Building a Synthetic Cell and Advancing Synthetic Genomics Technology
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For the past 17 years, the genomes of many organisms have been sequenced and deposited in databases. We recently showed that it is possible to reverse this process and synthesize bacterial cells starting from digitized information. To make this happen, our group needed to learn how to sequence, synthesize, and transplant genomes. Many hurdles had to be overcome, but we are now able to combine all of these steps to produce synthetic cells in the laboratory. As a proof of concept, we designed, synthesized, and assembled the 1.08–mega–base pair Mycoplasma mycoides JCVI-syn1.0 genome starting from digitized genome sequence information and transplanted it into a Mycoplasma capricolum recipient cell to create new M. mycoides cells that are controlled only by the synthetic chromosome. The only DNA in the cells is the designed synthetic DNA sequence, including “watermark” sequences and other designed gene deletions and polymorphisms, and mutations acquired during the building process. The new cells have expected phenotypic properties and are capable of continuous self-replication. We now will extend what we have learned in this proof of concept experiment to begin designing and producing new organisms with useful properties. For example, we will use available sequencing information to create cells that can produce energy, pharmaceuticals, and industrial compounds, and sequester carbon dioxide. In addition, we have already begun working on our ultimate objective which has been to synthesize a minimal cell that has only the machinery necessary for independent life. Now that we can produce a living cell from the genome we have synthesized, we can test for the functionality of the genome. We can whittle away at the synthetic genome and repeat transplantation experiments until no more genes can be disrupted and the genome is as small as possible. This will help us to better understand the function of every gene in a cell and what DNA is required to sustain life in its simplest form. The M. mycoides genome that we assembled is over one million base pairs in length and is the largest chemically defined structure ever synthesized in the laboratory. It is almost twice as large as the synthetic Mycoplasma genitalium genome we reported on in 2008, and is more than 30 times larger than any reported DNA sequence synthesized outside of the J. Craig Venter Institute. This work and new powerful methods for constructing small and large DNA molecules starting from chemically-synthesized oligonucleotides will be discussed.

Background Review Article:

[article available on CD]