# Biotech offers promise for producing fuel

August 9 2010, By Rachel Bernstein, Los Angeles Times

Fuel may be a messy business now, as the oil spill fouling the Gulf reminds us. But it might not always have to be. Scientists envision facilities that churn out black gold by enlisting engineered bacteria, yeast and algae to do all the dirty work.

Recently, scientists reported a significant step toward that futuristic goal: an engineered strain of the gut bacterium Escherichia coli that can make a diesel-like mixture of hydrocarbons.

The researchers, at South San Francisco-based biotech company LS9 Inc., created their biological hydrocarbon factory using genes from water-dwelling blue-green algae that naturally make tiny amounts of the fuel. They transplanted the genes into E. coli and, with a few more genetic tweaks, adjusted the bug's metabolism so it churned out 100 times more fuel than the algae did.

The finding, published in the journal Science, is the company's second announcement this year of a bacterium with fuel-production abilities.

"It's a very promising breakthrough," said Thomas Foust, a scientist at the National Renewable Energy Laboratory in Golden, Colo. Whether it will translate into a commercially successful product is another matter, he added - but he and others in the expanding field of "synthetic biology " are confident that sooner or later, something will.

In May, synthetic biology was brought into the national spotlight with the announcement of what many called "artificial life": Scientists at the J.

Craig Venter Institute in La Jolla chemically synthesized a whole bacterial genome and inserted it into a cell. The genetic material took over and turned the cell into a new type of organism.

This advance caught the public's eye, and President Barack Obama's as well - he instructed his bioethics commission to investigate the implications of the research and other synthetic biology work.

Most synthetic biologists, however, are doing something a little less Frankenstein-sounding than that. They are plucking genes from plants, bacteria, insects and more to make cellular factories that produce fuels and other chemicals such as pigments, fragrances and drugs.

They are also working toward creating catalogs of standardized genetic pieces that future designers can draw upon to make bugs with properties that scientists need.

Geneticists began altering genes almost 40 years ago, but those now in the field say the term "synthetic biology" signifies a new engineering mentality being brought to the enterprise.

In the past, usually just a gene or two was changed, with little sophisticated computer-modeling to predict the effect on a cell's delicate biochemical balance. Today, the whole mind-set is different - even the words the scientists use to discuss their tools: Things like genes and cells are described in engineering-speak as "parts" and "devices."

"This time," said Harvard genetics professor George Church, "we're trying to do the engineering right. It's a whole (different) attitude that's long overdue."

Biofuels are an especially hot target for this emerging field. Higher oil prices have improved their economic competitiveness, and there is a

growing scientific tool kit, more government funding and greater public demand for greener options.

Emeryville, Calif.-based Amyris Inc. uses engineered yeast to convert sugar into a molecule called farnesene that can be used as a diesel substitute.

The company got its start in the synthetic biology market by engineering a yeast strain to mass-produce artemisinin, a drug used to treat malaria. It has partnered with the French pharmaceutical company Sanofi-Aventis to develop a product for market by 2012.

Biofuels seemed the next logical step, said Jack Newman, Amyris' co-founder and senior vice president of research. A company trip to see Al Gore's environmental movie, "An Inconvenient Truth," he said, "sealed the deal."

Conveniently, the same metabolic system that produces the malaria drug can, with small changes, produce the fuel. The company made its first small quantities of the chemical in 2006, dubbed the "miracle droplet" by the scientists there.

In 2008, Amyris opened a pilot plant in Brazil, where sugar cane is cheap and plentiful, and last month began testing its fuel in six buses in Sao Paulo. It is working toward commercialization in 2011, Newman said.

LS9, meanwhile, has produced its fuels on a small scale and successfully tested them in engines. It is now renovating a demonstration plant in Okeechobee, Fla. The company aims to reach commercial capacity in 2013 with a plant in Brazil, said Stephen del Cardayre, LS9's vice president of research and development.

Such efforts may ultimately supplant ethanol, a well-established

alternative-energy fuel that has garnered criticism for driving up corn prices and hogging valuable agricultural land.

Ethanol was an early biofuel target because cells can make it relatively easily: Yeast naturally produces alcohol when fed corn, in a process similar to beer fermentation. Over the years, companies have worked to improve the microbe's ethanol-producing ability, but always by building on the organism's natural metabolism.

Synthetic biologists, in contrast, are granting yeast - and E. coli - entirely new metabolic capabilities to create the next generation of "green" fuels. These, they say, have advantages over ethanol: They store more energy per gallon, can be easily extracted and - importantly - can be used directly in existing diesel engines.

"Rather than changing the infrastructure to fit nature's fuel, let's change the biology," said Jay Keasling, an engineering professor at UC Berkeley who is involved with both the Amyris and LS9 efforts.

Many other alternative fuel efforts are under way - researchers are trying to move from sugar-based production toward methods that use plants and parts that aren't agriculturally useful, such as corn stalks and fast-growing switchgrass; others are working to capture algae's natural ability to convert sunlight into energy, but it will probably be 10 to 20 years before these methods reach large-scale implementation.

As young blood enters the field, ideas of what synthetic biology could do are expanding - sometimes in playful directions.

At this year's International Genetically Engineered Machine competition jamboree, to be held in November at MIT in Boston, an undergraduate team from Caltech will present its efforts toward making a three-dimensional printer out of plastic-producing E. coli.

Shine a light on the microbes and they release the plastic, explained team adviser and Caltech professor Richard Murray. By controlling the light and the location of the cells, the team proposes using the cells to lay down plastic in whatever pattern they're instructed to.

And in past competitions, college students made bacteria - dubbed "E. chromi" - that produce a rainbow of pigments, as well as others that, depending on where they are in their life cycle, smell either like bananas or wintergreen.