A game-changer in HIV diagnostics?

Martin Hedström from CapSenze HB and **Attila Agoston** of MFKK Invention and Research Centre Services discuss the development of a revolutionary technique for detecting HIV

Could you provide some background into the CapHIV proposal?

MH: The discussions that eventually led to the successful CapHIV proposal were initiated in the autumn of 2010 during the kickoff meeting for another EU Seventh Framework (FP7) project. The whole project idea started as a joint venture between MFKK Invention and Research Center, Lund University and CapSenze. With MFKK as the proposed coordinator, the other partners – Phenosystems, Lionex and Antibody Barcelona – were asked to join the consortium.

AA: We were looking for a partner with specific biosensor expertise for another project. This was our first contact with Martin. After the aforementioned kickoff meeting, he visited MFKK and presented his revolutionary label-free biosensor technology. We quickly found a fruitful synergy between the companies. We agreed to target HIV screening as an application in order to utilise the extremely high sensitivity of CapSenze sensor and to demonstrate its real capabilities.

What challenges do you foresee in translating the high-sensitive capacitive sensor concept from laboratory to praxis, and how do you plan to overcome them?

MH: There are a multitude of challenges when dealing with bioanalytical methods, especially with techniques aimed at the field of clinical diagnostics where the analytical answer certainly defines the specific treatment of a patient. Furthermore, when dealing with ultrasensitive measurements, the main challenges lie in the sensitivity of the method to external disturbances. Hence, both stability and robustness are parameters that need to be put into focus. Another major challenge for the development of the capacitive biosensor assay is the full automation to ensure ease of use in spite of the complexity of the method. Aiming for point-of-care diagnoses outside classified laboratories, the most important challenge is to ensure the biological safety of the operator.

AA: This would be a long list, but luckily most of it is already behind us! MFKK's role was to realise the sensor concept in a way that made the biologically active electrode easily replicable even outside the laboratory environment. This is a challenge when working with such highly classified pathogens like HIV. We succeeded in realising a disposable sensor cartridge with a hermetically sealed docking concept ensuring biological safety for the user as well as the precise electrode pair geometry for the measurement. This is just one example; there are several more challenges on the biochemical part. CapSenze, accompanied by Lund University, Lionex, and Antibody Barcelona, did a good job on that part.

How early do you see this new detection method being implemented?

MH: As mentioned, a complete validation process is needed for the technique to be accepted as a medical device within clinical diagnostics. However, with the current state of technological maturity, the instrument should have the potential to be on the market within two years.

How will the CapHIV detection system affect subsequent patient care and practice?

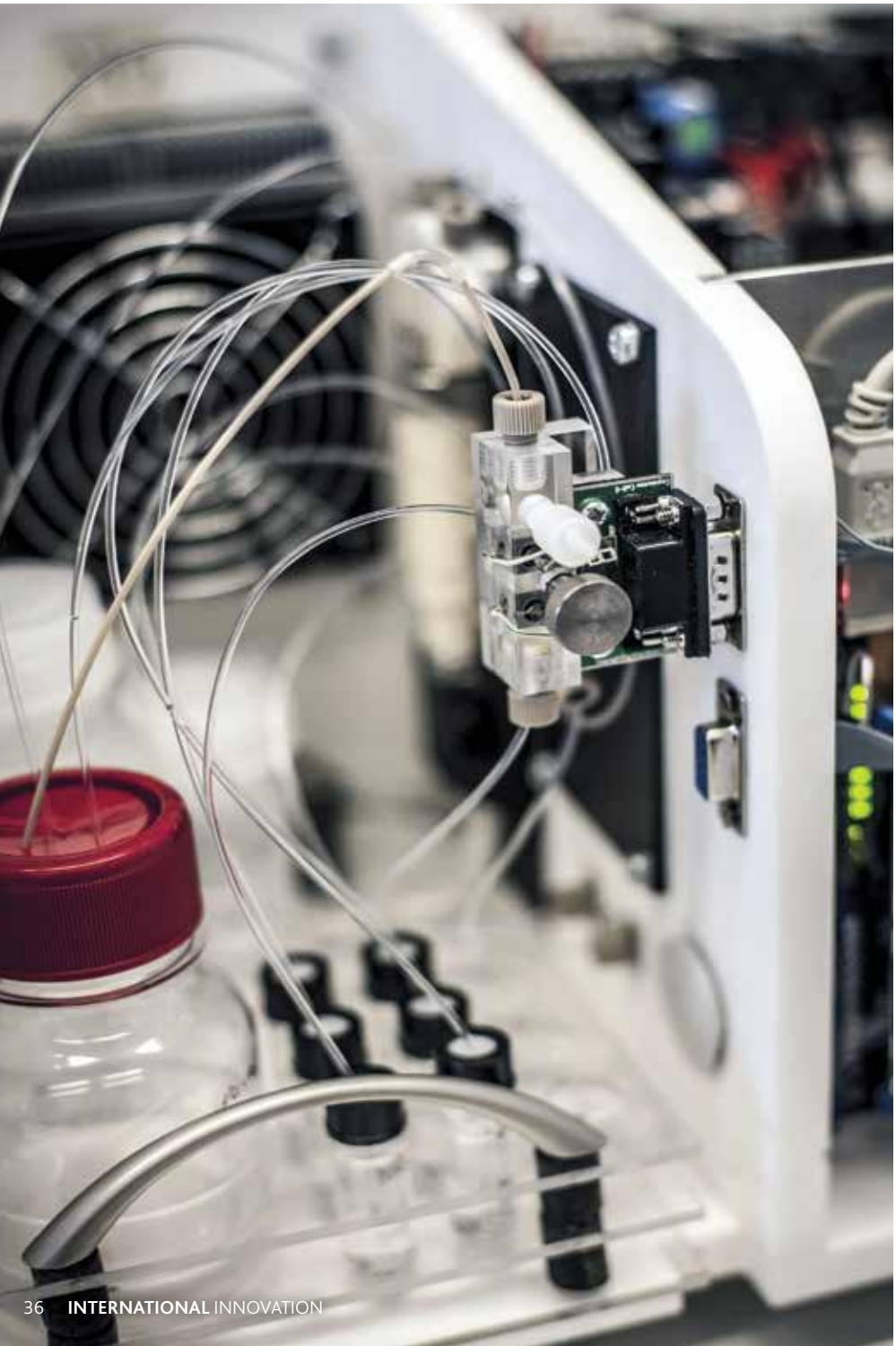
MH: The more sensitive the analytical instruments available, the sooner it will become possible to detect antibodies or other viral markers after infection. The benefit of early detection is primarily that the risk of further spread of infection is drastically reduced. It is also scientifically proven that early therapy significantly improves the effectiveness of the treatment over the whole course of the disease. This results in reduced patient agony, less handling and lower costs.

What does the future hold for CapSenze and the CapHIV proposal?

MH: As the core technology owner, CapSenze will of course set the pace for the technological development of the capacitive biosensor platform. Certainly, it is our ambition to focus much of our energy towards R&D, while building a sustainable company structure around the activities. For the CapHIV consortium, we foresee an interesting future, given that the FP7 DEMO project has already been approved by the EC. With a validated instrument, the opportunities clearly become interesting.

New screening technique for fast HIV diagnosis

Antiretroviral therapy (ART) may be helping to stop HIV in its tracks, but early diagnosis is essential for a good prognosis. With this in mind, Swedish scientists are at the forefront of game-changing research



ONE OF THE GREATEST challenges facing the HIV/AIDS research community today is the need to produce a definitive, low-cost, accurate and portable diagnostic system that delivers results in time to start saving lives.

As the leading viral cause of death worldwide, AIDS has devastated entire communities, most recognisably in Africa. Increasingly, the pandemic is affecting nations within the EU and the European Economic Area (EEA). World Health Organization (WHO) figures estimate that worldwide, 34 million people are living with HIV and 820,000 of these people live in the EU. Eastern European nations, in particular the Russian Federation states and Poland, are experiencing rising numbers of HIV diagnoses. In these economically deprived regions, 50 per cent of HIV infections go undiagnosed, compared with 30 per cent in the rest of Europe.

THE CONSEQUENCES OF LATE DIAGNOSIS

In theory, a rapid test would give a positive or negative diagnosis within 15 minutes. However, as things stand, laboratory confirmation is necessary and takes between two weeks and six months.

Unfortunately, current standard nucleic-acid-based tests (NATs) can deliver a false negative result during the most acute phase of the infection, which occurs during the first few weeks after exposure. This is the point at which an HIV sufferer is at his/her most infectious phase. The false negative reading occurs because the process of seroconversion – when the body produces a detectable amount of antibodies to fight an infection – can take three months and, in rare cases, up to six months. For those who have been recently exposed, the waiting only prolongs the misery. The aim of researchers now is to reduce false negative test results during this window.

The consequences of this problem are felt most tragically when it comes to babies born to women infected with HIV. As a newborn will display maternally-transferred antibodies, an antibody-based test will prove ineffective as it will always give a positive reading. When a baby is three months old a polymerase chain reaction (PCR) blood test can be conducted to search for the virus itself rather than antibodies. But PCR testing in isolated rural areas is labour-intensive and time-consuming at a very critical stage. Half of all babies born with the virus will die before the age of two if they do not receive treatment, so a test that does not rely on antibody detection is urgently needed.

The CapHIV consortium, coordinated by MFKK Invention and Research Center, has targeted this need and is working to produce a diagnostic technique that will help in these types of cases.

NEW TECHNIQUE

Rather than concentrating on the presence of antibodies, the CapHIV system targets the conserved viral capsid protein, p24 antigen, looking for extremely low levels in plasma

samples. In existing NAT assays, biological amplification is used to detect antibodies, yet antigen assays can deliver almost comparable sensitivity to NATs without the need for biological amplification. This, combined with the smaller window for antigens, results in a rapid, effective diagnosis.

The capacitive biosensor technology that CapSenze – the Swedish company behind the CapHIV project – is utilising draws upon research that was originally developed at Lund University, Sweden. It is based on the affinity-binding of the target protein p24-specific anti-p24 antibodies attached to the sensor surface. Via a flow-injection system connected to the analytical platform, blood samples can be consecutively analysed, which makes the technique highly suitable for screening purposes.

NEW MARKETS FOR TECHNOLOGY

The CapHIV consortium aims to address the need for lower costs in the diagnosis and treatment of HIV and AIDS.

As a consequence of late diagnosis, there is now a greater need for second- and third-line medications. In 2012 a WHO report into healthcare costs for HIV revealed that in middle-income countries such as Georgia, the cost of these drugs can be as much as US $27,000 per person annually, which is prohibitively expensive.

The CapHIV consortium hopes that an earlier diagnosis will curtail the risky behaviour that results in more infections during the window period, and could cut the interval to just two weeks. The new technology aims to give an accurate result in 30 minutes, which could then be delivered to the patient in a point of care location. In an age in which many patients only seek help 10 years after infection, every second counts.

Portability is also of concern. The current CapHIV prototype is approximately the same size as a shoebox, rendering it suitable for field use in both the inner city and rural Sub-Saharan Africa. Unlike NAT devices, the size of the CapHIV device reflects its purpose as a low-labour intensive, non-time consuming solution to testing in challenging environments.

It is hoped the system will be offered at a low cost of approximately €10 per test, with the device priced at around €30,000, with the potential for each disposable cartridge component to be used in 100 tests. The projected costs are aimed at eventually supplying hospitals in the developing world. In 2008, a European Network for HIV/AIDS Surveillance report estimated that 11 million HIV tests are being conducted annually within Europe alone, so the market for rapid testing is wide open.

The consortium also foresees new challenges emerging for its device, as it might rapidly be adapted for use in detecting other infections as new pandemics arise. In addition, the device could be used to test water supplies for infectious diseases such as cholera and to detect poisons used in biological terrorist attacks. This will create continuous new markets for SME partners.

ENCOURAGING RESULTS

US Federal Drug Administration (FDA) approval is vital in opening up the market for CapHIV and the device is on course to be available internationally, having passed the rigorous first assessment. Successful results have emerged from laboratory tests; the challenge now is to gain validation via on-site praxis.

CAPHIV SENSOR TECHNOLOGY

- Works label-free
- The target protein is immunologically immobilised on an active electrode in an electrode pair-forming capacitor
- p24 antibodies are used on the surface to immobilise the p24 proteins from the sample
- The protein layer acts electrically as a dielectric layer with measurable influence on the capacitance
- The detection principle is a high-sensitive capacitance measurement between the two electrodes

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CapSenze scientist Dmitry Berillo (foreground) operates the capacitive sensor. He is assisted by PhD student Ally Mahadhy (background).

INTELLIGENCE

CAPHIV

OBJECTIVES

The CapHIV proposal addresses the need to increase the competitiveness of SME partners by developing a cost-effective method to screen p24 capsid protein for the early diagnosis of HIV infection – a major health and economic threat to the quality of life of European citizens.

A CapHIV device will further exploit the results of the novel, ultra-sensitive capacitance based sensor technology by providing a fast, reliable early screening method in a cost efficient way.

PARTNERS

CapSenze HB, Sweden • Phenosystems SA, Switzerland • Lionex GmbH, Germany • AbBcn S.L., Spain

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DR ATTILA AGOSTON graduated in electrical and biomedical engineering at the Graz University of Technology in 2002. He obtained his PhD in the field of sensor technology at the Institute of Sensor and Actuator Technologies of the Vienna University of Technology in 2007, and currently works at MFKK as a head of department.

ASSOCIATE PROFESSOR MARTIN HEDSTRÖM has built his career at the Department of Biotechnology, Lund University, where he started his activities twelve years ago. He is now head of the Bioanalysis group at the department, with a main focus on the development of tools for various bioprocess monitoring applications. The group primarily focuses on research regarding bioanalytical platforms such as mass spectrometry, biosensors and flow-based assays.