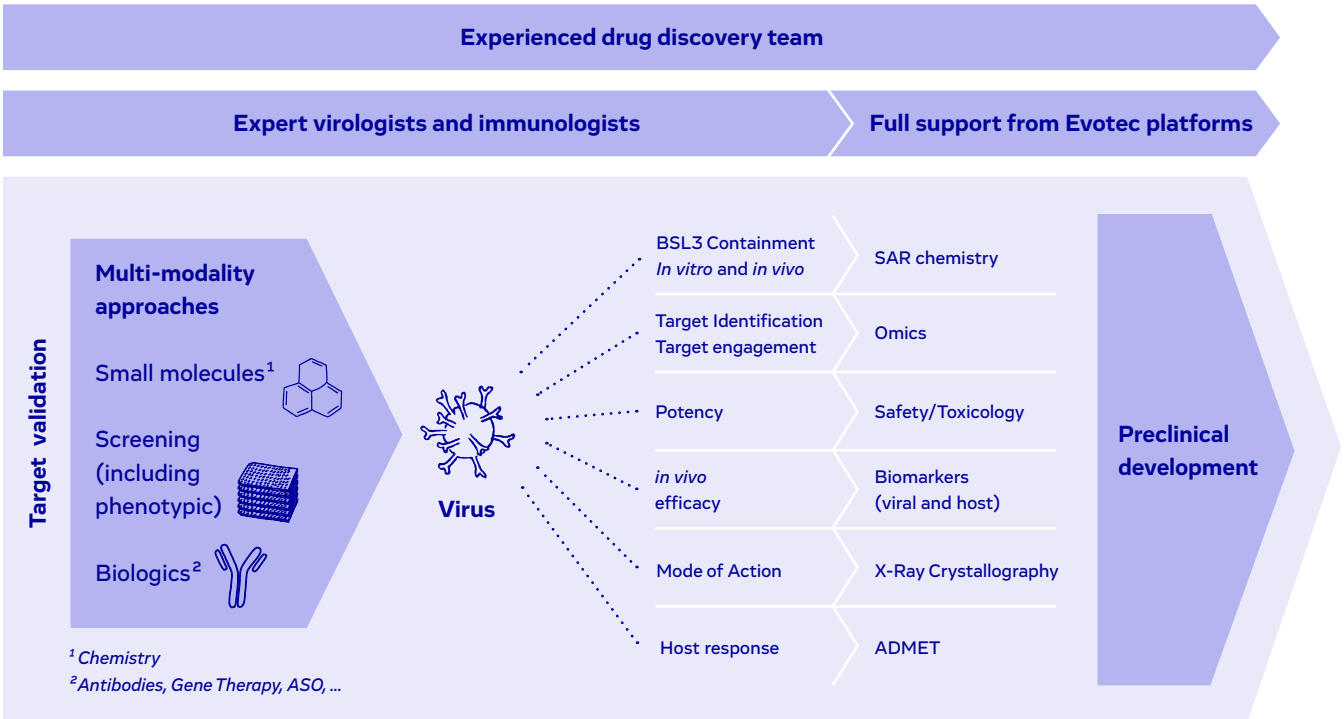
evotec

#RESEARCHNEVERSTOPS

Anti-Viral Drug Discovery

- Fully integrated R&D platform for fast and efficient identification and progression of novel anti-viral therapeutics
- Cutting-edge technologies and discovery platforms flexibly tailored around projects' scientific requirements
- Focus on respiratory viruses including SARS-CoV2 as well as Hepatitis B virus, capabilities ranging from screening to animal models
- Experience in multiple compound classes and MoA, including host targeting approaches and direct anti-virals
- Broad and deep immuno-virology capabilities and expertise, with assays to monitor innate and adaptive immunity
- Development of novel tools, assays and models bespokely tailored to project requirements
- State-of-the-art technology for hit finding and library screening to identify starting points for further profiling and modifications; screening capabilities up to BSL3 containment for target-based or phenotypic assays
- Identification and analysis of host biomarkers such as cytokines or innate signalling pathways



Contact our experts

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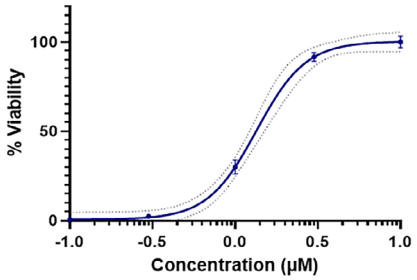
Viral Infections

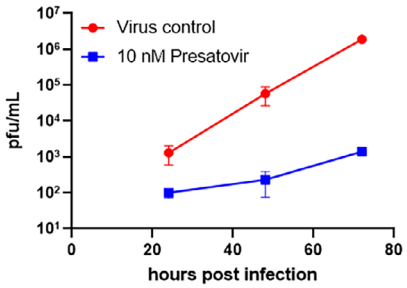
Human respiratory viruses including Coronaviruses (HCoV including endemic strains and most variants of SARS-CoV2), Respiratory Syncytial virus (RSV), Human Rhinovirus (HRV), Human Parainfluenza virus, Influenza virus.

- ***In vitro* infection systems:** Culture of virus and compound testing for potency and cytotoxicity in a range of different cell lines and virus or cell specific endpoints (cell viability, ELISA, RT-qPCR)
- **Air liquid interface system** with primary human bronchial and nasal epithelial cells

Cell viability assay



Human airway epithelial assay



In vivo models

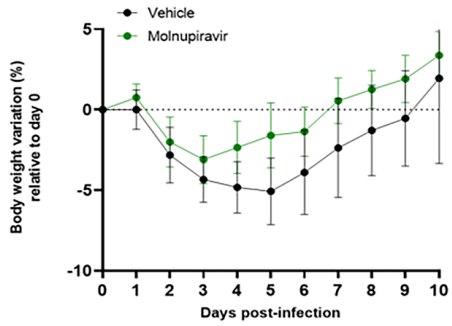
1) SARS-CoV2 hamster model with protocol tailored for specific applications (direct antivirals or host-targeting agents). Disease relevant readouts include: Body weights; Viral titre in tissues and oral swabs by RT-qPCR or plaque assay; Histopathology and Immuno-Histology of lung tissue; Cytokine/chemokine quantification in blood and tissue; Antibody characterisation by ELISA and neutralisation assay; Virus transmission between cage mates

2) ACE2 transgenic SARS-CoV2 mouse model with body weight and viral titre in tissues and oral swabs as endpoints

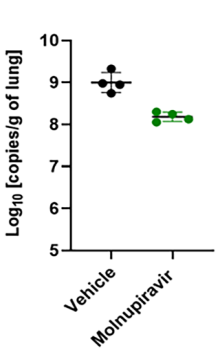
3) RSV cotton rat and mouse model; Cotton rat as gold standard model for RSV inhibitors, mouse for quicker access and availability of more biological tools, model has been used for vaccination and treatment studies. Validated endpoints include
   - Viral load in nasal and lung tissue by plaque staining assay and RT-qPCR
   - Antibody characterisation by ELISA and neutralisation assay
   - Immunohistochemistry
   - Cytokine/chemokine quantification in blood and tissue

SARS-CoV2 Hamster Model

Body weights



Viral burden

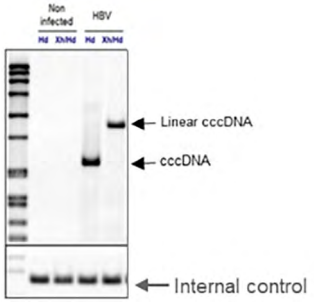


Hepatic viruses: HBV and HDV

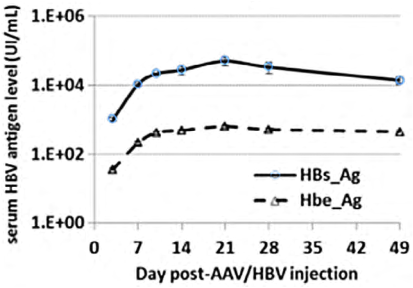
***In vitro* infection systems:** Culture of virus and compound testing in Primary Human hepatocytes as well as cell lines with parallel cytotoxicity testing. HBV/HDV co-infection in primary hepatocytes. Determination of cellular and secreted viral DNA and RNAs by RT-qPCR, cccDNA quantification by ddPCR and by Southern blot; Analysis of viral antigens HBeAg/HBsAg/HBx; analysis of host biomarkers including smc5/6 degradation, cytokines or innate signalling pathways.

HBV mouse model: Immune competent animals transduced with HBV via AAV carrier leading to persistent viral products over time with treatment protocol tailored for specific applications (direct antivirals or host-targeting agents). Disease relevant endpoints include:
Determination of circulating and liver viral DNA and RNAs by RT-PCR; cccDNA quantification by ddPCR and by Southern blot; Analysis of viral antigens HBeAg/HBsAg; profiling of Immune infiltrate and Cytokine release; Immuno-Histology of liver tissue and AST/ALT assessment.

cccDNA



Serum HBV antigen level

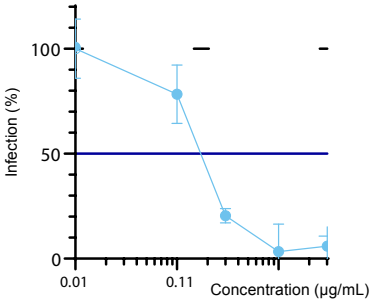


Emerging viruses

Pseudovirus constructs in VSV are available containing spike protein from several emerging viruses including SARS-CoV-2, SARS-CoV, MERS-CoV, Nipah and CCHF viruses to test entry inhibitors and neutralizing antibodies targetting different variants. This technique can be applied to many other viruses that normally need to be handled under BSL-3 and above containment. It can also be quickly adapted to include newly emerging variants.

Minigenomes are available for different viruses to rapidly evaluate polymerase inhibitors on wildtype and resistant mutants. These assays are more relevant than *in vitro* polymerase assays with a rapid read-out that is adaptable to HTS. It can be rapidly adapted to new emerging strains or variants with natural or induced resistance mutations

Neutralization using rVSV-SARS-CoV-2 Spike pseudovirus assay



Effect of pimodivir on PB2 mutants