IOWA STATE UNIVERSITY
Institutional Biosafety Committee

Guidance on Biosafety Level Designation for Adeno-Associated Virus Vectors

Background

Adeno-associated virus (AAV) is a small DNA virus which is commonly used as a viral vector for gene delivery. Although unrelated to Adenovirus, AAV was named such because it was discovered as a contaminant in Adenovirus preparations. AAV is a replication-defective, non-enveloped virus which requires the presence of a helper virus (typically Adenovirus or Herpesvirus) to replicate. Wild type AAV infects humans and other primate species but is not known to cause disease, and are considered non-pathogenic. Recombinant AAV (rAAV) vectors infect a wide range of mammalian cells. AAV can infect both dividing and non-dividing cells and may integrate its genome into the genome of the host cell. AAV vectors have been advantageous due to their efficient gene transfer, transient or stable transgene expression, and lack of induction of strong immune responses.

Biosafety Level Designation

The NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acids (NIH Guidelines) consider all AAV serotypes and recombinant or synthetic AAV constructs at risk group 1 (RG1) as long as the transgene does not encode either a potentially tumorigenic gene product (e.g., oncogene) or a toxin molecule and are produced in the absence of helper virus. However, rAAV that are produced in human cell lines are to be handled in accordance with the OSHA Bloodborne Pathogens Standard, under BSL2 containment.

The IBC will require BSL2/ABSL-2 containment if:
1) The transgenes express an oncogenic protein or toxin, or
2) The rAAV is produced using a helper virus of human origin, or
3) The rAAV is produced in human cell lines **without** purification prior to use.

The IBC may approve BSL1/ABSL-1 containment based on a risk assessment of the following criteria:
1) The nature of transgene expression
2) The use of a helper virus/production of replication competent virus or viral vector
3) The vector titer and the total amount of vector
4) Identification of the cell line in which the vector is produced
5) A description and analysis of purification procedures (e.g., column chromatography)
6) Risk factors including, but not limited to, aerosolizing procedures and the use of needles and sharps

References

Collins, D.E., J.D. Reuter, H.G. Rush, J.S. Vallano. 2017. Viral Vector Biosafety in Laboratory Animal Research. Comp. Med., 67(3), 215-221. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5482513/

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