	No	3.4%
7. In your opinion, do any of these online groups meet your expectations? (optional): **Do not use it**,[b] Less than satisfied, Satisfied, Exceeds, Exceptional	Facebook—High Content Screening	87.0%
	Google Group—High Content Imaging	77.3%
	LinkedIn—High Content Screening	46.7%
	Local—University, Institution, Center, etc.	67.6%
	Purdue University Cytometry Mailing List	77.0%
	Twitter—High Content Screening	89.5%
	Vendor (HCS) websites	31.5%

(*continued*)

Table 1. (Continued)

Question	Options	%
8. Please list **scientific meetings attended in the past 3 years.**[c] If a member of the society please list.	AAAS	2.5%
	AACR	19.8%
	ASCB	23.5%
	FASEB	8.6%
	ISAC	17.3%
	Society for Developmental Biology	3.7%
	SLAS	46.9%
	Society for NeuroScience	11.1%
	Society of Toxiciology	12.3%
	Cambridge HealthTech Institutes—HCA	43.2%
9. If interested in being part of organizing such a society, please let us know by filling out the form, otherwise skip the question.	Answered question: 45, 97.8% willing to help	
	Skipped question: 42	
	% of those taking survey willing to participate	50.6%

A questionnaire of nine questions were placed on SurveyMonkey and sent to a targeted audience of more than 100 people in the biomolecular imaging and informatics field. From 87 respondents (>95%), the majority consensus vote was to start a "society."

[a]Only the % "extremely important" responses are presented.

[b]Only the % "Do not use it" responses are presented.

[c]Only the % "attendance at scientific meetings" responses are presented.

Functional Genomics; Peter MacCallum Cancer Centre; and Renate Schnitzer, Director High Throughput Drug Discovery, Boehringer Ingelheim, RCV.

During the 2013 CHI-HCA meeting in San Francisco, members of the SBI² Board presented an introduction of the society at each of the vendor user group meetings and began planning for smaller regional meetings and a future annual conference.

SBI² REGIONAL MEETINGS 2012–2014

Consistent with the founding principles of SBI², since its launch in 2012, the society has striven to provide scientific conferences of very high scientific rigor at nonprohibitive costs, enabling broad participation by scientists and students from both academia and industry. The first SBI² regional meeting was held on October 11, 2012, in partnership with the Research Triangle Cytometry Association (RTCA) to co-sponsor the 3rd Annual High Content Cellular Imaging and Image Cytometry Symposium at the North Carolina Biotechnology Center. With the support of HCS vendors, collaborators, and a small grant, this one-day symposium was free for all participants from surrounding companies and universities to attend, anchored by an excellent keynote address by Professor John Russ (author of *Image Processing*), and several outstanding talks from scientists in the field. This SBI² Southeast regional meeting attracted around 100 participants and provided a scientific program, technology spotlights, and networking opportunities for participants and sponsoring vendors.

In 2013, on July 18 and 19, SBI² partnered with the Australian High Content Screening group to co-sponsor the Australian High Content Screening and RNAi meeting held at the Park Hyatt, East Melbourne, Australia. This workshop-styled meeting attracted 90 participants and provided an extraordinary opportunity for student and postdoctoral attendees to mix with international experts in a causal environment and to present and discuss their research. Another one-day symposium SBI² regional meeting was scheduled in October 2013 at the Promega site in Madison to coincide with a meeting of the assay development guidance group, but the government shutdown interrupted travel, and the meeting was postponed until January 2014. However, a severe winter storm forced SBI² to cancel the meeting, which has not yet been rescheduled.

On January 21, 2014, SBI² co-ran a successful special interest group on HCS/HCA data and informatics at the Society for Laboratory Automation and Screening (SLAS) annual conference in San Diego that attracted 60 participants. SBI² followed this up on January 23, 2014, with a West Coast regional meeting at the Sanford Burnham Medical Institute in La Jolla that was hosted by Dr. Jeff Price. The SBI² West Coast meeting was well received with excellent scientific presentations, good technology spotlights, a short course on automated imaging platforms and assay development for HCS/HCA, and networking opportunities for participants and sponsoring vendors. On July 17 and 18, 2014, SBI² was again affiliated with the annual Australian High Content Screening and RNAi meeting that was held at the Park Hyatt, East Melbourne, Australia. This year, 85 delegates attended the workshop-styled meeting, including international guests Professor Neil Carragher (Edinburgh Cancer Research Centre), Dr. Luke Lairson (Scripps), Dr. Krismunder Sigmundsson (Duke-NUS Singapore), and Dr. Annaleen Vermeulen (Dharmacon GE). In addition, the meeting focused on short 15-minute talks from students and postdocs working in the HCA, compound and RNAi screening areas, and a highly successful session hot topics roundtable discussion. As the society grows in Australia, the breadth of topics at the meeting was vast, and we heard from those starting out in the field to those who have recently published. The open and sharing forum of unpublished data was a key element to the success of the meeting. Delegates also enjoyed a networking cocktail function overlooking the Melbourne skyline at sunset.

1ST ANNUAL CONFERENCE

The 1st annual SBI² conference will take place on September 10–12, 2014, at the Joseph B. Martin Conference Center, Boston, Massachusetts, and comprises two major programs: a one-day educational program with a variety of short course topics taught by leaders in the field, and a two-day scientific program emphasizing the cutting edge of biomolecular imaging and informatics. Dr. Anne Carpenter is chair of the organization committee, and together with

members of her staff at the Broad Institute, they will be responsible for the onsite organization and logistics of the conference.

The SBI² educational program of short courses were developed and designed by Steve Haney and Anne Carpenter, and they have recruited expert instructors from the field of biomolecular imaging and informatics to teach a variety of topics for both novices and experienced users of HCS/HCA technologies. The morning session of the education program will be comprised of three introductory courses: Hardware and Image Acquisition, instructor Doug Bowman (Takeda Pharmaceuticals); Assay Types and Assay Development, instructors Steven Haney (Eli Lilly and Co) and Debra Nickischer (Bristol-Myers Squibb); and Image and Data Analysis, instructor Mark Bray (Broad Institute).

The afternoon session of the education program will cover more advanced elective courses, including:

- Assay validation for HCS, instructor Paul A. Johnston (University of Pittsburgh). The first step of validation is to confirm that the fully optimized HCS assay exhibits appropriate pharmacology and correctly identifies known activators/inhibitors with suitable EC50/IC50 values. We will illustrate the application of validation tests designed to aid with the selection of appropriate HTS data-processing methods, set quality control review standards, and select active criteria. We will describe the use of pilot screens to demonstrate that the assay performs well with compounds at an HTS scale, and strategies to identify and eliminate potential interference compounds that may be either cytotoxic or fluorescent intensity outliers.
- RNAi, instructor Kaylene Simpson (Peter MacCallum Cancer Centre, Melbourne). This short course will cover general considerations for high throughput automated siRNA screening from assay design, development, and implementation using high content image analysis as an assay readout.
- FIJI and open source image management tools, instructor Kevin Elicieri (University of Wisconsin). We will overview several tools for open source image informatics, including ones for acquisition, image analysis, and dissemination. A focus will be presenting FIJI and ImageJ, and efforts on interoperability with these tools.
- Tissue-based HCS, instructor Doug Bowman (Takeda Pharmaceuticals). This workshop will provide an introduction of applications of HCS in tissue, often referred to as quantitative digital pathology. We will review hardware and software technologies, image analysis, and challenges of tissue-based assays compared to *in vitro* cell-based assays. Lastly, we will highlight how these technologies are utilized with examples from preclinical and clinical studies.
- FRET/FLIM, instructor David Andrews (University of Toronto). We will cover what characteristics of fluorescence proteins are optimal, what biological controls are necessary, and how data collection and instrumentation differ from generally published methods in order to generate interpretable binding curves in live cells. We will also illustrate some of the caveats as well as some of the spectacular results that are possible.
- Single-cell analysis, instructor Bartek Rajwa (Purdue University). This course will present methods for analyzing imaging data that are analogous to flow cytometry, including co-variation of endpoints with samples to identify signaling dependencies. These methods are readily implemented on most imaging systems, and expand the information that can be extracted from experiments on cell signaling and development.
- Cell Profiler, instructor Mark Bray (Broad Institute). This workshop will instruct biologists in general concepts and techniques used for automated image analysis. Participants will learn the basics of using CellProfiler, an open-source, freely downloadable software package designed for large-scale, automated phenotypic image analysis. Lastly, we will also briefly discuss the basic principles of supervised machine learning in order to score phenotypes where phenotypic differences between samples are not visible by eye.
- Machine Learning, instructor Shantanu Singh (Broad Institute). The workshop will provide overview of data analysis/machine learning techniques for image-based high-throughput experiments. Free, open-source programs and languages (R and Python) will be used to demonstrate the concepts.

The 1st annual SBI² conference scientific program was developed and designed by Kaylene Simpson and Paul Johnston, with an emphasis on showcasing new HCS/HCA data and information that had not previously been presented or is at the cutting edge of biomolecular imaging and informatics. To develop a strong and rigorous scientific program for the 1st annual conference, Kaylene and Paul recruited a program committee composed of recognized leaders in the HCS/HCA field and tasked this committee with selecting speakers for four scientific sessions: assay development and HCS case histories; image analysis and informatics; physiologically relevant models; and emerging frontiers. Two speakers for each of the sessions were invited by the program chairs, and the remaining speakers were selected from abstracts submitted to the conference website (http://www.sbi2.org/abstract-submission/).

Session I—Assay Development and HCS Case Histories—will be chaired by Caroline Shamu, Director ICCB Longwood, Harvard Medical School, Boston, and Hakim Djaballah, Director HTS Facility, Memorial Sloan Kettering Cancer Center. The development, validation, and implementation of novel high content imaging assays combined with evolving strategies for compound and RNAi library screening seek to broaden both the scope of biological processes and/or target classes that can be addressed by HCS, and to improve the quality of information and actives emerging from HCS campaigns. This session will focus on recent innovations in HCS assay development and screening, with an emphasis on case histories where the technology has been successfully implemented to interrogate an important biological process and/or to discover novel leads for drug discovery.

Session II—Image Analysis and Informatics—will be chaired by Peter Horvath, Synthetic and Systems Biology Unit Hungarian Academy of Sciences, BRC, Szeged. The session will focus on the

development and application of novel image processing and multivariate data analysis methods for HCA, together with innovative strategies to manage, interpret, and share the large volume of images, data, and information produced. Practical examples highlighting the use of experimental design, image correction, image segmentation, data pre-processing, and multivariate statistical methods to analyze and extract quantitative data and information will be given priority, along with cases illustrating the integration of HCA data with other complex data sets, including but not limited to gene expression profiling, signaling pathway mapping, DNA sequencing, and mutational analysis.

Session III—Physiologically Relevant Models—will be chaired by Stephen Pak, Department of Pediatrics University of Pittsburgh Medical School, and Vance Lemmon, Department of Neurological Surgery University of Miami. HCS model systems range from 2D *in vitro* cell lines to whole organisms. Quite often, the direct outcome of drug or chemical screening in cell lines is to evaluate lead candidates in relevant model organisms. This session will focus broadly on different biological systems and their relevance to physiological environments. This could include but is not limited to novel cell culture imaging approaches (including primary cells, 3D conditions, co-culturing, cell-substratum interactions), strategies for imaging in a whole organism or part thereof and for quantitation of phenotypic outcomes.

Session IV—Emerging Frontiers—will be chaired by David Andrews, Director of the Sunnybrook Research Institute, University of Toronto, and Simon C. Watkins, Director of the Center for Biologic Imaging, University of Pittsburgh. We are seeking submissions on new material that is at the cutting edge of biomolecular imaging and informatics. We are looking to excite and inspire the current and next generation of researchers in the field. This session will include new single cell imaging and quantitation strategies, live cell imaging, novel staining methods, that is, biosensors, imaging modalities, quantitation algorithms, complex multi-parametric staining and detection followed by unsupervised clustering of data for analysis, and the development and application of new imaging platforms.

CONCLUSION

We would like to give an enormous amount of credit for the planning of the 1st Annual Conference to the BOD (past and present), Jonny Sexton, the SBI² Webmaster, and all of the folks on the organizing committee. Because SBI² is a young society and committee roles are immature, the Board has undertaken many of the duties required to ensure that the society and the conference will succeed. It is our hope and expectation that many of these duties will be transferred to committees populated by our membership. At the annual general meeting (AGM) to be held on September 11, 2014, at the conference, SBI² will asking for volunteers for new committees and will be electing two new Board members to help guide the direction of the society as it matures. Joe Trask's term as President will expire, and he will be stepping down to become Past-President. Paul Johnston will take on the role of President. The BOD position of President-Elect will therefore become open for nominations and will be voted on by society members at the AGM, and we welcome all participants of the conference to join us. In conclusion, we hope that you will join SBI² and become active participants on committees and/or the BOD to assist the society to achieve its goals to advance the field of HCS/HCA by promoting education and the development of standards within the scientific community.

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