Synthetic biology: Synthesis and modification of a chemical called poliovirus

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Synthetic biology is a newly emerging scientific field, encompassing knowledge of different disciplines, such as engineering, physics, chemistry, computer sciences, mathematics, and biology. Synthetic biology aims to create novel biological systems with functions that do not exist in nature. There seem infinite possibilities of constructing unique derivatives of existing organisms (bacteria, yeast, viruses). Apart from designing novel building elements for engineering biological systems, a fundamental requirement in synthetic biology is the ability of large-scale DNA synthesis and DNA sequencing.

Viruses can be described in chemical terms; the empirical formula of the organic matter of poliovirus being:[1]

$$C_{332,652}H_{492,388}N_{98,245}O_{131,196}P_{7,501}S_{2,340}.$$

Placing these atoms into order, a particle of high symmetry emerges[2] with all the properties required for its proliferation and "survival" in nature. These properties are encoded in the viral genome, which is a single stranded nucleic acid (RNA) of about 7,500 nucleotides. Guided by the published nucleotide sequence,[3] we have recently synthesized the DNA equivalent of the polio RNA genome and converted it by simple biochemical manipulations in a cell-free environment (outside living cells) into authentic poliovirus particles.[4] The synthesis of a replicating "organism" in the absence of a natural template was without precedence at the time of publication[4] and it provoked widespread responses – good and bad.

Poliovirus is a human virus that replicates after ingestion in the gastrointestinal tract. Infrequently, the virus invades the central nervous system (CNS) where it targets those cells (motor neurons) for destruction that control muscle movement.[5] This results in irreversible paralysis, and sometimes death, a disease called poliomyelitis. The virus has caused horrific epidemics in the first part of last century until two vaccines were developed controlling effectively the disease. We are studying the possibility to generate by chemical synthesis novel polioviruses whose ability to proliferate in the CNS is debilitated whereas its efficiency to replicate in tissue culture cells remains largely unchanged. The basis of the engineering of these new viruses is altered codon usage. We will present our results and discuss the possibilities that the synthesis of novel viruses offers to combat human disease.

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