News & Analysis

Highlighting the latest news and research in bioanalysis

Novel biosensor may be an important step towards diagnosing early-stage Parkinson's disease

ZnO nanowire/graphene foam electrode is capable of detecting low levels of uric acid in patients with Parkinson's disease

Researchers from Sungkyunkwan University (Suwon, Republic of Korea), in collaboration with Harbin University of Science and Technology (Harbin, China) and Chungnam National University Hospital (Daejeon, Republic of Korea), have reported on the development of a novel biosensor capable of detecting biomarkers associated with Parkinson's disease (PD), potentially representing a significant advance towards diagnosing PD in its early stages.

The study describes the fabrication of vertically aligned ZnO nanowire arrays on 3D graphene foam, which was used to selectively detect uric acid (UA), dopamine (DA) and ascorbic acid (AA) by a differential pulse voltammetry method. Speaking to *Future Science Group*, lead researcher Young Hee Lee, from Sungkyunkwan University, explained that low levels of DA are strongly linked to neurological disorders such as PD and schizophrenia. Since DA coexists with UA and AA in serum and the extracellular fluid of the CNS, Lee commented that, using conventional solid electrodes, "It is difficult to simultaneously detect DA, UA and AA in a mixture with high selectivity and sensitivity due to overlapping oxidation potentials, insufficient surface area and/or the limited kinetic accessibility of each species."

According to the study, the optimized ZnO nanowire/graphene foam electrode provided a high surface area and high selectivity with a detection limit of 1 nM for UA and DA. Lee commented, "The key features of our structural design are a large surface area with mesoporous 3D graphene structures to facilitate ion diffusion easily; high conductivity from 3D graphene foam; and active sites of ZnO surface for high selectivity."

In order to carry out the analysis, serum was extracted from human peripheral blood of healthy individuals, in addition to PD patients. This process involved proton and electron generation at the surface of the ZnO nanowire arrays, causing the transfer of electrons to the electrode. Using differential pulse voltammetry measurements with the ZnO nanowire/graphene foam electrode, the samples were analyzed for UA levels. The average UA concentrations for the healthy individuals and the PD patients were 355 ± 30 and 265 ± 20 µM, respectively. According to Lee, "This clear reduction in UA levels in the serum of PD patients with reliable statistics ($p < 0.001$) strongly implies that our approach is a significant step forward, which we believe will be beneficial for diagnosing PD and monitoring disease progression."

Currently, diagnosis of PD essentially relies on the assessment of clinical symptoms and a blood test for PD is a major goal for researchers. Speaking to *Future Science Group* about the significance of the study, Lee commented, "Being able to accurately test for biomarkers associated with the disease with simple blood tests would be a major breakthrough in diagnosing PD in the early stages when treatments are most likely to be effective."

In terms of future work, the team intends to improve on the electrode design in order to achieve the simultaneous and accurate detection of other disease biomarkers and biomolecules. Lee added that, "Since the oxidation potential of some biomolecules may overlap, there is no guarantee that they can always succeed. Therefore, we will proceed by testing individual diseases, including cancers, in order to improve their sensor design and make it as generally applicable as possible."

– Written by Hannah Coaker

Source: Yue HY, Huang S, Chang J *et al.* ZnO nanowire arrays on 3D hierachical graphene foam: biomarker detection of Parkinson's disease. *ACS Nano* 8(2), 1639–1646 (2014).

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Noninvasive probe developed for *Staphylococcus aureus* detection

In a recent publication in *Nature Medicine*, a group of researchers from the University of Iowa (IA, USA) present a novel method for *Staphylococcus aureus* detection. The approach is based on the activity of micrococcal nuclease – an enzyme secreted by *S. aureus*.

> "On assessment in mice bearing Staphylococcus aureus *muscle infections, the probe was activated at infection sites only, demonstrating potential for this probe in bacteria detection.*"

The team has developed a synthetic probe that contains both a flurophore and a quencher, which only emits light when cleaved. The probe has been optimized so that it is only cleaved by micrococcal nuclease, thus avoiding early cleavage in the bloodstream. On assessment in mice bearing *S. aureus* muscle infections, the probe was activated at infection sites only, demonstrating potential for this probe in bacteria detection.

> "*We believe that we are significantly improving the actual methods for detecting bacteria with a simple approach, which we expect to be cheap, fast and reliable.*"

Current diagnosis of *S. aureus* infection is a lengthy process, including biopsy and subsequent analysis. As corresponding author of the piece, James McNamara explains, "We've come up with a new way to detect staph bacteria that takes less time than current diagnostic approaches."

First author of the paper, Frank Hernandez, expands on this point, "Every year in the USA, half a million people become infected by *S. aureus* bacteria, and 20,000 of those who become infected die. We believe that we are significantly improving the actual methods for detecting bacteria with a simple approach, which we expect to be cheap, fast and reliable."

– Written by Alice O'Hare

Sources: A quicker, cheaper way to detect staph in the body: http://now.uiowa.edu/2013/07/quicker-cheaper-way-detect-staph-body; Hernandez FJ, Huang L, Olson ME *et al.* Noninvasive imaging of *Staphylococcus aureus* infections with a nuclease-activated probe. *Nat. Med.* 20, 301–306 (2014).

Mouth guard sensor to provide real-time fitness monitoring

Researchers based at the University of California, San Diego (CA, USA) have developed a sensor in the form of a mouth guard that can measure saliva metabolites to monitor the real-time health status of the wearer. The measurement of saliva via this method is noninvasive, and can provide a good indication of metabolism and hormone levels, as saliva has good correlation with blood concentrations of numerous analytes.

The research states that, "Until recently, most of the activity on wearable sensors has focused on monitoring vital signs from physical signals such as electrocardiography and pulse oximetry, while wearable chemical sensors have received limited attention." Previous saliva chemical sensors include dental tattoos and dentures; however, this method is much less invasive.

Lactate levels have been previously screened *in vitro* for monitoring fitness, therefore they were also tested in this study. The screen-printed electrode, which is incorporated into the sensor, produces a current in the presence of lactate. The sensor can selectively detect lactate and is stable in saliva for up to 2 h.

> "*The measurement of saliva via this method is noninvasive, and can provide a good indication of metabolism and hormone levels, as saliva has good correlation with blood concentrations of numerous analytes.*"

The study concludes, "Such noninvasive mouth guard metabolite biosensors could tender useful real-time information regarding a wearer's health, performance and stress level, and thus hold considerable promise for diverse biomedical and fitness applications."

> "*The sensor can selectively detect lactate and is stable in saliva for up to 2 h.*"

In the future the researchers intend to "focus on miniaturization and integration of the amperometric circuits and electronics for data acquisition, processing, and wireless transmission, as well as critical assessment of all potential toxicity and biocompatibility concerns."

– Written by Lisa Parks

Source: Kim J, Valdés-Ramírez G, Bandodkar A *et al.* Non-invasive mouthguard biosensor for continuous salivary monitoring of metabolites. *Analyst* 139(7), 1632–1636 (2014).

Partnership hopes to advance the discovery of therapies for idiopathic pulmonary fibrosis

Boehringer Ingelheim Pharmaceuticals, Inc. (Ingelheim am Rhein, Germany) and Duke Clinical Research Institute (DCRI; NC, USA) have entered into a partnership with the goal of achieving a deeper understanding of idiopathic pulmonary fibrosis (IPF), a progressive and fatal lung disease for which there are currently no US FDA-approved prescription medications.

The companies will work in collaboration to initiate a prospective, multi-center IPF registry in the USA, as well as establish a biomarker bank to identify potential blood or genetic markers of the disease that correlate with patient outcomes.

"We are excited by this research partnership with DCRI as it represents an important step to understanding a disease for which there has been a minimal amount of understanding," said Tunde Otulana, Senior Vice President at Boehringer Ingelheim Pharmaceuticals. "Our partnership with DCRI represents an important step for our company. We believe this approach will allow us to accomplish together certain research goals that we might not otherwise have achieved separately."

> *"The companies will work in collaboration to initiate a prospective, multi-center idiopathic pulmonary fibrosis registry in the USA, as well as establish a biomarker bank to identify potential blood or genetic markers of the disease that correlate with patient outcomes."*

According to a press release from Boehringer Ingelheim, the partnership plans to launch a project that will focus on the development of the IPF Outcomes Registry, a long-term study that will collect and analyze data over time from a large group of patients. This prospective, observational study is anticipated to afford a better understanding of the natural progression of IPF, with the view to developing treatment approaches for patients suffering with the condition.

– Written by Hannah Coaker

Source: Boehringer Ingelheim and Duke Clinical Research Institute form collaborative partnership to study the natural history of idiopathic pulmonary fibrosis: http://us.boehringer-ingelheim.com/news_events/press_releases/press_release_archive/2014/01-30-2014-boehringer-ingelheim-duke-clinical-research-institute-collaborative-partnership-study-natural-history-idiopathic-pulmonary-fibrosis-ipf.html

Microfluidic platform sheds light on metastasis

A global group of scientists have developed a microfluidic 3D *in vitro* model to analyze breast cancer metastasis to bone, which occurs in nearly 70% of patients with advanced breast cancer.

The microfluidic platform mimics the bone microenvironment, which the team used to study the extravasation of highly metastatic breast cancer cells. Using this platform, the study aimed to determine why certain breast cancers spread specifically to bone and not to other organs. Roger Kamm, a researcher on the study from the Massachusetts Institute of Technology (MA, USA), commented, "An example is that breast cancer will form metastatic tumors in bone, but not, for example, muscle. Why is this, and what factors determine it? We can use our model system both to understand this selectivity, and also to screen for drugs that might prevent it."

> *"Using this platform, the study aimed to determine why certain breast cancers spread specifically to bone and not to other organs."*

The study identified two important proteins, the bone-secreted chemokine CXCL5 and the cancer cell receptor CXCR2, which were demonstrated to play a key role in metastasis and, therefore, could be potential targets for drug development.

Looking to the future, the team is planning to study cancer metastasis in other organs. They hope that the platform could be used in personalized medicine to develop optimal cancer therapies for individual patients, as explained by Kamm, "One might envision using cells from the cancer patient to produce models of different organs, then using these models to determine the optimal therapy from a variety of available drugs."

– Written by Jessica Thorne

Sources: A microchip for metastasis: http://web.mit.edu/newsoffice/2014/a-microchip-for-metastasis-0206.html; Bersini S, Jeon JS, Dubini G *et al.* A microfluidic 3D *in vitro* model for specificity of breast cancer metastasis to bone. *Biomaterials* 35(8), 2454–2461 (2014).

The editorial team welcomes suggestions for timely, relevant items for inclusion in the news. If you have newsworthy information, please contact: Alice O'Hare, Commissioning Editor, *Bioanalysis*
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