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**Bauer Fellow Yaakov 'Kobi' Benenson: 'Each human cell already has all of the tools required to build these biocomputers on its own.'**

*In a first, scientists develop tiny implantable biocomputers*

## Devices' scans could revolutionize medicine

By David Baron

FAS Communications

Researchers at Harvard and Princeton universities have taken a crucial step toward building biological computers, tiny implantable devices that can monitor the activities and characteristics of human cells. The information provided by these "molecular doctors," constructed entirely of DNA, RNA, and proteins, could eventually revolutionize medicine by directing therapies only to diseased cells or tissues.

The results will be published this week in the journal *Nature Biotechnology*.

"Each human cell already has all of the tools required to build these biocomputers on its own," says Harvard's Yaakov "Kobi" Benenson, a Bauer Fellow in the Faculty of Arts and Sciences' Center for Systems Biology. "All that must be provided is a genetic blueprint of the machine and our own biology will do the rest. Your cells will literally build these biocomputers for you."

Evaluating Boolean logic equations inside cells, these molecular automata will detect anything from the presence of a mutated gene to the activity of genes within the cell. The biocomputers' "input" is RNA, proteins and chemicals found in the cytoplasm; "output" molecules indicating the presence of the telltale signals are easily discernable with basic laboratory equipment.

"Currently, we have no tools for reading cellular signals," Benenson says. "These bio-



Courtesy Kobi Benenson

**This work is a crucial step toward building biological computers, tiny implantable devices that can monitor the activities and characteristics of human cells.**

computers can translate complex cellular signatures, such as activities of multiple genes, into a readily observed output. They can even be programmed to automatically translate that output into a concrete action, meaning they could either be used to label a cell for a clinician to treat or they could trigger therapeutic action themselves."

Benenson and his colleagues demonstrate in their *Nature Biotechnology* paper that biocomputers can work in human kidney cells in a culture. Research into the system's ability to monitor and interact with intracellular cues such as mutations and abnormal gene levels is still in progress.

Benenson and colleagues, including Ron Weiss, associate professor of electrical engineering at Princeton, have also developed a conceptual framework by which various phenotypes could be represented logically.

A biocomputer's calculations, while mathematically simple, could allow researchers to build biosensors or medicine delivery systems capable of singling out very specific types or groups of cells in the human body. Molecular automata could allow doctors to specifically target only cancerous or diseased cells via a sophisticated integration of intracellular disease signals, leaving healthy cells completely unaffected.

Benenson and Weiss worked in collaboration with undergraduate Keller Rinaudo, postdoctoral researcher Leonidas Bleris, and summer intern Rohan Madamsetti, all at Harvard, and with Sairam Subramanian, a graduate student at Princeton. Their research is supported by Harvard University and a center grant from the National Institute of General Medical Sciences.