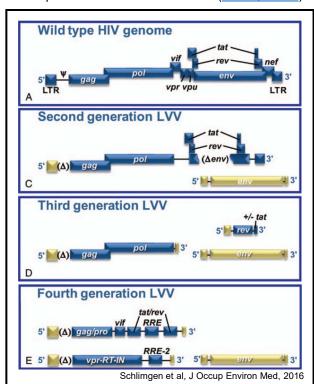


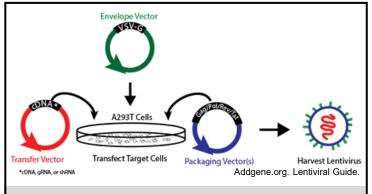
Working Safely with Lentiviral Vectors

Lentiviruses Characteristics

- Lentiviruses are a subtype of retroviruses that integrate the genes they need for replication into an infected host genome. Viral particles are made when the integrated lentiviral genomes are expressed into nucleic acids and proteins. This makes lentiviruses ideal tools for researchers to stably express or silence genes of interest in tissue culture and animal models.
- Safety concerns are primarily regarding generation of Replication-Competent Lentivirus (RCL) or oncogenesis as the result of integration of an oncogene or insertional mutations into an exposed researcher's genome.
- Lentiviruses are classified as Risk Group 2 agents, and work with lentiviral vectors should be performed in BSL-2/ABSL-2. (BMBL, 6th ed)



Lentiviruses are derived from wild-type HIV. By splitting up viral assembly genes onto separate plasmids, researchers can reduce the likelihood that transfected plasmids can recombine to form a full viral genome. EHRS recommends the use of 3rd and 4th generation lentiviral engineering.



Recombinant lentiviruses are synthesized by transfecting plasmids encoding lentiviral envelope and packaging proteins as well as gene(s) of interest into target cells. These target cells then express the proteins which self-assemble into recombinant viral particles; importantly, while these viruses are infectious, they lack the full-length genomes needed for replication.

PENN IBC Registration

- The <u>NIH Guidelines</u> specify the biosafety containment and practices for recombinant and synthetic nucleic acid research and require registration of such work with an Institutional Biosafety Committee (IBC) at all institutions receiving NIH funding.
- Registration of all lentiviral work is required with Penn's
 <u>IBC.</u> IBC registration numbers are also required on
 IACUC protocols involving all recombinant nucleic acid
 research. Registrations can be completed electronically
 on PIERS (ibc.research.upenn.edu).

Risk Mitigation

- Use 3rd and 4th generation lentiviral vectors to reduce likelihood of reconstituting RCLs.
- Recognize that using lentivirus for transducing oncogenes increases experimental risk.
- Select animal models that cannot support generation of RCLs.
- Reduce exposure likelihood by limiting the use of sharps while working with lentivirus.
- Self-monitor for symptoms of lentiviral infection (fever, myalgia, swollen lymph nodes, etc.).

Exposure Response

- · Report all spills and potential exposures to EHRS.
- Immediately proceed to Occupational Medicine (faculty, staff, and postdocs) or Student Health (graduate and undergraduate students) for medical treatment, which may include post-exposure prophylaxis (PEP).