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SBS

News

THE OFFICIAL MEMBERSHIP NEWSPAPER OF THE SOCIETY FOR BIOMOLECULAR SCIENCES

JUNE 2009 • ISSUE 40

from SBS' president

SHARING EXPERIENCE AND KNOWLEDGE

While returning from the successful 15th Annual SBS Conference & Exhibition held in Lille, France, my thoughts began to focus on how our Society will evolve in 2009 and over the next 15 years.



Jeff Paslay

The driving force for founding SBS in 1994 was to provide a forum for sharing, learning and networking with colleagues from both user and provider communities involved in screening technologies. The original founders recognized that there was no existing scientific organization that brought together the diverse participants in the various technologies and approaches that were evolving in screening laboratories. The success of that endeavor was recently echoed in the comments of Julio Martin, Derek Hook and Richard Ellson in the February 2009 (pre-conference issue) of *SBS News*, where they highlighted how membership in the society over many years has enriched their careers. The fact that they represent industry, academia, and technology suppliers reflects the importance of these communities in our past and, more than ever, in our future.

We have witnessed many changes during our 15-year history. From my perspective, three have had major impact on all of our member communities—industry, academia and providers:

Industry Consolidation: The first change is the consolidation that we have witnessed in both the biotechnology and pharmaceutical industries. Starting in the early 1990s with discussions of health care reform and proclamations by several consulting groups on the necessary scale required to fuel pipelines, survival strategies by large pharma companies initiated a wave of mergers and acquisitions that continues today.

In parallel, there was an explosion of bio-
(continued on page 6)

leading edge

Unique Symposium Merges Screening Technologies with Stem Cell Biology



Interview by Marilyn Larkin

On September 2-3, 2009, a new SBS symposium, *Screening Stem Cells: From Reprogramming to Regenerative Medicine*, will be held at the Boston Park Plaza Hotel in Boston, Massachusetts, USA. *SBS News* talked with symposium chair, Kelvin Lam, Ph.D., Director of High-Throughput Screening at the Harvard Stem Cell Institute and Harvard University, about the topics that will be covered in the symposium, why SBS members and drug-discovery scientists should attend, and why he was drawn to stem cell screening.

WHAT'S UNIQUE ABOUT THIS STEM CELL SYMPOSIUM, COMPARED WITH ALL THE OTHERS "OUT THERE"?

If you want to know more about screen cells generally, there are plenty of meetings you can go to. But if you want to learn about screening "stem cells", this is the meeting for you. We will be talking about what drug-discovery professionals need to know about stem cell biology in order to use screening techniques with stem cells. For example, whereas most compounds subject to traditional screening last only two or three days, generally stem cells last more than three weeks. So to manage stem cells, you need to assemble new skills in compound management, in image-based HCS assays, in cell-based assays, and in assay development for long term cell culturing systems. Traditional drug-discovery skills alone perhaps are not sufficient, and knowledge of stem cell biology alone is not adequate to establish a valid stem cell screen. You need both skills. Whereas the field used to be thought of only in terms of small molecules, now stem cell therapeutics, as well as biotherapeutics and antibodies, are all part of drug discovery.



Kelvin Lam

WHAT KEY ISSUES WILL BE COVERED?

Key issues with respect to stem cells include understanding their fundamental biology; how to characterize and standardize them; using HTS against stem cells to identify small molecule cell-fate modulators; how to move from induced pluripotent cells (iPS) to patient-specific pluripotent cells; and therapeutic

applications of embryonic cell-based therapy, including replacing diseased cells with healthy cells in a process similar to organ transplantation.

To address these issues, the program committee decided to organize the conference around four major themes:

1. The promise of stem cells;
2. Access, distribution and quality control;
3. Stem cell screening systems; and
4. Therapeutic applications.

How to best realize the vast potential of stem cells is the first theme of the conference, and will be addressed by our keynote speakers (see box, p. 7).

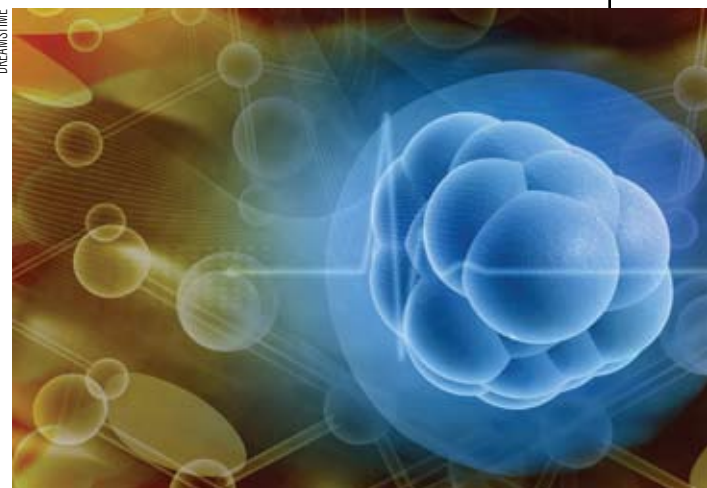
The second session covers stem cell standardization, which is essential not only in laboratory settings, but also for developing safe and effective stem cell therapies for patients. The topic will be addressed in a panel format to stimulate a dialogue aimed at generating the highest scientific standards.

The third session addresses how HTS technologies that have been successful in exploiting traditional targets can be applied against stem cells. For example, we will cover how stem cell-directed differentiation assays can be used to target disease-specific therapies.

The fourth session will provide real-life examples of how stem cell technologies are moving from concept to the clinic, including an update from Geron on the

(continued on page 7)

DREAMSTIME



New skills are needed to manage stem cells



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what's up at SBS

— compiled by David Roman

Here's the latest from SBS. As always, we welcome your suggestions and feedback.

New Virtual Course: ADMET

SBS is pleased to present the latest in its series of online educational courses. *Fundamentals of ADME and Toxicology Assessment for Pre-Clinical Drug Discovery* will run on four Tuesdays in September, on the following schedule:

MODULE 1: Introduction to the Principles of *in vitro* ADME

Presenters: Jianling Wang, Novartis and Suzanne Tilton, Novartis

Sponsored by PerkinElmer

Date: September 8, 2009

MODULE 2: Drug Metabolism and Drug-Drug Interactions

Presenter: Albert Li, *In Vitro* ADMET Laboratories

Date: September 15, 2009

MODULE 3: Safety/Toxicology Integrated Risk Assessment

Presenters: Willi Suter, Novartis and

Francois Pognan, Novartis

Date: September 22, 2009

MODULE 4: Major Elements of Organ-Toxicity

Presenters: David Brott, Astra Zeneca, James Xu, Merck, and Laszlo Urban, Novartis

Date: September 29, 2009

JBS Reviewer Excellence Awards Presented

Four reviewers received the *Journal of Biomolecular Screening* Reviewer Excellence awards for their contributions in 2008. *JBS* Editor-In-Chief, Robert Campbell, presented the awards during a luncheon in Lille, France, at SBS 2009. The lunch, which was hosted by Sage Publications, honored Dr. Michael Entzeroth, Dr. Ilona Kariv, Dr. Shaoyou Chu, and Dr. Derek Hook. According to Dr. Campbell, all reviewers do a great job of reviewing and researching the materials submitted, but several stand out for the quality of their reviews, the number of articles reviewed, and rapid turnaround time. We at SBS congratulate these four members of the *JBS* Editorial Board.

2009 SBS President's Award

Dr. Richard Eglen accepted the President's Award at the recent SBS 15th Annual Conference & Exhibition. The award is one way of expressing the Society's appreciation for Dr. Eglen's many contributions and support over the years. Dr. Eglen, who is President of Bio-discovery at PerkinElmer Life and Analytical Sciences in Massachusetts, has continually shown his willingness to contribute whenever needed, not only during his tenure on the SBS Board of Directors, but at many other times, as well.



Richard Eglen

Label-Free Symposium in November

Advances & Challenges in Label-Free Technologies for Drug Discovery, the second symposium being presented this year, will take place November 2-3 in San Diego, California at the Marriott Mission Valley. This meeting will explore the latest scientific and technological advances in label-free technologies, which continue to demonstrate their value in characterizing new therapeutic targets. It will consist of four main sessions, listed below. Visit www.sbsonline.org for details.

SESSION 1: Chemical Compounds & Therapeutic Targets

SESSION 2: Antibodies, Cells, Biopharmaceuticals & Biomarkers

SESSION 3: Systems Biology

SESSION 4: Technologies

Poster PDFs Online

As a bonus to SBS Members, PDFs of the posters presented at the 15th Annual Conference & Exhibition are now available for viewing. Members can access these posters by clicking through the "Members Only" section of the SBS web site. You can read the full posters at your leisure and listen to the principal investigators provide additional details of their work. *

people changing places

Ute Egerland, formerly with Elbion GmbH, has accepted a position at Biotie Therapies GmbH., **Jack Elands**, formerly with Sidec AB, has joined Elands & Partners as Managing Director. **Teresa Ferragamo**, formerly with BD Biosciences, has accepted a position at VisEn Medical Inc., as Agent Sales Manager. **David Green**, formerly with Amgen, Inc., has joined Vertex Pharmaceuticals as Senior Director. **Hugo Klaassen**, formerly with Galapagos NV, has accepted a position at CISTIM Leuven Vzw. **Philippe Verwaerde**, formerly with iNovacia, has joined Alzprotect as Chief Science Officer.

SBS virtual course

Enzymology Course Emphasizes Knowledge, Practical Skills, Problem-Solving

Paul England
Proxara Biotechnology, Ltd
Bristol, UK

A few months ago (March-April 2009), Peter Lowe (Biomolecular Interactions, Herfordshire, UK), Tom Meek (GSK, Collegeville, PA, USA) and I developed and taught an SBS virtual course, *Enzymology in Drug Discovery*. The objective of the course was to give a theoretical and practical grounding in the more commonly encountered situations where enzymes are being studied as drug targets.

Why is enzymology important in drug discovery, and why is there a need for an appropriate course? Estimates suggest that up to 50 percent of current drug targets are enzymes, and hence anyone working in drug discovery has a high probability of needing to understand some aspects of enzyme kinetics and mechanisms.

Unfortunately, enzymology is often perceived as a difficult and “mathematical” branch of biochemistry, and many biochemistry graduates have only a fragmentary understanding of the subject. However, it is essential that anyone undertaking drug discovery on enzyme targets have a good basis on which to design their experiments, and to understand the theoretical and practical issues sufficiently to be able to provide accurate data with appropriate interpretation to their colleagues. It was our intention that the virtual course would provide such an understanding, with emphasis on commonly-encountered problems and on practical advice for conducting enzyme kinetic experiments. The course was designed to teach participants how to ensure inhibitors are properly evaluated for potency, selectivity, and mode of action, to produce correct information for colleagues, and to give some insights into how inhibitors work on enzyme targets.

Why Enzymes?

Why are so many current drug targets enzymes? Two reasons can be highlighted. Firstly, enzymes are extremely important in the functioning of all aspects of life, and many enzymes are key control points in pathways that can be modulated to therapeutic advantage. For example, many growth factor receptors are protein kinases which control the growth and differentiation of cells. Several of these receptor enzymes have been successfully targeted for treatment of cancer.

Secondly, enzymes make very good drug targets for low molecular weight compounds - that is, they are extremely “drugable.” The active sites of enzymes are usually small pockets in the protein structure, well designed for small molecule interactions. Of course, this is also true for many receptor ligand-binding sites, but the key function that enzymes have evolved to perform is to catalyse breakage or formation of covalent bonds using specific chemical reaction pathways. This can often be exploited by designing mechanism-based inhibitors, which rely on the catalytic activity of the enzyme to produce the active inhibitor, and can result in very potent and long-acting therapeutic agents.

Enzymes have come rather later to prominence in drug discovery than might have been expected, given their importance in cell function and regulation. One reason may be that many enzymes are intracellular, and hence the complication of cell penetration must be overcome in designing effective inhibitors. It is certainly true that quite a few successful early enzyme drug targets were extracellular, which obviated the need for appropriate

membrane permeability. Also, it is only with the recent understanding of signal transduction pathways that individual enzymes can be pinpointed as having potential therapeutic relevance.

The Time Factor

What specific features of enzyme mechanisms important for drug discovery does a course in enzymology need to explain? One key aspect that distinguishes enzymes from many other isolated biological systems such as simple equilibrium binding assays, is time. Because enzymes catalyze reactions that deplete substrates and generate products, the extent to which an enzyme reaction is allowed to proceed can have a significant effect on the measured potency of inhibitors. More importantly, it can also have an effect on the apparent mechanism of inhibition in certain cases.

Some of the most potent enzyme inhibitors react covalently with the enzyme and form “irreversible” complexes that are very long-lived. In these cases, time becomes a critical parameter in its own right, since the length of time of incubation has a direct influence on the extent of inhibition. A detailed analysis of the time course of inhibition can provide much useful information on the design of inhibitors.

Time can also be important in a class of inhibitors that show a time-dependent change in the affinity with the enzyme, even if covalent bonds are not formed between the enzyme and inhibitor. It is important not only to recognize that time-dependent binding is taking place, but also to characterize the precise time course of inhibition, since this will have a major effect on the measured potency of the inhibitors.

Overcoming Assumptions

Many enzymes catalyze reactions involving multiple substrates and products. Protein kinases, which are currently a very important drug target enzyme family, are a good example of enzymes with two substrates and two products. The two substrates will show different types of inhibition with respect to a given inhibitor. This has real significance on how an assay is configured to discover or study inhibitors against multi-substrate enzymes, and can have a major effect on how *in vitro* potencies translate to *in vivo* efficacy. It is therefore very important in drug discovery to characterize the mechanism of inhibitors, and to understand how to distinguish between types of inhibition.

Too often in drug discovery an assumption is made as to the type of inhibition shown by a particular class of inhibitors, sometimes based on extrapolation from the literature or results with similar types of molecules. However, without experimental measurement, these assumptions may be incorrect. It is also necessary within a series of related inhibitors to check that the mechanism has not changed with modification of structure. Incorrect assumptions also can have significant effects on the *in vivo* efficacy of enzyme inhibitors. It is also necessary to be aware that as inhibitors become very potent (so-called “tight binding inhibitors”), incorrect potencies can be obtained if the concentration of inhibitor is similar to that of the enzyme—unless the appropriate kinetic analysis is used.

Enzymology is a practical subject, even though many texts and courses deal with it in an abstract mathematical way. Appropriate design of experiments, choice of concentrations of enzyme, substrates and inhibitor, and the time course of the reaction are all extremely impor-



Paul England

tant. Enzyme-inhibitor interactions can also be studied using a variety of techniques that do not rely on measuring the rate of the enzyme reaction, and these can give much additional useful information. These, too, rely on a correct practical design of the studies. Many computer packages now exist to allow calculation of enzyme parameters such as K_m , IC_{50} , K_i , etc, but use of these without a full understanding of the assumptions in the equations chosen can lead to erroneous results.

All the above might lead the reader to think that enzymology is best left to the experts, and a short web-based course will not provide sufficient understanding to allow design of good enzyme experiments. For most enzyme drug targets, this is not true. Many enzymes in current drug-discovery programs have relatively simple kinetics; inhibitors work in clearly-defined ways; and high quality information can be obtained by anyone with the knowledge included in the SBS *Enzymology in Drug Discovery* course!

For more information or to purchase a CD or streaming video of this and other SBS virtual courses, please go to www.sbsonline.org and click on “Education.” *

SBS Welcomes Its New MEMBERS

The value of belonging to SBS is enriched by the shared knowledge of the society’s members. Welcome to the following new members, who bring their unique experience and information to the community.

Emilie Bureau	MRC Technology
Michael Cane	UCLA
Sean Cobin	Merck & Co.
Gabor Csucs	ETH Zurich
Dion Daniels	GlaxoSmithKline
Sebastien Dasnoy	GlaxoSmithKline Bio
Jon de Vlieger	VU University
Carsten Degenhart	Lead Discovery Center GmbH
Jan Eickhoff	Lead Discovery Center GmbH
Steve Ernst	Veris Communications
Daniela Fischer Russell	McMaster University
Jacob Gopas	Ben Gurion University
Chris Hempel	Galenea Corp.
Jorrit Hornberg	Bayer Schering Pharma
Victoria Knight-Connoni	Cubist Pharmaceuticals
Richard Kuo	Novartis Institutes for Biomedical Research
Pascal Iaeng	Galenea Corp
Jane Lamerdin	Odyssey Thera, Inc.
Karl-Johan Leuchowius	Uppsala Universitet
Arne Lundin	BioThema AB
Sara Lundqvist	AstraZeneca R&D Molndal
Franck Madoux	Scripps Florida
Irene Mile	AstraZeneca
Iva Navratilova	College of Life Sciences Univ. of Dundee
Charlotta Otter	AstraZeneca
Kathy Paschetto	AstraZeneca
Wilt Peters	Molecular Sensing Inc.
Laurel Provencher	Caliper Life Sciences
Rafael Rojas	Neurocrine Biosciences
Gerry Ronan	Farfield Group Ltd
Pascal Schenk	F.Hoffman La Roche Ltd
Matthew Scullion	Idaho Technology
C. Ian Spencer	Fluxion Biosciences Inc
Erik Wade	Sealed BioBusiness Consulting
Fredrik Wagberg	AstraZeneca
Jonathan Wrigley	AstraZeneca
Zhong-Hua Yan	Millennium Pharmaceuticals
Francisco Ylera	AbD Serotec/MorphoSys AG
Peder Zipperlen	3-V Biosciences

member profile

Diane Stark: Boat Racing—Like Science—is a Pleasure and a Challenge

Interview by David Roman

Dr. Stark is a Research Scientist at VaxInnate in New Haven, Connecticut, where she leads the Discovery Group in evolving Toll-like receptor ligands. After years of sailing in San Francisco Bay, she recently returned to New England where she learned to sail as a child. Dr. Stark was also one of the Ten Best Poster winners at the SBS 14th annual in St. Louis, Missouri.

WHEN DID YOU FIRST BECOME INTERESTED IN SAILING?

DS: I grew up on the water on Peconic Bay between the Twin Forks of Long Island. My parents were power boaters (or ‘stink potters,’ as we sailors lovingly refer to them). So my siblings and I have been on boats since birth. I’m quite proud of my three sisters who are all accomplished mariners. I’m the only ‘rag picker’ (sailor) in the family. I learned to sail as a child. My grandparents had a Sunfish, which is one of those little day-sailor boats, and I taught myself how to sail.

YOU NOW RACE—ON WHAT TYPE OF BOAT?

DS: I have raced on many different types and sizes of boats over the years. I enjoy racing on smaller boats, particularly ultra-lights and dinghies. I’m not as disadvantaged by lack of upper body strength on small boats and there are many ‘One Design’ fleets in the 24-foot size range on the San Francisco Bay. Because all of the boats are the same make and model in these fleet races, there is a higher level of skill and competition. For example, I used to sail in the “Wylie Wabbit” fleet. The Wabbits are 24 feet long with a mainsail, jib, and spinnaker. They are really meant for lake sailing because they are so light. On the Bay, with its strong winds, at least one crew member is always suspended on a wire from the mast so that weight can be moved outboard to keep the boat from tipping over. It’s a wild ride.

These days I’m doing more PHRF, or handicapped racing, on larger boats. Participants with different sized boats that go at different speeds are “handicapped” according to a rating system. This type of sailing is a little more relaxed than One Design racing. The biggest boats I have sailed have been 50 footers.

HOW DO YOU PRACTICE FOR THIS TYPE OF SPORT?

DS: For the more serious races, we may go out and run drills. For example, we may practice hoisting and taking down the spinnaker, which is the large colorful sail that flies in front of the boat when it’s going down wind. More importantly, especially for women, is to train. Sailboat racing is athletic and you need to have upper body strength and balance. Therefore, one needs to be in good physical condition, and work-



Gearing up for a race on San Francisco Bay

ing out at the gym helps. Recently, some of my old team mates from San Francisco asked me to race with them in the Heineken Regatta in St. Martin. After a winter hibernating in New England, I was so out of shape I was afraid that they would jettison me from the boat at the first mark! So I went to the gym for six weeks for two hours every night after work to get ready for the race.

HOW OFTEN DO YOU GET TO RACE?

DS: Because I live in Connecticut now, the weather here dictates my racing schedule. I don’t get to race as often as I did in the San Francisco Bay, where the season is all year long. On the east coast, some people do don dry-suits and sail in the winter, but being less hardy, I prefer warm weather sailing. So, this means we start in April/May and continue into September/October. I sail on average twice a month.

WHERE DO THE RACES START AND FINISH?

DS: It depends. Generally, they use established landmarks, as well as temporary buoys, for the courses. A series of races takes place over a period of weeks, and the courses are set around different “marks” for each race.

DO YOU HAVE ANY FAVORITE SAILING SPOTS?

DS: It is always more pleasant to be sailing in warm water, but it is also great to have a decent breeze. The crew is generally more important to me than the venue. Being on a boat with a fun, top-notch, skilled crew is such a treat, and makes all the difference in the world.

ARE YOU ATTRACTED AT ALL BY THE SPEED OR DANGER OF BEING ON THE WATER?

DS: Actually, I don’t enjoy being out in extreme conditions or when the equipment and skill level of the crew is not well matched to the conditions. I have been out in very bad conditions with a very experienced crew, and had no qualms at all. On the other hand, I have been in races, like the one off the Western Coast of Mexico, where driving into a storm with a slow boat and an inexperienced crew made for a very unpleasant few days. I personally like enough wind to make for a fun and interesting race. “A good day sailing” for me would be a race with nice conditions where we as a crew execute very well.

ANY “UNFORGETTABLE” MOMENTS?

DS: There have been some bad times due to inclement weather. I suppose some of my best moments have been taking a little boat over to one of the clam beds on Long Island. Park the boat, stick a clam knife in your bathing suit and float around on your back digging up clams, shucking them and eating them on site! I can think of no better way to spend a Saturday afternoon!

ARE THERE ANY MYTHS ABOUT SAILING THAT SHOULD BE DE-BUNKED?

DS: Even though sailing is perceived as a male-dominated sport, there are a growing number of women on the water, many of whom are now professionals. And the amazing thing about these professional women sailors is that they are inspiring and supporting novices in the sport. Women like Dawn Riley, who was captain of the historic all-women America’s Cup team, will come out, race and coach other women on the San Francisco Bay. The other myth that we women are debunking is that you can’t talk about shoes between tacks and still win the race. We can multitask.

ARE YOU EXHAUSTED AT THE FINISH LINE, OR EXHILARATED?

DS: Well, it depends what place we come in. If we are in first place, I am exhilarated, and if we come in last place I am exhausted!

DO YOU EVER SAIL FOR PLEASURE INSTEAD OF RACING?

DS: I find racing pure pleasure. Although it is physically challenging, it relaxes me. Sometimes, when we are “short tacking” (zig zagging) up an estuary and I am “grinding” (turning the crank to trim the sails) I have been known to trade jobs with a crew member if I felt I couldn’t do my job well.

DO OTHER SCIENTISTS PARTICIPATE IN THE SPORT?

DS: In San Francisco, sailing seems to attract a lot of engineers. This is probably because it is challenging intellectually as well as physically. It resembles a moving chess game. Your strategy for a race changes constantly as the positions of the surrounding boats change and the winds shift. Also there seems to be no middle of the road for boaters or scientists: they have a passion for what they do. ✧

cutting edge

Howard Hughes Funds KwaZulu-Natal Research Institute to Meet Global Health Challenges of HIV, Tuberculosis

By Howard Hughes Medical Institute Staff

A groundbreaking partnership between the Howard Hughes Medical Institute (HHMI) and the University of KwaZulu-Natal (UKZN) in South Africa will establish an international research center focused on making scientific contributions to the worldwide effort to control the co-epidemic of tuberculosis and HIV, and on training a new generation of scientists in Africa.

"This initiative adds a new dimension to HHMI's commitment to international research," said Thomas R. Cech, former president of HHMI. "Our cross-Atlantic partnership reflects a shared view that direct and substantial investment in basic, clinical, and translational research in the heart of the pandemics of HIV and TB will yield significant discoveries that will alleviate the human suffering caused by these diseases."

The creation of the KwaZulu-Natal Research Institute for Tuberculosis and HIV (K-RITH) reflects nearly two years of discussion between HHMI and UKZN and was announced in March 2009 at simultaneous events in Washington, D.C., and Durban, South Africa. HHMI has committed \$60 million to the initiative over the next 10 years. "The HHMI-UKZN partnership is a major and unique investment into one of humanity's major global health challenges, that of HIV and TB co-infection. The partnership is addressing a real problem that affects real people," said Professor Malegapuru William Makgoba, UKZN's vice chancellor.

The institute will be located on the campus of the Nelson R. Mandela School of Medicine in Durban in a six-story facility that will include two floors of high-level biosafety (BSL-3) laboratories equipped for TB research. HHMI will provide \$20 million toward the construction of the new building, with UKZN and LIFE Lab, a biotechnol-

ogy center of the government of South Africa, making substantial commitments to the project. The total cost of the project—which will be integrated with the existing Doris Duke Medical Research Institute—is estimated at about \$30 million. Construction is expected to begin in late September.

HHMI awarded seed grants totaling more than \$1.1 million to scientists in the United States and South Africa in 2008 as part of the long-term plan to develop K-RITH. This year, the institute will provide an estimated \$3 million in grant funding and support construction of temporary laboratory facilities to support the TB research program.

"This initiative is one of the most challenging we have embarked upon in our international program," said Robert Tjian, HHMI's president (as of April, 2009). "I look forward to seeing how K-RITH realizes the potential for developing new strategies to combat the dual scourge of HIV and tuberculosis—both for South Africa and the entire world."

HIV, XDR-TB in Focus

South Africa has more residents infected with HIV than any other nation in the world. By 2007, the nation accounted for 17 percent of the global HIV disease burden—an estimated 5.4 million people are infected—and it has one of the highest per capita rates of tuberculosis in the world. Tuberculosis, a major problem in pre-AIDS South Africa, emerged as a public health crisis in its own right, particularly with the emergence of both multi-drug resistant and extensively drug resistant (XDR) strains of tuberculosis in persons already infected with HIV.

KwaZulu-Natal province, home to more than 10 million people, bears an even greater burden of disease than the nation as a whole; as much as 40 percent of the population may be positive for HIV. When an outbreak of XDR-TB was reported in the rural area of Tugela Ferry in 2006, the region became a focus of international concern even as additional cases of XDR-TB surfaced elsewhere in the world.

"The projects defined in the K-RITH program are there to address important research questions that would provide greater insights, understanding and the potential for solutions. All these should bring hope to people who are infected and affected," said Professor Makgoba. "Most critically, this partnership is an investment into the future, in the training of a new generation of scientific leaders in this



Howard Hughes has committed \$60 million to K-RITH



The atrium at KwaZulu-Natal Research Institute for TB and HIV (K-RITH)

important area of health research."

HHMI and UKZN will jointly recruit a permanent director for K-RITH. Barry R. Bloom, former dean of the Harvard School of Public Health, and a well-known TB researcher, will chair the search committee.

Scientific Support

But the commitments by HHMI and UKZN go beyond the financial. Two leading HHMI investigators with longstanding expertise in TB and HIV research will participate actively in the program: William R. Jacobs,



Malegapuru William Makgoba

Jr., of the Albert Einstein College of Medicine, and Bruce D. Walker of the Massachusetts General Hospital, who directs the HIV Pathogenesis Program in Durban, a joint initiative of Harvard University and UKZN. Dr. Walker also directs the newly formed Ragon Institute, which will focus on development of a vaccine against HIV.

UKZN scientists helping to direct and plan K-RITH are A. Willem Sturm, a noted TB researcher and dean of the Mandela School of Medicine, who serves as K-RITH's interim director, and Salim S. Abdool Karim, UKZN Pro Vice-Chancellor (Research) and director of the Center for the AIDS Program of Research in South Africa.

Key Research Areas

K-RITH will initially focus on four major research areas, led by teams of U.S. and South African scientists and their clinical collaborators:

- *Development of rapid and more effective tests for tuberculosis that will be built with the use of engineered bacteriophages, viruses that infect bacteria. Tuberculosis is a slow-growing organism and difficult to culture, which*

(continued on page 6)

SBS' President

(continued from page 1)

technology companies attempting to avoid some of the pitfalls of large pharma through increased focus, more nimble organizations, and the application of rapidly evolving technologies. The difficulties (time and money) in moving therapies from concept to market coupled with less friendly financial markets have driven mergers and acquisitions of a significant percentage of the biotechnology companies.

Globalization: The second change is the globalization that has occurred in both research and development. Outsourcing to access additional skilled capabilities at reduced costs and the establishment of research or development centers in areas with increasing scientifically trained workforces and large patient populations have truly made our industry global over the last five years. Every major pharmaceutical company has either a dedicated site and workforce, or significant R&D collaborations in India or China.

Emergence of Academic Screening Centers: The third change is the relatively recent establishment of over 100 academic screening centers at numerous universities and institutes. Funds from federal and local governments plus significant private endowments have enabled the development of capable screening labs focused on understanding the complexities of biological systems, discovering and developing research probes, and even engaging in early drug discovery. Thirty years ago, when some of our early members left academia to move into industry, professors and colleagues advised that those were "career-ending decisions." Much has changed.

Implications of Change

Together, these three factors have changed our industries, our careers and our Society. Most often, discussions on outsourcing or industry consolidation focus on the negative impacts—loss of jobs, fewer opportunities, global shifts in technology bases, etc. Though these effects can not be denied, these factors have also produced some favorable outcomes. As jobs related to screening technologies have decreased in one sector, there has been growth in another, which has driven significant movement of talented staff between industry, academia and technology providers. The transition from "user" to "provider" and often back to user has been, is, and will continue to be common. This cross fertilization has been instrumental in driving many of the technological advances related to all aspects of screening.

The growth of academic screening centers has also provided new and enriching opportunities for many of our members. These members bring years of experience,

which allows academic laboratories to grapple with complex biological problems. They also bring expansive knowledge to share with the next generation of "screeners."

And many of our friends and colleagues now work in China, India or other distant locations in newly established research or development centers, in professional roles broader than just screening.

Experience and Knowledge

What has enabled our members to make these transitions in what others would consider troubling times? I think the answer is obvious—our experiences and knowledge are extremely valuable. It is important for us to remember that our involvement in advancing the science of screening over the last 10-15 years has provided each of us with opportunities to develop unique skills and a broad body of knowledge applicable far beyond lead identification and drug discovery. Our members are the world thought leaders in sample management, assay development, assay performance, data management and informatics, automation engineering, and process implementation.

One underlying theme that often comes to mind when I try to understand the "hows" and "whys" of the success of both our Society and our members during the last 15 years, even given the impact of all the changes, is a long-standing mantra used in medical education: "see one, do one, teach one." SBS has been *the* scientific society in which we have shared and learned from each other. It has provided access to the tools that enabled application of screening technologies in our laboratories. It has been the forum in which we have collaboratively developed and advanced technologies now affecting R&D beyond its roots in HTS.

The continued growth and success of SBS and our members will rely on continued application of the philosophy of "see one, do one, teach one" as the Society expands globally and we embrace the rapidly emerging participants in academic laboratories. Over the last two years, the SBS Board of Directors, the Presidents, and the Executive Director have engaged in developing the strategic direction for the society. At a high level, three key goals have emerged: increased global presence, educational offerings enhancing the knowledge of our members, and meeting formats (annual conferences, symposia, regional meetings, etc.) providing opportunities for our global membership. The specifics around these strategies will be communicated in the upcoming months, but they are all supported by SBS' unique position to share our experiences and knowledge across the globe in numerous industrial and academic settings. *

Research Institute

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means that tests used to diagnose patients or identify those with drug-resistant strains of the disease take too long. Some newer tests are more rapid, but miss resistant strains or require too much high-tech equipment. The lack of effective diagnostic tools poses a particular threat to individuals vulnerable to infection because their immune systems are weakened by HIV or other diseases.

Principal investigator: William Jacobs Jr.

- Characterization of the *genotypic and phenotypic characteristics of drug resistant strains of tuberculosis*—both MDR and XDR—as a step toward understanding the



K-RITH will be led by teams of US and South African scientists

biological factors that drive bacterial pathogenesis. This research will be coupled with clinical and epidemiological data on strains of tuberculosis as a step toward developing a comprehensive understanding of the role that each plays in determining patient outcomes. Ultimately, this research may lead to rapid genetic testing for drug resistance. **Principal investigator:** A. Willem Stum.

- *Analysis and characterization of the complex immune response to tuberculosis*—specifically among individuals already infected with HIV—with a goal toward understanding the factors that may predict disease progression or long-term control of the TB infection. Understanding how the immune system responds to TB will be essential to the development and testing of vaccines for both HIV and TB. **Principal investigator:** Bruce Walker.

- *Study of recurrent tuberculosis in patients with HIV* to assess the nature of the recurrence: Is it a function of re-infection with TB or has the patient's latent TB infection become reactivated? This research has important public health implications because each scenario requires a different treatment response and poses different risks—for example, as South Africa greatly expands highly active retroviral therapy in the coming years, what will be the best strategies for managing large numbers of individuals at high risk for TB in a crowded clinic? **Principal investigator:** Salim S. Abdool Karim.

For more information, see www.hhmi.org. *

SBS 2010 call for papers

Take this opportunity to submit an abstract for oral or poster presentation at the 16th Annual Conference & Exhibition. The conference theme is Advancing the Science of Drug Discovery. Session topics include the following:

- Lead Discovery in Immunoinflammation Research
- Lead Discovery in Oncology Research
- Lead Discovery in Neuroscience Research
- Lead Discovery in Epigenetics: An Emerging Target Class
- Critical Reagents: Design of Synthetic & Natural Product Libraries
- Critical Reagents: Sample Storage, QC & Distribution
- Critical Reagents: Bioreagent Preparation for Lead Discovery
- Assays & Automation: Best Practices in Automation & Miniaturization
- Assays & Automation: Novel Screening Technologies for Hit Discovery
- Assays & Automation: Novel Screening Technologies for Lead Optimization

All abstracts must be submitted electronically via the online abstract submission system at www.sbsonline.org. Specific formatting requirements are included on the submission form. Upon submission, authors give SBS the right to publish abstracts in any format before, during or after the 2010 Conference & Exhibition.

Deadlines:

Oral abstracts: November 4, 2009

Poster abstracts: March 5, 2010

from SBS' executive director

Come to Phoenix, Arizona, USA for SBS 2010

By Christine Giordano, CAE

The dust has yet to settle from our conference in Lille, and we are in full swing planning the next annual conference, which will take place in Phoenix, Arizona, USA from April 11-15, 2010. Phoenix is the sixth largest city in the United States, with a cosmopolitan ambiance balanced

by the lure of the spirit of the Southwest.

The real character of Phoenix is in its desert location and Native American culture. In the heart of the scenic Sonoran desert, you can relax at one of the many spa resorts and behold soul-searching sunsets. There are also countless opportunities for fun should you wish to arrive early or extend your stay. Businesses will find it's a great location for corporate meetings and team-building events (teepee building,



anyone?). For family vacations, activities can range from the usual—playing golf, outdoor shopping and dining, museums, casinos—to wilderness adventures (jeep, ATV desert tours, star-gazing), western adventures (Fort McDowell, dude ranches, horseback riding, cattle drives), sightseeing tours (helicopter, hot-air balloon flights), side trips to the Grand Canyon for whitewater rafting, or a visit to the red rocks of Sedona, known for its art culture and spiritual vortices.

April also marks the start of major league baseball (Phoenix is home to the Arizona Diamondbacks), the Arizona Asian Festival, the Jazz and Blues Festival, NASCAR Nextel Cup auto racing, the Phoenix Film festival, and even the Southwest Salsa Challenge. Phoenix is definitely a location you will want to plan a vacation around. Every year brings an average of 310 days of sunshine and low humidity. Temperatures in April generally range from 53 to 83 degrees Fahrenheit (11 to 28 degrees Celsius).

Transportation to Phoenix is easy. Phoenix Sky Harbor International Airport boasts nearly 500 non-stop flights to over 100 domestic and international destinations. A modern light rail system links the airport to the downtown area with a multitude of restaurants, museums and active nightlife.

Removing my "tour hat" for a moment, I'd like to remind you that attending the annual conference and taking advantage of the opportunities it provides for professional development and networking is one of the most important benefits of your membership. Although the 2010 conference program is

still in the early planning stages, I can share with you that it will provide content designed to accommodate a wide breadth of topics on advances in screening technologies, as well a deeper appreciation of targeted topics in drug discovery. You are invited to check our web site at www.sbsonline.org for up-to-date information on the program as it develops, and to submit an abstract for oral or poster presentation (see box, 4).

I look forward to seeing you in Phoenix. ✱

PHOTO: COURTESY GREATER PHOENIX CIB



Atrium lobby at the Phoenix Convention Center

Stem Cell Symposium

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first human clinical trial using embryonic stem cell-based therapy.

WHAT EXCITES YOU PERSONALLY ABOUT WORKING WITH STEM CELLS?

When I came to the Harvard Stem Cell Institute, I was immediately struck by the passion of the scientists at the Institute to understand cutting-edge stem cell biology. Now I have the opportunity to utilize my industrial screening experience in an academic research environment to collaborate with some of the most brilliant minds in this emerging discipline. We are currently working on an exciting project to identify small molecules that determine cell fate, and we're making significant progress.

On a personal note, I volunteered to work with a patient with diabetes who had severe impairments. That experience helped me understand how devastating that disease can be. Collaborations between screeners and stem cells experts will allow us to identify therapeutic agents that could one day help these patients.

I would like to add, too, that in the 1990s, I worked for a small biotechnology company (ScriptGen Pharmaceuticals), where I was introduced to HTS. SBS had just been founded at that time, and I remember reading every article in the society's peer-reviewed Journal of Biomolecular Screening. Being a "screener" was not my original career plan, and I had no idea I would end up as a "career screener." Later, when I joined a large pharmaceutical company (Pfizer, Inc.), I continued my professional development, this time in the broader world

of industrial screening. By then, both SBS and HTS were well established. Now, both are expanding into areas such as stem cells screening, and I'm pleased to be able to play a small role in helping that expansion of knowledge in drug discovery.

One way to fulfill the promise of stem cells is to

integrate "screening" with "stem cells" by bridging the screening focus of SBS with dedicated stem cell organizations like the Harvard Stem Cell Institute and the International Society for Stem Cell Research (cosponsors of the symposium) to enable collaborations that synthesize these kinds of symposia. ✱

symposium presenters

KEYNOTES

Michael Clarke, MD - Stanford Institute for Stem Cell & Regenerative Medicine, USA
Douglas Melton, PhD - Harvard Stem Cell Institute (HSCI) & Harvard Univ., USA

SPEAKERS

Petter Björquist, PhD - Cellartis, Sweden
George Daley, MD, PhD - HSCI & Children's Hospital Boston, USA
Hakim Djabballah, PhD - Memorial Sloan-Kettering Cancer Center, NYC
Kevin Eggan, PhD - HSCI &

Harvard Univ., USA
Derek Hei, PhD - Univ. of Wisconsin Stem Cell and Regenerative Medicine Center, USA
Konrad Hochedlinger, PhD - HSCI & Massachusetts General Hospital, USA

Hans Keirstead, PhD - Univ. of California at Irvine, USA

Morey Kraus, PhD - Viacell, Cambridge, USA

Daniel Marshak, PhD - PerkinElmer, Inc., China

Christine Mummery, PhD - Leiden Univ. Medical Center, Netherlands
Thomas Okarma, MD, PhD -

Geron, USA

Michelle Palmer, PhD - Broad Institute, USA

Lee Rubin, PhD - HSCI & Harvard Univ., USA

Clive Svendsen, PhD - Waisman Center, Univ. of Wisconsin Madison, USA

Lilian Wikstrom, PhD - NeuroNova AB, Sweden

Amy Wagers, PhD - HSCI & Joslin Diabetes Center, USA

Shu Wang, PhD, National Univ. of Singapore, Singapore

Leonard Zon, MD - HSCI & Children's Hospital Boston, USA

symposium program preview

Reprogramming somatic cells to a pluripotent state could generate a rich supply of patient-specific stem cells and mature cells for regenerative medicine and compound screening. Studies show that viral-mediated gene delivery of four transcription factors, including two potential oncogenes, can directly reprogram somatic cells to induced pluripotent stem (iPS) cells.

Unfortunately, the resulting iPS cells are unsuitable for many therapeutic applications because the viral transgenes can spontaneously reactivate a process that has led to tumor formation. Therefore, discovering small molecules through high-through-

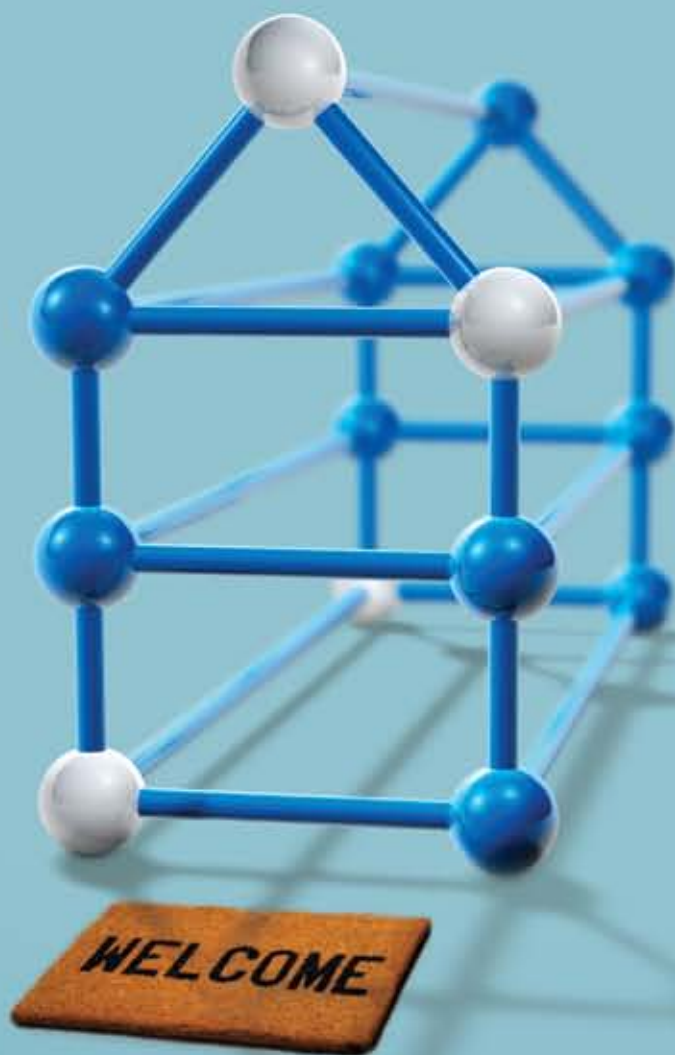
put technologies capable of reprogramming cells—without relying on viruses or oncogenes—would be extremely valuable to therapeutic applications.

Furthermore, using stepwise differentiations of pluripotent cells and/or embryonic stem cells to terminally differentiated functional cells via small molecule treatment would be useful for transplantation therapy, identifying targets for drug discovery and for toxicology testing. HTS and HCS technologies against stem cells offer great potential for identifying novel small molecules to reprogram cells and to induce formation of terminally differentiated functional cells.

HUMAN HEALTH

ENVIRONMENTAL HEALTH

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