High Throughput Screening Platform For Inhibitors of Viral Membrane Fusion

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Overview

Enveloped viruses pose significant health risks and lack effective treatments. Inhibiting viral membrane fusion, a crucial step in infection, holds promise for antiviral drug development. Dr. Ori Avinoam and his team developed a high throughput screening (HTS) platform to identify small molecule inhibitors of viral membrane fusion, starting with the SARS-CoV-2 spike protein, whose fusogenic domain is highly conserved. The platform can be extended to target other enveloped viruses.

Background and Unmet Need

Enveloped viruses, including SARS-CoV-2, influenza, Nipah virus, Hendra virus, HIV, and Ebola, pose significant threats to human health, yet effective treatments are limited. Membrane fusion plays a critical role in these viruses' ability to invade host cells, presenting an appealing target for antiviral interventions. Notably, the highly conserved fusogenic (S2) domain within the Spike protein of SARS-CoV-2 enables the fusion of the virus with host cells. This conserved domain serves as an attractive therapeutic target, offering the potential for developing broad-spectrum antivirals that extend their effectiveness to other viruses, such as Hendra and Nipah, which are among the most deadly emerging bat-borne viruses.

The Solution

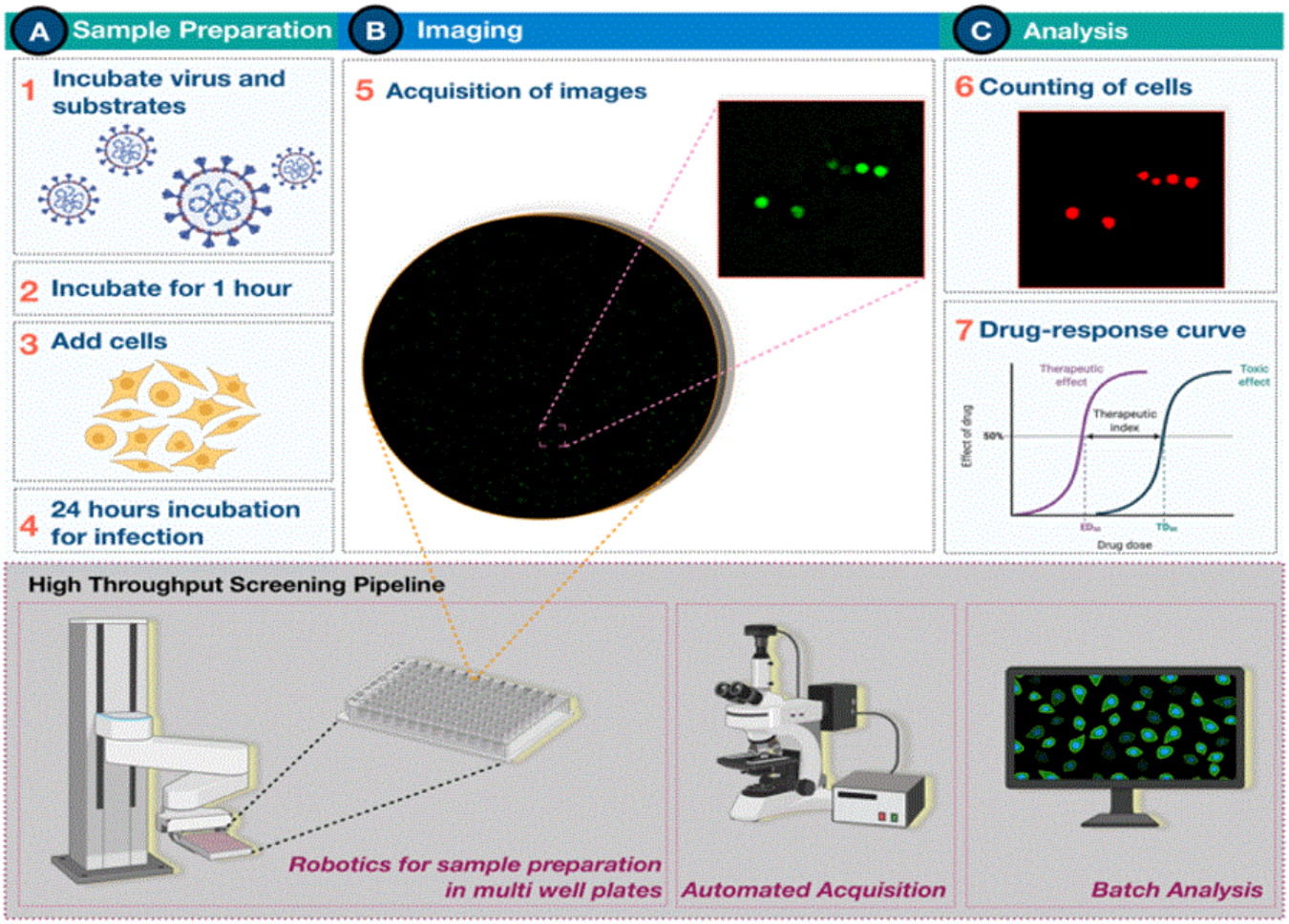
Dr. Ori Avinoam and his team developed an HTS platform to identify small molecules that inhibit the membrane fusion of the SARS-CoV-2 and other enveloped viruses.

Technology Essence

The platform utilizes a recombinant Vesicular Stomatitis Virus (VSV) expressing the SARS-CoV-2 S protein and a green fluorescent protein (GFP) as a reporter gene. GFP expression is dependent on viral envelope fusion, enabling accurate detection of viral infection at the single-cell level.

Applications and Advantages

- A robust and efficient platform for high-content screening of viral membrane fusion inhibitors
- Discovery of novel antiviral drugs with a unique mechanism of action
- High signal-to-noise ratio, single-cell resolution, and automated analysis options
- Addressing present and future pandemics by developing broad-spectrum, universal viral inhibitors



Development Status

The team has completed screening ~200,000 compounds and identified novel small molecules that inhibit Bona fide SARS-CoV-2 infection. The current focus is on hit-to-lead optimization.

Patent Status

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