The pseudo-natural peptides therapeutic innovation

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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 Peptides Integrated Discovery) system as a novel "molecular technology", the libraries of natural product-inspired (pseudo-natural) macrocycles with a variety ring sizes and building blocks can be screened (selected) against various drug targets inexpensively, less laboriously, and very rapidly. This lecture will discuss the most recent development of their technology and therapeutic applications toward drug discovery innovation.

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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, and Nagoya Medal Silver 2017, etc. He is also a founder of PeptiDream Inc. Tokyo, a publicly traded company in the Tokyo First Stock Exchange Market (the market capitalization is over JY 600 billions), which has many partnerships with pharmaceutical companies in worldwide.