Researchers expand synthetic biology's toolkit: New method could enable reprogramming of mammalian cells

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Boston University Biomedical Engineer Ahmad Khalil led the research team that engineered a new method for developing the genetic components synthetic biologist use to build networks. Credit: Boston University

Through the assembly of genetic components into "circuits" that perform logical operations in living cells, synthetic biologists aim to artificially empower cells to solve critical problems in medicine, energy and the environment. To succeed, however, they'll need far more reliable genetic components than the small number of "off-the-shelf" bacterial parts now available.

Now a new method developed by Boston University biomedical engineers Ahmad S. Khalil and James J. Collins -- and collaborators at Harvard Medical School, Massachusetts General Hospital and MIT -- could significantly increase the number of genetic components in synthetic biologists' toolkit and, as a result, the size and complexity of the genetic circuits they can build. The development could dramatically enhance their efforts not only to understand how biological organisms behave and develop, but also to reprogram them for a variety of practical applications.

Described in the August 2 online edition of *Cell*, the method offers a new paradigm for constructing and analyzing genetic circuits in eukaryotes -- or organisms whose cells contain nuclei, which include everything from yeasts to humans. Instead of constructing these circuits with off-the-shelf parts from bacteria and porting them into eukaryotes, as most synthetic biologists do, Khalil and his collaborators have engineered these circuits using modular, functional parts from the eukaryotes themselves.

With funding from the Howard Hughes Medical Institute, the Defense Advanced Research Projects Agency and other sources, the research team built their synthetic genetic circuit parts from a class of proteins, known as zinc fingers, which can be programmed to bind desired DNA sequences. The modularity of the new parts enables a wide range of functions to be engineered, the construction of much larger and more complex genetic circuits than what's now possible with bacteria-based parts, and ultimately, the development of much more powerful applications.

"Our research may lead to therapeutic applications, such as the dynamic modification and control of genes and genetic networks that are important in human disease," said Khalil. Potential medical applications include stem cell therapeutics for a wide variety of injuries and diseases

and in-cell devices and circuits for diagnosing early stages of cancer and other diseases. The new method may also equip groups of cells to perform higher-order computational tasks for processing signals in the environment in sensing applications.

Provided by Boston University