Engineers build first-ever multi-input 'plug-and-play' synthetic RNA device

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Engineers from the California Institute of Technology have created a "plug-and-play" synthetic RNA device--a sort of eminently customizable biological computer--that is capable of taking in and responding to more than one biological or environmental signal at a time.

In the future, such devices could have a multitude of potential medical applications, including being used as sensors to sniff out tumor cells or determine when to turn modified genes on or off during cancer therapy.

A synthetic RNA device is a biological device that uses engineered modular components made of RNA nucleotides to perform a specific function--for instance, to detect and respond to biochemical signals inside a cell or in its immediate environment.

Created by Caltech's Christina Smolke, assistant professor of chemical engineering, and Maung Nyan Win, postdoctoral scholar in chemical engineering, the device is made up of modules comprising the RNA-based biological equivalents of engineering's sensors, actuators, and information transmitters. These individual components can be combined in a variety of different ways to create a device that can both detect and respond to what could conceivably be an almost infinite number of environmental and cellular signals.

This modular device processes these inputs in a manner almost identical to the logic gates used in computing; it can perform AND, NOR, NAND, and OR computations, and can perform signal filtering and signal gain operations. Smolke and Win's creation is the first RNA device that can handle more than one incoming piece of biological information. "There's been a lot of work done in single-input devices," notes Smolke. "But this is the first demonstration that a multi-input RNA device is possible."

Their work was published in the October 17 issue of the journal *Science*.

The modular--or plug-and-play--nature of the device's design also means that it can be easily modified to suit almost any need. "Scientists won't have to redesign their system every time they want the RNA device to take on a new function," Smolke explains. "This modular framework allows you to quickly put a device together, then just as easily swap out the components for other ones and get a completely different kind of computation. We could generate huge libraries of well-defined sensors and assemble many different tailored devices from such component libraries."

Although the work in the Science paper was done in yeast cells, Smolke says they have already shown that they can translate to mammalian cells as well. This makes it possible to consider using these devices in a wide variety of medical applications.

For instance, ongoing work in Smolke's laboratory is looking at the packaging of these RNA devices--configured with the appropriate sensor modules--in human T cells. The synthetic device would literally be placed within the cell to detect certain signals--say, one or more particular biochemical markers that are given off by tumor cells. If those biomarkers were present, the RNA device would signal the T cell to spring into action against the putative tumor cell.

Similarly, an RNA device could be bundled alongside a modified gene as part of a targeted gene therapy package. One of the problems gene therapy faces today is its lack of specificity--it's hard to make sure a modified gene meant to fix a problem in the liver reaches or is inserted in only liver cells. But an RNA device, Smolke says, could be customized to detect the unique biomarkers of a liver cell--or, better yet, of a diseased liver cell--and only then give the modified gene the go-ahead to do its stuff.

Source: California Institute of Technology

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