Peptide dendrimers as novel vehicles for mRNA transfection

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The Sars-Cov-2 pandemic of the last years has led to a surge in the application of mRNA vaccines as viable prevention for infectious diseases. Although this technique has proven as highly efficient, certain shortcomings have been highlighted, among them instability of lipid nano particles, the degradation of the coding mRNA and the inability to escape endosomes to achieve translation to the final immunogen[1]. Recently, peptide dendrimers have been found to spontaneously aggregate into nano particles with siRNA[2] and facilitate endosome escape through formation of alpha-helices, which perforate the endosomal membrane, therefore enabling efficient transfection[3].

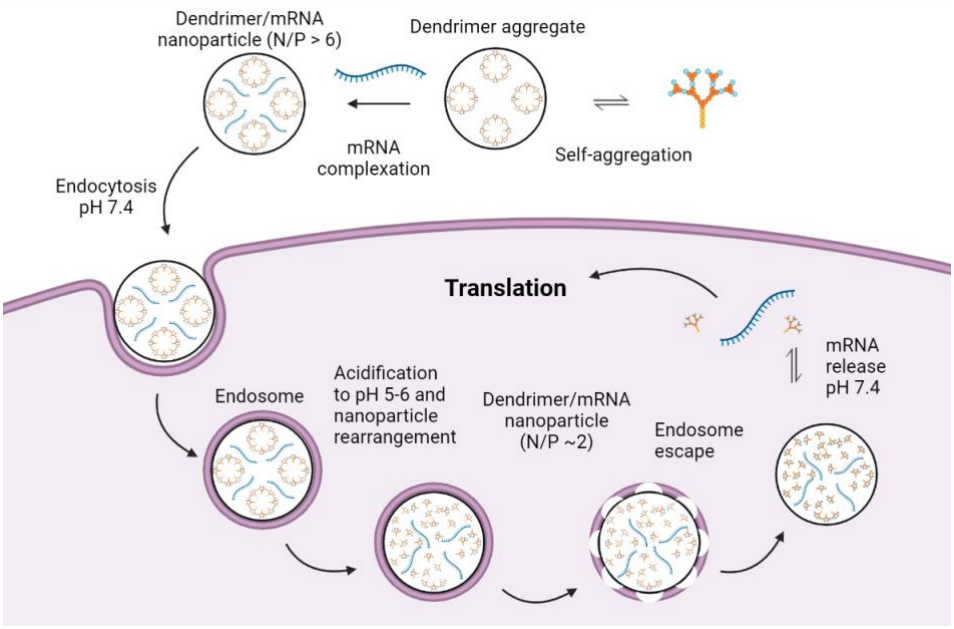

Figure: Schematic representation of peptide dendrimer mediated mRNA transfection.

In this research project peptide dendrimers are being employed as new transfection agents for mRNA molecules with sizes up to 3420 nucleotides. Confocal microscopy as well as beta-galactosidase Assays have been employed to compare transfection efficiency with the current gold standard Lipofectamine. Our research has led to new compounds with activity on par with Lipofectamine and viability surpassing the current gold standard. The final goal of this project is to generate peptide dendrimers, that facilitate mRNA transfection with high efficiency and great ease to further progress the development of mRNA vaccines for infectious diseases.

[1] X. Hou, T. Zaks, R. Langer, Nature Reviews Material, 2021, 1078–1094
[2] M. Heitz, S. Javor, T. Darbre, J.-L Reymond, Bioconjugate Chemistry, 2019, 30 (8), 2165-2182
[3] M. Heitz, S. Zamolo, S. Javor, J.-L. Reymond, Bioconjugate Chemistry, 2020, 31 (6), 1671-1684