Lentiviral Vector Exposure Treatment

Introduction**:**

Detroit Medical Center’s (DMC) Occupational Health Services (OHS) has developed a Lentiviral Vector (LVV) post-exposure management plan that is applicable to Wayne State University (WSU) researchers. The treatment plan includes the option for research personnel to receive anti-retroviral drugs that are commonly used as prophylaxis following HIV exposure. It is important to note that any researcher that is exposed to LVV should report to OHS (or the Detroit Receiving Hospital Emergency Department (ED) after hours), but it is up to the patient, in consultation with the medical professional, as to whether or not they receive treatment. As a consequence, it is essential that WSU researchers are informed about the potential treatment strategies and knowledgeable about the risks associated with the specific lentiviral constructs being used within their laboratory. The following information and form are designed to facilitate discussion and document the pertinent information for individual research groups at WSU.

Laboratory Acquired Infections**:**

To date, there have been no documented cases of laboratory acquired infections/disease associated with LVV exposures. However, the consequence of exposure is difficult to measure due to a paucity of medical evidence relating to the specific outcomes of infection. In addition, adverse effects may occur years after the exposure incident.

Education:

The physicians at both the DMC Occupational Health Clinic and Detroit Receiving Hospital (DRH) Emergency Room will have access to the post-exposure management plan.

It is not practical for the Occupational Health Clinic to ensure physician knowledge about the specifics of lentivirus. The DMC OHS post-exposure management plan is written with this in mind.

The researcher is the most informed individual with regard to the specific hazards associated with the virus they are using. As such, prior education should be provided to research personnel by their Principal Investigator on:

1. Evaluating risk associated with the lentivirus being used
2. Routes of Transmission
3. What represents a significant exposure
4. Treatment options following exposure

1. Evaluating Risk: Lentivirus Vectors Information:

The risks from LVV exposure include; insertional mutagenesis, transgene expression, and generation of replication competent retrovirus. It is important that each construct being used in the lab is assessed and the potential risk associated with the LVV be evaluated. This will enable research personnel to make informed decisions when selecting medical treatment options in the event of an exposure incident.

Table 1: Information to help perform risk assessments of viral vectors1

|  |  |  |
| --- | --- | --- |
| **Vector variable** | **Low-risk Examples** | **Clinically Relevant Examples** |
| Transgene Function | Protein based fluorescence (e.g. GFP) | Silence a tumor-suppressor or Oncogene expression |
| Number of plasmids used to generate virions | 3-4 plasmids | 2 or less plasmids |
| Mutations within LVV | Self-inactivating LTRs | WT LTRs, Drug resistance  |
| Expression Control Elements | Weak promoters | Strong promoters (e.g. CMV, SV40) |
| Production volume | <100mL | >100mL |
| Concentrations | <1 x 109 IU/mL | >1 x 109 IU/mL |
| Percentage of genome deleted or substituted | >2/3 | <2/3 |

Modified from Schlimgen et al, 2016

2. Routes of Transmission:

Within the laboratory, the following represent the potential routes of transmission:

* Direct parenteral inoculation
* Contact with mucous membranes or non-intact skin
* Direct contact at a close range to droplets from an aerosol generating procedure outside of primary containment

3. What Represents a Significant Exposure?

Significant Exposures

* Contact with mucous membranes: eyes, nose, or mouth
* Contact with non-intact skin
* Skin puncture or injection
* Ingestion
* Droplets from an aerosol generating procedure

Low Risk Exposures

* Bite from recently infected animal
* Contact with body fluids from recently infected animal
* Intact skin contact with liquid solution or droplets

4. Treatment Options Following Exposure:

* The new treatment regimen is modeled on current HIV prophylaxis.
* The efficacy of the drugs being used is unknown with regard to lentivirus exposure, but believed to help to reduce risk based upon analogy to HIV treatment.
* Due to the viral vectors inability to replicate, the duration of the course of treatment is shortened in comparison to the standard treatment for HIV exposure.
* Prophylaxis is not usually indicated 72 hours post-exposure
* Drugs offered are an integrase inhibitor (Raltegravir2) with or without a NRTI (Truvada3) daily for 7 days
* The side effect profiles of the drugs are described as “tolerable” for most healthy individuals.
* OHS defined drug regimen is subject to change. The OEHS will endeavor to keep this document current but all treatment options should be discussed with the physician at the time of treatment.

Treatment options:

1. Decline intervention with anti-viral drugs
2. Accept treatment with Integrase inhibitor alone
3. Accept treatment with integrase inhibitor in combination with NRTI

Decision to treat:

* The decision to treat is based on an individual’s personal decision following consultation with the attending physician
* With regard to the decision to treat, primary consideration is given to the patient’s risk tolerance level
* Consultation with an infectious disease specialist and the patients primary care physician will occur if the patient has pre-existing illness or health concerns that may complicate treatment, including pregnancy, breastfeeding, and family planning.
* The patient is to be counseled and supported in whatever decision he or she makes

References:

1. <http://journals.lww.com/joem/Fulltext/2016/12000/Risks_Associated_With_Lentiviral_Vector_Exposures.1.aspx>

2. Raltegravir; Integrase Inhibitor: <https://www.isentress.com/raltegravir/isentress/consumer/common_side_effects_for_isentress/>

3. Truvada; NRTI: <http://www.truvada.com/patients>

**LENTIVIRUS EXPOSURE RESPONSE PLAN**

|  |  |
| --- | --- |
| **Lentivirus Vector Name:** |  |
| **Number of plasmids used to generate virions:** |  |
| **Mutations within LVV (SIN LTR or resistance):** |  |
| **Transgene Function:** |  |
| **Expression Control Elements:** |  |
| **Production volume:** |  |
| **Concentration:** |  |
| **Greater than 2/3rds of the HIV genome remaining?** |  |

**Routes of Transmission:**

Significant Exposures

* Contact with mucous membranes: eyes, nose, or mouth
* Contact with non-intact skin
* Skin puncture or injection
* Ingestion
* Droplets from an aerosol generating procedure

Low Risk Exposures

* Bite from recently infected animal
* Contact with body fluids from recently infected animal
* Intact skin contact with liquid solution or droplets

**First Aid:**

* Call emergency personnel if immediate medical care is needed (WSU Police: 313 577 2222)
* Stabilize the individual and provide first aid for injuries that require immediate medical care (e.g. deep cuts, bleeding, etc.)
* Skin Exposure: wash with soap and water: flush area with water 10-15 minutes
* Eye(s), Nose, Mouth Exposure: irrigate with running water for 15 minutes
* **Seek Professional Medical Treatment in the event of an exposure**

**Post-exposure Prophylaxis:**

Based upon discussion before the incident, the following treatments may be offered.

* As soon as possible but within 72 hours, initiate a 7-day course of a NRTI and/or an integrase inhibitor
* Observation and treatment of overt effects of the exposure incident

If no prior discussion about treatment has occurred, treatment with a NRTI and/or an integrase inhibitor should be considered and begin within 72 hours and continued based upon a discussion and acceptance of the risks and benefits of treatment.

**Report Incidents & Seek Care:**

* Take a copy of this document with you to the medical care facility
* Care should be sought as soon as possible, within 2 hours after exposure at OHS-4K Clinic or DRH-ER Department. After 72 hours, prophylactic medications may not be effective (although clinical follow-up remains essential).
* Notify PI of all accidents, injuries, or exposures involving lentiviruses
* Document incidents on WSU ‘Report of Injury From’ <http://idrm.wayne.edu/risk/rofi.pdf>

**EXPOSURE RESPONSE CONTACTS**

* **Principal Investigator (PI):**
* **WSU Public Safety:** 313-577-2222, emergency transportation
* **Occupational Health Services (OHS-4K):** 313-745-5123, available 7am-4:30pm
* **Detroit Receiving Hospital ER:** 313-745-3355, available outside OHS hours
* **Office of Environment Health & Safety:** 313-577-1200, spills or clean-up
* **Institutional Biosafety Committee Contact:** Richard Pearson. PhD, 313-993-7597

Reference:

 1. <http://journals.lww.com/joem/Fulltext/2016/12000/Risks_Associated_With_Lentiviral_Vector_Exposures.1.aspx>