

Timely automation for ultra-sensitive immunodiagnosics

High sensitivity immunoassays allow earlier detection and diagnosis of patient conditions, leading to earlier interventions and better patient prognoses. Immunodiagnosics company Singulex's unique immunoassay technology allows early detection of even low abundance biomarkers for a wide range of conditions, and the company has partnered with Tecan to develop an intuitive, fully automated platform – the Singulex Clarity® system – which will allow clinical labs to take advantage of this novel technology for routine diagnostics.



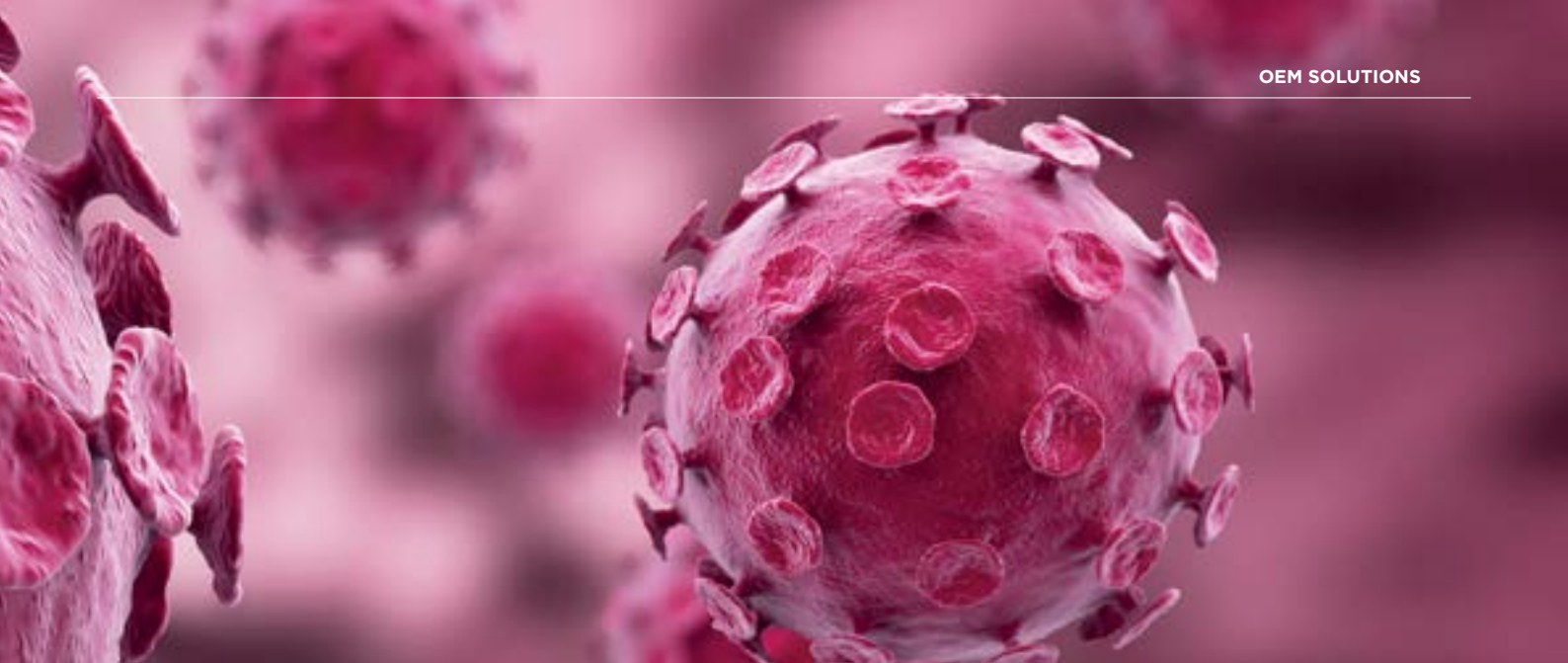
The Singulex development group

Singulex®

Singulex is a California-based immunodiagnosics company at the forefront of Single Molecule Counting technology. The company's proprietary technology provides unprecedented sensitivity, enabling the precise measurement of biomarkers at previously undetectable levels, offering a clearer and more definitive picture of a patient's health, as Dr Jeff Bishop, Senior Vice President of Diagnostic Operations at Singulex, explained: "Single Molecule Counting is a very sensitive optical system that allows us to analyze low abundance biomarkers in blood samples in an extremely precise way. It offers up to 1,000-fold greater

sensitivity than other technologies and is independent of any specific disease or biomarker; we have already developed assays for cardiovascular, infectious disease and oncology applications."

Single Molecule Counting technology uses a familiar 'sandwich-type' immunoassay format that combines capture antibodies immobilized onto paramagnetic microparticles with fluorescently-labeled detection antibodies. However, this is where the similarity ends, as Jeff highlighted: "After a wash step to remove unbound assay components, we disrupt the antibody-antigen complex to yield free,



dye-labeled detection antibodies in an optically-inert buffer solution. By removing the analyte and magnetic particles, this significantly reduces potential sources of assay 'noise', allowing individual fluorescently-labeled molecules to be detected as they pass through the narrow interrogation window of a confocal detection system. This method doesn't rely on the total fluorescence within the sample, and so we're able to detect low abundance biomarkers – such as proteins and nucleic acids – down to the femtogram per milliliter level."

The unprecedented sensitivity of Single Molecule Counting enables much earlier detection of time-critical biomarkers – such as the cardiac biomarker troponin – or bacterial infections, for example *C. difficile*, than would be possible with traditional immunoassays. This allows appropriate care to be initiated much sooner. "By the time other systems can detect these biomarkers, the patient is really sick," Jeff continued. "Single Molecule Counting can effectively identify much lower concentrations of these diagnostic markers much sooner, leading to earlier intervention and better patient outcomes."

Singulex began using the early detection capabilities of this technology for clinical applications in 2010, through a service provided, at the time, by its CLIA-certified laboratory. "Physicians all over the US would send blood samples to us, and we ran them in our lab and reported the results. In 2012, we decided to develop a fully automated platform with ready-to-use reagents – the Singulex Clarity system – creating a streamlined

'sample in, result out' workflow that could be deployed at customer sites."

"We had two main goals for this project," Jeff added. "The first one was to get this system into the market as quickly as possible, and the second was to ensure the same level of assay performance as in our clinical lab. Tecan's engineers had already created a number of complete clinical platforms based on the Freedom EVO® system, and so we felt that, with this experience, they could help us get to market more quickly than anybody else. We already had more than 10 Freedom EVO platforms in the laboratory, so we were familiar with Tecan and the technology, and knew the assays could be automated on this system. Because Tecan has a portfolio of detection instruments, we were also confident that the company had the expertise to replicate the design of our reader and incorporate it into the system. This took a lot of the risk out of the instrument development program."

"When we first started out, we thought that as much as 80 % of the system would use off-the-shelf Freedom EVO parts, but it became more customized over the course of the development. Our technology uses a unique, eight-well reaction vessel, so the gripper fingers, pipetting heads and integrated HydroFlex™ washer had to be modified to accommodate our consumables. The system also has a four-channel Air LiHa™ pipetting arm, a Robotic Manipulator Arm™, a MIO™ incubator and a shaker. The software is based on Freedom EVOware®, but uses a custom, touchscreen-based graphical user

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interface to guide the user through each step of the workflow.”

"During the development process, we had weekly meetings with the Tecan development team; we visited the company's sites in both Switzerland and Austria several times, and Tecan engineers came to our lab here in California. There were very few days when somebody from Tecan wasn't talking with somebody from Singulex. Tecan isn't just our development and manufacturing partner though. We now have a service relationship with the company, whereby Tecan's engineers will be helping us to service the systems that are placed out in the field, ensuring support is available for the global Clarity landscape," Jeff concluded.

To find out more about partnering with Tecan, visit partnering.tecan.com

To learn more about Singulex and the Clarity system, go to www.singulex.com