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A GOLDEN OPPORTUNITY FOR IMPLANTABLE SENSORS

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Science is awash with implantable sensors, but most are developed to measure just one analyte. This is a problem, according to Dr. Katharina Kaefer, a postdoctoral biomedical chemist in the Nanobiotechnology group at the University of Mainz. "Many platforms are not generalizable and cannot be easily changed to detect something different," she says.

A gold star sensor

Kaefer and her team set out to create a subcutaneous sensor suitable for patients who need long term monitoring of a molecule in the blood. They turned to gold for several reasons: it is non-toxic and stable in the body, and its colour doesn't fade over time. "Gold nanoparticles act like small antennae for light," says Kaefer, "they strongly absorb and scatter light, and therefore appear colourful." The nanoparticles can be attached to a variety of "hooks" or receptors that capture the molecule of interest. For their proof-of-concept experiments, the scientists used a short DNA sequence called an aptamer that specifically hooks the antibiotic kanamycin. As the aptamer wraps around kanamycin, the modified refractive index changes the colour of the gold nanoparticles.

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"Gold nanoparticles act like small antennae for light."

From sensor to implant

The aptamer-gold system was then embedded into a porous hydrogel to create a wafer-thin implant. Hydrogels have a similar consistency to tissues, allowing them to evade immune rejection, says Kaefer. To test their device, the team implanted the sensor into a fold of skin in the belly of hairless rats. Once implanted, cells and capillary blood vessels grow into the pores in the hydrogel, streaming blood past the sensor. When the team injected kanamycin into the rat's tail vein, they could detect a colour change in the sensor by shining white light onto one side of the skin flap and measuring the absorbance spectrum on the other side.

Endless possibilities

The beauty of this sensor is that by modifying the receptor "hooks" it can be adapted to measure nearly anything in the blood. "We could also use proteins or polymers as different classes of receptors to specifically bind an analyte that we are interested in," says Kaefer. Aptamers are endlessly adaptable, explains Kaefer, as well as being stable and already available for many different molecules. "It's a really generalizable approach," she says.

Kaefer and her team carefully engineered their sensor for long-term implant, paying attention to stability in the body and minimizing immune rejection. This makes the sensor particularly useful for tracking how an analyte in the blood changes over time. There is a myriad of applications for such a sensor, such as glucose sensing in diabetes. This technology could even track inflammation in chronic disease, spot evidence of rejection in transplant recipients or flag disease progression in cancer. "You could also monitor drug concentrations," says Kaefer. "So many drugs have a small therapeutic window. It's important that patients receive the right dose so that they do not metabolize the drug too fast or too slow." The device could even be used to establish the pharmacokinetics of drugs.

Next steps

The team is brimming with ideas for future work. To make the system more user friendly for real people, they want to work on measuring the output via reflection off the skin surface. Another task on the list is to shrink the device even further.

They also want to try measuring different analytes. "We hope to find more and more specialist collaboration partners who are interested in different questions," says Kaefer who would especially like to hear from medical doctors with requests for measuring specific molecules with clinical applications.

Challenges

The team has sidestepped many of the challenges in this project by integrating multidisciplinary working from the start. Kaefer was lucky to have mentors with complementary expertise in chemistry and physiology. "This was the perfect combination," she says. According to her, a project like this requires interdisciplinary teams to handle the biology and the chemistry, not forgetting the physics. "If you want

to shine light on your sensor and detect in skin, you have to see how you arrange your optical components etc.," she says.

Luckily, the cost of gold nanoparticles was not one of the challenges of this project. "People often ask if its really expensive to use gold," laughs Kaefer, " but you use really tiny amounts, so price is not really a problem."

REFERENCES

¹ Implantable Sensors Based on Gold Nanoparticles for Continuous Long-Term Concentration Monitoring in the Body. Katharina Kaefer et al, Nano Letters 2021 21 (7), 3325-3330. DOI: 10.1021/acs.nanolett.1c00887

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