

What is claimed is:

1. A method of determining the stoichiometry of protein components of an intact, non-enveloped viral particle, comprising:

subjecting a sample comprising said viral particle to hydrophilic interaction liquid chromatography (HILIC) to separate the protein components of the viral capsid of the viral particle;

determining the masses of protein components of the viral capsid to identify the protein components separated by HILIC;

determining the relative abundance of the protein components of the viral capsid from the HILIC separation, thereby determining the stoichiometry of protein components of the viral capsid of said viral particle.

2. The method of claim 1, wherein the viral particle comprises an adeno-associated virus (AAV) particle.

3. The method of claim 2, wherein the protein components of the protein capsid comprise VP1, VP2 and VP3 of the AAV particle.

4. The method of claim 2, wherein the masses of VP1, VP2, and VP3 are compared to theoretical masses of one or more of an AAV1 capsid, an AAV2 capsid, an AAV3 capsid, an AAV4 capsid, an AAV5 capsid, an AAV6 capsid, an AAV7 capsid, an AAV8 capsid, AAVrh8 capsid, an AAV9 capsid, an AAV10 capsid, an AAV11 capsid, an AAV12 capsid, or a variant thereof.

5. The method of claim 3, wherein the AAV particle comprises an AAV1 capsid, an AAV2 capsid, an AAV3 capsid, an AAV4 capsid, an AAV5 capsid, an AAV6 capsid, an AAV7 capsid, an AAV8 capsid, AAVrh8 capsid, an AAV9 capsid, an AAV10 capsid, an AAV11 capsid, an AAV12 capsid, or a variant thereof.

6. The method of claim 2, wherein the AAV particle comprises an AAV1 inverted terminal repeat sequence (ITR), an AAV2 ITR, an AAV3 ITR, an AAV4 ITR, an AAV5 ITR, an AAV6 ITR, an AAV7 ITR, an AAV8 ITR, an AAV9 ITR, an AAV10 ITR, an AAV11 ITR, or an AAV12 ITR.

7. The method of claim 2, wherein the AAV particle is a recombinant AAV (rAAV) particle or an AAV vector encoding a heterologous transgene.

8. The method of claim 2, wherein the AAV particle has a capsid serotype selected for transduction of cells of a subject's liver.

9. The method of claim 8, wherein the AAV particle has a capsid serotype AAV7, AAV8, or AAV9.

10. The method of claim 9, wherein the AAV particle has a capsid serotype AAV9.

11. The method of claim 2, wherein the AAV particle has a capsid serotype AAV9 and is a viral vector encoding Lysosomal Alpha Glucosidase (GAA) linked to an anti-CD63 antibody.

12. The method of claim 1, wherein the viral particle comprises a viral vector encoding a heterologous transgene or belongs to a viral family selected from the group consisting of Adenoviridae, Parvoviridae, Retroviridae, Baculoviridae, and Herpesviridae.

13. The method of claim 12, wherein the viral particle belongs to a viral genus selected from the group consisting of Atadenovirus, Aviadenovirus, Ichtadenovirus, Mastadenovirus, Siadenovirus, Ambidensovirus, Brevidensovirus, Hepadensovirus, Iteradensovirus, Penstyldensovirus, Amdoparvovirus, Aveparvovirus, Bocaparvovirus, Copiparvovirus, Dependoparvovirus, Erythroparvovirus, Protoparvovirus, Tetraparvovirus, Alpharetrovirus, Betaretrovirus, Deltaretrovirus, Epsilonretrovirus, Gammaretrovirus, Lentivirus, Spumavirus, Alphabaculovirus, Betabaculovirus, Deltabaculovirus, Gammabaculovirus, Iltovirus, Mardivirus, Simplexvirus, Varicellovirus, Cytomegalovirus, Muromegalovirus, Proboscivirus, Roseolovirus, Lymphocryptovirus, Macavirus, Percavirus, and Rhadinovirus.

14. The method of claim 12, wherein the Retroviridae is Moloney murine sarcoma virus (MoMSV), Harvey murine sarcoma virus (HaMuSV), murine mammary tumor virus (MuMTV), gibbon ape leukemia virus (GaLV), feline leukemia virus (FLV), spumavirus, Friend virus, Murine Stem Cell Virus (MSCV) Rous Sarcoma Virus (RSV), human T cell leukemia viruses, Human Immunodeficiency Viruse (HIV), feline immunodeficiency virus (FIV), equine immunodeficiency virus (EIV), visna-maedi virus; caprine arthritis-encephalitis virus; equine infectious anemia virus; feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); or simian

immunodeficiency virus (SIV).

15. The method of claim 1, wherein the HILIC uses a mobile phase A comprising trifluoroacetic acid in water or a mobile phase B comprising trifluoroacetic acid in acetonitrile.

16. The method of claim 15, wherein the mobile phase A or the mobile phase B comprises about 0.1% trifluoroacetic acid.

17. The method of claim 15, wherein the proportion of mobile phase A in the chromatography increases over time.

18. The method of claim 17, wherein mobile phase A increases from about 15% to about 100%, over about 45 minutes.

19. A method of determining the heterogeneity of protein components of a capsid of an intact, non-enveloped viral particle comprising:

subjecting a sample comprising said viral particle to hydrophilic interaction liquid chromatography (HILIC) to separate protein components of the viral particle's capsid;

determining the masses of protein components of the capsid;

comparing the determined masses of the protein components of the viral particle's capsid with theoretical masses, wherein a deviation of one or more of the masses of protein components of the viral particle's capsid from the theoretical masses is indicative of capsid heterogeneity.

20. The method of claim 19, wherein the heterogeneity comprises one or more of mixed serotypes, variant capsids, capsid protein amino acid substitutions, truncated capsid proteins, or modified capsid proteins.