

Novel Multi-Marker Screening Platform Cell line and Primary Human Hepatocyte Screening

ImQuest has developed a multi-parameter screening platform to expedite the screening of antiviral agents against hepatitis B virus (HBV) and gain immediate insight into mechanism of action. The assay can be customized to meet your development needs. HBV replication markers which can be evaluated include:

- Production of cccDNA
- Generation of pgRNA
- Synthesis of viral DNA
- Translation of viral proteins
- Viral DNA Encapsidation

The multi-parameter assay has been optimized for standard cell lines – HepG2 2.2.15, Hep AD38 and Hep AD79 – and also for primary human hepatocytes (PHH). PHH have been pre-screened for their ability to support HBV infection and replication, and can also be utilized to assess multiple endpoints of HBV replication.

Our suite of anti-HBV services includes assays to evaluate range of action, efficacy in drug combinations, potential for resistance selection, and characterization of resistant strains.

HBV Virus Stock Production

ImQuest also has the capability to produce HBV virus stocks and can achieve virus concentrations of approximately 1×10^{11} genome equivalents per milliliter. Virus production services include:

- Production of crude virus preparations
- Concentration of virus from crude preparations
- Isolation of viral proteins, RNA & DNA
- Determination of virus concentration
- Preparation of inactivated virus
- Quantification of proteins and nucleic acids

About ImQuest BioSciences

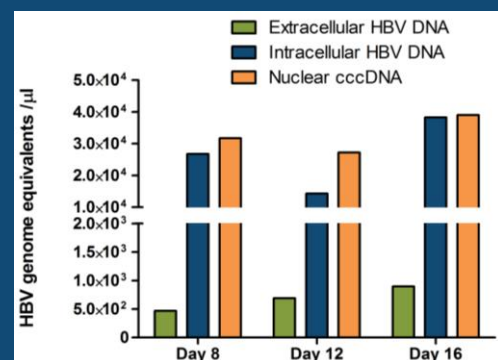
ImQuest BioSciences is a preclinical contract research and development company that evaluates the potential of new and novel pharmaceutical products. We specialize in services for the development of drugs, vaccines and biologics for the treatment and prevention of infectious disease, cancer and inflammatory disease.

Primary Human Hepatocyte Screening

ImQuest BioSciences has established a robust antiviral assay using primary human hepatocytes which can be used to assess the effectiveness of anti-HBV products. Cells are available fresh or cryoplateable; all PHH lots are tested for infectability prior to use at variable MOIs*. Numerous qPCR and ELISA-based endpoints are currently available including quantification of the following:

- Extracellular HBV DNA
- Intracellular HBV DNA
- cccDNA
- Pre-genomic RNA
- HBsAg
- HBeAg
- HBcAg

The figure below demonstrates the successful quantification of extracellular DNA, intracellular DNA and cccDNA from infected PHH. Contact us to learn more.



*Multiple PHH lots have been screened for their ability to support HBV replication. Cell lots are subject to availability; multiple lots may need to be tested prior to initiation of screening studies.

Using state-of-the-art and established *in vitro*, *ex vivo* and *in vivo* models, ImQuest BioSciences helps our clients rapidly identify antiviral agents with the potential to inhibit the replication of viruses.

Services

- Determination of efficacy and toxicity in established and fresh human cells
- Range of action assays, including:
 - Efficacy evaluation in a variety of phenotypically distinct human cell types
 - Efficacy evaluation against drug-resistant virus isolates
 - Efficacy evaluation in chronic and latent models of infection
 - Cell-to-cell virus transmission assays
 - Virucidal activity evaluation
 - Effect of serum and serum protein on antiviral activity
 - Effect of time-of-drug addition and viral multiplicity of infection
 - Efficacy against a range of infectious viruses
- Mechanism of action evaluations using cell-based, molecular/biochemical and enzymatic assays
- Combination therapy evaluation with other FDA-approved and experimental inhibitors
- Drug resistant virus selection and characterization analysis
- Pharmaceutical product characterization and formulation

Approach

Our work begins with drug discovery screening programs and follows a well-defined antiviral developmental pathway, guided by documents such as the FDA Points to Consider. We provide support from initial discovery to lead identification and IND-directed preclinical development.

Virus Panels

Human Immunodeficiency Viruses

- Hundreds of clinical and laboratory HIV-1 strains representative of Group M and O
- Drug-resistant and multi-drug resistant HIV-1 isolates
- Clinical and laboratory HIV-2 strains

Hepatitis and Flaviviruses

- Hepatitis B Virus
- Hepatitis C Virus surrogate - Bovine Viral Diarrhea Virus (BVDV)
- Hepatitis C Virus replicon system
- Zika Virus
- Chikungunya Virus
- Dengue Virus subtypes 1 through 4
- Yellow Fever Virus

Respiratory Viruses

- Influenza Virus (A & B)-numerous wild-type and drug-resistant strains
- Human Parainfluenza Viruses
- Respiratory Syncytial Viruses
- Human Rhinoviruses
- Measles Virus
- Human Adenoviruses

Herpes Viruses

- Herpes Simplex Virus type 1 and 2
- Human Cytomegalovirus
- Varicella Zoster Virus

Enteric Viruses

- Enteroviruses
- Echoviruses
- Coxsackie Viruses
- Poliovirus