UC RIVERSIDE
Occupational Health

Working with Viral Vectors: Herpesvirus

Introduction: viruses and viral vectors have become a staple of the molecular biology community. As such, it is important for users to understand the origins of these tools and potential implications of their use. The Herpesvirus section contains information on virology, clinical features, epidemiology, treatment, laboratory hazards, Personnel Protective Equipment (PPE), disinfection, instructions in the event of an exposure, and use with animals.

Herpesvirus: Herpesviruses include infectious human viruses such as herpes simplex virus type-1 (HSV-1), which is the most commonly used vector system. HSV-1 is common in the general population, but can cause encephalitis in rare cases; its utility as a vector system stems from its broad host cell range, ability to transduce neurons, and its large insert capacity. Biosafety Level 2 **(BSL2)** is appropriate for many constructs.

Virology: *Herpesviridae*, *Alphavirinae*, genus *Simplexvirus*; double-stranded linear DNA virus, icosahedral, lipid envelope, 110 - 200 nm diameter, HSV types 1 and 2 can be differentiated immunologically. Vectors derived from Herpes simplex virus (HSV) have some unique features. The vectors have a wide host range and cell tropism, infecting almost every cell type in most vertebrates that have been examined. In addition, the natural property of the virus to infect and establish latent infection indefinitely in post-mitotic neurons has generated substantial interest in using it to deliver therapeutic genes to the nervous system.

Clinical Features: Classic presentation of primary HSV-1 is herpes gingivostomatitis - oral mucosa, HSV 1 - primary infection is usually mild (10% of cases can be severe) and in early childhood; reactivation of latent infection results in fever blisters or cold sores, usually on the face and lips which crust and heal within a few days, may be CNS involvement (meningoencephalitis), 70% mortality rate if left untreated; causes about 2% of acute pharyngotonsillitis; Classic presentation of a primary HSV-2 infection is herpes genitalis, HSV 2 - genital herpes, sexually transmitted, associated with aseptic meningitis, vaginal delivery can cause risk to newborn, encephalitis and death; either HSV-1 and HSV-2 may infect the genital tract or oral mucosa.

Epidemiology: Type 1 - contact with saliva of carriers, infection of hands of health care personnel; Type 2 - usually by sexual contact; infected secretions from symptomatic or asymptomatic individuals. Virus may be secreted in saliva for up to 7 weeks after recovery and from genital lesions for 7-12 days: asymptomatic oral and genital infections, with transient viral shedding, are common; reactivation can be precipitated by over-exposure to sunlight, febrile, physical or emotional stress or foods and drugs, especially chemotherapy; HSV may be shed intermittently from mucosal sites for years, possibly life long.

HSV is spread by direct contact with epithelial or mucosal surfaces. Additionally,

approximately 50% - 90% of adults possess antibodies to HSV type 1; 20% - 30% of adults possess antibodies to HSV type 2. This is a concern as reactivation from latency is not well understood. Infection by HSV vectors into latently infected cells could potentially reactivate the wild-type virus, or spontaneous reactivation of a latent infection could produce an environment where replication defective vectors could replicate.

Treatment of Symptomatic Infection: If clinical disease develops (vesicular lesions, herpetic whitlow, ocular infection, etc.):

- **Oral acyclovir, valacyclovir, or famciclovir** for mucocutaneous disease.
- **Ophthalmology referral + topical antivirals** for ocular involvement.
- **IV acyclovir** for severe or disseminated disease.

Special Considerations

Pregnant or immunocompromised workers should be evaluated with high priority due to risk of severe disease and neonatal transmission. For more information contact Occupational Health or call (951) 827-5528.

Workers with active herpetic lesions (especially on hands) should not handle animals or cultures until cleared by Occupational Health Physician.

Ocular HSV Infection:

Topical antivirals: Trifluridine, idoxuridine, or vidarabine.

Oral antivirals: Acyclovir, valacyclovir, or famciclovir.

Laboratory Hazards: Ingestion; accidental parenteral injection; droplet exposure of the mucous membranes of the eyes, nose, or mouth; inhalation of concentrated aerosolized materials

Laboratory Hazards	PPE
Exposure of mucus membrane (eyes, nose, mouth)	**Use of safety goggles or full face shields. Use of appropriate face mask**
Injection	**Use of safety needles; NEVER re-cap needle or remove needle from syringe**
Aerosol inhalation	**Use of appropriate respiratory protection**
Direct contact with skin	**Gloves, lab coat, closed shoes**

The above PPE are often required IN ADDITION to working in a certified Biosafety Cabinet.

Susceptibility to disinfectants: Susceptible to common disinfectants - 1% sodium hypochlorite, iodine solutions containing ethanol, 70% ethanol, glutaraldehyde, formaldehyde

Use in Lab: BSL 2

Use with Animals: ABSL2housing.

Instructions in the Event of an Exposure

EXPOSURE FROM SPLASH OR AEROSOLS – INHALATION

Report the incident to your supervisor and refer to UCR Animal Researchers Occupational Health Guidance. At UCR, all injuries, regardless of severity, must be reported through the injury, incident, or safety concern form on the EH&S website Injury Reporting Form. You may contact **Occupational Health or call (951) 827-5528.**

EXPOSURE FROM SPLASH OR AEROSOLS – EYE CONTACT, SKIN AND/OR MUCOUS MEMBRANE

Rinse a minimum of 15 minutes in eye wash or flush area with water, report the incident to your supervisor and refer to UCR Animal Researchers Occupational Health Guidance for Researchers. At UCR, all injuries, regardless of severity, must be reported through the injury, incident, or safety concern form on the EH&S website Injury Reporting Form.

NEEDLESTICK AND/OR SHARPS EXPOSURE

Contaminated skin should be thoroughly scrubbed for several minutes with soap or a 10% povidone solution (Betadine) and copious amounts of water. Report the incident to your supervisor. All injuries, regardless of severity, must be reported through the injury, incident, or safety concern form on the EH&S website Injury Reporting Form. Undergraduate Student Employees report your injury to your supervisor (or go to Employee Injuries).

First and foremost, for life-threatening injuries call 911 immediately and obtain emergency treatment.

For all other injury types, seek Medical Treatment at UCR's preferred Occupational Clinics. Visit the Medical Treatment Facilities webpage to learn more on where to seek medical treatment.

References

1. Stanford University, "Working with Viral Vectors," https://ehs.stanford.edu/topic/biosafety- biosecurity/viral-vectors

University of California, Riverside
INFECTIOUS AGENT CARD

My job requires me to work with the agent Herpes Simplex Virus (HSV) and animals injected with HSV.

If the person with this card exhibits any of the symptoms listed on the back, immediately contact the UCI Medical Center Infectious Disease Fellow on call at (714) 456-6011. For immediate medical counseling on what to do right away, proceed to the nearest Emergency Department and present this card. For more information or to report an incident call: UC Riverside, Occupational Health, at (951) 827-5528.

Herpes Simplex Virus (HSV) is transmitted by skin contact with infected secretions from infected individuals.

INCUBATION PERIOD: 6-8 days

SYMPTOMS: Blisters in the skin or mucous membranes of the mouth, lips or genitals.

TREATMENT: Acyclovir or Valacyclovir. No full treatment is available.

Acknowledgement of Working with Viral Vectors: Herpesvirus

By signing below, I confirm that I have reviewed and understood the requirements for working with Herpesvirus viral vectors. I agree to comply with all outlined responsibilities, including:

- **Safe care practices**
- **Appropriate first aid procedures**
- **Prompt reporting of any exposures or incidents**

Name (Print)	Identification*	Signature	Date	Supervisor / Principal Investigator

*Identification: Provide your UCR Student ID, Employee ID, UCR NetID, UCR Email, or Date of Birth.