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Artificial life

Nearly there

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The penultimate step towards the creation of artificial life has just been announced

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LIKE a striptease artist in front of an eager audience, Craig Venter has been dropping veils over the past few years without ever quite revealing what people are hoping to see: the world's first artificial organism. He has been discussing making one since 1995, when he worked out the first complete genetic sequence of a natural living organism. And, after a lot of hard graft and blind alleys, he and his team have almost got there. As they report in this week's *Science*, they have replicated the genome of *Mycoplasma genitalium*, the species that was the subject of that original sequencing effort. It is not actual life, but it is surely the tease before the last veil finally falls away.

Though Dr Venter (pictured above at the helm of his yacht, *Sorcerer II*) is the public face of the effort, and the 17-strong team that did the work are all employed by the J. Craig Venter Institute in Rockville, Maryland, the synthetic genome project is equally the brainchild of his collaborator, Hamilton Smith. Indeed, it is in Dr Smith's name that the paper announcing the synthesis is published—along, of course, with the 16 others including Dr Venter himself.

It is a formidable effort. But what is, perhaps, most noteworthy is that the starting point for the project was not the raw nucleotides (the chemical letters of which DNA is composed), but a set of pre-assembled “cassettes” of DNA that the team had ordered from commercial suppliers. The point where any Tom, Dick or Harriet with a reasonably well equipped genetics laboratory could do likewise is not, therefore, that far off.

All you create

M. genitalium's genome is a single, circular chromosome that is 580,076 letters long, and contains 485 protein-coding genes. The team divided it on paper into 101 units (the cassettes), each containing four or five genes. They also took the precaution of editing one gene in particular, so that it would not work. The gene in question is crucial to *M. genitalium*'s ability to stick to mammalian cells, and thus become infective (it lives naturally in the urinary tract and is thought to cause urethritis). Disrupting it thus forestalled the risk of creating anything nasty.

The team placed orders for the cassettes with three firms that turn such things out routinely. They then used a variety of techniques, some old and some specially invented, to link the cassettes together into larger and larger units until they had two half chromosomes which, with the aid of some yeast cells, they turned into a whole one. All that remains to create what most researchers in the field would be willing to recognise as an artificial organism is to insert such a chromosome into a bacterial cell that has had its own chromosome removed. At the moment, no one is clever enough to make all of the cellular machinery that translates genes into the stuff of life. Hence the need for this shortcut. But if the newly reconstituted cell were able to grow and reproduce, the nature of its progeny would be dictated by the implanted chromosome. That, not the nature of the host "shell", would define the species of the progeny.

Dr Venter's purpose in synthesising artificial genomes is twofold. Scientifically, he wants to understand how life works. One way to do this is to discover what he refers to as the minimal genome. This is a Platonic ideal of life, which would contain only the genes absolutely necessary for survival and reproduction, and might shed light on the nature of Luca, the last universal common ancestor of life on Earth. In practice, that ideal is difficult to realise, since many genes cover for each other. He knows that 100 of *M. genitalium*'s genes can be eliminated individually without killing it, but eliminate all of these and it dies. Assembling mix-and-match genomes with lots of different combinations of cassettes that each contain but a handful of genes should shed light on the question.

But Dr Venter is also a practical man, who wants to turn genomics into technology. Indeed, one of his other enterprises is a firm called Synthetic Genomics and he is one of the leading lights of the emerging field of synthetic biology. This seeks, among other things, to create a parts list of biological components such as DNA cassettes that could be ordered from catalogues in the way that electronic components can be.

Synthetic Genomics itself is a bit cagey about exactly which molecular products it is working on, but one of Dr Venter's interests is in using modified bacteria to make fuels. Natural bugs can turn out both hydrogen and methane. There is talk of modifying them to produce high-value liquid fuels, for jets, say.

He is not alone in this idea. Several Californian firms are also seeking to make advanced biofuels using modified bacteria. But if Dr Venter can take the final step of kicking the new, wholly synthetic genome into reproductive life, he will not only have made a great technological leap forward, he will also have erased one of the last mythic distinctions in science—that between living and non-living matter. Watching that veil drop will have been worth the wait.