

S4-7

SYNTHESIS OF FUNCTIONAL GENES BY MIXING MICROGENES

Kiyotaka Shiba

Department of Protein Engineering, Cancer Institute, Japanese Foundation for Cancer Research and CREST, JST, 3-10-6, Ariake, Koutou-ku, Tokyo 135-8550, JAPAN. E-mail: kshiba@jfc.or.jp

Creation of artificial proteins is a synthetic approach to understanding the dynamic behavior of protein evolution. The approach also represents a new way to establish novel pharmaceutical strategies for development of tailor-made medications. In this presentation, I describe a strategy for synthesizing artificial proteins by combinatorial assemblage of reading frames from a single microgene. Short peptide motifs that are related to apoptosis induction and protein transduction were encrypted into different reading frames of a microgene, which was then polymerized; random frame shifts at junctions between microgene units yielded combinatorial polymers of the motifs. Among the proteins created, some clones were found to exert a strong apoptotic effect on several cancer cell lines when added to their culture medium. It is noteworthy that a simple conjugation of these motifs did not give a multi-functional peptide. A combinatorial approach enabled us to create a functional protein that efficiently entered cells and induced apoptosis. Continued identification of peptide motifs from existing proteins and selection of artificial peptides from phage display libraries should provide us with the flexibility to create artificial proteins having a wide variety of functions.