Bioengineering team's 'circuit' work may benefit gene therapy

March 6 2018

From left: Dr. Leonidas Bleris, associate professor of bioengineering, and Tyler Quarton, bioengineering graduate student, said they hope their work has a big impact on synthetic biology and gene therapy. Credit: University of Texas at Dallas

Researchers at The University of Texas at Dallas have designed genetic "circuits" out of living cellular material in order to gain a better understanding of how proteins function, with the goal of making improvements.

Tyler Quarton, a bioengineering graduate student, and Dr. Leonidas Bleris, associate professor of bioengineering in the Erik Jonsson School of Engineering and Computer Science, said they hope their work, published in *Systems Biology and Applications*, has a big impact on synthetic biology and gene therapy.

The Genetic Symphony

Every living cell contains a compilation of genes, which serves as the blueprint for all the biological activity within a cell. Bleris explained this system by comparing genes to musicians. Their collective expression creates a genetic symphony that can invoke a multitude of cellular emotions, calming or exciting the cell when appropriate. Stretching this analogy, the conductor of this symphony, equipped with a waving baton, can quiet an individual or whole section if they begin to play too loudly.

In the genetic context, consider this hushing gesture as the expression of small non-coding RNA molecules called microRNA. They are responsible for the fine-tuning of gene expression—which results in an output such as a protein—through repression. MicroRNA are integral components of a cell's development and homeostasis. MicroRNA that misfire can contribute to progression of various diseases, including cancer.

Quarton and Bleris engineered a custom microRNA-based system by stitching together pieces of genetic material taken from a variety of living organisms, including humans, viruses and jellyfish. Their plan was to place this system inside human cells and use its output to analyze the nuanced behavior of microRNA.

"We built genetic circuits that operate in individual cells that are able to detail how microRNA repression changes in different biological contexts," Quarton said.

Potential Applications

Quarton said he hopes their research influences future designs of genetic circuits that will be used in personalized medicine and gene therapy. Gene therapy involves transplanting normally functioning genes into cells to replace missing or damaged material in order to correct genetic disorders.

Quarton's background is in physics. He used mathematics and statistics to create simple models that other scientists could use as they develop their own systems.

"These models can help other researchers trying to understand or use microRNAs," he said. "By using principles of math and physics in synthetic biology, we uncovered specific properties of microRNA that can be used in future applications for targeted and smart therapeutics."

He also said that this research could shed light on natural genetic redundancies and other diseases where microRNA are not at physiological levels.

"Synthetic biology is important for gene therapy applications, and our methodology may assist in building more robust and reliable therapeutics in the future," Bleris said.

More information: Tyler Quarton et al, Mapping the operational landscape of microRNAs in synthetic gene circuits, *npj Systems Biology and Applications* (2018). DOI: 10.1038/s41540-017-0043-y

Provided by University of Texas at Dallas