Researchers quicken drug discovery method via zombie-like cells

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Jessica Irvin, an undergraduate research assistant from Galloway, New Jersey, grinds a plant as preparation for creating a plant extract to be used in research. Credit: University of Alabama in Tuscaloosa

Researchers are using zombie-like cells that behave normally on the outside, but are filled with magnetic particles inside, to screen potential drugs from natural products.

Discovered at The University of Alabama, the method could quicken a laborious task that slows drug discovery, according to findings in a paper published in the journal *Nanoscale*.

The method uses magnetic nanoparticles coated with a biological cell membrane as a lure to fish out pharmacologically active compounds from plants and other natural organisms such as fungi. It quickly sorts through hundreds, possibly thousands, of compounds found in a natural product in a few days, a process that can take weeks or months using traditional screening methods.

The work was done in the labs of Dr. Lukasz M. Ciesla, UA assistant professor of biological sciences, and Dr. Yuping Bao, UA associate professor of chemical and biological engineering. The lead author is Dr. Jennifer Sherwood, a former researcher in Bao's lab who earned her doctorate from UA in 2018.

"This solves one of the main problems and bottlenecks in drug discovery from natural products," Ciesla said. "It dramatically speeds up the process of the identification of new drug leads."

About 70 percent of drugs approved by the federal Food and Drug Administration were first identified in nature, but teasing out possible chemical compounds from the abundance of plants is time consuming.

Pharmaceutical research has turned mostly to libraries of synthesized chemical compounds tuned for a specific purpose. However, nature is more diverse in the compounds it creates, and plants produce compounds designed for a biological response. The same pathways a chemical uses to ward off an insect, for example, can interact with humans.

"Plants produce chemicals with structures we cannot possibly imagine," Ciesla said.

Dr. Lukasz Ciesla examines a plant extract in his lab on the UA campus. Credit: University of Alabama in Tuscaloosa

Natural samples, though, are complex. An extract of a plant produces scores of chemical compounds, and finding one that shows pharmacological promise is done by isolating and screening them individually.

The new method uses ionic solvents to leech out the innards of a cell and wrapping the cell's shell around iron oxide nanoparticles. They are inserted into a plant extract.

The encapsulation of the magnetic beads of iron oxide with a cell membrane keeps the function of the transmembrane proteins that act as receptors for active compounds, which bind to the coated nanoparticles.

Like a zombie moving despite being dead, the cell is no longer an active human cell, yet its membrane continues to function. This advantage differentiates it from computational methods that simulate chemical interaction in one, static state, Ciesla said.

"We have the receptor in its natural environment behaving the way it normally behaves in a cell," he said.

If there is a compound in the natural extract that can interact with the receptor, they will stick to the surface of the nanoparticles. A magnet can be used to separate the nanoparticles from the extract, and solvents can detach them, yielding the possible pharmacologically active compounds.

The UA team used cell membranes with nicotinic receptors as a coating, but any transmembrane receptor could be used as way to search for compounds, Ciesla said.

"The cool thing of this project is it's not limited," Bao said. "All you need to do is switch out the cell type, and you can fish out a different type of drug candidate."

Ciesla stresses this method is only a first step in the long process of creating drugs to treat a disease, but it shows promise in helping find medicinal uses from natural products.

More information: Jennifer Sherwood et al. Cell-membrane coated iron oxide nanoparticles for isolation and specific identification of drug leads from complex matrices, *Nanoscale* (2019). DOI: 10.1039/C9NR01292C

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