Scientists remove yeast cell's sex drive and turn it into a cannabis tracker

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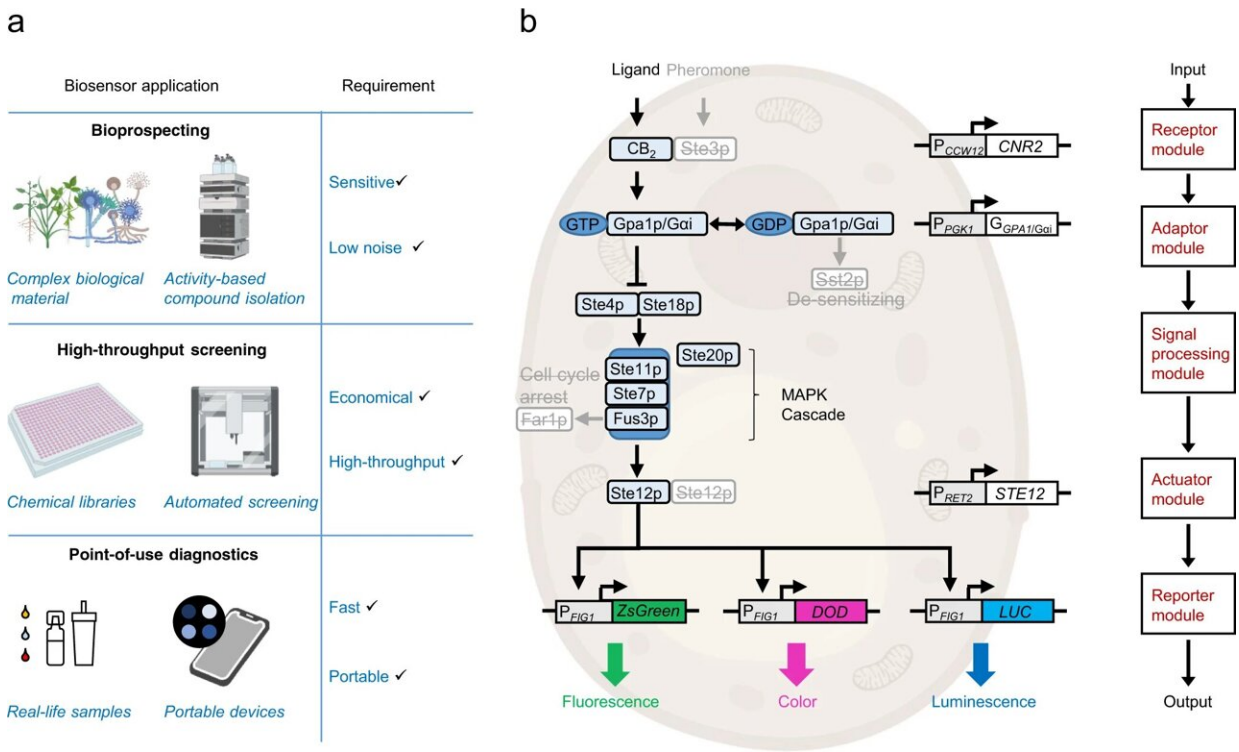

The CB_2 cannabinoid biosensor design. **a** The biosensor was developed to enable diverse applications with different requirements. For example, bioprospecting of complex biological material requires the biosensor to be sensitive but with low background. This is because the bioactive compounds are often present in minute amounts among many other compounds potentially interfering with detection. On the other hand, screening of chemical libraries requires a biosensor that is robust, economical, and amenable to high-throughput workflow. For this, fast-growing and easy-to-prepare cells that can be handled with non-expensive material and equipment are desirable. In the case of a biosensor for point-of-use diagnostics outside the lab, this needs to be easy to use, fast, and operable by the

equipment available to non-experts. **b** The cannabinoid biosensor is based on a modular design. Interchangeable parts can be introduced into the receptor, adaptor, actuator, or reporter modules (red), while the native yeast Gβ and Gγ subunits and the MAPK cascade are employed as a signal-processing module without further modification. The parts are integrated into a chassis strain KM111 where genes encoding the yeast pheromone pathway components to be replaced (pheromone receptor *STE3*, Gα subunit *GPA1*, and pheromone pathway master regulator *STE12*) have been removed (strikethrough) alongside with *SST2* (which returns Gα to its inactive state) and *FAR1* (which triggers cell-cycle arrest). This design enables the functional insertion of different GPCR receptors by pairing them with the corresponding Gpa1p/Gα chimera. According to the specific requirements of each application, the biosensor can be fitted with an optimal reporter construct including, for example, a fluorescence, color, or luminescence reporter. Credit: *Nature Communications* (2022). DOI: 10.1038/s41467-022-31357-6

Researchers at the University of Copenhagen's Faculty of Science have modified a yeast cell to sense the active substances in cannabis and get it to turn red when it does. The result paves the way for more actors to discover new medicinal substances and for a new type of drug test that can be done with a smartphone.

Yeast cells are simple organisms. They do two things in life: eat and propagate. Now, researchers at the University of Copenhagen's Department of Plant and Environmental Sciences have equipped common baker's yeast cells with a new function.

The researchers substituted the yeast cell's sex drive with a sense of taste and smell that allows it to detect cannabinoids, the active substances in cannabis. Going one step further, the researchers made the yeast turn red or glow when it successfully detects cannabinoids. The study has been published in *Nature Communications*.

"We have made a living sensor out of the yeast cell, which can now sense cannabinoids or molecules that have the same function as cannabinoids even if they look very different than cannabinoids. Among other things, the biosensor can be used to look for new substances with the same properties as cannabinoids. This could democratize medicinal development so that pharmaceutical companies aren't the only ones equipped to discover new substances," says Professor Sotirios Kampranis of the Department of Plant and Environmental Sciences, who headed the research.

Turns red when sensing cannabinoids

Humans use hundreds of different GPCRs (G-protein-coupled receptors) to taste and smell. In our noses alone, 400 different GPCRs make it possible for us to detect and distinguish between the smell of roses and freshly baked bread, each of which activates different GPCRs that then signal the brain.

Along with his research colleagues, Professor Kampranis swapped the GPCR that yeast cells use to sense the opposite sex in an environment, with the GPCR we humans use to recognize cannabinoids. At the same time, the researchers complemented the yeast cell's genetic material with a set of new genes that make it turn red or even glow when it senses cannabinoids nearby.

"The yeast cell now emits a signal when there are cannabinoids in the yeast cell's environment. This allows us to screen thousands of plants for substances with therapeutic potential. And we can also investigate whether people are on drugs or whether someone is trying to smuggle illegal cannabinoids or "designer drugs" through an airport checkpoint," explains Professor Sotirios Kampranis.

Discovered four new substances in one day

Cannabinoids are known to be connected with sleep, appetite and pain relief. In fact we have them naturally in our bodies where they are called endocannabinoids. This is precisely why the researchers chose to encode the ability to find cannabinoids in the yeast cells. But in principle, they could have done so for opioids or any other group of medicinal substances.

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There is no doubt that the yeast cell can find new substances. In initial tests, the researchers used the yeast cell to study 1600 random substances from a vast chemical compound library available at the University of Copenhagen. It didn't take long to get a bite.

"In a single day, the yeast cell found four undiscovered substances that had never been associated with anti-inflammatory properties or pain relief, but could potentially be used for these purposes," says Sotirios Kampranis.

When drug companies look for new drugs today, it is with the help of state-of-the-art robotics and laboratory equipment that universities and other non-commercial entities will never be able to afford. That the researchers have developed an alternative, may allow for more people to hunt for helpful substances in nature.

"It's a crowdsourcing approach whereby smaller laboratories can find more new potential substances for pharmaceutical use. I don't see it as competition with pharmaceutical companies—but as something that can create a synergy between independent players in the scientific world and

the pharmaceutical industry," says Professor Kampranis.

Smartphone accessory can find drugs

The researchers also developed a portable plastic device with a yeast cell biosensor in it. Plant material, saliva, urine, blood, material from a suitcase, or whatever one would like for the yeast cell to test, is placed into the gizmo.

The device then uses the smartphone's camera to see if the yeast cells light up, delivering its result in just 15 minutes. The application could be able to help police officers and others track down drugs at airports or administer drug tests.

"We can test for both natural cannabinoids and designer drugs—chemical substances that have very different structures—with the same effects as cannabinoids. In principle, we could also adapt the yeast cell to be able to detect opioids like morphine, fentanyl and oxycodone," says Sotirios Kampranis.

The device can be 3D printed or assembled using materials easily obtained online. The researchers are now working to make the test tool available free of charge, for as many people as possible, but at the same time be able to maintain control for maintenance and further development.

More information: Karel Miettinen et al, A GPCR-based yeast biosensor for biomedical, biotechnological, and point-of-use cannabinoid determination, *Nature Communications* (2022). DOI: 10.1038/s41467-022-31357-6

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