Detecting levels of antibiotics in blood paves the way to individualized treatment

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A new methodology for rapidly measuring the level of antibiotic drug molecules in human blood serum has been developed, paving the way to applications within drug development and personalised medicine.

The study, published today in *Nature Nanotechnology*, describes the exploitation of a sensor for measuring the concentration of effective antibiotics in blood, giving an indication of their efficiency against disease causing pathogens, for instance multidrug resistant hospital "superbugs".

This development could potentially give a far greater understanding of the effectiveness of drug dosages required for different individuals, reducing potential toxic effects, allowing personalised treatment for patients and leading to new insights into optimal clinical regimes, such as combination therapies.

When effective, antibiotic molecules impose cellular stress on a pathogen's cell wall target, such as a bacterium, which contributes to its breakdown. However, competing molecules in solution, for example serum proteins, can affect the binding of the antibiotic to the bacterium, reducing the efficacy of the drug. Serum proteins bind to drugs in blood and, in doing so, reduce the amount of a drug present and its penetration into cell tissues.

As the amount of antibiotics that bind to serum proteins will vary between individuals, it is extremely valuable to be able to determine the

precise amount of the drug that is bound to serum proteins, and how much is free in the blood, in order to be able to accurately calculate the optimum dosage.

Existing biosensors on the market do not measure cellular stress, however, the nanomechanical sensor exploited by a group of researchers from the London Centre for Nanotechnology (LCN) at UCL, the University of Cambridge, the University of Queensland and Jomo Kenyatta University of Agriculture and Technology, can accurately measure this important information even when antibiotic drug molecules are only present at very low concentrations.

The researchers coated the surface of a nanomechanical cantilever array with a model bacterial membrane and used this as a surface stress sensor. The sensor is extremely sensitive to tiny bending signals caused by its interactions with the antibiotics, in this case, the FDA-approved vancomycin and the yet to be approved oritavancin, which appears to deal with certain vancomycin-resistant bacteria, in the blood serum.

This investigation has yielded the first experimental evidence that drug-serum complexes (the antibiotics bound to the competing serum proteins) do not induce stress on the bacteria and so could provide realistic in-vitro susceptibility tests for drugs and to define effective doses which are effective enough but less toxic to patients.

In the future, the researchers believe that with a suitably engineered surface probe, this sensor could be paired with customised drug delivery for anaesthetics, anti-cancer, anti-HIV and antibacterial therapies.

The lead author of the study, Dr. Joseph W. Ndieyira of the LCN, said "This discovery represents a major advance in our fundamental understanding of the pathways between chemical and mechanical signals in a complex media, such as blood serum, and how this information can

be used to tune the efficacy of drugs and to minimise the potential toxic side effects."

Dr. Ndieyira added, "Monitoring the levels of active free drugs in serum can be crucial in honing therapeutic solutions for patients to enhance drug administration. This will be particularly helpful in addressing problems of drugs which have to be used in very precise quantities and where there are large differences in how drugs affect individuals and groups. For example, overuse of antibiotics can fuel resistance to drugs or underuse of anaesthetics may lead to a patient regaining consciousness during an operation."

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