Synthetic Biology Approach
towards Creation of an Organism
with a New Genetic Code

Barry L. Wanner, Ph.D.
Department of Microbiology
Harvard Medical School, USA

≪Summary≫
Recoding—the repurposing of genetic codons—is a powerful strategy for enhancing genomes with functions not commonly found in nature. I will discuss the computational design, synthesis, and experimental progress toward assembly of a 3.97-megabase, 57-codon Escherichia coli genome in which all 62,214 instances of seven codons are being replaced with synonymous codons across all protein-coding genes. Our testing of 55 segments of about 50-kilobases showed that 63% of the recoded genes have been validated. We found 91% of the tested essential genes retained functionality with a limited fitness effect. We demonstrate identification and correction of lethal design exceptions, only 13 of which were found in 2229 genes. This work underscores the feasibility of rewriting genomes and establishes a framework for large-scale design, assembly, troubleshooting, and phenotypic analysis of synthetic organisms.

Barry L. Wanner, Ph.D.
Department of Microbiology
Harvard Medical School, USA

加藤 純一:
E-mail  jun@hiroshima-u.ac.jp  TEL 082-424-7757

（世話人：加藤 純一教授
大学院先端物質科学研究科
分子生命機能科学専攻）

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