| TITLE: UAB LENTIVIRUS VECTOR EXPOSURE RESPONSE PLAN (TIME CRITICAL) | | ACTIVATION DATE: 11/16/2017 |
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**A. Purpose:** Lentivirus vectors are derived from HIV and similar complex retroviruses and are popular research and gene therapy tools, due to their efficient delivery of transgenes to a broad range of target cells. While most researchers are working with replication-incompetent vector systems, these systems retain the ability to deliver and integrate their genetic material into the genome of exposed human cells. **The purpose of this program is to decrease the risk of insertional mutagenesis and/or transgene-associated malignancies resulting from an accidental exposure to lentiviral or retroviral vectors.**

**B. Scope:** UAB faculty, staff, or students exposed to lentiviral or retroviral vectors

**C. Risk Factors for considering post-exposure treatment recommendations:**

- **Exposure level:** Estimates of titer, volume, and potential exposure routes of are critical for determining the relative risk associated with a lentivirus exposure. The average viral load of an untreated HIV patient is 100,000 viral copies/ml of serum. Most lab viral constructs are at least this concentrated and would have an elevated risk of infection due to their enhanced properties.
- **Viral tropism (host or cell type specificity):** The envelope gene used to package a lentivirus will determine the species or cell type specificity of the vector. For example, most lentivirus preparations are pseudotyped with the vesicular stomatitis virus G protein, which infects a broad range of species and cell types, whereas lentivirus pseudotyped with an ecotropic envelope will only infect murine cells.
- **Generation of Packaging System:** The lentiviral vector systems used in the laboratory are generally "replication incompetent," meaning that they cannot cause an infection that will become self-perpetuating in the host to produce more virus. The "generation" of a lentivirus system conveys the degree of safety features engineered into the vectors to reduce the relative risk that a reversion to wild type (replication competent) virus can occur. Third and 4th generation systems are less likely to revert, compared to 1st and 2nd generation systems.
- **Insertional Mutagenesis:** Replication incompetent vectors MAINTAIN the ability to insert their genetic material into the genome of exposed cells, with the potential for insertional mutagenesis of tumor suppressor or activation of proto-oncogenes.
- **Transgenes expressed:** While the impact of experimental genetic material on human cells is usually unknown, there is presumed to be some level of risk from all inserted genetic material. There is a greater risk for vectors that express oncogenes, proto-oncogenes, cancer promoters, and toxins (e.g., proto-oncogenes used to induce pluripotent stem cells).
- **HIV rescue or amplification: UAB does not screen researchers for HIV. This Exposure Control Plan is designed to decrease the risks for all persons exposed to lentivirus vectors. Thus, there is one post-exposure protocol for all persons.** The impact of a lentiviral vector exposure to a person who is already HIV positive is unclear. There is a concern that the "wild type" HIV will supply the viral attributes necessary to produce replication-competent virus propagating the research DNA in the infected person. This is particularly concerning if the lentivirus expresses an oncogene or other adverse transgene.

## D. PROCEDURES FOR THE EXPOSED INDIVIDUAL:

1. Wash the exposure site:
   a. dermal/percutaneous: 15 minutes with soap and water
   b. mucous membranes: 15 minutes with water only

2. While washing the exposure area, have a colleague contact and report the incident to your supervisor (Supervisor's Phone Number: _____). Work with your colleague or supervisor to collect the agent specific information below to determine the magnitude of risk (see page page 1):
   a. titer: _____
   b. volume: _____
   c. route: _____
   d. transgene: _____
   e. tropism: _____

3. Seek treatment immediately (**Bring this exposure protocol with you**):
   - **During work hours (Monday-Friday, 7 AM - 4:00 PM):**
     The Workplace Clinic, 1201 11th Avenue South, Birmingham, AL 35205
     (205) 930-7007
   - **After hours or weekends:**
     UAB ED, 1802 6th Ave S, Birmingham, Alabama 35233,
     (205) 934-4011
   - Timing: goal is to obtain prophylaxes within 2 hours post-exposure
   - Prophylaxes acting on preintegration targets (integrase, reverse transcriptase) are only relevant for lentiviral vector exposures.

4. If you are seeking medical treatment at the Workplace Clinic, have a colleague or supervisor fill out an Initial Medical Evaluation Authorization form. Have your supervisor sign the form (if your supervisor is unavailable, seek a signature from an alternate departmental superior or OH&S representative). This form is required for reimbursement.

5. Schedule a 1-week follow-up appointment with The Workplace Clinic. In the Workplace Clinic a risk assessment (with the assistance of the Biosafety officer and appropriate scientists) will be completed to make a recommendation to continue or suspend treatment with antiretrovirals.

6. The supervisor should contact OH&S Occupational Medicine to report the incident as soon as possible
   - During work hours (8 AM – 5 PM): call 205-934-2487 and ask to be connected with an Occupational Medicine representative.
   - After hours or weekends: call UAB PD Dispatch at 205-934-4434 and ask to speak to "OH&S Directors on Call." The Director on Call can put you in touch with an Occupational Medicine representative.

7. If you have an injury requiring medical treatment that would cause a bill to be generated, you MUST fill out an OJI Application for Benefits form as well as a Release of Information form. The Trend Tracker Incident Report must also be completed before any bills will be paid.

## E. RESPONSE PROCEDURES FOR THE WORKPLACE CLINIC/UAB ED STAFF:

**THIS PATIENT HAS BEEN EXPOSED TO A LENTIVIRUS.**

1. **For treatment to be effective, it is critical that prophylaxis antivirals must be started immediately (preferably within 2 hrs).**

2. **An OJI Form is not a prerequisite for treatment in this situation.**

3. Verify exposure area has been washed/irrigated

4. For percutaneous exposures (needlestick) or exposures that include mucosal surfaces, initiate the following post-exposure prophylaxis:
   - Dispense one week supply of **Truvada 200/300 Daily and Raltegravir 400 mg BID**
   - Have the patient take the initial dose of both medications immediately
   - Draw the following screening labs: HIV 1 & 2 screening antibody

5. Inform the patient that it is very important that they start taking the medication immediately.

6. If there are questions concerning exposure risk to the patient and treatment, medical staff should contact OH&S Occupational Medicine
   - During work hours (8 AM – 5 PM): call 205-934-2487
   - After hours or weekends: call UAB PD Dispatch at 205-934-4434 and ask to speak to "OH&S Directors on Call" to arrange communication with an OH&S Occupational Medicine representative.

7. Advise the patient to schedule a 1-week follow-up at The Workplace clinic
   (205) 930-7007

## F. REFERENCES:

1. R. Schlimgen *et. al.* **Risks Associated With Lentiviral Vector Exposures and Prevention Strategies**. J Occup Environ Med. 2016 Dec;58(12):1159-1166.

2. **Biosafety in Microbiological and Biomedical Laboratories (BMBL).** 5th Ed., Dec. 2009.