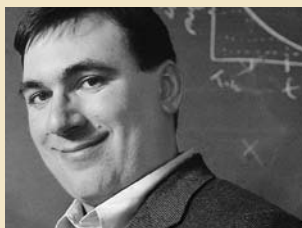


Electrifying Cells

CELLS “SPEAK” THEIR OWN, ELOQUENT LANGUAGE. HOW TO TRANSLATE THIS biochemical banter into signals understandable by electronic gadgetry has been a major technical challenge for scientists. Using electronics is appealing, as it would eliminate the need for the bulky optical instrumentation used routinely today to visualize cellular activities.

Now, HHMI investigator Milan Mrksich and his colleague Joel H. Collier have devised an ingenious approach to making cells that are themselves “electric” in that they produce a readily detectable electrochemical output of their own. Their achievement could create the cellular equivalent of bloodhounds—biosensors that send an electrical signal when biowarfare agents, pollutants, or clinical diagnostic molecules are present. Also, drug companies could use such cells to screen libraries of compounds to detect those that switch on specific disease targets on the cell.

Mrksich, at the University of Chicago, and Collier, of the University of Cincinnati, reported their new approach in the February 14, 2006, issue of *Proceedings of the National Academy of Sciences*.



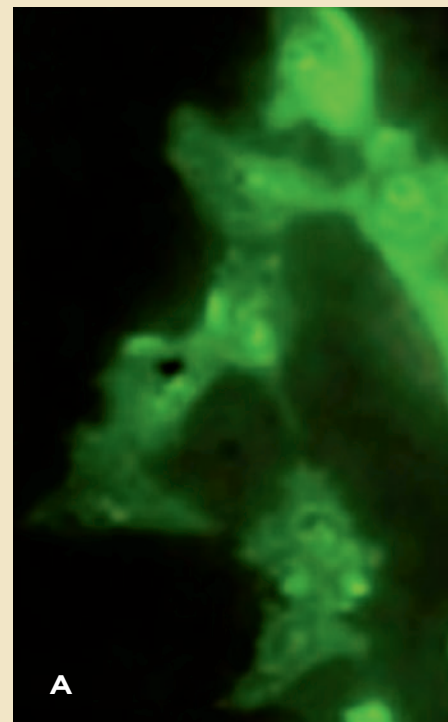
MILAN MRKSICH

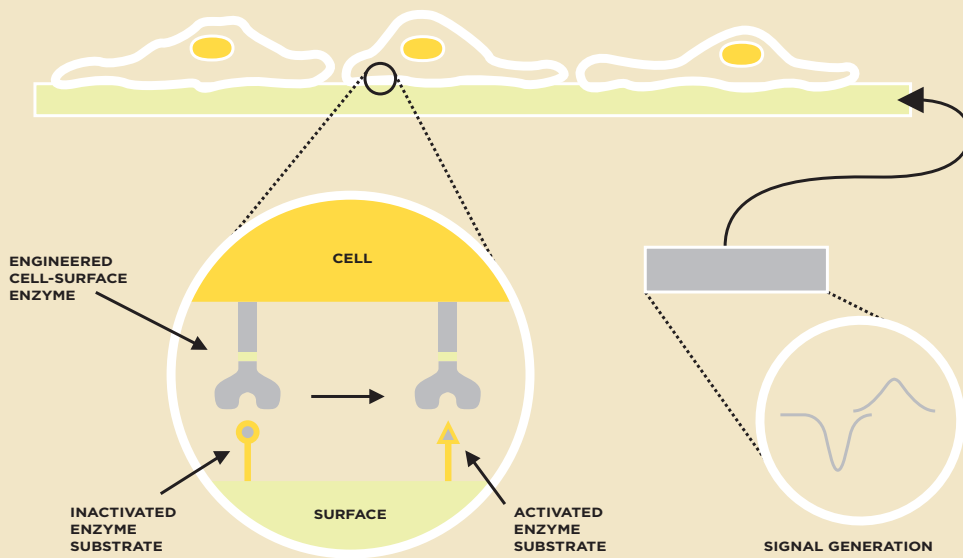


JOEL H. COLLIER

First the researchers engineered Chinese hamster ovary cells to produce on their surfaces a fungal enzyme called cutinase, which is not normally made by mammalian cells. Cutinase was chosen because it catalytically transforms its target compound, or ligand, from an electrically inert substance into an electroactive one. To be able to detect this transformation, the researchers tethered a synthetic form of the ligand on an engineered electrode surface. When cutinase acts on the ligand, an electric signal materializes and is detected.

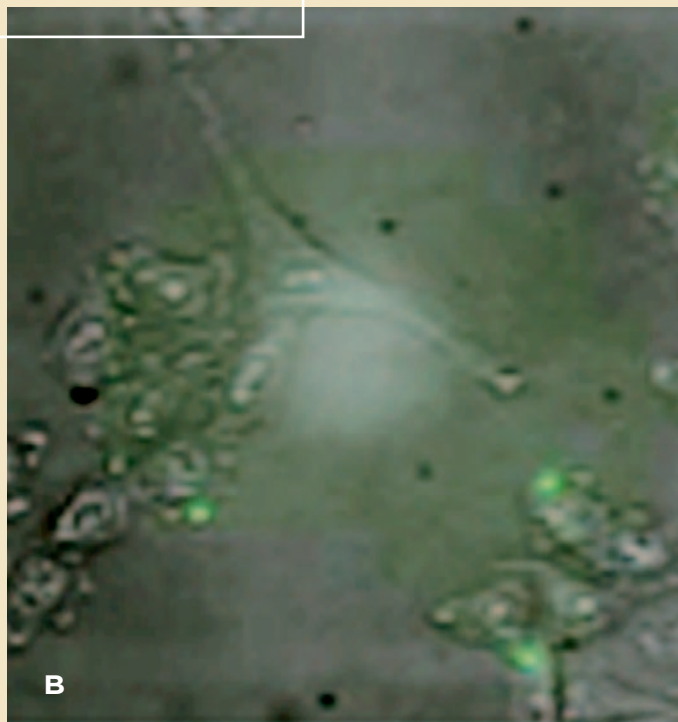
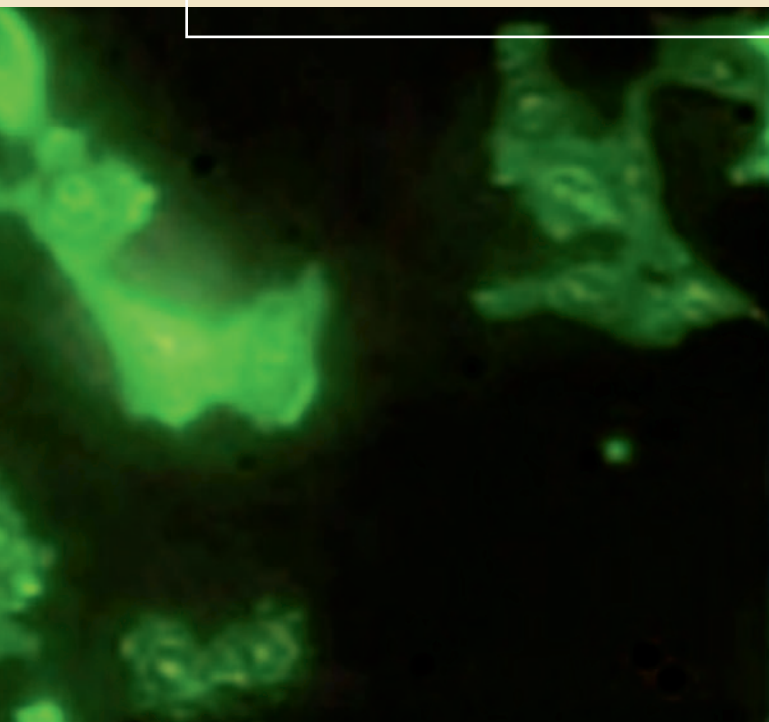
With this technique, the researchers aim to have a cell that speaks not only its own “native language” but also a telltale electrical signal. ■ —DENNIS MEREDITH





LEFT: In the technique invented by Milan Mrksich and Joel Collier, Chinese hamster ovary cells engineered to produce the fungal enzyme cutinase are adhered to a receiver surface containing the enzyme's target molecules. When the cutinase transforms its target from an electrically inactive state to an active one, the electrodes in the receiver surface can detect a signal. Importantly, the researchers found, normal cellular processes are not disrupted by either the production of cutinase or the attachment of the cells to the receiving surface. And because cutinase is not native to mammalian cells, the chemical reaction it triggers is distinct from those of its host cell, greatly reducing biochemical "noise."

BELOW: By staining their engineered cells with a fluorescent antibody to cutinase, the researchers confirmed that the cells (A) were actively expressing the enzyme, as compared to normal cells (B). The researchers believe their proof-of-concept experiment with cutinase raises the possibility of engineering cells to produce other such signaling molecules as well, thereby enabling "multichannel" monitoring of many cell processes simultaneously.



Science images: Courtesy of Mrksich and Collier labs; adapted from PNAS 103(7): 2021-2025. ©2006. Mrksich; Aynsley Floyd/AP © HHMI / Collier; Courtesy of Joel Collier