Manufacturing of mRNA nanomedicines using thermoreversible aqueous biphasic systems and ionic liquids

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The COVID-19 pandemic has unlocked the potential of messenger RNA (mRNA) vaccines as an effective tool to contain infectious disease outbreaks. Over conventional vaccines, mRNA vaccines show advantages, namely improved safety and efficacy, and the possibility of repeatedly administration [1]. However, mRNA nanomedicine 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.

Ionic liquids (ILs) are molten salts comprising organic cations, with a remarkable structural diversity and with promising applications as solvents and catalysts. 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]. Accordingly, 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 using a T7 polymerase-based cell free system and its purification using conventional methods, followed by the implementation of quality control methods to evaluate mRNA purity. Considering the most promising ILs able to maintain the stability and integrity of mRNA, 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 to be developed can be used to overcome the challenges of mRNA nanomedicine production, namely by lowering costs and environmental impact of current manufacturing processes while improving mRNA stability, yield, and speed of production.

Acknowledgements:
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.

Keywords: mRNA nanomedicines; ionic liquid; thermoreversible aqueous biphasic system; in vitro transcription.

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