World-first automation for influenza surveillance

Researchers at the Victorian Infectious Diseases Reference Laboratory have completely automated an influenza hemagglutination inhibition assay on a Freedom EVO® workstation using the newly developed FluHema™ module from SciRobotics. It is the first laboratory in the world to achieve this, now running and analyzing up to 128 microplates daily with far better flexibility, reproducibility and overall assay performance.

WHO Collaborating Centre for Reference and Research on Influenza
VIDRL

VIDRL
Victorian Infectious Diseases Reference Laboratory

SCIROBOTICS

The WHO Collaborating Centre for Reference and Research on Influenza – part of the Victorian Infectious Diseases Reference Laboratory (VIDRL) in Melbourne, Australia – is one of five centers around the world that oversee the surveillance of human influenza viruses in the global population. As part of the World Health Organization's Global Influenza Surveillance and Response System (GISRS), information from the Center is used by the WHO to make recommendations on the appropriate viruses to be included in the annual seasonal human influenza vaccines for the northern and southern hemispheres. Dr Ian Barr, Deputy Director, explained: "Our laboratory performs molecular and serological assays on influenza viruses isolated from samples gathered around the region. After growing the viruses in cell culture, we look for any significant changes in the circulating human influenza viral population which might require an update to the biannual recommendations for the influenza vaccine composition."

"Despite sample processing and culture growth being predominantly manual activities, we automated our analytical workflow some years ago to standardize the processes as much as possible, as well as to ensure high quality data. More recently, we have introduced a Tecan Freedom EVO workstation to increase flexibility and improve the reproducibility of some of our assays. The first assay we automated on this platform was our routine neuraminidase inhibitor resistance testing. This fairly straightforward assay involves a series of

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Rob Shaw, Iwona Buettner and Ian Barr with the automated workstation

pipetting steps followed by fluorimetric analysis – which is fully automated using the system's integrated microplate reader – but transferring it to the Freedom EVO has certainly improved performance in terms of assay reproducibility and lower CVs. However, our main reason for purchasing the platform was the automation of our hemagglutination inhibition (HI) assay."

Developed over 70 years ago, the HI assay can be used to detect even small changes in the viral serotype using specific antisera, and relies on the influenza virus' ability to agglutinate red blood cells. Ian continued: "By using a series of very specific, post-infection antisera from ferrets, we are able to selectively block this agglutination process. The ferret sera are serially diluted to determine the point at which the serum no longer blocks agglutination, allowing us to profile the characteristics of each viral sample, comparing them to a reference panel to identify new variants. Until now, identifying the point at which agglutination is no longer inhibited has always been performed visually by a trained technician. Using a Freedom EVO workstation, we have been able to develop a fully automated system that can not only do all of the liquid handling steps, but can also 'read' the plates, and this breakthrough was made possible through Tecan's connection with SciRobotics. By combining our knowledge of this assay with the liquid handling capabilities of the Freedom EVO 200 platform and SciRobotics' expertise in imaging and analysis, we can now automatically process and analyze the HI assay plates."

The VIDRL worked closely with SciRobotics to develop a new automated imaging system – the FluHema module – which photographs the plates and analyzes images from individual wells and columns. Depending on the red blood cell type, the 96-well plates can be tilted at angles of up to 65 degrees, allowing compact cell 'buttons' shaped like inverted teardrops to form, offering more precise endpoints and easier interpretation. The module's software uses specially developed algorithms to determine the settling patterns, recognizing where changes in shape and size occur across a dilution series. Data is then exported to an Excel® spreadsheet, which shows the final results along with photos of each well.

"Overall, our collaboration with Tecan and SciRobotics has been very successful. Reliable automated interpretation of the HI assay is now possible, enabling a typical run of around 64 plates to be performed in just a few hours and doubling our previous daily throughput. Our technical expert at Tecan Australia, Luke Danielewski, played a significant part in this, and his knowledge and expertise were invaluable. The platform has given us a very flexible, reproducible and precise system, freeing up staff time for other activities," Ian concluded.

To view a short video of the fully automated HI system in action, go to **www.youtube.com/watch?v=fvZ034BDSqQ**

To learn more about Tecan's clinical solutions, visit **www.tecan.com/clinicaldiagnostics**

To find out more about the WHO Collaborating Centre for Reference and Research on Influenza, visit **www.influenzacentre.org**