

## YAAKOV BENENSON

Age: 28 | Graduate student | Weizmann Institute of Science

Yaakov Benenson wants to shrink your doctor. Or more accurately, he wants to replace physicians with molecular machines that diagnose and treat diseases with phenomenal precision, each what he calls a “doctor in a cell.” ■ In just five years, Benenson has taken the concept from drawing board to test-tube prototype. Working at the Weizmann Institute of Science in Rehovot, Israel, he has built molecular devices—essentially DNA strands and enzymes—able to analyze genetic changes associated with lung and prostate cancers and to release a drug in response. These prototypes are “a beautiful work of molecular and conceptual integration, pointing the way toward truly integrating diagnostics with therapeutics,” says George Church, director of the Center for Computational Genetics at Harvard Medical School. ■ “Using these tiny diagnostic machines, we could selectively treat only the diseased cells,” Benenson says. For example, the prototype device for small-cell lung cancer assesses the activity of four genes. Cancerous cells produce extra RNA copies of each of these genes. Consecutive sections of the DNA strand in the prototype bind, in turn, to these RNA strands; when they do, an enzyme chops them off. If all of the cuts are made properly, the enzyme releases and activates an anticancer drug that has been tethered to the DNA in an inactive form. ■ Benenson’s molecular machines offer a unique combination of precision and flexibility. A single one of them can be designed to look for up to 10 different diagnostic markers before it releases its drug payload. The devices can also be tailored to several different diseases through simple-to-make changes in their DNA sequences. ■ These machines represent a quantum leap not only in medicine but also in DNA computing. Benenson’s molecular “doctors”—which are computers in the sense that they store information and analyze it following a yes/no logic—are “directed at a practical interface with biomedicine rather than losing an abstract race with existing computers on their own turf,” says Church. ■ It will be a while before molecular machines replace existing systems of diagnosis and treatment: Benenson estimates three or four years before even simple versions that work in a living cell are ready, and perhaps decades before they can be tried in people. If the DNA doctors prove as successful in the body as they have in the lab, though, they might spark a revolution in medicine.

