

Chemists solve biological challenge

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Chemistry professor Ronald Kluger and PhD candidate Svetlana Tzvetkova have made discoveries that could not only allow scientists to generate new kinds of proteins —the building blocks of life—but also eventually lead to practical applications such as simplifying drug development and manufacturing.

These chemists have stretched the bounds of nature and genetics by chemically, rather than biologically, modifying the steps involved in creating proteins. Kluger became interested in the possibility of manipulating proteins after learning about efforts to produce “designer amino acids.”

“I was intrigued by the possibility that someone could actually attempt to make proteins with amino acids that aren’t specified in the genetic code at all,” Kluger explained.

Nature defines 20 different amino acids that can link together to make proteins. But protein creation begins with deoxyribonucleic acid (DNA), which sends out genetic instructions via an RNA message (mRNA) to the ribosomes in our cells. Transfer ribonucleic acids (tRNA) collect the amino acids and bring them to the ribosomes. The tRNA then aligns with mRNA so the amino acids can join to form proteins. The catch is that an amino acid has to be activated by a specific enzyme before the tRNA can scoop it up.

Kluger and former student Lisa Cameron found that they could mimic

the critical action of this enzyme when they combined common inorganic chemicals called lanthanum salts with a chemically activated amino acid. It was Tzvetkova who showed that this chemical mimic will allow an amino acid to attach to the complex tRNA molecule in just the right place. These results were e-published in the Dec. 4 issue of the *Journal of the American Chemical Society*. In principle, this research could be developed to allow tRNA to collect new “unnatural” amino acids, which according to Kluger, could “give anyone the ability to create totally new materials that have nothing to do with the genetically defined functions of proteins.”

Kluger and Tzvetkova aren't the first researchers to try to create a “ribosome-ready” tRNA. Scientists have been attempting this type of modification for years but “their method involved a lot of difficult steps. They started to mutate the enzymes instead of doing a chemical alteration,” said Kluger, who explained that the elegance of his method is that it changes how amino acids are added to tRNA “in one step, just the way nature does it.”

But just because the solution was simple doesn't mean that finding it was. This type of approach has never been tried before. Kluger said that he and his students “were constantly told that this direct chemical route was impossible” and added that “we were novices from day one in this project. Each time we got to another stage of this, we were novices again.”

These researchers are continuing their work by incorporating their artificially attached amino acids into proteins. Kluger feels that the “possibilities are well beyond our imagination or our lifetime.”

Source: University of Toronto

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