BPP 2022 POSTER ABSTRACT SUBMISSION

Maria I. Sousa, Mara G. Freire, Francisca A. e Silva, Augusto Q. Pedro

CICECO – Aveiro Institute of Materials, Department of Chemistry, University of Aveiro, Portugal

TITLE: Integrated manufacturing of mRNA nanomedicines using thermoreversible aqueous biphasic systems and ionic liquids

Keywords: mRNA nanomedicines; ionic liquid; integrated manufacturing processes; thermoreversible aqueous biphasic system; *in vitro* transcription; T7 RNA polymerase.

Abstract (250 words)

The COVID-19 pandemic has unlocked the potential of messenger RNA (mRNA) vaccines as an effective tool to contain infectious diseases outbreaks. Over conventional vaccines, mRNA vaccines show advantages, namely improved safety and efficacy, and the possibility of repeatedly administration. In addition to infectious diseases, mRNA offer enhanced therapeutic approaches for a wide range of diseases including cancer, myocardial ischemia, genetic diseases, among others [1]. However, mRNA nanomedicines production is still complex and expensive, requiring improved technologies to produce more stable and widely accessible products by meeting a timely and sufficient manufacturing capacity. If properly engineered, ionic liquids (ILs) can improve the stability of RNA [2] and contribute to the achievement of highly selective purification processes when applied as components of aqueous biphasic systems (ABS) [3]. To overcome the described bottlenecks, this work proposes the integration of production and clarification steps of mRNA manufacturing processes using thermoreversible ABS comprising ILs to simplify subsequent purification steps.

So far, we have accomplished the production of mRNA by *in vitro* transcription, and its purification using conventional methods, followed by the study of mRNA stability and integrity in ILs with different chemical structures. Based on these results, ongoing work is focused on the selection of the best production-clarification platform resorting to thermoreversible IL-based ABS.

In conclusion, the integrated production-clarification platform herein developed can be essential to overcome the challenges of mRNA nanomedicines production, namely by lowering costs and environmental impact of current manufacturing processes while improving mRNA stability, yield, and speed of production.

References (250 words)

[1] Pardi, N.; Hogan, M.J.; Porter, F.W.; Weissman, D. mRNA vaccines — a new era in vaccinology. *Nature Reviews Drug Discovery* 2018, *17*, 261-279, doi:10.1038/nrd.2017.243.
[2] Pedro, A.Q.; Pereira, P.; Quental, M.J.; Carvalho, A.P.; Santos, S.M.; Queiroz, J.A.; Sousa, F.; Freire, M.G. Cholinium-Based Good's Buffers Ionic Liquids as Remarkable Stabilizers and

Recyclable Preservation Media for Recombinant Small RNAs. *ACS Sustainable Chemistry & Engineering* 2018, *6*, 16645-16656, doi:10.1021/acssuschemeng.8b03900.
[3] Ventura, S.P.M.; e Silva, F.A.; Quental, M.V.; Mondal, D.; Freire, M.G.; Coutinho, J.A.P. Ionic-Liquid-Mediated Extraction and Separation Processes for Bioactive Compounds: Past, Present, and Future Trends. *Chemical Reviews* 2017, *117*, 6984-7052, doi:10.1021/acs.chemrev.6b00550.

Acknowledgements (250 words)

This work was developed within the scope of the following projects: CICECO-Aveiro Institute of Materials, UIDB/50011/2020, UIDP/50011/2020 & LA/P/0006/2020, financed by national funds through the FCT/MEC (PIDDAC); EIC-Pathfinder YSCRIPT project with reference 101047214, supported by the budgets of the Horizon Europe Program; and mVACCIL (EXPL/BII-BTI/0731/2021, Improving the manufacturing of mRNA vaccines applying ionic liquids and integrated production-clarification processes), financially supported by national funds (OE), through FCT/MCTES. Augusto Q. Pedro and Francisca A. e Silva acknowledge FCT respectively, for the research contracts CEEC-IND/02599/2020 and CEEC-IND/03076/2018 under the Scientific Stimulus – Individual Call.

Submitted and presented at BPP 2022 - Biopartitioning & Purification Conference 2022, Aveiro, Portugal (September 2022).