Understanding how drug carrier physico-chemical properties shape their interactions in complex biological environments and with cells

Anna Salvati

Department of Nanomedicine & Drug Targeting, Groningen Research Institute of Pharmacy, University of Groningen, Groningen, Netherlands

a.salvati@rug.nl

Our research is focused on understanding at a fundamental level how the drug carriers used in nanomedicine interact with and are processed by cells. In this talk, we will show you how we combine optimization and physico-chemical characterization of drug delivery systems with different methods in cell biology to determine their interactions with cell receptors, mechanism of uptake and intracellular behavior. In addition, we will present novel methods to characterize cellular pathways, which we developed by taking advantage of nanoparticle properties. [1,2]
Particular attention is given to the modifications drug carriers encounter upon administration: once in contact with complex biological fluids, biomolecules adsorb on the drug carrier surface, forming a corona that strongly affects the subsequent interactions with cells. For instance, we previously showed that the adsorbed corona molecules can interact with specific cell receptors and affect the mechanisms cells use for internalizing the drug carrier.[3,4] Similarly, we found that the adsorbed corona can modulate the transfection efficiency of lipid nanoparticles for RNA delivery, such as those used for the RNA vaccines against COVID-19.[5]
Next, we focus on nanoparticle interactions with cells, and in particular the interaction with cell receptors, mechanisms of uptake and intracellular behavior, and study how these processes can be controlled by tuning nanoparticle physico-chemical properties. As an example of this, we used liposomes of different compositions in order to obtain nanoparticles with different rigidity and study how nanoparticle mechanical properties affect their cell behavior. Similarly, we modulated liposome charge to obtain positively charged nanoparticles that are stable in biological fluids and are not toxic to cells and used them to understand at a fundamental level why positively charged nanoparticles usually are internalized by cells more than negatively charged ones. [6]
Our findings highlight the importance of understanding how drug carrier physico-chemical properties shape their interactions in complex biological environments and with cells in order to be able to design nanomedicines with the desired outcomes at the cell level.

Keywords:
Drug delivery, nanomedicine, biomolecule corona, liposomes, lipid nanoparticles, cell uptake

References:

[1] Garcia Romeu, H. et al., *Time-and Space-Resolved Flow-Cytometry of Cell Organelles to Quantify Nanoparticle Uptake and Intracellular Trafficking by Cells* , **Small** 2021, 17 (34), 2100887.
[2] Garcia Romeu, H. et al., *Organelle Sorting and Proteomic Analysis to Identify Proteins Involved in the Uptake and Intracellular Trafficking of Nanoparticles* , **Small Methods** 2025, e02004.
[3] Francia, V. et al. *Corona Composition Can Affect the Mechanisms Cells Use to Internalize Nanoparticles* . **ACS Nano** 2019, 13, 11107-11121.
[4] Montizaan, D. et al, *Genome-wide forward genetic screening to identify receptors and proteins mediating nanoparticle uptake and intracellular processing,* **Nature Nanotechnology** 2024, 19 (7), 1022-1031.
[5] Liu et al, *Multiomics analysis of naturally efficacious lipid nanoparticle coronas reveals high-density lipoprotein is necessary for their function* , **Nature Communications** 2023, 14 (1), 4007.
[6] Zhao et al, *Effect of positive charges on liposome stability, uptake efficacy and impact on cells* , **International Journal of Pharmaceutics** 2025, 681, 125881.