

New biosensors measure toxic drugs in cancer, arthritis, and organ transplant patients

December 19 2021



Researchers are a step closer to transforming a US\$70 billion global diagnostic industry with new designer biosensors that 'switch on' colour or electrical responses to drugs used in cancer, arthritis, and organ transplant treatment. Credit: Queensland University of Technology (QUT)

Researchers are a step closer to transforming a US\$70 billion global diagnostic industry with new designer biosensors that 'switch on' color or electrical responses to drugs used in cancer, arthritis, and organ transplant treatment.

Researchers from the CSIRO-QUT Synthetic Biology Alliance have proven their modular approach to constructing small molecule biosensors—[artificial proteins](#) designed to capture biomarkers of choice and produce measurable responses—in collaboration with Clarkson University in the US and Pathology Queensland.

In two separate studies, biosensors were adapted to accurately measure immunosuppressant drugs cyclosporine A, tacrolimus and rapamycin, and anticancer drug methotrexate, which requires close monitoring to reduce toxicity and organ damage.

Lead researcher Professor Kirill Alexandrov said the [protein](#) biosensors had potential to expand [patient care](#) by enabling sophisticated tests on cheaper lab equipment and new point-of-care devices.

"Proteins are at the core of a US\$70-billion-dollar global diagnostic market that relies heavily on central lab processing," Professor Alexandrov said.

"Our [biosensor technology](#) will enable tests like therapeutic drug monitoring on less sophisticated equipment that you are more likely to find in small, regional or remote labs and hospitals."

Future tests may also require smaller biological samples with researchers proving a biosensor could accurately measure cyclosporine A levels in one microlitre blood samples.

"With further development, the [biosensor technology](#) could lead to a

fingerstick test that potentially provides doctors with patient results in 3-5 minutes during a standard consultation," Professor Alexandrov said.

Professor Alexandrov said protein complexity and fragility made construction and use of protein biosensors difficult, but the [modular design](#) helped alleviate the problem and could be adapted to potentially target any small molecule—not just therapeutic drugs.

He said the new proteins were produced by engineered bacteria, altered using recombinant DNA technology to produce artificial switch molecules that were tailored to recognize a particular drug.

"The protein biosensors are 'switched off'—like an electrical circuit with a missing piece. Only the targeted biochemical in human fluids like blood or saliva can complete the circuit and 'switch on' a signal proportional to the amount of biomarker detected," he said.

When activated, the different protein biosensors produce either a change of color for hue-based readings, or electrochemical current.

Professor Alexandrov said the team experimented with applications using common glucometer technology to develop a cheap, portable, and accurate device.

"Activated electrochemical biosensors broke down glucose and generated electrons as by-products to produce electrical current proportional to the amount of captured [target molecule](#)," he said.

"The Clarkson team also demonstrated the feasibility of multiplexing this technology to detect two different biomarkers at the same time."

Despite experiment success, Professor Alexandrov said glucometer technology was use-specific, and researchers would need to re-engineer

devices and [manufacturing processes](#) for new clinical uses.

"There are a huge number of parameters to reconcile when building a medical device. It's incredibly hard and that's why new diagnostic technologies come to the market very slowly," he said.

Professor Alexandrov is from the QUT Centre for Genomics and Personalised Health, the QUT Centre for Agriculture and the Bioeconomy, and the QUT Faculty of Science. He said future research would focus on protein biosensor stability, sensitivity, and manufacturability.

Studies validating different biosensor designs have been recently published by [Angewandte Chemie](#) (11 October 2021) and [Nature Communications](#) (8 December 2021).

More information: Zhong Guo et al, Design of a methotrexate-controlled chemical dimerization system and its use in bio-electronic devices, *Nature Communications* (2021). [DOI: 10.1038/s41467-021-27184-w](#)

Provided by Queensland University of Technology

Citation: New biosensors measure toxic drugs in cancer, arthritis, and organ transplant patients (2021, December 19) retrieved 11 May 2024 from <https://medicalxpress.com/news/2021-12-biosensors-toxic-drugs-cancer-arthritis.html>

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