mRNA Drug-Nanoparticles: Polymer and Liposomes - Study by SANS and DLS

Siewert C.[1], Ziller A.[1], Nogueira, S.[3], Nawroth T.[1],
Haas H.[3], Radulescu A.[4], Sahin U.[2,3], Langguth P.[1]

[1] *Pharmacy and Biochemistry Inst., Pharma-Technology, Gutenberg-University, D-55099 Mainz, Germany*
[2] *Exp. Oncology, III. Med Clinics, TRON, University Medicine Gutenberg-University, D-55131 Mainz, Germany*
[3] *BioNTech AG – Individualisierte Immuntherapien, An der Goldgrube 12, D-55131 Mainz, Germany*
[4] *Jülich Centre for Neutron Science JCNS at Heinz Maier-Leibnitz Zentrum MLZ, D-85748 Garching, Germany*

mRNA pharmaceuticals represent a new area of therapeutics, with a large range of application, including cancer vaccination, tumour therapy and protein substitution [1-2]. For administration, formulations are required to carry messenger RNA (mRNA) to the target side. These Nano carriers bear additional excipients for the induction of genetic transfection after receptor mediated cell uptake. Such mRNA nanoparticles can be setup as polyplexes containing a polymer matrix.
In the current study mRNA containing polyplexes and basic excipients were investigated in structure by D-contrast SANS, SAXS and dynamic light scattering DLS. The bio-medical ability was demonstrated by transfection of cell cultures with luciferase mRNA nanoparticles. The polymer Diethylaminoethylen (DEAE) - Dextran formed nanoscaled poly-cationic/poly-anionic complexes with mRNA. A typical nanoparticle size of 60 - 100 nm was estimated by SANS at the JCNS, Garching, and DLS, while the absence of large aggregates was demonstrated. Due to the composition of at least two materials of different hydrogen content, structure and domains are distinguished by neutron scattering SANS with the deuterium contrast method giving us additional information in comparison to SAXS. The Dextran nanoparticles depicted SANS profiles with multiple side maxima, as it is typical for a macro-helical structure (Fig. 1 b). In contrast to SAXS measurements, main particle structure signal, side maxima, and mRNA were investigated by the solvent contrast variation technique at various H_2O/D_2O mixtures. The different D-matching points (scattering length density SLD) indicated the formation of local contact domains between polymer and mRNA. Using SANS measurements it was possible to obtain detailed structural informations for active pharmaceutical polyplexes unattainable with SAXS.

a) SAXS of DEAE-Dextran-mRNA polyplex **b) SANS of DEAE-Dextran-mRNA polyplex**

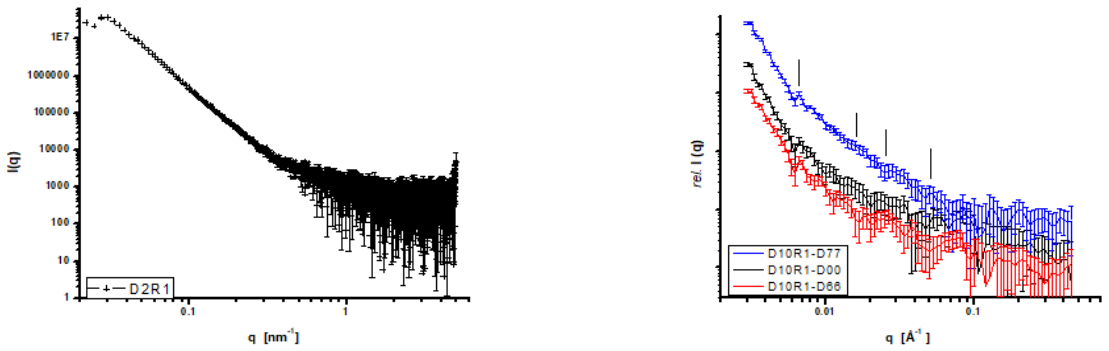

Figure 1. a) SAXS of DEAE-Dextran/mRNA nanoparticles b) SANS of DEAE-Dextran/mRNA nanoparticles at different H_2O/D_2O mixtures

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[2] Stadler C.R., Bähr-Mahmud H, Celik L, Hebich B, Roth AS, Roth RP, Kariko K, Sahin U (2017) Nature Medicine doi:10.1038/nm.4356
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