Minilab never misses a tumour

A new nanosensor developed by the Universities of Twente and Wageningen is designed to track down cancer in the body with a single drop of blood. No tumour particle will escape notice, think the researchers, thanks to antibodies and smart electrochemistry. 'This sensitivity is unprecedented.'

TEXT ROELOF KLEIS **PHOTO** SVEN MENSCHEL

Pepijn Beekman, a PhD candidate in the Organic Chemistry chair group, carefully holds out a Petri dish. In it are two ultrathin chips barely two centimetres wide. These are nanosensors, a kind of miniscule laboratory on a chip. Once the chip is fully developed, it should be capable of detecting the presence of tumour cells in the body with just a drop of blood.

Body cells are constantly secreting tiny sacs containing substances with which they communicate with one another. Called extracellular vesicles, these little sacs are also secreted by tumour cells, in which case they are called tumour-derived extracellular vesicles (tdEVs). Beekman uses these vesicles to demonstrate the presence of tumour cells. On the surface of the vesicles of the tumour cells is a particular protein (EpCAM). The sensor distinguishes between tumour vesicles and those from other cells.

The sensor makes use of antibodies and electrochemistry. The antibodies detect the tumour vesicles and an enzyme that is attached to the antibody causes a measurable electrical signal to be produced.

The electrodes that detect the signal are spaced 120 nanometres apart. The vesicles themselves are no more than 100 nanometres in size. 'If you stare at your thumbnail for one minute, it will have grown 100 nanometres': this is Beekman's favourite analogy to show how small yet how high-tech this technology is.

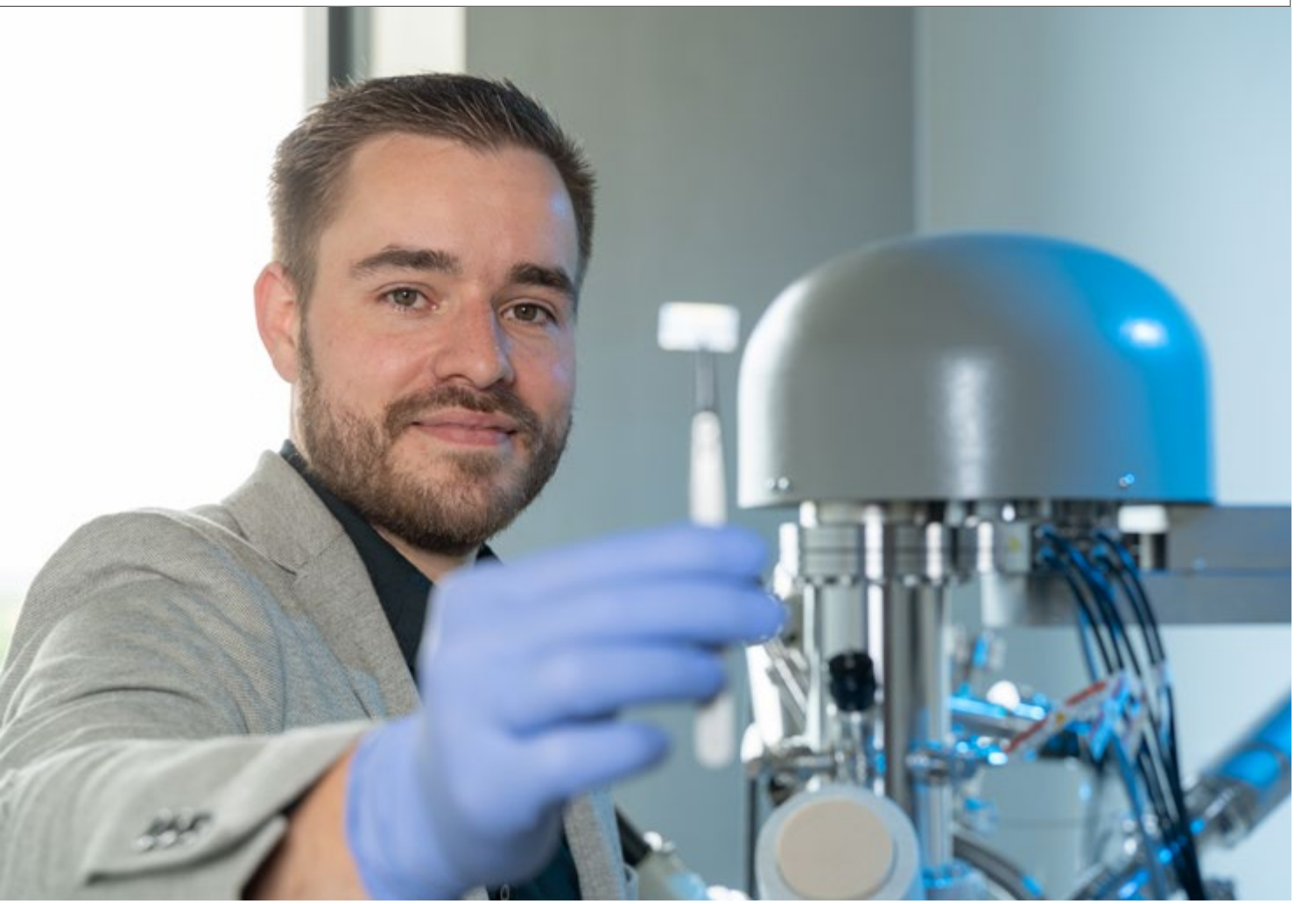
BIOMARKERS

Beekman, who also does research at the University of Twente, developed the nanosensor with his colleague at Twente, Dilu Mathew, in their start-up ECsens. They met on their MSc programme in Nanotechnology at Twente, and decided to join forces.

Beekman: 'My research is focused on biomarkers and Dilu concentrates on the sensor technology.'

Their first nanosensor only worked with a concentration of at least 10 tumour vesicles per microlitre of fluid from tumour cells cultured in the lab. It nevertheless got Beekman and Mathew onto the cover of *Nano Letters*, a leading journal published by the American Chemical Society. 'We're very proud of that,' says the PhD candidate. 'But that sensitivity is not good enough for proper detection. The sensor needs to be at least 100 times more sensitive.'

They have now achieved that. But Beekman is a bit secretive about the improvements they have made. 'We haven't described this new technique in the scientific literature yet, but we have done so in a patent application. We've used electrochemistry to ensure that the tumour particles come to



Pepijn Beekman displays the nanosensor, a lab on a chip.

> ‘Tumour particles come to the detector themselves’

the detector of their own accord. That way you don’t miss a single one. That sensitivity is unprecedented.’

WORLD EXPO

At the end of 2019, Beekman and Mathew’s invention won them the 4TU Impact Challenge, an innovation competition run by the four science and technology universities in the Netherlands. The prize will take the researchers and their company to the World Expo in Dubai in early 2022. ‘It’s nice to be allowed to present it at the same event at which innovations such as the television and the computer were introduced to the world. It is the ultimate opportunity to draw the attention of potential investors to our technology.’

Beekman and Mathew also received grants to the tune of nearly half a million euros to perfect the sensor. That means testing it with real blood rather than material from cultivated tumour cell lines. ‘The question is whether we can improve the chemistry so that it also works in blood plasma. Plasma contains a lot of biomaterials that could disturb the signal,’ says Beekman.
The prospects look promising at this early stage. ‘We are introducing measures involving a coating on the electrons that repels certain components in blood. That worked fine in the experiments we have done with healthy donor blood. We are now ready to repeat those experiments in combination with actual detection, but that research has been held up due to the coronavirus crisis.’ ■

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