# New detection technologies for bacterial pathogens

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In FP7 jargon, RAPTADIAG is categorised as a 'small or medium-scale focused research project'. However, the past two years have seen the consortium turn a novel diagnostic test for bacterial meningitis into what is likely to become a full-blown set of sensor technologies for detecting bacterial pathogens of all kinds.

Whilst the sector has made some giant leaps over the past few years, much contemporary medicine still revolves around symptom-based treatments and costly diagnosis methods. In the case of 'bacterial meningitis' (BM), symptoms would usually develop within three to seven days after initial exposure if at all, as some people can carry the bacteria without getting sick. No treatment means a 50 % chance of dying, and the treatment's effectiveness depends on how soon it is administered.

According to Morten A. Geday, coordinator of the RAPTADIAG (Rapid Aptamer based diagnostics for bacterial meningitis) project and professor, treatment effectiveness is dragged down by the fact that early diagnosis is currently possible only through use of very expensive technologies. Not only are these methods taking too long to give an accurate result, but they are also too complex to be used outside major hospital facilities.

Together with partners from Switzerland and Denmark and thanks to EUR 2.2 million of EU funding, Prof. Geday set out to overcome these obstacles with a fast, easy-to-use and inexpensive diagnostic test for Neisseria meningitides (aka meningococcus) and Streptococcus pneumonia, which are responsible for 80 % of BM cases. He and his team have already developed three groundbreaking technologies, including a microacoustic-resonating sensor and a liquid crystal-based sensor, and are now planning to take their project to the next level.

In this interview, Prof. Geday explains his consortium's journey since the project started in 2011. He also elaborates on the findings that made them reconsider the project's raison d'être, from better diagnosis for BM to detection of a much larger spectrum of bacteria, in contexts as varied as food or water borne pathogens entering the food chain, water resources, or even air conditioning units.

## What's so new or innovative about this test? How does it work?

The new diagnostic tests will be faster (minutes rather than hours or days) and cheaper (euros rather than several 10s of euros) than the currently-available technologies. They were intended to address the clinical need for a diagnosis of these diseases with a high degree of morbidity, reducing the possibility of misdiagnosis and abuse of

antibiotics.

To enable microorganism recognition, we use novel aptamer receptors rather than conventional antibodies. In a nutshell, aptamers are short single-stranded DNA/RNA molecules which can undertake a three-dimensional structure by intra-strand pairing of the nucleic bases. This structure is then selected based on its high affinity and specificity towards the desired antigen or target.

Three different sensor technologies are being developed in parallel. The first technology is the adaptation of the commercial evanescent biosensor technology (Eva-sensor) using aptamer receptors instead of antibodies. Two more experimental (university-developed) technologies are being employed to develop a rapid test at a significantly lower cost, i.e. a microacoustic-resonating sensor and a liquid crystal-based sensor. The challenge in developing these two sensors was first of all to show that it is possible to develop microacoustic-resonating sensors with the necessary sensitivity, and then that we could develop liquid crystal-based sensors with the potential for single cell detection.

## What were the main difficulties you faced and how did you resolve them?

The project has been marred by two problems, one technical and one scientific. Shortly after the kick-off, one of the principal partners went bankrupt. This meant that the project found itself without the possibility of developing the key receptor molecules, i.e. the aptamers. The solution eventually came from one of the partners who took on this responsibility by employing key staff members from the bankrupted partner. The handling of the bankruptcy, the redefinition of responsibilities, and getting the project back up to speed has led to a six-month delay in execution. However, the highly successful development of both the

liquid crystal-based sensor and the microacoustic resonators is closely related to the choices we made then.

The second scientific problem is the development of the BM-specific aptamers. As the project is progressing, it is becoming increasingly clear that the necessary affinity and specificity towards the targets will reach the limits of the consortium's abilities as it stands. To what extent this reflects the limitations of the consortium or the limitations of the aptamer technology is not entirely clear. The workaround is the employment of BM-specific antibodies and existing aptamers targeting alternative pathogens in the testing and validation of the developed technologies.

## So you progressively moved away from BM to focus on other types of pathogens. How did that happen?

During the execution of the project, it has become increasingly clear that while the development of cheaper and faster BM detection could impact the detection and subsequent limitation of a BM epidemic in the Third World, the clinical impact in the West would probably be limited.

At the same time, we have realised that the technologies being developed for BM detection have a significant impact on the detection of bacterial pathogens in a large number of contexts, most notably food or water borne pathogens either in the food chain, in water resources or in air conditioning units. Similarly, these technologies may pave the way for novel means of detection of human pathogens in saliva or other bodily fluids.

As a consequence, various proposals aiming to further mature these technologies were presented in the last round of FP7, and a much more ambitious project—which to some extent is building on the experiences

gained during RAPTADIAG—is currently being evaluated in a Horizon 2020 Call.

## Where do you stand with your objective of delivering at least one commercial product by the end of the project?

The project is well on track. The Eva-sensor can already be purchased, and Davos Diagnostics have proven that their technology is suitable for bacterial detection using aptamer recognition or otherwise. On the other hand, both the microresonators and the liquid crystal sensors are still too immature. These technologies require a strong industrial partner. In the light of the financial situation in Spain, it is unlikely that funding for a spin-off involving the participating scientists can be found, and thus the technology must be transferred to an existing entity. We will, together with the technology transfer office at the University, start looking for potential partners in the near future.

## Would you say that the project results meet your expectations?

The project, originally scheduled to finish in June 2015, has already achieved a great number of its objectives. We have proven the use of the aptamers as receptor molecules for bacterial pathogens in the Eva-sensor, resulting in fast and easy pathogen detection (patents pending). At the same time, the microacoustic-resonating biosensor technologies are already approaching the sensibility needed to potentially detect the binding of one microorganism alone, which is the ultimate detection limit, while the liquid crystal sensor is opening the way for an exceedingly simple and inexpensive detection method, with either visual (without the need for any instrumentation!) or simple optoelectronic inspection with miniature readers or even mobile phone cameras. The

microacoustic resonators have already been published in various peer-reviewed journals, while a patent has been submitted in order to protect the liquid crystal sensor technology.

Thus from a technological bio-sensor development point of view, the project has vastly exceeded even the participants' expectations.

## When do you think patients and health workers could realistically start benefiting from your findings?

The payback to society will depend to a large extent on the conservatism of the medical sector. It will be immensely difficult even for our finished product, Eva-sensor, to have a significant impact over the next two years, even though Davos Diagnostics, during—and to some extent, thanks to—this project, has become ISO certified. Over the longer term (three to five years), we expect the Eva-sensor to become widespread in hospital wards, providing faster and easier detection of a large number of pathogens and other biological targets. The future of both the liquid crystal and the micro-resonating sensors will entirely depend on the industrial partners that the consortium gets interested in its technologies.

**More information:** For further information, please visit RAPTADIAG: www.raptadiag.eu/

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