VAMAS

Synthetic Biomaterials

Technical Work Area 40

Project 5

An intracellular distribution number of virus-like particles per cell

Objectives

The aim of this work is to provide a comparability dataset for a distribution number of virus like particles (VLPs) in mammalian cells. The work is to support the characterisation of VLPs as reference materials for intracellular gene and drug transfer. This study will measure the number of the particles and their distribution in cells after transfection using high resolution microscopy.

Background

The lack of biologically relevant reference materials that are suitable for the comparative characterisation of advanced medicinal products remains a major barrier for commercialisation in cell and gene therapies (2007/1394/EC).

Bio-functional particles are of increasing importance as candidate reference materials due to their high performance profiles in terms of drug loading capacities and intracellular transfer. Therefore, quantitative measures of their uptake into cells and biophysical properties in relevant environments, that is in cells and between cells, as accurately as deemed feasible, is essential for standardisation and commercialisation.

Despite the importance of and need for such reference materials, none is available to date.

Standardization needs

The pre-standardisation needs focus on:

- protocols for the preparation of cell samples transfected with virus-like materials
- assigned values consistent between laboratories and using different techniques
- procedures for quantitative analysis of the values by reproducible measurements of the highest metrological order
- performance validation of reference materials in biologically native and near-native environments.

Relevant generic Standards

ISO Guide 35 Reference materials
SO 29301: 2017
ISO 13022:2012
CHMP/GTWP/671639/2008

Relevant Committees

ISO/TC 276—Biotechnology
ISO/TC 229—Nanotechnology
ISO 15194: 2009—CRMs

Work Programme

- Rodent macrophages will be transfected with synthetic VPLs, fixed, processed for electron microscopy and microtomed to give thin sections (70 nm).
- The thin sections will be distributed to the participants for characterisation.
- Analysis of the results including statistical evaluation
- Repeatability and reproducibility of the results will be tested from a smaller group of participants.

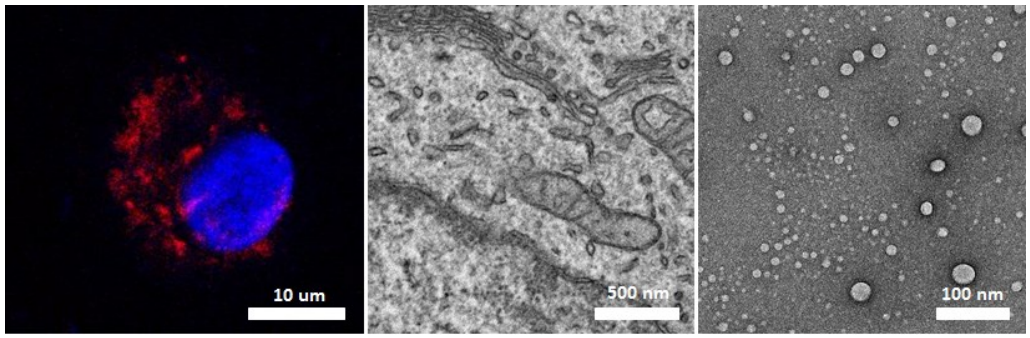
Second stage analysis

- Measurement protocols that give accurate distribution numbers of VLPs per cell and per cell area of transfection will be used for correlated imaging using super-resolution microscopy.

Knowledge Transfer

International round-robin tests, good practice guidelines, peer-review publications and presentations.

Call for Participation



Fluorescent micrograph showing the uptake of VLPs (red) into macrophages (nucleus in blue) - (A) and electron micrographs of macrophage (B) and VLPs (C).

Status

Study in progress since October 2018.

Additional Volunteers Welcome
Participants fund their own study in the project

For more information on participation, please contact:

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April 2019