Revolutionizing the discovery processes of de novo bioactive peptides and biologics

Hiroaki Suga

Department of Chemistry, Graduate School of Science, The University of Tokyo, Japan
hsuga@chem.s.u-tokyo.ac.jp

Macrocyclic peptides possess a number of pharmacological characteristics distinct from other well-established therapeutic molecular classes, resulting in a versatile drug modality with a unique profile of advantages. Macrocyclic peptides are accessible by not only chemical synthesis but also ribosomal synthesis. Particularly, recent inventions of the genetic code reprogramming integrated with an in vitro display format, referred to as RaPID (Random non-standard Peptides Integrated Discovery) system, have enabled us to screen mass libraries (>1 trillion members) of non-standard peptides containing multiple non-proteinogenic amino acids, giving unique properties of peptides distinct from conventional peptides, e.g. greater proteolytic stability, higher affinity (low nM to sub nM dissociation constants similar to antibodies), and superior pharmacokinetics. The field is rapidly growing evidenced by increasing interests from industrial sectors, including small start-ups as well as mega-pharmas, toward drug development efforts on macrocyclic peptides, which has led to several *de novo* discovered peptides entering clinical trials. This lecture discusses the aforementioned screening technology, the RaPID system, and several showcases of therapeutic potentials of macrocyclic peptides. This lecture also discusses an application of the RaPID peptides to biologics development.

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Hiroaki Suga is a Professor of the Department of Chemistry, Graduate School of Science in the University of Tokyo. He was born in Okayama City, Japan in 1963. He received his Bachelor of Engineering (1986) and Master of Engineering (1989) from Okayama University, and Ph. D. in Chemistry (1994) from the Massachusetts Institute of Technology. After three years of post-doctoral work in Massachusetts General Hospital, he was appointed as a tenure-track Assistant Professor in the Department of Chemistry in the State University of New York at Buffalo (1997) and promoted to the tenured Associate Professor (2002). In 2003, he moved to the Research Center for Advanced Science and Technology in the University of Tokyo as an Associate Professor, and soon after he was promoted to Full Professor. In 2010, he changed his affiliation to the Department of Chemistry, Graduate School of Science. His research interests are in the field of bioorganic chemistry, chemical biology and biotechnology related to RNA, translation, peptides and pseudo-natural products. He is the recipient of Akabori Memorial Award 2014, Japanese Peptide Society, Max-Bergmann Gold Medal 2016, Nagoya Medal Silver 2017, and Vincent du Vigneaud Award 2019. He is also a founder of PeptiDream Inc. Tokyo, a publicly traded company in the Tokyo First Stock Exchange Market, which has many partnerships with pharmaceutical companies in worldwide.