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Therapeutic Potentials of Pseudo-Natural Peptides, Products and Neobiologics

Hiroaki Suga obtained his Ph. D. in Chemistry (1994) from the Massachusetts Institute of Technology; post-doctoral fellow in Massachusetts General Hospital/Harvard Med School (94–97); a tenure-track Assistant Professor in the Department of Chemistry in the State University of New York at Buffalo (1997); the tenured Associate Professor (2002); Research Center for Advanced Science and Technology in the University of Tokyo, Associate Professor (2003–2005), Full Professor (2005–2010); Department of Chemistry, Graduate School of Science in the University of Tokyo (2010–current). He is the recipient of Akabori Memorial Award 2014 of Japanese Peptide Society; Max-Bergmann Gold Medal 2016; Nagoya Medal Silver 2017; Vincent du Vigneaud Award 2019; Research Award of the Alexander von Humboldt Foundation 2020; MIT T.Y. Shen Lectureship 2022; ETHZ Prelog Medal Lecture 2022; Wolf Prize in Chemistry 2023; Nelson J. Leonard Distinguished Lecture of the University of Illinois at Urbana-Champaign; Van't Hoff Award Lectureship of the Royal Netherlands Academy of Science. He is also an academic founder of and the Board of Directors of PeptiDream Inc. Tokyo (2006–2018), a publicly traded company in the Tokyo Premier Stock Exchange Market, which has many partnerships with pharmaceutical companies in worldwide. He is also an academic co-founder of MiraBiologics Inc. and the Board of Directors since 2017.

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 or eukaryotes, the usage of amino acids is generally restricted to 20 proteinogenic (standard) kinds, and thus the expressed peptides are composed of only such monomers. However, 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 most recent development in the genetic code reprogramming approach that enables us to express natural product-like non-standard peptides. The technology involves (1) efficient macrocyclization of peptides, (2) incorporation of non-standard amino acids, such as N-methyl amino

Keynote presenter

acids and beta/gamma-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 Peptide Integrated Discovery) system, the non-standard cyclic peptide libraries with various ring sizes can be screened (selected) against various drug targets inexpensively, less laboriously, and very rapidly. Moreover, this technology was integrated with post-translational modifying enzymes to display pseudo-natural products. This lecture discusses therapeutic potentials using such pseudo-natural macrocyclic peptides and products, and more recent advance in generating neobiologics by means of LassoGraft technology.