Sensor technology can improve accuracy of prostate cancer diagnosis, research shows

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New research has shown how a smart sensor chip, able to pick up on subtle differences in glycoprotein molecules, can improve the accuracy and efficiency of prostate cancer diagnosis.

Researchers at the University of Birmingham believe that the novel technology will help improve the process of early stage diagnosis.

Glycoprotein molecules, proteins that are covalently bound to one or more carbohydrate chains, perform a wide range of functions in cell surfaces, structural tissues and blood. Because of their essential role in our immune response, they are useful clinical biomarkers for detecting prostate cancer and other diseases.

The team of chemical engineers and chemists, created a sensor chip with synthetic receptors along a 2D surface to identify specific, targeted glycoprotein molecules that are differentiated by their modified carbohydrate chains.

In doing so, they developed a more accurate and efficient way of diagnosing prostate cancer than the current tests which rely heavily on antibodies.

These antibodies are expensive to produce, subject to degeneration when exposed to environmental changes (such as high temperatures or UV light) and more importantly, have a high rate of false-positive readings.

Professor Paula Mendes said, "There are two key benefits here. Crucially for the patient, it gives a much more accurate reading and reduces the number of false positive results. Furthermore, our technology is simple to produce and store, so could feasibly be kept on the shelf of a doctors' surgery anywhere in the world. It can also be recycled for multiple uses without losing accuracy."

Most previous research on detecting glycoproteins centered on the protein of the molecule. Problematically for diagnosis, the protein part of glycoproteins does not always change if the body is diseased.

The findings, published in the journal *Chemical Science*, show how the rate of false readings that come with antibody based diagnosis can be reduced by the smart technology that focuses on the carbohydrate part of the molecule.

The complex sugar structure in glycoprotein can be subtly different between samples from healthy and diseased patients. In order to achieve more accurate readings, the team wanted to identify the presence of disease by detecting a particular glycoprotein which has specific sugars in a specific location in the molecule.

Professor Mendes added, "Biomarkers such as glycoproteins are essential in diagnostics as they do not rely on symptoms perceived by the patient, which can be ambiguous or may not appear immediately. However, the changes in the biomarkers can be incredibly small and specific and so we need technology that can discriminate between these subtle differences - where antibodies are not able to."

To engineering the sensor chip, the team developed a smart surface with nano-cavities that fit the particular target glycoprotein.

To create the nano-cavities, the sugar part of the prostate cancer

glycoprotein is reacted with a custom-designed molecule that contains a boron group at one end (the boron linkage forms a reversible bond to the sugar). The other end of this custom molecule is made to react with molecules that have been tethered to a gold surface. The glycoprotein is then bound to the surface via its sugar groups, before the rest of the surface is blocked with a third molecule.

When the glycoprotein is removed (by breaking the reversible boron bonds) it leaves behind a perfect cast. Within that cast, there was a special area with boron-containing molecules that can recognise a specific set of sugars.

Professor Mendes said, "It is essentially a lock, and the only key that will fit is the specific prostate cancer glycoprotein that we're looking for. Other glycoproteins might be the right size, but they won't be able to bind to the very specific arrangement of boron groups."

Dr John Fossey added, "It's estimated that one in eight men will suffer from prostate cancer at some point in their life, so there's a clear need for more accurate diagnosis. By focussing on the sugar, we appear to have hit the 'sweet spot' for doing just that. Our focus now is to take this technology and develop it into something accessible to people across the world."

The team also hope that further investment, and collaboration with commercial partners, will open the door to adapting the current technology for other diseases.

Dr Fossey continued, "We believe that this could be applicable to other diagnostic challenges. Lots of diseases produce specific glycoproteins, so there are a number of possible avenues to improve the accuracy of our diagnoses."

Provided by University of Birmingham