Title	**Development of RNA delivery systems**
PI	**Francesca Mastrotto**
Research Group	**Drug delivery and Biopharmaceutic**
Curriculum	**Pharmaceutical Sciences**
Location	Ed. B Dep. of Pharmaceutical and Pharmacological Sciences
Contact	**web: https://www.dsfarm.unipd.it/francesca-mastrotto**
	email: francesca.mastrotto@unipd.it

Project description:

The project concerns the development of innovative polymer and lipid-based delivery systems for therapeutic nucleic acids, and in particular RNA. The COVID-19 pandemic has brought new light on the efficacy of mRNA vaccines and, in general, on RNA therapeutics. Of note, RNA treatments are often developed for rare diseases, where there is no alternative. This is due to the fact that once the delivery system is optimized for a specific type of RNA (e.g. mRNA, siRNA etc), it can be easily applied to other RNA sequences belonging to the same family, although with a different therapeutic purpose. This is supported by the number of clinical trials ongoing on RNA both as therapeutics and as biomarkers for several disfunctions, with a lot of research dedicated to the identification of the role of different miRNAs on the onset and prognosis of the disease. Two are the key points to achieve an effective RNA therapy: 1. The chemistry of the nucleic acid used to stabilize the structure and make it more “active” and, 2. The vehicle adopted to protect the RNA from degradation after injection into our body, to favour its internalization by target cells, and to facilitate the endosomal escape preventing its degradation in the lysosomes. Thus, this project aims at generating block copolymers composed of a cationic fraction for RNA complexation, a targeting portion to direct the system towards selected cells, and a third block to facilitate the endosomal escape. In parallel, the polymeric platform will be compared with solid lipid nanoparticles specifically designed for RNA transport and decorated with newly designed targeting agents. Once synthesized, the delivery systems will be screened for their complexation ability of RNA therapeutics, and characterized for their physico-chemical properties and stability in physiological medium. In vitro studies will be devoted to investigate their transfection efficiency, and, possibly, the more promising candidates will be tested in vivo.

Hosting group(s) for the period abroad (tentative list, may change):

Prof. Francisco Fernandez Trillo, Chemistry Department, University of Coruna (SP)
Prof. Giuseppe Mantovani, Faculty of Pharmacy, University of Nottingham

Publications:

[1] Bellato F. *et al. Biomacromolecules,* 2022, 23 (12), 5148-5163.
[2] Mastrotto *et al. JACS*, *2022, 144, 50, 23134–23147.*
[3] Malfanti *el al. JCR, 2019, 310, 58-73.*
[4] Loczenski Rose, V., *Polymer Chemistry*, 2017, 8(2), 353–360.