Wild Types

A blog for ASBMB Today by Rajendrani Mukhopadhyay

An artificial peptide-making machine

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Ribosomes (http://en.wikipedia.org/wiki/Ribosome) are huge machines inside biological cells that build proteins by attaching amino acids, one by one, to each other in a specific sequence. In this week's issue of Science, researchers describe (http://www.sciencemag.org/content/339/6116/189.abstract) a synthetic version of the ribosome made out of simpler, nonbiological molecules. David Leigh (http://www.catenane.net/publicats/profbio2.html) at the University of Manchester (http://www.chemistry.manchester.ac.uk/index.html)says the work demonstrates that "highly modular small-molecule machines can be designed to perform useful and complex tasks in synthesis."

Leigh says his group's interest has been in designing molecular-scale machines (http://www.catenane.net/index.html). Indeed, there has been a longstanding effort among scientists to make machines out of chemicals that can mimic the complex biological machinery of life. For example, molecular machines have been designed to do mechanical work and store information.

Leigh's group decided to tackle a nonbiological version of the ribosome because the organelle "is an awe-inspiring machine that performs a task that cannot be achieved using conventional chemistry other than through multistep synthesis," says Leigh.

The machine they designed is based on a molecular ring threaded through a molecular axle. The ring and axle are called a rotaxane (http://en.wikipedia.org/wiki/Rotaxane). The machine moves along a molecular strand, picking up amino acids that block its way. A thiolate group on the ring removes amino acids and transfers them to a peptide-elongation site where they get fashioned into a peptide chain in an orderly manner.

Leigh admits that the design of this machine was challenging because “lots of different components are required to do different jobs.” The investigators had to come up with a way to make sure that the chemistry of one component didn’t interfere with that of another. For example, says Leigh, if the machine is not designed correctly, the amide groups of the strand can sequester the copper ions needed to direct the threading, which stops the machine from coming together.

The investigators demonstrated that ~10^{18} molecular machines could work act in parallel to make impressive milligram quantities of a peptide with a single sequence. But Leigh hastens to add that “it’s important to stress that our molecular machine is extremely primitive in comparison to the ribosome and is nowhere near as functional.”

But still, he envisions artificial ribosomes could be used for other types of chemical reactions that use different building blocks, opening up the possibility of making new types of molecules with different properties and functionalities. For now, Leigh’s group is focusing on making larger peptides and proteins with their artificial ribosome. They hope to watch the peptides and proteins fold at the single-molecule level and better understand the elusive relationship between protein sequence and function.