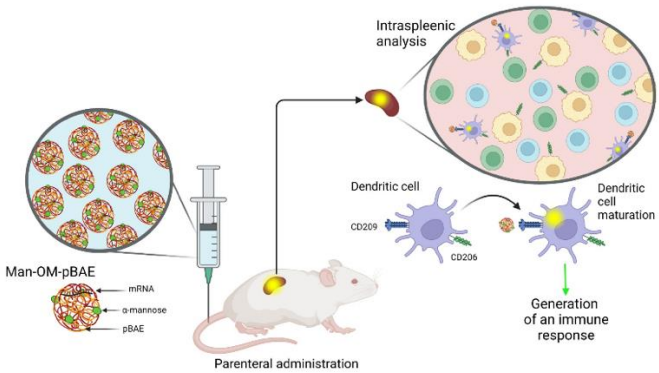
MANNOSE-FUNCTIONALIZED NANOPARTICLES AS MRNA VACCINES SELECTIVELY TARGETED TO ANTIGEN-PRESENTING CELLS

Magda Faijes[a], Nil González-Ríos[a,b], Maria Bericat[a,b], Antoni Planas[a], Salvador Borrós[b], Cristina Fornaguera[b]

[a] Laboratory of Biochemistry, Institut Químic de Sarrià, Ramon Llull University, Barcelona, Spain
magda.faijes@iqs.url.edu
[b] Grup d'Enginyeria de Materials,Institut Químic de Sarrià, Ramon Llull University, Barcelona, Spain

Cancer represents one of the most devastating diseases without an effective treatment, with lung cancer ranking among the most lethal. Immunotherapies, especially therapeutic vaccines that use mRNA as an active compound, stand as the most promising solutions [1]. Poly b-(amino esters) (pBAE) have been demonstrated to efficiently encapsulate mRNA generating small polymeric nanoparticles, the protection and controlled release of the genetic material, their biocompatibility; and their ability to promote cellular internalization and transfection [2,3]. However, their selectivity is not fully controlled due to the lack of an active targeting moiety.
It is of utmost importance to design selective vectors to selectively target them toward antigen presenting cells (APCs), and specifically, to dendritic cells (DCs). Knowing the significance of glycobiology [4], in which the carbohydrates exposed on the nanoparticles interact with the targeted cells surface proteins, this project aims at engineering α-mannose-nanoparticles to enhance cell dendritic targeting presenting lectins like DC-SIGN and MMR.
Three different polymer candidates were synthesized with variable-length mannose functionalization [5,6]. Fine formulation of these polymers with mRNA resulted in nanoparticles decorated with surface-exposed α-mannoses with sizes around 180 nm and positive surface charge (see figure: Man-OM-pBAE). Notably, these particles maintained their properties after freeze-drying and subsequent redispersion. Finally, our mRNA carriers preferentially targeted and transfected APCs in vitro and in vivo. In conclusion [5, 6], we demonstrated, at a preclinical level, that the mannose functionalization enables more selective targeting of APCs and, thus, these polymer and nanoparticles are candidates for a new generation of mRNA immunotherapy vaccines.



References:
1. Esfahani, Roudaia, Buhlaiga, Del Rincon, Papneja and Miller, Current Oncol., 27(S2), 87–97, **2020.**
2-3. Shi, Beasock, et al., Adv. Drug Deliv. Rev.180, 114079 **2022**. Magaña Rodriguez JR, Guerra-Rebollo M, Borrós S, Fornaguera C., Drug Deliv Transl Res. (12):3477-3493 **2024.**
4. Feinberg et al, CD206, JBC, 296, 100368, **2021**.
5. González-Ríos, Artigues, Guerra-Rebollo, Planas, Borrós, Faijes Fornaguera, Journal of Materials Chemistry B. 11, 6412-6427 **2023**.
6. Patent: EP24383477.7: Polymers comprising two building blocks obtained by click chemistry and uses thereof **2024.**