

PL9008: Key publications on the characterization of gene vectors by light scattering

Summary

This document lists key publications using high-throughput dynamic light scattering (HT-DLS), size exclusion chromatography combined with multi-angle light scattering (SEC-MALS), and field flow fractionation combined with MALS (FFF-MALS) to characterize various gene delivery nanoparticles including viral vectors/virus like particles (VLPs), lipid nanoparticles (LNPs), extracellular vesicles (EVs), and other gene carriers.

Viral vectors and virus-like particles

HT-DLS

- **Virus-derived nanoparticles**

Dashti, N.H., Sainsbury, F. *Protein Nanotechnology*. Humana, New York, NY (2020). 149-162.
https://doi.org/10.1007/978-1-4939-9869-2_9.

- **Virus-like particle formulation optimization by miniaturized high-throughput screening**

Mohr, J. et al. *Methods* **60**(3), 248-256 (2013).
<https://doi.org/10.1016/j.ymeth.2013.04.019>

SEC-MALS

- **Comprehensive characterization and quantification of adeno-associated vectors by size exclusion chromatography and multi angle light scattering**

McIntosh, N.L. et al. *Scientific Reports* **11**:3012 (2021)
<https://doi.org/10.1038/s41598-021-82599-1>

- **Comparison of analytical techniques to quantitate the capsid content of adeno-associated viral vectors**

Werle, A.K. et al., *Molecular Therapy: Methods & Clinical Development*. **23** (December 2021)
<https://doi.org/10.1016/j.omtm.2021.08.009>

- **Detailed protocol for the novel and scalable viral vector upstream process for AAV gene therapy manufacturing**

Silveraj, N. et al., *Human Gene Therapy*. **32** (August 2021) <https://doi.org/10.1089/hum.2020.054>

FFF-MALS

- **Quantitative real-time single particle analysis of virions**

Heider, S., Metzner, C. *Virology* **462**, 199-206 (2014).
<http://dx.doi.org/10.1016/j.virol.2014.06.005>

- **Quantitative analysis of virus-like particle size and distribution by field-flow fractionation**

Chuan, Y.P. et al. *Biotechnology and Bioengineering* **99**(6), 1425-1433 (2008).
<https://doi.org/10.1002/bit.21710>

- **Characterization of virus-like particle assembly for DNA delivery using asymmetrical-flow field-flow fractionation and light scattering**

Citkowicz, A. et al. *Analytical Biochemistry* **376**(2), 163-172 (2008).
<https://doi.org/10.1016/j.ab.2008.02.011>

IEX-MALS

- Biophysical Characterization of Adeno-Associated Virus Vectors Using Ion-Exchange Chromatography Coupled to Light Scattering Detectors

Wagner, C. et al. *Int. J. Mol. Sci.* **23**(21), 12715 (2022)
<https://doi.org/10.3390/ijms232112715>

Lipid nanoparticles

HT-DLS

- Automated high-throughput preparation and characterization of oligonucleotide-loaded lipid nanoparticles

Yuchen, F. et al. *International Journal of Pharmaceutics* **599**, 120392 (2021)
<https://doi.org/10.1016/j.ijpharm.2021.120392>

- Impact of lipid nanoparticle size on mRNA vaccine immunogenicity

Hassett, K.J. et al. *Journal of Controlled Release* **335**, 237-246 (2021) <https://doi.org/10.1016/j.jconrel.2021.05.021>

- Polysarcosine-functionalized lipid nanoparticles for therapeutic mRNA delivery

Nogueira, S.S et al., *ACS Applied Nano Materials* **3**(11), 10634-10645 (2020).
<https://doi.org/10.1021/acsanm.0c01834>

- High-throughput in vivo screen of functional mRNA delivery identifies nanoparticles for endothelial cell gene editing

Sago, C.D. et al. *PNAS* **115**(48) (2018)
<http://doi.org/10.1073/pnas.1811276115>

SEC-MALS

- Polydispersity characterization of lipid nanoparticles for siRNA delivery using multiple detection size-exclusion chromatography

Zhang, J. et al. *Analytical Chemistry* **84**(14), 6088-6096 (2012).
<https://doi.org/10.1021/ac3007768>

- Enabling online determination of the size-dependent RNA content of lipid nanoparticle-based RNA formulations

Jia, X. et al. *Journal of Chromatography B* **1186**, 123015 (2021).
<https://doi.org/10.1016/j.jchromb.2021.123015>

FFF-MALS

- Improved multidetector asymmetrical-flow field-flow fractionation method for particle sizing and concentration measurements of lipid-based nanocarriers for RNA delivery

Mildner, R. et al. *European Journal of Pharmaceutics and Biopharmaceutics* **163**, 252-265 (2021)
<https://doi.org/10.1016/j.ejpb.2021.03.004>

- Physical characterization of liposomal drug formulations using multi-detector asymmetrical-flow field flow fractionation

Parot, J. et al. *Journal of Controlled Release* **320**, 495-510 (2020).
<https://doi.org/10.1016/j.jconrel.2020.01.049>

- Liposome size analysis by dynamic/static light scattering upon size exclusion-/field flow-fractionation

Hupfeld, S. et al. *Journal of Nanoscience and Nanotechnology* **6**(9-10), 3025-3031 (2006).
<http://doi.org/10.1166/jnn.2006.454>

Polymeric nanoparticles

SEC-MALS

- Synthesis of biocompatible PEG-based star polymers with cationic and degradable core for siRNA delivery

Cho, H.Y. et al. *Biomacromolecules* **12**(10), 3478-3486 (2011).
<https://doi.org/10.1021/bm2006455>

SEC-MALS, DLS, ELS

- Molecular weight-dependent activity of aminated poly(α)glutamates as siRNA nanocarriers

Krivitsky, A. et al. *Polymers* **10**(5), 548 (2018).
<https://doi.org/10.3390/polym10050548>

Extracellular vesicles

HT-DLS

- Profiling plasma extracellular vesicle by pluronic block-copolymer based enrichment method unveils features associated with breast cancer aggression, metastasis and invasion

Zhong, Z. et al. *Journal of Extracellular Vesicles* **7**(1), 1458574 (2018).

- Plasma exosome profiling of cancer patients by a next generation systems biology approach

Domenyuk, V. et al. *Scientific Reports* **7**, 42741 (2017).
<https://doi.org/10.1038/srep42741>

FFF-MALS

- Separation and characterization of extracellular vesicles from human plasma by asymmetrical flow field-flow fractionation

Wu, B. et al. *Analytica Chimica Acta* **1127**, 234-245 (2020).
<https://doi.org/10.1016/j.aca.2020.06.071>

- Evaluation of exosome separation from human serum by frit-inlet asymmetrical flow field-flow fractionation and multiangle light scattering

Kim, Y. B. et al. *Analytica Chimica Acta* **1124**, 137-145 (2020). <https://doi.org/10.1016/j.aca.2020.05.031>

- Asymmetric-flow field-flow fractionation technology for exomere and small extracellular vesicle separation and characterization

Zhang, H., Lyden, D. *Nature Protocols* **14**(4), 1027-1053 (2019).
<https://doi.org/10.1038/s41596-019-0126-x>

- Identification of distinct nanoparticles and subsets of extracellular vesicles by asymmetric flow field-flow fractionation.

Zhang, H. et al. *Nature Cell Biology* **20**, 332-343 (2018).
<https://doi.org/10.1038/s41556-018-0040-4>

- Size characterization and quantification of exosomes by asymmetrical-flow field-flow fractionation

Sitar, S. et al., *Analytical Chemistry* **87**(18), 9225-33 (2015).
<https://doi.org/10.1021/acs.analchem.5b01636>

Other gene carriers

FFF-MALS

- The utility of asymmetric flow field-flow fractionation for preclinical characterization of nanomedicines

Hu, Y. et al. *Analytical and Bioanalytical Chemistry* **412**(2), 425-438 (2020).
<https://doi.org/10.1007/s00216-019-02252-9>



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