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Rapid quantitation of virus-neutralizing antibodies in biosamples – a novel BSL1 approach based on virus-like particles (VLPs)

Neutralizing antibodies, virus-free assay, VLP, SARS-CoV-2, EBV

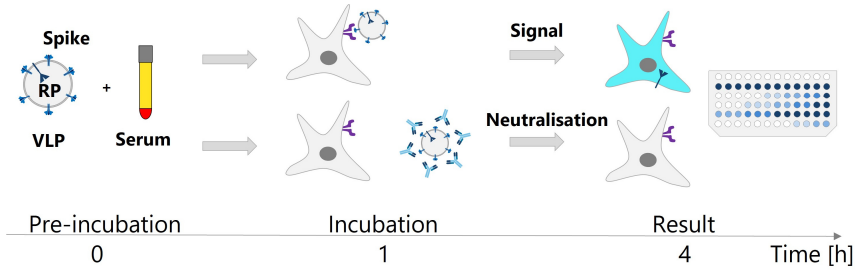
INVENTION NOVELTY

Serum, saliva and other body fluids of virus-infected individuals contain virus-specific antibodies, which are important diagnostic biomarkers. The functions of these antibodies may vary, but the biologically most relevant are so called „neutralizing antibodies“, which neutralize viral infectivity and thus directly contribute to viral clearance. Assays for the measurement of virus-neutralizing antibodies require elaborate cell culture models and are tedious, time-consuming tasks. All standard assays require the handling of infectious virus and, depending on the virus type, read-outs that build on cytopathic effects (CPEs). Alternative methods exist, but are restricted to laboratories certified according to national laws to handle infectious agents and providing specialized equipment and at least biosafety level 2 (BSL2) containment.

The present invention provides an easy and fast qualification and quantification method to determine presence and titer of virus-neutralizing antibodies in a sample, comprising VLP carrying one or more viral glycoproteins and a label, thereby omitting the use of infectious virus and being adaptable to all enveloped viruses.

VALUE PROPOSITION

The invention provides a highly flexible and reliable method to specifically detect virus-neutralizing antibodies in a sample without the need to use infectious viruses. This advantage and the use of engineered VLPs opens the way to high-throughput screens which are not compatible with other neutralization assays. The detection of neutralizing antibodies using this new assay provides very valuable insights into the course of viral infection, its clinical prognosis or outcome and delivers critical information if patients have mounted robust and virus-specific immune responses, for example in the current COVID-19 pandemic.



VLPNT Assay (source: Prof. Hammerschmidt, HMGU)

TECHNOLOGY DESCRIPTION

The inventors engineered extracellular vesicles (EV) to carry viral glycoproteins (or viral glycoproteins together with a viral nucleo- or tegument protein from the same virus) and a label. The EV are detectable via the label, wherein the label is attached to the glycoprotein or the nucleo or tegument protein of the EV. The label can either be a functional enzyme (e.g. luciferase, β-lactamase) reacting with a substrate added to the cells which are capable of taking up the EV (e.g. HEK 293), or a split protein, wherein a first part of the split protein is comprised in the EV and a second part of the split protein is comprised in the cells, forming an active complex after the EV has been taken up in the cells. So far, EV has been engineered to express the spike proteins of different field isolates of SARS-CoV-2 and the gp350 glycoprotein of EBV. Preincubation of the engineered EV with human serum samples showed characteristic neutralization curves when neutralizing antibodies are present in the sera. The neutralizing antibodies present bind to the viral glycoproteins hereby preventing the EVs to be incorporated in the cells via receptor-specific (e.g. ACE2, CR2) adsorption to and penetration into the cell.

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COMMERCIAL OPPORTUNITY

The Virus-like particle neutralization test (VLPNT), mimicking an infection process without using infectious viruses, can serve a broad range of applications such as vaccine and drug development, clinical trial evaluation, and immune status monitoring. The technology is open for licensing, further co-development is highly welcomed.

DEVELOPMENT STATUS

In addition to the already validated cell-based assay, a cell-free assay has been established, providing a donor type of EV (carrying the viral glycoprotein and the first part of a split label protein) and a recipient type of EV (carrying the respective receptor of the viral glycoprotein and the second part of the split label protein). Fusing of both EVs effect the split proteins to complex and after adding a substrate of the label e.g. emitting light can be measured.

PATENT SITUATION

A PCT application has been filed in 2021 with priority of Oct. 9, 2020.

FURTHER READING

Roessler et al. (2021), medRXIV preprint “Quantitation of SARS-CoV-2 neutralizing antibodies with a virus-free, authentic test"

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