Analytical Metrology for Isolating, Purifying and Characterizing Extracellular Vesicles (EVs) for Development and Delivery of Gene and Protein-Based Therapeutics

NIST NRC Postdoctoral Fellowship Solicitation

Extracellular vesicles (EVs), and in particular exosomes, have the potential to revolutionize the development and efficient delivery of gene and protein therapeutics. Due to their natural non-immunogenicity and their inherent capacity to target specific cell types with no or minimal off-target selection, exosomes are currently being investigated as therapeutic agents in multiple disease models.[1] The most established method for isolating exosomes from biological samples (biofluids and/or cell cultures) is based on differential centrifugation (preparative ultracentrifugation), although other methods such as magnetic or immunoaffinity separation and size exclusion chromatography are also utilized.[2] Robust purification and analytical characterization of the purified exosome fractions is required due to sample heterogeneity (e.g., microvesicles mixed with exosomes) and sample contamination by exomeres, protein aggregates, microsomes, etc., before the isolated exosomes can continue down the development pipeline toward the therapeutic stage. In addition, it is important to be able to discriminate between the different sub-classes (membrane compositions) of purified exosomes that will potentially be loaded with therapeutic agents. Some techniques for the purification of isolated exosomes include field flow fractionation and sucrose density gradient centrifugation. Standardized methods for isolating and/or purifying exosomes from biological samples do not exist and this is a critical research gap that has been recognized by the International Society for Extracellular Vesicles.[3] This postdoctoral solicitation features an opportunity to address this urgent need by inviting motivated investigators to comprehensively examine and expand upon current methods or to develop completely new, reproducible methods for isolating, purifying and characterizing exosomes from biological samples. Method development efforts should focus on the incorporation of a robust and optimized experimental design aimed at assessing the sources of variability, repeatability and reproducibility for isolating and purifying exosomes from a representative biological model. Measurements should incorporate the use of process controls, rigorous statistical analysis techniques and method robustness evaluations appropriate for high-quality protocol development.

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Keywords: characterization; drug delivery; exosomes; extracellular vesicles; isolation; measurement assurance; method development; microvesicles; therapeutics

References:

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