

ISWAVLD 2⁽¹⁾23

International Symposium of the World Association of Veterinary Laboratory Diagnosticians

29 JUNE-1 JULY 2023 Congress Centre

Lyon

Towards the veterinary diagnostics of the future

Main topic : Other Topics

ImpedanCELL: a core facility to screen and evaluate antiviral compounds against Equid alphaherpesviruses.

PRONOST S. 12.3, NORMAND C. 1,2, THIEULENT C. 1,2,4, SUTTON G. 1,2,5, CARNET F. 1,2, GUENOUX A. 1,2, BROTIN E. 3,6,7, FORTIER C. 1,2,3, DENOYELLE C. 3,6,7, HUE E. 1,2,3

¹ LABEO, Caen, France; ² Université de Caen Normandie, BIOTARGEN, CAEN, France; ³ Université de Caen Normandie, Unité de Service PLATON, ImpedanCELL (IBiSA), Caen, France; ⁴ Department of Pathobiological Sciences, School of Veterinary Medicine, Louisiana State University, Baton Rouge, United States; ⁵ Microbiology, Infectiology and Immunology Department, Faculty of Medicine, University of Montreal, Montreal, Canada; ⁶ Université de Caen Normandie, Inserm, ANTICIPE UMR (1086), Caen, France; ⁷ Comprehensive Cancer Center François Baclesse, UNICANCER, Caen, France

ImpedanCELL (IBiSA) is an innovative and original core facility for the study of real-time high?throughput cellular activity using impedance measurement (xCELLigence technology) and real-time cellular imaging. It is localised on two different geographical sites in Caen (Normandy, France): LABEO (Normandie Equine Vallée research platform) for all applications in virology and in bacteriology (biosafety level 2) and Comprehensive Cancer Center F. Baclesse for all non-microbiological applications. The core facility is equiped with cutting-edge technologies based on xCELLigence RTCA analysers (including 3 MP, 1 SP, 1 DP, 1 S16 and 1 CardioECR) and live-cell imaging devices (3 Incucyte S3) both allowing the study of proliferation, cell death, adhesion, migration and invasion in various domains including virology, bacteriology, immunology, toxicology, neurosciences and marine biology. This study will illustrate an application of the ImpedanCELL platform for the screening and identification of antiviral compounds against equid herpesviruses (EHVs).

Based on xCELLigence technology, a high-throughput screening of 2891 compounds was performed against equid herpesvirus 1 (EHV-1) [1]. Among the nine EHVs (1-9) described in equids today, EHV-1, responsible of respiratory, ocular, abortion and neurological forms of the disease, generates some of the greatest concern to the global equine industry, as evidenced by recent neurological outbreaks [2]. EHV-4 is responsible for the respiratory form of rhinopneumonia, EHV-3 is responsible for coital exanthema and the two most recent EHVs (EHV-8 and -9) could also cause neurological forms of disease similar to those observed with EHV-1 infections.

Among these 2891 molecules, 22 compounds have been found to be effective in vitro against EHV-1. Data were confirmed by viral DNA quantitation and microscopy observation. Valganciclovir, ganciclovir, decitabine, aphidicolin, idoxuridine and pritelivir are the six most effective compounds identified, and their antiviral potency was confirmed on 3 different cell lines (E. Derm, RK13 and EEK cells) and against 3 different EHV-1 variants (ORF30 2254 A/G/C). These six most effective compounds were then tested, alone or in combination against other EHVs. The results demonstrated that five of the six most effective compounds were effective in vitro against EHV-3 and among them Aphidicolin was the most effective. The different compounds were also effective against EHV-8 and EHV-9. As ganciclovir was identified as one of the most potent molecules, it was tested in combination with other compounds of interest. A synergically effect was observed between ganciclovir and decitabine co-treatment against EHV-1.

This work has shown that impedancemetry is very useful for screening antiviral compounds, but also for identifying synergistic effects between molecules of interest. This will contribute to the identification of the best cocktails to combat the neurological form of the disease observed with EHV-1, EHV-8 and EHV-9. In line with one ImpedanCELL's mission, the core facility is open to any scientists with high?throughput study needs for dynamic tracking of real-time cellular behaviour. ImpedanCELL (IBISA, https://impedancell.fr/) is open to collaborations and services for both academic and industrial partners and offers theoretical and practical courses.