

Japan-UK Science, Technology & Innovation Symposium 2014 in London

Expanding the Protein and Peptide Universe

Symposium by a cofounder of PeptiDream Inc; Professor Hiroaki Suga (The University of Tokyo, Japan) and Professor Christopher J Schofield (University of Oxford, UK) on Wednesday, March 5th, 2014, at Embassy of Japan in the United Kingdom.

The aim of this symposium is to introduce to the science and technology community in the UK, a seminal global contribution originating from Japan in science, technology and innovation. For this event, we invite a Japanese scientist who has brought about substantial impact on our life and society, enabling our current prosperity with sustainability.

Professor Hiroaki Suga



Professor Christopher J Schofield



At this symposium, Prof. Suga will lecture on “*Pseudo-Natural Product Synthesis and Drug Applications*”, and Professor Schofield will lecture on “*The Chemistry of Oxygen Sensing in Humans*”.

Some natural products generated from microorganisms show efficacies on the mechanisms of occurrence of human diseases, and thus provide precursors of drug development. Meanwhile, the discovery of such molecules relies on “the matter of luck” rather than a platform technology. We here conduct research to devise platform technologies that enable us to discover functional “natural product-like” molecules in a systematic manner. Such molecular technologies can lead a paradigm shift from a “by chance” to “reliable” drug discovery process, which brings about a new stream of innovation contributing to human health. Prof. Suga will introduce some of his unique and exciting achievements this in his lecture.

We hope that this special opportunity of meeting these leading scientists at the Embassy will be a memorable occasion where scientists from Japan and the UK will reinforce the strong scientific and cultural ties between the two countries.

Co-hosts	<i>Embassy of Japan in the UK / The Chemical Society of Japan / PeptiDream Inc</i>
Supported by	<i>Royal Society of Chemistry</i>
Date:	<i>Wednesday, March 5th, 15:00-17:15, followed by Reception Party</i>
Venue:	<i>Embassy of Japan in the UK 101-104 Piccadilly, London W1J 7JT http://www.uk.emb-japan.go.jp/en/embassy/index.html#locmap</i>
Registration:	<i>RSVP no later than February 28th through stisympo0305@ld.mofa.go.jp *Note that all visitors to the Embassy are required to show your Photo ID as well as the registration form to this Symposium at the entrance. *Dress code for this event is lounge suits.</i>
Fee:	<i>Registration of the Symposium and reception party is free.</i>
Contact:	<i>Atsushi Oku, First Secretary (Science and Technology) atsushi.oku@mofa.go.jp</i>

Symposium Programme

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| 14:30-15:00 | Registration |
| ■ 15:00-15:05 | Master of Ceremony Mr. Atsushi Oku, First Secretary ; Embassy of Japan in the UK |
| 15:00-15:05 | Welcome
Mr. Nobuyuki Kawashima, Executive Director, The Chemical Society of Japan |
| 15:05-15:15 | Opening Remarks
H.E. Mr. Keiichi Hayashi, Ambassador of Japan |
| ■ 15:15-16:15 | Chairman Mr. Atsushi Oku, First Secretary (Science and Technology) |
| 15:15-16:15 | Professor Hiroaki Suga, The University of Tokyo
<i>'Pseudo-Natural Product Synthesis and Drug Applications'</i> |
| 16:15-17:15 | Professor Christopher J Schofield, University of Oxford
<i>'The Chemistry of Oxygen Sensing in Humans'</i> |
| 17:15-17:30 | Closing Remarks |
| 17:30- | Reception Party |

Profile of Professor Hiroaki Suga

Education and Professional Career

- **Bachelor of Engineering** (1986) Department of Applied Chemistry, Okayama University, Okayama
- **Visiting Scholar** (1987-1988) University of Laussane, Switzerland (with Dr. Manfred Schlosser)
- **Master of Engineering** (1989) Department of Applied Chemistry, Okayama University, Okayama
- **Ph.D.** (1994), Department of Chemistry, Massachusetts Institute of Technology, Cambridge, MA (with Dr. Satoru Masamune)
- **Post-doctoral Fellow** (1994-1997), Harvard Medical School/Massachusetts General Hospital, Boston, MA (with Dr. Jack W. Szostak)
- **Assistant Professor** (1997-2002) Department of Chemistry, University at Buffalo (SUNY), Buffalo, NY
- **Associate Professor** (2002-2003) Department Of Chemistry, University at Buffalo (SUNY), Buffalo, NY
- **Associate Professor** (2003-2005) Research Center for Advanced Science and Technology, The University of Tokyo, Tokyo
- **Professor** (2005-2010) Research Center for Advanced Science and Technology, The University of Tokyo, Tokyo
- **Professor** (2010-present) Department of Chemistry, School of Science, The University of Tokyo, Tokyo
- **Co-founder & Board Member** (2006-present) PeptiDream Inc, Tokyo

Editor and Editorial Board

- Editor, Chemistry and Biology Cell Press, Elsevier (2011–present)
- Associate Editor, Bioorganic Chemistry, Elsevier (2013–present)
- Editorial Board Member, Current Opinion in Chemical Biology, Elsevier (2012–present)
- Editorial Board Member, C ACS Chemical Biology, American Chemical Society (2010–present)
- Editorial Board Member, ChemBioChem, Wiley-VHC (2001–present)
- Editorial Board Member, Biotechnology Journal, Wiley-VHC (2009–2012)
- Editorial Board Member, Chemistry and Biology Cell Press, Elsevier (2008–2011)

Current Awards

- 2012 President Award of Science Council of Japan for New Inventions in Government-Industry-Academic Relation, Cabinet Office
- 2012 Boehringer Ingelheim Lectureship at Montreal University
- 2013 Award of The Chemical Society of Japan for Creative Work
- 2013 Lilly Distinguished Lecturer at Colorado State University

Abstract

Pseudo-Natural Product Synthesis and Drug Applications

Hiroaki Suga

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The genetic code is the law of translation, where genetic information encoded in RNA is translated to amino acid sequence. The code consists of tri-nucleotides, so-called codons, assigning to particular amino acids. In cells or in ordinary cell-free translation systems originating from prokaryotes, the usage of amino acids is generally restricted to 20 proteinogenic (standard) kinds, and thus the expressed peptides are composed of only such building blocks. To overcome this limitation, we recently devised a new means to reprogram the genetic code, which allows us to express non-standard peptides containing multiple non-proteinogenic amino acids in vitro. This lecture will describe the development in the genetic code reprogramming technology that enables us to express natural product-inspired non-standard peptides and pseudo-natural products. The technology involves (1) efficient macrocyclization of peptides, (2) incorporation of non-standard amino acids, such as N-methyl amino acids, and (3) reliable synthesis of libraries with the complexity of more than a trillion members. When the technology is coupled with an in vitro display system, referred to as RaPID (Random non-standard Peptide Integrated Discovery) system, the libraries of natural product-inspired macrocycles with a variety ring sizes and building blocks can be screened (selected) against various drug targets inexpensively, less laboriously, and very rapidly. Moreover, the RaPID system has further evolved to a new system for the discovery of pseudo-natural products. This lecture will discuss the most recent development of their technology and therapeutic applications as well as an entrepreneur to establish PeptiDream Inc. Tokyo.

References

1. Y. Tanaka, C. J. Hipolito, A. D. Maturana, K. Ito, T. Kuroda, T. Higuchi, T. Katoh, H. E. Kato, M. Hattori, M. K. Kumazaki, T. Tsukazaki, R. Ishitani, H. Suga, O. Nureki, "Structural basis for the drug extrusion mechanism by a MATE multidrug transporter." *Nature* **2013**, 496, pp. 247-251.
2. K. Ito, T. Passioura, H. Suga, "Technologies for the synthesis of mRNA-encoding libraries and discovery of bioactive natural product-inspired non-traditional macrocyclic peptides." *Molecules* **2013**, 18, pp. 3502-3628.
3. J. Morimoto, Y. Hayashi, H. Suga, "Discovery of macrocyclic peptides armed with a mechanism-based warhead that isoform-selectively inhibit a human deacetylase SIRT2" *Angew. Chem., Int. Ed.* **2012**, 51, pp. 3423-3427
4. Y. Hayashi, J. Morimoto, H. Suga, "In Vitro Selection of Anti-Akt2 Thioether-Macrocyclic Peptides Leading to Isoform-Selective Inhibitors" *ACS Chem. Biol.* **2012**, 7, pp. 607-613.
5. Y. Yamagishi, I. Shoji, S. Miyagawa, T. Kawakami, T. Katoh, Y. Goto, H. Suga, "Natural product-like macrocyclic N-methyl-peptide inhibitors against a ubiquitin ligase uncovered from a ribosome-expressed de novo library" *Chem. Biol.* **2011**, 18, pp. 1562-1570.
6. Y. Goto, T. Katoh, H. Suga, "Flexizymes for genetic code reprogramming" *Nat. Prot.* **2011**, 6, pp. 779-790.

Profile of Professor Christopher J Schofield

Short Biography:

Christopher J Schofield studied for a first degree in chemistry at the University of Manchester (1979-1982). In 1982 he moved to Oxford to study for a DPhil with Professor Jack Baldwin on the synthesis and biosynthesis of antibiotics. In 1985 he became a Departmental Demonstrator in the Dyson Perrins Laboratory, Oxford University followed by his appointment as Lecturer in Chemistry and Fellow of Hertford College in 1990. In 1998 he became Professor of Chemistry, and in 2011 was appointed Head of Organic Chemistry. He is a Fellow of the Royal Society of Chemistry and of the Royal Society. His research group works at the interface of chemistry, biology and medicine. His work has opened up new fields in antibiotic research, oxygen sensing and gene regulation. His work has identified new opportunities for medicinal intervention that are being pursued by numerous academic and commercial laboratories.

Abstract

The Chemistry of Oxygen Sensing in Humans

The lecture will describe studies aimed at identifying the role of oxygenases in the regulation of protein biosynthesis. Attempts to correlate the biochemical properties of oxygenases with their physiological roles, in particular with respect to oxygen sensing will be described. In addition to work on enzymes involved in transcriptional regulation, recent work including on the oxygen-dependent modification of ribosomes will be described.