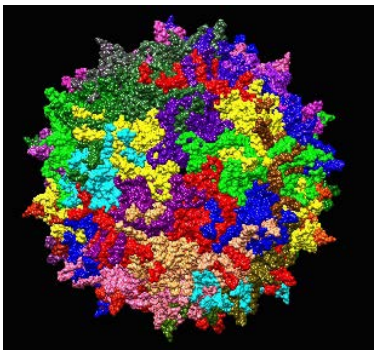
UNIVERSITY of GUELPH

RESEARCH INNOVATION

ADENO-ASSOCIATED VIRUS VECTOR WITH IMPROVED TRANSDUCTION FOR ANTIBODY EXPRESSION AND GENE THERAPY



Status

Development Status: TLR-4

Patent Status: Granted US 10,806,802 and Pending CA 3,023,706

License Status: Seeking non-eclusive licensees and product development collaborators

Opportunity

Drs. Sarah Wootton, Bernard Thebaud et al. have developed a novel triple mutant AAV6 capsid with significantly improved transfection, expression and tropism for respiratory epithelium. Also, this capsid has very efficient intramuscular expression of monoclonal antibodies useful for emergency vaccine and prophylactic applications or mAb drug delivery.

Advantages and Applications

Gene Therapy

- Highly trophic for respiratory alveolar type-2 cells
- Improved potency and response time compared to any vector
- 49 fold greater transgene expression in lung at 24h vs WT AAV6
- 5 fold greater resistant to antibody neutralization vs WT AAV6
- In vivo efficacy validated using surfactant replacement model in surfactant deficient (SPB-/-) mice
- Lower viral vector dose required for efficacy
- Rapid therapeutic levels achieved within 3 days post-administration
- Easily purified using heparin columns –lowering manufacturing costs
- Potential vector for treating other monogenic lung diseases and for gene editing in the lung

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mAb Expression

- Robust and sustained in vivo expression of mAb-based kinase inhibitors and vascular normalizing agents
- Validated as a rapid intramuscular mAb gene delivery vector using Ebola mouse model and proven anti-Ebola antibodies: (published)
- 100% protective in a mouse adapted Ebola challenge model
- Highly efficient intramuscular expression of mAb or single chain variable fragment
- Almost immediate transgene (antibody) production in serum
- 101 fold greater transgene expression in muscle at 24h vs WT AAV6
- 10 fold greater resistance to immunoglobulin neutralization vs WT
- Maintained heparin sulfate binding useful for large-scale production
- Improved in vitro transduction makes culture methods easier vs WT
- Transgene (antibody) expression persists for > 1 year, perhaps longer…

References

Lieshout LP. et al. (2018) A Novel Triple-Mutant AAV6 Capsid Induces Rapid and Potent Transgene Expression in the Muscle and Respiratory Tract of Mice. Molecular Therapy, Methods & Clinical Development, Vol 9:323-329.

Lieshout LP. et al. (2018) Intramuscular Adeno-Associated Virus–Mediated Expression of Monoclonal Antibodies Provides 100% Protection Against Ebola Virus Infection in Mice. Journal of Infectious Diseases, Vol 217:916–925.

Lieshout LP. et al. (2019) AAV-Mediated Gene Delivery to the Lung. In: Michael J. Castle (Eds.), Adeno-Associated Virus Vectors Methods in Molecular Biology, Vol. 1950, 361-372.

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