SYNTHETIC LIFE, WHAT FOR AND WHAT FUTURE?

ARMANDO ARANDA-ANZALDO

In late May 2010, a group of researchers lead by J. Craig Venter reported the creation of a bacterial cell controlled by a synthetic genome, implying that such a genome had been artificially created in the lab [1]. This technological development was widely quoted in the media followed by an aura, not to say noise, of big words and big worries: synthetic life, artificial life, creation of life, man playing god, very much fuelled by Venter himself, as he seems to be convinced of the awesome philosophical meaning of this work [2]. The plain facts are that a genome from a well-known bacterium (M*ycoplasma mycoides*) was synthesized and assembled in pieces and then cleverly introduced into a closely-related host bacterium (*Mycoplasma capricolum*) where the transplanted genome directed the production of the cellular components now corresponding to those coded by the *M. mycoides* genome, leading to the propagation of this new variant of *M. mycoides* that Venter has unabashedly characterized as a new species worth of his own name (*Mycoplasma mycoides JCVI-syn1.0*). Venter's claim for having created a new species is based on the fact that the synthetic *M. mycoides* genome has not exactly the same nucleotide sequence of the natural *M. mycoides*, as the researchers deliberately introduced "watermarks", meaning artificial nucleotide sequences altogether meaningless from the functional point of view, as molecular labels for distinguishing the synthetic genome from the natural one [3]. This was an important control step in order to prove that the resulting newly made bacterial cells carry the synthetic genome and so do not correspond to natural *M. mycoides* bacteria that may have contaminated the bacterial cell cultures formerly populated by *M. capricolum*. Thus, this technological feat is analogous to an imaginary Honda takeover of the failing Ford factories, during the recent world financial crisis, in order to produce brand new Honda cars. Indeed, the spatiotemporal order of molecules and biochemical interactions that result in the cellular organization represented by the host *M. capricolum* was "kidnapped" by the transplanted synthetic genome that from then on repro-

Laboratorio de Biología Molecular, Facultad de Medicina, Universidad Autónoma del Estado de México, Toluca, México. / aaa@uaemex.mx

This text answer the question, posted by the editor, on the philosophical, scientific and social problems followed from the synthetic ensemble of the modified genome of the bacteria *M. Mycoides,* announced in May 2010 by the J. Craig Venter Institute.

duced such a preexisting cellular organization but using *M. mycoides* components. In no way the synthetic genome was able to determine the preexisting cellular organization and so the old dictum attributed to Pasteur *Omne vivum ex vivo* (all life arises from preexisting life) remains as valid and mysterious as ever, despite Venter's claims on the contrary.

Interestingly, Venter says that the synthetic assembly of a working bacterial genome is a major step in an ongoing fifteen year-old research project whose central aim is achieving the creation of a living cell with a minimal working genome [1]. Apparently, a major question for Venter and associates is which genes are essential and which genes are dispensable for cellular life. For example, a single base pair deletion that creates a frameshift in *dnaA*, a gene that codes for an enzyme essential for chromosome replication, was enough to preclude the successful transplantation of the synthetic genome. On the other hand, unexpected accidental insertions of transposons occurring during the procedure for assembling the synthetic genome, resulted in the disruption of two genes whose inactivation did not preclude the successful transplant of the synthetic genome that was able to replicate in the new host [3]. Hence, Venter qualifies *dnaA* as an essential gene while the disrupted genes are non-essential.

One wonders about this obsession with simplifying a genome that is the natural result of evolution. Indeed, classifying genes as essential or non-essential is a risky business. It all depends on the arbitrary criteria chosen for such an evaluation. For example, in the case of metazoans there may be genes whose mutation is non-compatible with embryonic development (embryonic lethal genes) and so development is early aborted. Yet, other genes that cause no harm to the embryo when mutated and so are apparently non-essential for development, may nevertheless cause the sterility of the adult animal then unable to reproduce. In both cases, there is a breakdown in the ability to pass a given genotype to an offspring. Moreover, there is overwhelming evidence that redundancy at both the genetic and functional levels is a fundamental condition of life [4]. Such a redundancy is a critical feature that guarantees the resilience and adaptability of living things in an always shifting environment. Living things are not built like cars in a factory where quality control checks are applied to newly-made lots of parts and pieces before being used for the assembly of new cars, which are also selectively subjected to further quality-control checks before going into the market. In this case, an economy of savings in operational costs and avoidance of costly consumer's lawsuits determines the industrial practices. However, nature is rather wasteful when building things and the quality control is carried *ex post* by natural selection [5]. The goal of creating synthetic cells or organisms based on minimal working genomes may be appealing from a financial perspective, aiming at maximum revenues from minimal investment, yet it carries the seed of

disaster as the loss of redundancy within the system increases its frailty and potential for critical malfunction. Indeed, highly important and expensive man-made devices have significant built-in redundancy: space shuttles, nuclear submarines, nuclear-power plants, jet airliners, and so forth, in order to reduce the risk of critical failure.

In any case, more than wasting our time with the exegesis of Venter's achievements it is worth considering the rationale behind the synthetic biology fad. At the end of the day, all these efforts are justified with the classical argument for the benefit of mankind: new bacteria that will eat and degrade the oil from spills, vegetables that will produce useful drugs in their saps, cells that will secrete the right products for making the right vaccines against dreadful diseases, and so forth [1]. That sounds nice and marvelous. Yet one wonders. When there are no oil spills to tame what happens to the oil-eating bacteria, will they remain safely latent, frozen in their liquid nitrogen casks? And if by some mistake they happen to fell into the oil-storage tanks of a major oil refinery? That would be the ultimate feast for such synthetic organisms! Then, shall we need massive amounts of antibiotics (perhaps produced by another synthetic organism) in order to kill the oil-eating bacteria menacing to wreak havoc on the oil industry? Moreover, once the former useful drug for controlling gastroesophageal reflux is replaced by a better drug, what would happen to the synthetic vegetables that produced the former drug in their sap? Will such plants go into nostalgic display in botanical gardens? Will they undergo the same fate as 33 rpm acetate records, Betamax videos, cassette tape-recorders, typewriters, floppy disks? What would happen to all these man-modified or man-created life forms once their useful purpose has been fulfilled and superseded by new human needs, trends and fashions? Then I am afraid, we will begin to worry about what to do with that invasion of useless, out of fashion, synthetic life-forms in the same way that today we have piles of discarded TV sets, old computers, used batteries and nuclear waste posing a serious problem of containment and disposal.

NOTES

1 See video at http://www.ted.com: "Craig Venter unveils synthetic life" (YouTube)

2 Cho, M.K. and Relman, D. A. (2010), "Synthetic "life", ethics, national security, and public discourse," *Science* 329: 38-39.

3 Gibson, D. G., et al. (2010), "Creation of a bacterial cell controlled by a chemically synthesized genome," *Science* 329: 52-56.

4 Aranda-Anzaldo, A. and Dent, M. A. R. (2003), "Developmental noise, ageing and cancer," *Mech. Ageing Dev.* 124: 711-720.

5 Aranda-Anzaldo, A. and Dent, M. A. R. (2007), "Reassesing the role of p53 in cancer and ageing from an evolutionary perspective," *Mech. Ageing Dev.* 128: 293-302.