Final Report

Project acronym: *MagicCELLGene*

Project number*: 4174*

M-ERA.NET Call 20*16*

Period covered: 01/09/2017 to 28/02/2021

Publishable project summary

The MagicCELLGene consortium, formed by Consejo Superior de Investigaciones Científicas (CSIC, project coordinator, Spain), Universidad de Zaragoza (UNIZAR, Spain) and Associação para a Inovação e Desenvolvimento da FCT (NOVA.ID-FCT, Portugal) worked on bringing together for the first time two independent areas of knowledge: **magnetic hyperthermia** and **cell transfection**. The **ultimate goal** of the project was to **develop a novel methodology for artificial introduction of nucleic acids into cells** through pores on the cell membrane generated by **"hotspots" triggered by magnetic hyperthermia (MH)**. This represented an **unprecedented application of MH,** which typically uses the ability of magnetic nanoparticles (MNPs) of transforming magnetic energy into heat under an alternating magnetic field (AMF) for cancer treatment or drug delivery purposes. Our approach was based on the covalent immobilization of magnetic nanoparticles (MNPs) on living cell membranes through bioorthogonal click chemistry. We hypothesised that, under the application of an alternating magnetic field (AMF), MNPs would induce a controlled and localized heating of nanometric regions of the cell membrane (so-called "hotspots"), without causing alterations in cell viability (sub-lethal magnetic hyperthermia). Our efforts were specially directed towards increasing transfection efficiency of hard-to-transfect cells (primary cells), while maintain a high cell viability. Currently used non-viral transfection methodologies are usually rather cytotoxic and do not achieve adequate transfection rates, which imposes limitations to several therapeutic applications where the genetic modification of these cells is a key factor (e.g. *ex vivo* cell transfection for gene and cell-based therapy). At the end of the project, **we were able to demonstrate the feasibility of the proposed methodology as a novel transfection technology** using different nucleic acids and representative established (MCF7 - breast cancer) and primary cells (immature and mature dendritic cells).

Despite some technical and administrative problems in the first half of the project and the delays caused by the COVID-19 health crisis in the second half, we achieved most of the project objectives. In addition, progress has been made in all work packages in terms of TRL level, exceeding the initial level of TRL2 (technology concept formulated), with all the proposed activities achieving a TRL level higher than 2.