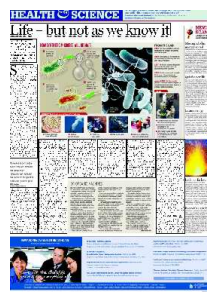


Mediaportal Report

24/09/2009

▶ **Life but not as we know it**
Sydney Morning Herald, 24/09/09, Health & Science, Page 21
By: None

Clip Ref: **00057455242**
1223 words



Life – but not as we know it

It could end hunger, or even help solve global warming. Or it could put us on a deadly path from which there is no return. **Deborah Smith** reports on the imminent creation of artificial life.

Sometime soon, researchers are expected to announce they have achieved an extraordinary feat in science: the creation of artificial life. Far from a lumbering Frankenstein monster, the first life form from the lab will be a minuscule new bacterium, invisible to the human eye.

Although tiny, its existence will represent the crossing of a technological threshold to an uncharted future that could hold both promise and peril. The bacterium will be a fully functioning, self-replicating organism that has never existed before: its DNA will have been man-made from scratch.

This dawn of synthetic life will come as a surprise to many; the research has progressed rapidly, below the radar of most people except interested scientists and concerned onlookers.

Advocates hope the technology will be used to design and build new microbes that will help tackle climate change, power the globe, clean up pollution, make drugs and feed the hungry. But critics are concerned mankind's creations could escape the lab and harm the environment, or become new weapons for terrorists.

Cliff Hooker, a professor of philosophy at the University of Newcastle, says new synthetic life forms will have three critical characteristics that are reason for caution: they will be extremely small, able to reproduce, and able to evolve.

"If something goes wrong with them, it is impossible to recall them back from the environment."

Strong international regulations, as well as clever technology, will be needed to safeguard society, says Dr Michael Selgelid, deputy director of the National Centre for Biosecurity at the Australian National University.

Synthetic biology could greatly benefit humanity, but "the worry is the very same science and technology can

be used for malevolent purposes."

Georgia Miller, of the environmental group Friends of the Earth, says the lack of regulation, and the hundreds of millions of dollars being poured into research, makes this a "cowboy industry". The environmental release of any synthetic microbes should be prohibited "until strong governance is established", she says.

Hooker adds, however, that concern about how to manage these scientific developments is no reason to stop pursuing the research. "We walk a razor's edge every time we increase our knowledge [because] we increase our capacity for greater harm and greater good," he says. "To tell us to stop is to tell us to not be human."

Synthetic biology has been pioneered by Dr Craig Venter, the controversial American scientist and entrepreneur who most famously competed with a public consortium of researchers during the 1990s to sequence the human genome, a race that was eventually declared a tie by president Bill Clinton in 2000.

While Venter and his colleagues have been trying to create new life forms for years, last month they announced they had overcome the last of three hurdles. All they need do now is put the steps together in order. Success is expected before the end of the year.

Scientists have been tweaking life for decades, producing genetically modified microbes, plants and animals, by knocking out or adding a gene or two, but synthetic biology represents a much bigger leap, in which entirely new forms of life are engineered.

There are two approaches – bottom up, and top down. In the bottom up approach, scientists are like children with Lego, choosing from a library of thousands of basic biological building blocks, called biobricks, to assemble new microbes (*see box*).

These biobricks, for example, may include packages of genes that allow a

microbe to operate at higher or lower temperatures than normal, or to soak up more carbon dioxide, or digest woody plant material efficiently to produce ethanol, or latch onto heavy metals in the environment.

The top down approach Venter follows involves designing and making a synthetic genome in the lab and inserting it into an existing bacterial cell, which will then activate and generate the new, useful organism.

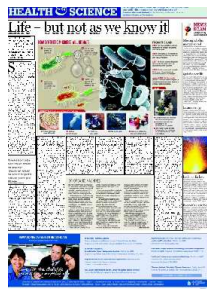
The research has been spurred on by the existence of more than 50 companies that churn out lengths of DNA for scientific customers, carefully building up the letters, or chemical bases of the DNA code, in the requested order.

In July 2002, American scientists used this service to create the world's first virus from scratch, choosing to make polio, a relatively small killer with only about 7700 letters, or base pairs, in its genetic blueprint.

The State University of New York team wanted "to prove it could be done", as a warning to the world. Their synthetic virus was indistinguishable from the real thing, paralyzing and killing mice infected with it.

At the time scientists thought it would be extremely difficult to synthesise bigger genomes, but by January 2008, researchers at the J. Craig Venter Institute in Rockville, Maryland, a not-for-profit lab founded by Venter, had created the largest man-made DNA structure ever – the genome of a bacterium, *Mycoplasma genitalium*.

It took them several years to work out how to chemically synthesise fragments of the genome, which has almost 583,000 letters, or base pairs, and then assemble them. "This extraordinary accomplishment is a technological marvel that was only made possible because of the unique and accomplished JCVI team," Venter enthused at the time, explaining that as the strands of DNA got longer they got more brittle and difficult to work with.



In June 2007, his team had shown they could put a natural genome into a bacterium, and get it to activate, converting one species of life into another. Their breakthrough last month was to devise a way to take a natural genome, modify it in a yeast cell, and transfer this semi-synthetic genome into a bacterium and activate it to produce a strain of bacterium "that had not previously existed".

The final step will be to put a fully synthetic genome into a bacterium and kickstart it into life.

Selgelid says there is a risk terrorists could use the technology to create deadly viruses and bacteria they could not otherwise obtain, such as ebola. Most worrying would be any attempt to make the smallpox virus, "one of the worst diseases in human history", against which few are immune.

Synthesising smallpox, which has about 185,000 pairs of letters in its genome, is regarded as technically feasible by experts, he says.

DNA synthesis companies, based mainly in Europe and the US, have begun to develop voluntary screening standards for the industry, which includes genes in a customer's order be-

ing automatically compared to a list of dangerous organisms.

But different protocols have been proposed by different companies on whether staff are then assigned to act on suspicious requests. There are also concerns this system cannot deal with unknowns, such as genes from harmless organisms that can be modified in some way to make them dangerous.

Selgelid says the situation is similar to that of nuclear science in the early 20th century, and new international bodies, laws and reporting systems are required to avoid rogue use of the biological technology. "What we need is a web of prevention," he says.

This could include, for example, a requirement for all buyers of gene sequences to be registered with authorities, he says. Scientists also need to be better educated about the risks of harmful use of their discoveries.

Miller says the environmental risks from accidental or deliberate release of new organisms are impossible to predict, making strict regulation of synthetic biology necessary "before it becomes a reality". New microbes could infect other species, disrupt ecosystems, or

become impossible to eliminate. "The potential to mutate in unpredictable ways is of great concern."

More debate is also needed on the potential for the technology to increase corporate control of essential processes like energy generation and food production, she says.

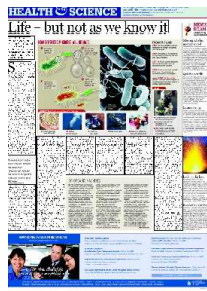
Hooker says it may be possible to develop a range of classes for the new synthetic organisms. At one end would be those never to be released; at the other, those with very low likelihood of causing problems.

For organisms in the middle, special approaches may need to be developed – for example, an in-built self-destruct mechanism in case a problem arises.

He says the same concerns apply to other new technologies, such as self-replicating nanobots and computer viruses, because they have the same three worrying characteristics: tinniness, ability to reproduce and ability to evolve. The creation of a synthetic microbe will be a milestone but "there is nothing special about it being life that will cause us social problems", he says.

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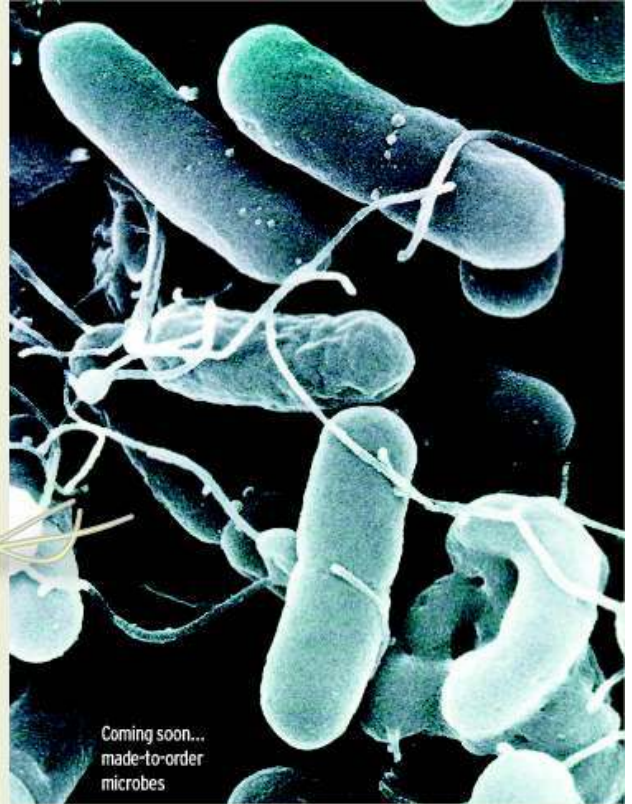
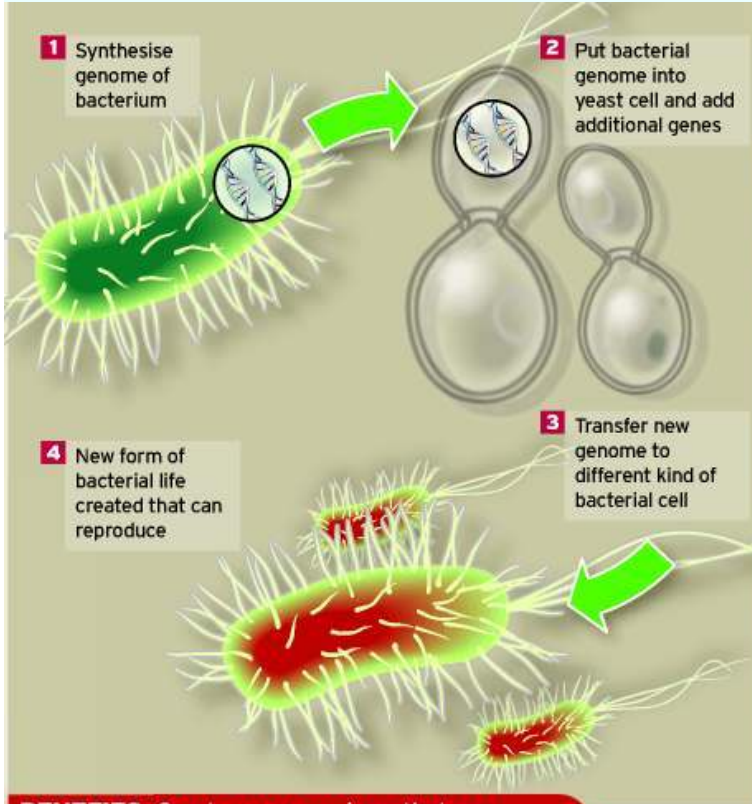
Cliff Hooker,
philosophy professor



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HOW SYNTHETIC MICROBES WILL BE MADE



BENEFITS: Create new organisms that can



■ Produce biofuels more efficiently



■ Soak up carbon dioxide



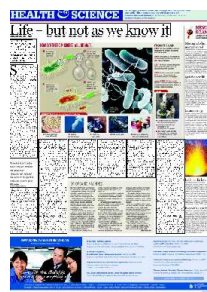
■ Clean up toxic waste



■ Mop up oil spills



■ Make new antibiotics and anti-cancer drugs



FROM THE LAB

2002 Polio virus created from scratch by synthesising 7741 base pairs of its genetic code. Took two years.

2003 Bacteriophage, or virus that infects bacteria, created by synthesising 5386 base pairs. Took just two weeks.

2007 One life form converted into another by transferring full genetic code of one bacterium into another bacterium.

2008 Scientists create largest man-made DNA structure - the genetic code of a bacterium containing 582,970 base pairs.

August 2009 The final hurdle: genome of a bacterium modified in a yeast cell and then inserted into a different bacterium to create an entirely new organism.

RISKS



- Accidental release from the lab of harmful organisms.
- Deliberate release that could harm the environment or people.
- Technology could be used by terrorists to create new or old deadly viruses such as smallpox.