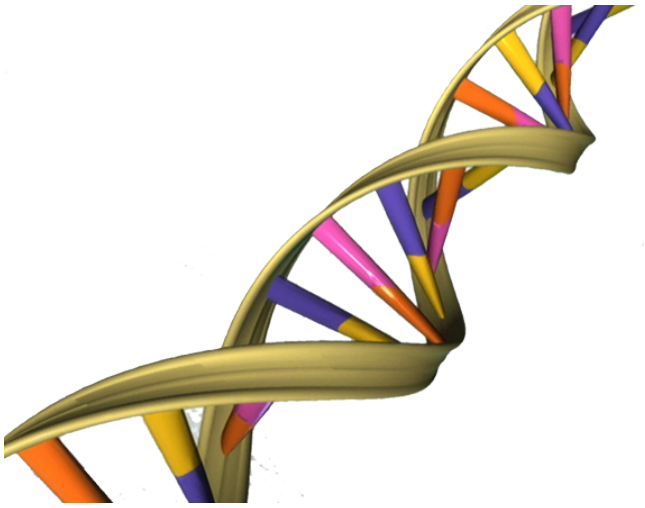
Programming human cells to follow sets of logical instructions

29 March 2017, by Bob Yirka



A depiction of the double helical structure of DNA. Its four coding units (A, T, C, G) are color-coded in pink, orange, purple and yellow. Credit: NHGRI

(Phys.org)—A team of researchers at Boston University has developed a new way to engineer mammalian cells that allows for programming them to behave in desired ways. In their paper published in the journal *Nature Biotechnology*, the team describes their technique and where they believe such technology is heading.

As scientists around the world look for new ways to prevent and treat diseases, new techniques are emerging, some of which involve programing human cells to behave in desired ways—such as killing cancer cells. In this new effort, the researchers have developed a new way to program mammalian cells using DNA recombinases.

To learn how to program cells researchers have worked with simple organisms such as bacteria, which has led to the use of proteins called transcription factors that regulate genes.

Unfortunately, that technique has proven unsuitable for programming mammalian cells because it does not produce the same results consistently in all environments. To get around that problem, the researchers instead chose to work with DNA recombinases—enzymes that can be used to cut DNA in predesignated ways and put them back together in new and useful ways.

Cutting DNA and sewing it back together allows for programming cells because DNA controls which proteins a cell makes. By cutting and sewing in a certain way, the researchers were able to induce a human kidney cell to produce a fluorescent protein which caused the cell to light up under desired conditions. Inserting other snippets allowed for modifying recombinases that were activated only in the presence of a certain chemical. By cutting multiple DNA snippets, adding new ones and sewing them back together, the researchers found that they were able to create 113 unique circuits that demonstrated a 96.5 rate of success. In one instance, they created a bio-circuit that mimicked a Boolean lookup table—it had six inputs that allowed for executing 16 logical operations.

The work by the team was a proof of concept, they're optimistic that their technique could be used to create new therapies such as bolstering the immune system by programming T cells—perhaps causing them to attack tumor cells. Another possibility is using the technique to program stem cells to grow into desired tissue.

More information: Benjamin H Weinberg et al. Large-scale design of robust genetic circuits with multiple inputs and outputs for mammalian cells, *Nature Biotechnology* (2017). DOI: 10.1038/nbt.3805

Abstract
Engineered genetic circuits for mammalian cells often require extensive fine-tuning to perform as intended. We present a robust, general, scalable

system, called 'Boolean logic and arithmetic through DNA excision' (BLADE), to engineer genetic circuits with multiple inputs and outputs in mammalian cells with minimal optimization. The reliability of BLADE arises from its reliance on recombinases under the control of a single promoter, which integrates circuit signals on a single transcriptional layer. We used BLADE to build 113 circuits in human embryonic kidney and Jurkat T cells and devised a quantitative, vector-proximity metric to evaluate their performance. Of 113 circuits analyzed, 109 functioned (96.5%) as intended without optimization. The circuits, which are available through Addgene, include a 3-input, two-output full adder; a 6-input, one-output Boolean logic look-up table; circuits with small-molecule-inducible control; and circuits that incorporate CRISPR–Cas9 to regulate endogenous genes. BLADE enables execution of sophisticated cellular computation in mammalian cells, with applications in cell and tissue engineering.

APA citation: Programming human cells to follow sets of logical instructions (2017, March 29) retrieved 29 November 2021 from https://phys.org/news/2017-03-human-cells-logical.html