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Artificial DNA Presents Real Dangers

May 2nd, 2012

As concerns grow about dangers posed by the emergent field of synthetic biology, a novel discovery threatens to make this "extreme" form of genetic engineering even more risky.

Since Watson and Crick discovered the double-helix structure of DNA in 1953, it's been a common assumption that DNA and RNA are the only molecules that can store genetic information and pass it on. That belief, according to a recent article in *Science*, may no longer hold.

New Discoveries in Synthetic Biology - XNA

The article's conclusion is summarized by its title, "Synthetic Genetic Polymers Capable of Heredity and Evolution." "There is nothing Goldilocks about DNA and RNA," noted Phillip Holliger, a co-leader along with Vitor Pinheiro of the research team who authored the paper. "There is no overwhelming functional imperative for genetic systems or biology to be based on these two nucleic acids." DNA, as one article about the new study puts it, no longer has "reason to feel special."

Holliger and Pinheiro's team of researchers, based at the MRC Laboratory of Molecular Biology in Cambridge, UK, demonstrated that six alternative nucleic acids are capable of storing and transmitting genetic information. These molecules, collectively dubbed XNAs or Xeno-Nucleic-Acids ("Xeno" is Greek for foreign or alien) carry the same nucleic acid base pairs as do DNA and RNA (the well-known A, C, T, and G), but do so on a sugar backbone different from the deoxyribose of DNA or the ribose of RNA.

The Cambridge team induced one of the XNAs to undergo an evolution-like process, thus demonstrating that "replication, heredity and evolution are possible in these alternative [XNA] backbones."

Just as significant is the set of techniques developed in conducting the research. XNAs have been in scientific use for some time, but scientists used to have to make them one at a time, limiting their experimental value. The new research has made that process obsolete. As one researcher put it, "if I give you a few XNAs in the morning, I can come back in the afternoon and you can give me trillions of copies."

Media Buzz and Scientific Hype

The study has been greeted with a wave of media buzz not seen for synthetic biology since Craig Venter's team declared they had created the first (so-called) synthetic life form back in 2010. Prominent articles covered it excitedly in the, *Los Angeles Times*, *Boston Herald*, *The Guardian*, *Scientific American*, *New Scientist*, and *BBC News*, just to name a few.

The scientific community has also been enthusiastic. One of the study's authors, molecular biologist John Sutherland, called the discovery a "game changer." In a commentary in *Science* titled "Toward an Alternative Biology," Gerald Joyce, a researcher at the Scripps Research Institute who is unaffiliated with Holliger's team, proclaimed that:

> The work heralds the era of synthetic genetics, with implications for exobiology, biotechnology, and understanding of life itself.

The work done by Holliger and his team is no doubt scientifically significant. However, it is just as significant for the new risks it poses. It is worth summarizing some of the projected applications and risks of this new research.

New Biomedical Applications and Risks

Scientists, media outlets and biotech industry figures are already envisaging a variety of applications for replicable XNA. Hollinger stated that "there are a whole host of opportunities in biotechnology which now become possible" on the basis of his new research. Professor of Biochemistry Andrew Ellington, at the Center for Systems and Synthetic Biology at the University of Texas, called the research a "tour-de-force" that could have "direct therapeutic impact."

In addition to general proclamations like these, a number of more specific biomedical possibilities have been raised. Ana Pallasen of *BioNews* suggested

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CONTRIBUTORS

- Marcy Darnovsky
- Osagie K. Obasogie
- Pete Shanks
- Doug Pet
- Emily Beitiks
- Daniel Sharp
- Jesse Reynolds
- Jillian Theil

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that the study "opens avenues" for "gene therapy." (Let the hype cycle begin.)

The rationale is as follows. Compared to transferred DNA and RNA, which are "rapidly broken down by enzymes called nucleases, XNAs are "more resistant to degradation by biological nucleases." As Gerald Joyce puts it, XNAs are "bullet proof."

That means that XNA circumvents an essential hurdle that most gene therapies face. As Victor Pinheiro points out, "since these molecules can now be selected directly on XNA, medicinal chemistry should no longer be limiting" for gene therapy.

Such applications are speculative, given the early stage of this research. But it's not too soon to note that caution is in order. While XNA research using synthetic biology techniques might overcome one hurdle to effective gene therapy, it certainly doesn't avoid all the risks associated with the field. In fact, it may amplify them. Since the body's natural defense mechanisms aren't adapted to recognize, let alone break down, synthetic XNA, human biology is essentially defenseless against it.

Synthetic Xeno-organisms

The new XNA research has also triggered speculation about its use to create artificial biological systems not based on DNA. Though it has not yet been demonstrated that XNAs can be successfully introduced into cells, the *Guardian*, for example, has suggested that "the creation of alternatives to DNA could enable scientists to make novel forms of life in the laboratory."

As Gerald Joyce notes, research is still "miles and miles" away from yielding a synthetic, XNA-based life form. But with speculation about xeno organisms already rampant, it's important to get ahead of the curve in terms of understanding the risks.
As has been extensively documented by risk analysis experts, bioethicists, and critics of synthetic biology, the behavior of synthetic organisms is inherently unpredictable.

The way such organisms will interact with their environments cannot be known ahead of time, and could produce negative ecological consequences. On the basis of such concerns, 112 civil society organizations have called for a moratorium on the environmental release of synthetic organisms in a document entitled *Principles for the Oversight of Synthetic Biology*.

A similar precautionary approach should be taken towards any potential "xeno organisms," which again amplify the standard concerns about synthetic organisms. Since "XNAs are unnatural and would pass through the biosphere unscathed," they would have an immense evolutionary advantage. As one commentator (whose name could not be located) from the Leukippos Institute for synthetic biology wisely pointed out, xeno organisms could have potentially devastating ecological consequences:

> XNA organisms might still be able to interact with their natural counterpart on an ecological level. It has to be avoided, that xeno
>
> organisms alter habitats, food webs or on extreme wipe out the native population due to an evolutionary advantage. Moreover, it has to be avoided that xeno organisms produce unintended toxic substances or other harmful metabolites.

These environmental risks belie the hope that XNAs could serve as "the ultimate biosafety tool." Bioethicist Marcus Schimdt first proposed this idea back in 2010, envisioning XNA systems as a panacea for every biotechnological risk:

> Whatever new or improved physical containment mechanisms are developed, there is one key problem that cannot be solved: all biotech (and nanobiotech) use the same "software program," namely DNA. DNA occurs in all naturally evolved and domesticated microbes, plants, and animals. Instead of bug fixing, and poorly adjusting biosafety regulations, red taping R&D, or painfully trying to fight off public resistance, why not switch to a different genetic software program altogether? … Why not construct a genetic firewall that solves this problem once and for all?...
>
> Xenobiology could become a fundamental safety device capable of limiting any kind of genetic interaction with the natural world. What xenobiology could bring about is no less than to provide an isolated genetic enclave within the natural world.

Certainly this way of thinking – a one-size-fits-all solution to the problems concerning biotechnology – will be attractive to advocates of synthetic XNA research. However, the new research demonstrating that XNA can be induced to interact with DNA seems to undermine the feasibility of its use as a "genetic firewall." If XNA can be induced to evolve and interact with DNA, xeno organisms might be capable of breaching any "genetic firewall" altogether.

Moreover, even if such a "genetic firewall" were feasible, it would not be equivalent to a biological firewall. Since xeno organisms, as Schmidt himself admits, could still interact with natural organisms on the biological level, the ecological concerns about the release of novel xeno organisms remain pressing. In short, a biotechnology-based cure-all for biotech risks is a pipe dream.

Harm to Our Biology?

A number of leading scientists have voiced similar concerns. In the end of his review in Scicnce, Gerald Joyce points to the need for caution:

> The benefits of their unusual chemical properties must be weighed against their greater cost, both literally and with regard to operating in the uncharted waters of XNA biochemistry.
>
> As one contemplates all the alternative life forms that might be possible with XNAs and other more exotic genetic molecules, the words of Arthur C. Clarke come to mind. In 2010: Odyssey Two, HAL the computer tells humanity: "All these worlds are yours" but cautions: "Except Europa. Attempt no landings there." Synthetic biologists are beginning to frolic on the worlds of alternative genetics but must not tread into areas that have the potential to harm our biology.

Even George Church, a leading proponent of synthetic biology, acknowledged that "the risk could go up by increasing the survivability of XNA relative to [DNA or RNA]."

But discussions of ecological risk have been largely absent from reports on the new XNA findings, and some seem willfully blind to them. One science blogger even openly ridiculed Joyce's proclamation that scientists should proceed with caution when creating artificial life:

> What exactly does "potential to harm our biology" mean? Cancer alone has an enormous potential to harm our biology-in fact it has gone far beyond potential because many people's biology has been brought to its knees by cancer! Let's not lose sight of the bigger picture here. Sure synthetic biology has risk, but the problems it promises to address are so pervasive and devastating that to limit our inquiry based on arbitrary, unfounded
>
> proclamations (reminiscent of Eden's Tree of Knowledge, really!) is unacceptable.

Such responses partake of a techno-scientific ideology whose adherents are so spell-bound by the allure of biotechnology that they are unable even to contemplate that serious safety and social risks might exist. A number of leading synthetic biologists have already publicly advocated for the reengineering of the human genome via synthetic biology techniques. Developments in XNA research might further advance this dubious agenda.

The Way Forward

Toward the end of his 2010 article on xenobiology, Marcus Schmidt speaks of a coming "paradigm shift" in the way life is conceptualized:

> Xenobiology could easily trigger the next paradigm change in the way we understand nature and life. Just as the Earth lost its place as the center of the universe, or men lost its unique status in the animal world, our natural world could lose its unique status as being synonymous with "life."

These developments are indeed radical, and there can be no doubt that synthetic biology and xenobiology are transforming our scientific conceptions of what constitutes life.

But such transformations need not – indeed, they shouldn't – undermine the basic moral precepts of protecting human health and ecological integrity. Scientists, policy makers and the rest of us must acknowledge the profound risks that attend the creation of artificial life, and work to prevent them ahead of time.

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