

Label-free technology benefits drug discovery

High throughput screening for drug discovery depends on reliable liquid handling, like that provided by Tecan's Freedom EVO® platform. Chicago-based company SAMDI Tech has automated its proprietary label-free SAMDI technology on a Freedom EVO system for performing rapid and quantitative analysis of challenging biochemical targets.

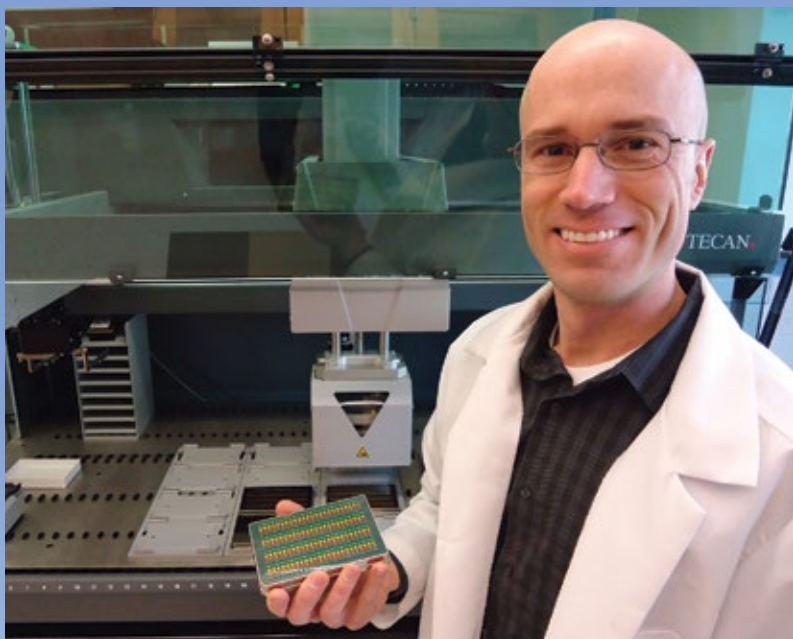
“It can accurately dispense from 0.5 µl up to 3 µl onto the SAMDI array, pipetting very reproducibly at the same height each time.”

SAMDI Tech, Inc. is an early-stage technology company, spun out of the University of Chicago, USA, that offers label-free assay services for high throughput screening and peptide substrate discovery. The Company's proprietary SAMDI¹ technology, developed by Professor Milan Mrksich, combines surface chemistry, high density biochip arrays and MALDI-TOF² mass spectrometry (MS) for rapid

and quantitative measurement of analytes in biochemical reactions. Michael Scholle, Director of Technology and Operations at SAMDI Tech, explained: “Label-free technology for high throughput screening is now a reality, eliminating the need for cumbersome antibodies, fluorescent and radiolabeled compounds that can interfere with activity. SAMDI is a high throughput, label-free technology for sample preparation prior to analysis by mass spectrometry. At the core of SAMDI is the biochip, which consists of self-assembled monolayers of alkyldisulfides arrayed on a very thin film of pure gold. Peptides, proteins, small molecules or even nucleic acids can be efficiently captured onto the surface of biochips, allowing enzyme activity on these substrates to be observed.”

“Until fairly recently, SAMDI was used mainly as a research tool. We wanted to progress from the benchtop to fully automated high throughput screening in a robust and reproducible format that was commercially viable. When we were at the University of Chicago, we used a Freedom EVO 200 platform, which was ideal for developing the biochip and establishing screening protocols. It was a high performance system





The Freedom EVO allows Michael Scholle and his team at SAMDI Tech to run hundreds of 384-well plates every day

that could provide us with the accurate pipetting volumes and height we needed. Our workstation is equipped with a Robotic Manipulator Arm, and we upgraded from a MultiChannel Arm™ (MCA) 96 to an MCA 384 to give us even greater flexibility and throughput. We use the system for multiple processes, from liquid handling for reaction set-up to sample transfer to the SAMDI arrays, as well as for pipetting small molecule libraries into 384-well plates for high throughput screening in drug discovery.”

Michael continued: “We typically begin the process with an enzyme and substrate from a client, which are then integrated into a high throughput screening process, generally using a small molecule library. The assay is performed on the Freedom EVO and, once complete, we use the MCA to transfer the analytes from 384-well plates to SAMDI arrays in 384 format for analyte capture. It is critical that the MCA tips do not touch the biochip, as this damages

the surface chemistry; to avoid this was simply a matter of programming the Freedom EVO with the new labware and the specific pipetting height. Next, unbound components are removed by washing the biochip, and a 2',4',6'-trihydroxyacetophenone monohydrate (THAP) matrix is applied for MALDI-TOF analysis of the alkyldisulfide-analyte conjugates. With MALDI-TOF MS, we can automatically collect the data from all 384 individual spots on the SAMDI biochip array in just 20 minutes. Mass spectrometry gives us the ability to monitor both substrates and products simultaneously, whereas many labeled assays only monitor the products. The ability to monitor multiple analytes – for example mono-, di-, and tri-methylated histone tails – helps to provide a better understanding of enzyme function and aids the discovery of early stage modulators of enzymes involved in human disease.”

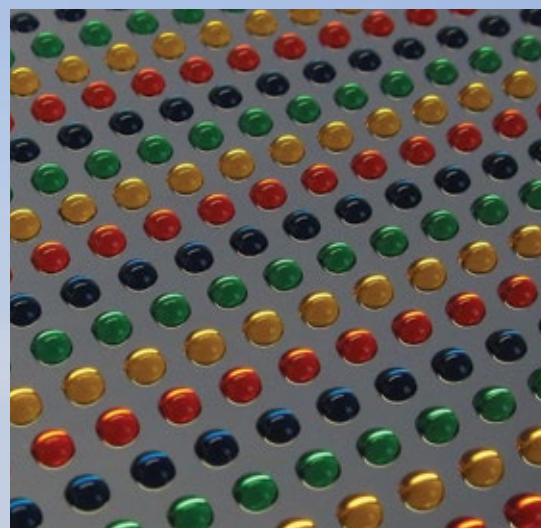
“Automating the SAMDI process on the Freedom EVO has given us greater throughput – allowing us to run hundreds of 384-well plates every day – and it can accurately dispense from 0.5 µl up to 3 µl onto the SAMDI array, pipetting very reproducibly at the same height each time. The system is straightforward to operate and the software user friendly, so it is also easy for us to make adjustments on the fly. In the future, we plan to transfer four 384-well plates to the higher density 1,536 SAMDI biochip arrays, which is quite a challenge as it requires accurate transfer of volumes of 0.5 µl or less. This will enhance throughput even further, allowing four times the density on a single array and saving time downstream as only one plate, rather than four, will need to be loaded into the MALDI-TOF system. We are entering a very interesting time, where automated technology and label-free assays will help elucidate the function of difficult targets and expedite drug discovery,” concluded Michael.

To find out more on Tecan’s drug discovery solutions, visit www.tecan.com/drugdiscovery

To learn more about SAMDI technology, go to www.samditech.com

¹SAMDI: self-assembled monolayers and matrix-assisted laser desorption ionization

²MALDI-TOF: matrix-assisted laser desorption ionization time of flight



SAMDI technology offers rapid, quantitative MALDI-TOF analysis of biochemical reactions