New sensors streamline detection of estrogenic compounds

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Researchers have engineered new sensors that fluoresce in the presence of compounds that interact with estrogen receptors in human cells. The sensors detect natural or human-made substances that alter estrogenic signaling in the body.

The study appears in the journal *Biotechnology and Bioengineering*.

Estrogen occurs naturally in the body (in the form of 17-beta-estradiol), and a variety of plants (such as soybeans), pharmaceuticals, microbial byproducts and industrial chemicals (such as bisphenol A, in plastics) are also known to activate or block the activation of estrogen receptors in human cells.

"There are so many estrogenic compounds in our environment, and some of them could be a danger to health," said University of Illinois chemical and biomolecular engineering professor Huimin Zhao, who led the research. Zhao also is an affiliate of the chemistry and biochemistry departments, the Center for Biophysics and Computational Biology, and the Institute for Genomic Biology, all at Illinois. "We are concerned about estrogenic compounds because they interact with the estrogen receptor, which plays an important role in many important biological processes, like reproduction, bone growth, cell differentiation and metabolism."

The estrogen receptor is also implicated in a majority of breast cancers, he said, with compounds that activate it potentially spurring the growth of cancer cells.

The researchers used part of the estrogen receptor itself in the design of their new sensors. They took the region of the receptor that binds to estrogenic compounds (called the "ligand-binding domain) and added two halves of a fluorescent protein that glows only when the halves are reunited. The ligand-binding domain changes its conformation when it binds to an estrogenic compound. This change, the researchers hoped, would draw the two parts of the fluorescent protein together to produce a signal.

In a series of trials, the researchers found that two of their sensors reliably signaled the presence of estrogenic compounds. The first, "sensor 2," differentiated between compounds that activate and those that block estrogen receptors, glowing more brightly in the presence of one and dimming when bound to the other. A second bioengineered molecule, "sensor 6," fluoresced in the presence of both types of compounds, making it a reliable indicator of chemicals that bind to the receptor.

When incubated in human cells, the sensors responded to estrogenic compounds within a few hours, Zhao said, with the fluorescent signals gradually increasing in strength up to 24 hours. "And also the sensitivity is pretty high," he said. "Of course it depends on the compound that you're testing; different compounds will have different affinities. But for a truly estrogenic compound, we can detect at the nanomolar level, a very low level."

These are the first such sensors to work in human cells without costly additional chemical steps, he said.

The new sensors will help researchers and clinicians quickly and efficiently determine whether a food, drug or chemical substance interacts with estrogen receptors in human cells, Zhao said.

More information: "A New Fluorescence Complementation Biosensor for Detection of Estrogenic Compounds," onlinelibrary.wiley.com/doi/10 … 2/bit.23254/abstract

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