Harvard Scientists' Discovery Opens Door to Synthetic Life

By John Lauerman

March 7 (Bloomberg) -- Harvard University scientists are a step closer to creating synthetic forms of life, part of a drive to design man-made organisms that may one day be used to help produce new fuels and create biotechnology drugs.

Researchers led by **George Church**, whose findings helped spur the U.S. human genome project in the 1980s, have copied the part of a living cell that makes proteins, the building blocks of life. The finding overcomes a major roadblock in making synthetic self-replicating organisms, Church said today in a lecture at Harvard in Cambridge, Massachusetts.

The technology can be used to program cells to make virtually any protein, even some that don't exist in nature, the scientists said. That may allow production of helpful new drugs, chemicals and organisms, including living bacteria. It also opens the door to ethical concerns about creation of processes that may be uncontrollable by life's natural defenses.

"It's the key component to making synthetic life," Church said yesterday in a telephone call with reporters. "We haven't made synthetic life and it's not our primary goal, but this is a huge milestone in that direction."

The work may be immediately helpful to companies such as Synthetic Genomics Inc., headed by **J. Craig Venter**, trying to make new organisms that perform specific tasks, such as converting buried coal into methane gas that's easier to extract from the ground.

Microbes for Coal

Venter's plan is to create man-made microbes that can help break down the coal in the earth, much as bacteria speed decomposing plant material.

In a conference for alumni today at Harvard, Church described how his team assembled a reconstituted **ribosome**, the first artificial version of the structure capable of remaking itself.

Naturally occurring ribosomes are used now when biotechnology companies genetically engineer cells to make the proteins for vaccines and drugs, such as **Genentech Inc.**'s Herceptin. Normal ribosomes make some drugs slowly, and others can't be made at all, said **Anthony Forster**, a Vanderbilt University pharmacologist who has collaborated with Church on synthetic biology projects.

A man-made, or reconstituted, ribosome may be programmable to make all kinds of molecules, Forster said.

Efficient Protein Making

"There would be advantages to having ribosomes that would only make specific proteins" said **James Collins**, a Boston University biomedical engineer, in a telephone interview. "Then you could program ribosomes so that they shut down much of the rest of the cell, only making the proteins you want to produce. You could shift the cell's machinery to making certain products or fuels, for example, and really increase efficiency."

Specially programmed ribosomes might also have the ability to make mirror images of the active molecules in existing drugs, Church said. These mirror-image versions, sometimes called **chirals**, would be impervious to enzymes that the body usually uses to break down chemicals.

"They would have a longer stability in natural environments," Church said.

Ribosomes have been synthesized before, some as long as 40 years ago. Because they were made only under specialized conditions of temperature and salt concentration, scientists couldn't get them to recreate

themselves, a key requirement in making artificial life.

Security Concerns

Artificial life and drugs that can't be broken down by the body's natural enzymes raise a number of serious concerns, said David Magnus, director of the **Stanford Center for Biomedical Ethics**.

As the tools of synthetic biology become easier to use, bioterrorists and criminals may attempt to exploit them, he said. Well-meaning scientists might also release potentially deadly organisms and chemicals into the environment.

"A number of proposals have been made about controlling access to this technology," Magnus said in a telephone interview. "The synthetic biology community takes these issues seriously and are talking about what it will take to make sure we have effective oversight."

The first artificial organisms are likely to be grown in highly controlled conditions, and would probably be unable to exist outside the laboratory, said Vanderbilt's Forster.

Lab Escape Improbable

"It might sound scary initially, but it would almost be on life support," he said. "It would probably be highly dependent on someone feeding it 30 or more small molecules. It wouldn't be likely to escape into the environment and run amok."

Church has advised 22 companies on genetic sequencing since 1984. Technology he developed was licensed to **Applied Biosystems** Inc., purchased last year by **Life** Technologies Corp. The technology is used to make Life's sequencing products.

The Harvard geneticist last year received backing from **Google** Inc. for a project to decipher the genomes of 100,000 people using sequencers, machines that quickly read the genetic code, the instructions for making all its proteins that is stored in **DNA** molecules. A complementary molecule, called RNA, sends the genetic messages to structures called ribosomes that act like factories producing proteins.

New Help

To reach his latest goal, Church last year hired **Michael Jewett**, a chemical and biological engineer who had been at Stanford University near Palo Alto, California. Jewett was one of the few people who had the knowledge of protein synthesis to move the effort forward. The project was done within a year.

"We really thought this was going to be hard, I can't overemphasize that," Church said. "I'm probably not articulating how exciting this is."

Jewett quickly found ways to make and assemble the 54 proteins and three RNA molecules that go into making a ribosome. Church said he now has a "tubeful" of reconstituted ribosomes, containing millions of the artificial structures. While the findings haven't been published, Church said they've been replicated many times.

Church "is a pioneer in biotechnology who, with this latest study, has established himself as a pioneer in synthetic biology," said Boston University's Collins.

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