Antiviral Research Branch
Enteric Diseases Branch
National Institute of Allergy and Infectious Diseases
National Institutes of Health

In Vitro Antiviral Screen & Antiviral Evaluation in Animal Models

A major goal of NIAID's Antiviral Research Branch and Enteric Diseases Branch is to identify promising agents for therapy of human viral infections (other than AIDS) and facilitate their development. The Branches interact with commercial and academic scientists in both the pre-clinical and clinical evaluations of their compounds. All rights to the compounds evaluated remain entirely with the compound sponsor. The sole interest of the government is to ensure that effective therapies for viral diseases are identified, developed, and licensed as expeditiously as possible.

I. Three in vitro antiviral screening facilities have been established to expediate the identification of compounds with inhibitory activity for herpes, respiratory viruses, and/or hepatitis B virus (HBV). In these facilities:

1. Selective indices of potential antiviral compounds are determined;
2. Active compounds are further evaluated in additional cell lines using virus strains including clinical isolates and resistant strains (except HBV); and
3. More extensive studies on mechanism of action and activity in drug combinations are conducted with the consent of the sponsor. Confidentiality is strictly maintained. Screening of compounds for antiviral activity is available for:

Herpesviruses: HSV-1, HSV-2, HCMV, VZV, EBV
Respiratory Viruses: Flu A, Flu B, RSV, Paraflu 3, Ad 5, Measles
Hepatitis B Virus

II. A major aspect of the pre-clinical antiviral evaluation occurs in animal model systems that mimic a viral disease process in man. The models currently supported by the Branches include:

1. HCMV in rabbits, guinea pig CMV, murine CMV.
2. HSV encephalitis in mice, neonatal herpes in mice, genital herpes in mice and guinea pigs.
3. Varicella-zoster virus infection of guinea pigs, rabbits.
4. RSV in cotton rats, measles in cotton rats.
5. Influenza in mice, parainfluenza in cotton rats.
6. Shope papillomavirus infection of domestic rabbits.
7. Xenograft system for growth of HPV 11 papillomas in nude mice.
8. Woodchuck hepatitis virus in woodchucks (HBV model).

For more information, contact:

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Developmental Therapeutics Branch
Division of AIDS
National Institute of Allergy and Infectious Diseases
National Institutes of Health

In Vitro and Animal Model Evaluation of Antiviral and Antiinfective Therapies

The mission of the Developmental Therapeutics Branch (DTB) is to facilitate the discovery of therapies for HIV and AIDS-associated opportunistic infections and to assist in their development into clinical trial candidates. DTB provides the resources listed below to assist academic and industrial scientists in preclinical aspects of drug development. All rights to compounds developed with the assistance of DTB remain entirely with the compound sponsor. The sole interest of the government is to ensure that effective therapies are developed and licensed as quickly and efficiently as possible.

Confirmatory in vitro testing for anti-HIV activity can be performed in T-cells and macrophages using standard laboratory strains, clinical isolates, and drug-resistant strains of HIV. Various virologic endpoints are available, including evaluation of virucidal potential using cervical epithelial cells. Combinations of antiviral agents are routinely evaluated. In vivo testing against HIV can be performed using a SCID/hu murine model. SIV, FIV, FeLV, and MuLV animal models of AIDS are available. Immune-based therapies can be evaluated in these animal models.

Primary screening of potential therapies against a variety of opportunistic infections that affect AIDS patients can be performed. In vitro or in vivo models can be used to determine drug efficacy against Pneumocystis carinii, Mycobacterium avium complex, Toxoplasma gondii, Cryptococcus neoformans, Candida albicans, Histoplasma capsulatum, Cryptosporidium parvum, and Mycobacterium tuberculosis. High throughput biochemical screens which use purified target and host enzymes are available for some of these organisms.

Facilities are available to provide preclinical, critical path development resources necessary to satisfy IND requirements, including scale-up synthesis, formulation development