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Supervisor's contact details

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Title of the project

Molecular Spherical Nucleic Acids as Next generation therapeutics

MSCA-PF Research Panel

☒ Chemistry (CHE)

☐ Social Sciences and Humanities (SOC)

☐ Economic Sciences (ECO)

☐ Information Science and Engineering (ENG)

☐ Environment and Geosciences (ENV)

☒ Life Sciences (LIF)

☐ Mathematics (MAT)

☐ Physics (PHY)

Description of the project

The interest of pharma companies towards oligonucleotides (ONs) as therapeutics has exponentially increased in recent years and even further boosted by the success of COVID-19 vaccines. However, ON drugs suffers from the known obstacles in delivery. Thus, their functionality is limited to diseases that can be treated by intrathecal, -muscular and -vitreal administration and intravenously via blood stream in liver hepatocytes only. Bioorganic group/Utu (https://bioorganic.utu.fi/) has recently investigated atomically uniform molecular [C60]fullerene-based SNAs (MSNAs) as delivery warheads. The radial formulation of MSNAs may be used to hide unfavourable biodistribution properties of negatively charged ONs and simultaneously enhance cell-specific ligand effect on the outer sphere. These low valency MSNAs do not activate scavenger receptors strongly, and their delivery can bypass organs, rich by cells of the mononuclear phagocyte system (MPS), such as liver, spleen and lungs. These characteristics may open possibilities to targeted tissue-specific delivery of ONs. Preliminary in vivo PET imaging study verifies that MSNAs do not accumulate in liver, like most NPs, but a prolonged activity in blood circulation is observed. In this project (fellow's aim) readily available core units and optimized synthetic strategies will be used for the assembly of MSNAs, which with appropriate outer sphere decoration will yield next generation delivery warheads for therapeutic ONs. To find the best delivery warheads, the role of bio-corona, in depth cellular uptake, and in vivo biodistribution of the MSNAs will be investigated.

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Research objectives or research questions of the project

For more systematic evaluation of how the core unit, valency and structural design of the MSNAs affect the delivery and biological activity, a set of MSNAs will be assembled. The oligonucleotide loading and its density correlate with Scavenger A-mediated endocytosis and, consequently, with efficacy of polydisperse SNAs in vitro and in topical delivery. However, the role of the core unit, structural design and valency of MSNAs for the in vivo-biodistribution is unknown, which needs to be investigated in detail.

MSNAs of most promising structures will be decorated with cancer cell-specific ligands to aim targeted delivery. The ligands may include small molecular ligands, constituents of glycans and aptamers that show affinity to cell surface receptors of breast cancer cells.

An attention to the synthetic availability, how homogeneous MSNAs can be assembled in a scalable and sustainable manner, will be paid. For this purpose, entirely in liquid phase occurring synthetic strategies will be developed.