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High-throughput Screening for anti-herpesviridae Drugs

Keywords: High-throughput Screening, Cytomegalovirus (CMV), anti-herpesviridae Drugs

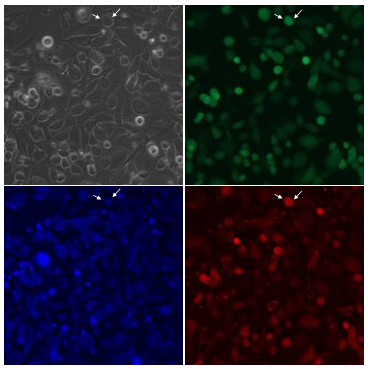
INVENTION NOVELTY

The offered technology is an ideal tool for fast and simple high-throughput screening for the identification of new anti-herpesviridae active ingredients. CMV was used as a first virus to show the proof-of-principle. By modifying the technology, it can also be used for screening of antiviral drugs against any member of the large family of Herpesviridae DNA viruses.

VALUE PROPOSITION

Cytomegalovirus (CMV) infection is highly prevalent worldwide. Although the majority of infections are asymptomatic, morbidity and mortality is high for immunocompromised individuals, and congenitally infected infants. Currently approved drugs to treat CMV infections are often inefficient and can lead to severe side effects. In order to make therapies safer and more efficient in the future, there is an urgent need for new antiviral drugs.

Targets for antiviral drug candidates can be found in all phases of viral lifecycle. These different phases are characterized by expression of immediate early, early and late genes. To investigate the mode and time of action of new drugs screening tools are needed that are able to differentiate between the different phases of viral replication cycle.



Reporter virus visualizing the expression of Immediate Early-, Early- und Late-Genes by co-expression of fluorophores.

TECHNOLOGY DESCRIPTION

A reporter virus is used to visualize the three different phases (Immediate Early, Early and Late) of the lytic replication cycle of CMV. For this purpose, different-colored fluorophores are coupled by P2A linkers to, and thus co-expressed with essential genes of the three phases. Coupling to essential genes generates a specific readout because inhibition of these genes results in both reduced fluorescence and interrupted replication cycle.

The fluorescence intensity is proportional to the amount of expressed viral proteins and indicates the activity of potential antiviral drugs. Since each phase of the replication cycle is represented by a different color, it is possible to investigate in which phase potential drugs inhibit the replication cycle and the virus multiplication. This makes the reporter virus an ideal tool for screening for new inhibitors of virus multiplication. The technology allows the monitoring of events at single cell level, and thus amenable to high-throughput-, or cell on-a-chip screens.

COMMERCIAL OPPORTUNITY

The technology is offered for in-licensing and co-development.

DEVELOPMENT STATUS

Proof-of-principle for the detection of anti-viral compounds was achieved.

PATENT SITUATION

Priority application was filed in July 2017. PCT application was filed in July 2018. 2020 entry into the European phase.

FURTHER READING

Rand U et al. A Novel Triple-Fluorescent HCMV Strain Reveals Gene Expression Dynamics and Anti-Herpesviral Drug Mechanisms. Front. Cell. Infect. Microbiol., 08 January 2021; doi: 10.3389/fcimb.2020.536150

Kasmapour B et al. Myeloid Dendritic Cells Repress Human Cytomegalovirus Gene Expression and Spread by Releasing Interferon-Unrelated Soluble Antiviral Factors.
J Virol. 2017 Dec 14; 92(1): e01138-17.

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