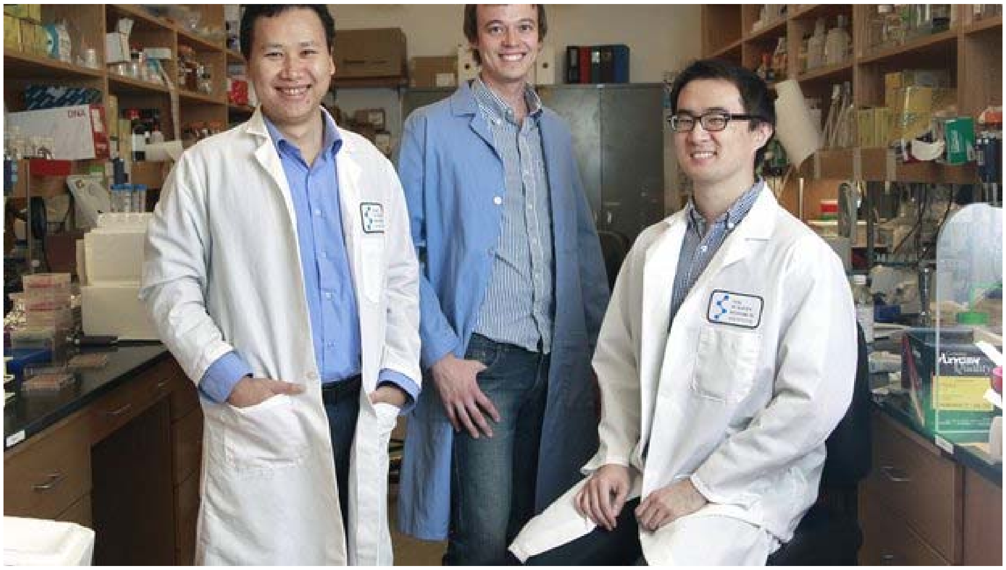
Synthorx: DNA of a new San Diego biotech

By Bradley J. Fikes (/staff/bradley-fikes/) 8:22 p.m. May 7, 2014



Tingjian Chen, left, Denis Malyshev, and Yorke Zhang of The Scripps Research Institute are part of the team that created a bacterium with artificial DNA, expanding the genetic code from four letters to six. The technology has been licensed to a new biotech in La Jolla, Synthorx — *K.C. Alfred*

As adept as scientists have become at manipulating the code of life, there's only so many words you can spell with DNA's four-letter alphabet.

Adding two letters to that alphabet, as Floyd Romesberg and colleagues at The Scripps Research Institute announced Wednesday (http://www.utsandiego.com/news/2014/may/07/romesberg-dna-scripps-d5SICSTP/), exponentially increases the possibilities. La Jolla's Synthorx (http://synthorx.com/) was founded on those possibilities, including more targeted medicines, vaccines and nanoscale electronics.

For nanoelectronics, the DNA with the expanded alphabet can be used outside of cells to precisely position components, said Court Turner, president of Synthorx and a partner at La Jolla's Avalon Ventures.

Romesberg designed the expanded alphabet to allow addition of molecular linkers, which could attach to drugs, or, as it turns out, various metals. This could lead to something the electronics industry constantly demands, smaller batteries, microprocessors and higher data density on microchips, Turner said.

"You can arrange the unnatural DNA in any architecture you like, and link metals, which you can then make nanowires out of," Turner said. "You could link on gold or magnesium, then you would be able to go across the architecture in nanowires."

The metals would line up only where the linkers are, forming wires running parallel to the DNA. After the nanowires are laid down, the DNA could be burned off if desired, since its function as a molecular scaffold is no longer needed, Turner said.

Synthorx will need a partner with nanoelectronics expertise to pursue that application, he said.

"It's not unheard of to use charged bioorganic materials whether peptides (protein fragments) or others to make batteries on a smaller scale, with more power," Turner said. "That's certainly possible with Floyd's technology."

The unnatural DNA could also be used to identify items, either to track them or identify them as genuine, Turner said.

"People, including the Secret Service, are now trying to find ways to use DNA for tracking or anti-counterfeiting for currency," Turner said. "You could imagine taking specific sequences, similar to a bar code, and spraying it on currency or guns or anything you would want to keep track of."

For biomedical uses, the expanded six-letter alphabet makes it possible to design a much greater assortment of large-molecule protein drugs, Romesberg said. Protein drugs such as the cancer medicine Rituxan, made in genetically engineered cells, are big commercial success stories.

“The cell does all the work for you,” Romesberg said. “It makes those proteins. All you have to do is purify it.”

But DNA makes proteins with just 20 naturally occurring amino acids.

“These amino acids, in a lot of cases, just aren’t that interesting from a chemist’s perspective,” Romesberg said. “There’s a lot of things they can’t do.”

With an expanded genetic alphabet of two unnatural letters along with the four natural ones, the bacterium used by Synthorx can use up to 172 amino acids. This will allow production of better drugs that bind more tightly to their target, he said.

Synthorx now has two employees, and may expand to six by year’s end, Turner said. The company’s website is Synthorx.com (http://Synthorx.com).