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Robotics and proteomics: A partnership with a promising future in biomarker discovery

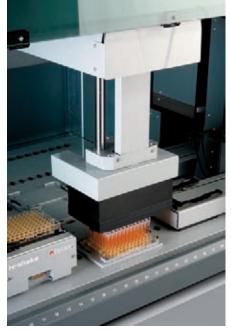
High throughput proteomics was the goal of researchers in France who turned to Tecan to automate their sample preparation protocols for biomarker discovery in patient samples.







Freedom EVO 100 with integrated Te-Stack



The search is on for novel disease biomarkers that will ultimately lead to a more tailored and personalized approach to treatment for a number of diseases, including many cancers, diabetes and all kinds of metabolic diseases. For researchers like Dr Patrick Ducoroy, manager in the Clinical Innovation Proteomic Platform (CLIPP, based at Dijon and Besancon in France), of which the health department is based at the Hospital and Cancer Center in Dijon, high sample numbers and throughput are critical factors for getting good results. As Patrick explained: "These things are of paramount importance to us in order to identify good, robust biomarkers for investigation. It is also vitally important to standardize the procedures and the treatment of samples and, in this early discovery phase, stringent quality control is a must. Quite simply, automation is essential to achieve all these objectives."

To this end, Patrick's laboratory uses two versatile Freedom EVO® liquid handling platforms to extract purified protein samples from patients' blood, for longterm storage or further downstream analysis using mass spectrometry. "Our two Tecan robots are integrated and totally compatible with one another; they use exactly the same software for their operation, and therefore automation and standardization of the pipetting procedures during sample preparation are maximized," he said. Patrick is a firm believer in the use of quality control and considers the Freedom EVO platforms crucial to achieve a standardized procedure that can be reproduced in good faith, time and time again. The Freedom EVO 200 has an 8-tip liquid handling arm for sample aspiration from tubes. For the clinical studies, the Freedom EVO 200 is used to aliquot the samples, which arrive in different types of tubes, to 96-well microplates, which are compatible with the MultiChannel Arm™ 96 in the Freedom EVO 100. Protein and peptide purification is carried out in the Tecan Freedom EVO 100, which also allows for additional downstream analysis of protein and peptide samples."Both the Freedom EVO 200 and the Freedom EVO 100 include a 37 °C incubator for performing protein digests directly after purification in order to retrieve the peptides", Patrick added.

"The main advantage of our Tecan systems is the ability to process 96 patients in parallel in one hour, from the initial step of putting the sample tubes onto the first worktable, to isolate the plasma, purify the peptide and put the peptide on the target matrix, ready for mass spectrometry. The rapid processing helps us to achieve excellent reproducibility – we have analyzed the reproducibility of our instruments over time and we have had very good results. It is very important that we can process a very high number of patients in one week; ultimately we are aiming for a thousand and Tecan's technology will be central to us achieving this goal".

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proteomics

Another important consideration is that it is imperative to minimize crosscontamination between patient samples at all costs, and this concern is addressed with the Freedom EVO's ability to switch to using disposable tips. The tips are changed between samples, and this is key for the avoidance of contamination. In addition, all source tubes and destination plates are identified through their barcodes with Tecan's PosID[™] positive identification system.

For analysis and identification of the separated proteins, and for the detection of new biomarkers in clinical studies by profiling comparison, the team uses Matrix Assisted Laser Desorption Ionization (MALDI) mass spectrometry. In this technology, the ionized protein samples are accelerated through an analysis chamber (vacuum or flight tube) to separate the molecules according to their mass to charge ratio. The timeof-flight (TOF) analyzer determines the mass of a peptide by the amount of time it takes to reach the detector within the flight tube. Afterwards they employ a variety of different statistical tools for the treatment and analysis of the data obtained. Interestingly, the team is currently working with Tecan to obtain an informatics software solution, which will hopefully lead to good traceability of process between the Freedom EVO software and the mass spectrometer software.

Scientific instrumentation. Not for use in human clinical or in vitro diagnostic procedures.



The team at Clinical Innovation Proteomic Platform (CLIPP), Dijon, France

Support from the Tecan engineers has been critical to the success of the project. Patrick added: "We have had very good support from Tecan, particularly with regard to modifying the different parameters of the robotic workstations. I am sure this has helped us to achieve such excellent reproducibility of results, with the throughput that we need." For more information about Tecan's Protein Science solutions, visit www.tecan.com/proteinscience

Tecan's technology will be central to us achieving our goal.



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