Acadamh Ríoga na hÉireann
Royal Irish Academy

# Charlemont grant report

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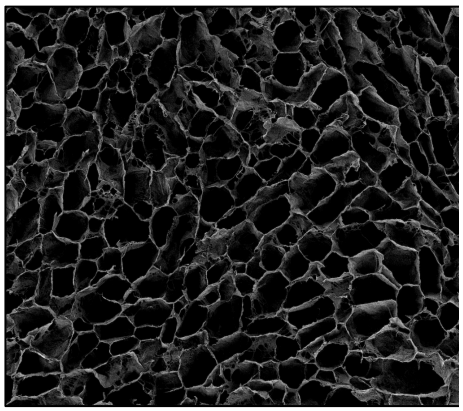
| Recipient name: | Dr. Joanna Sadowska |
| Discipline and subject area: | Sciences |
| Amount and year awarded: | €2,500. in 2023 |
| Title of project: | Development of novel gene-activated scaffolds delivering mRNA encoding bone morphogenetic protein-2 and bone morphogenetic protein-7 for bone regeneration. |

**Summary of findings:**

The project titled 'Development of novel gene-activated scaffolds delivering mRNA encoding bone morphogenetic protein-2 and bone morphogenetic protein-7 for bone regeneration,' focuses on addressing the challenge of treating large-volume bone defects in bone tissue engineering.

The project consisted of the use of collagen–nanohydroxyapatite scaffolds, developed at the Tissue Engineering Research Group (TERG) at RCSI with chemically modified messenger RNA (cmRNA) encoding for BMP-2 and BMP-7 (the most potent bone proteins) designed at the MERLN Institute at Maastricht University.



The project firstly evaluated the scaffolds in vitro with human mesenchymal stem cells and in vivo using a subcutaneous nude mouse model. The in vitro characterisation has been finalised while the in vivo study will finalise in December with the analysis of the data scheduled for Q1 and Q2 of 2024.

The key achievements of the in vitro study are:

1. Demonstrated osteogenic differentiation of human mesenchymal stem cells using BMP-2 and BMP-7 cmRNAs: This opens the door for using mRNA technology, originally used in vaccine development, for regenerative medicine approaches.
2. Development of an effective scaffold system delivering BMP-2 and BMP-7 cmRNAs: This system provided controlled and sustained delivery of the genetic cargoes up to 7 days post-transfection.
3. Demonstrated osteogenic potential of the scaffold system: The research demonstrated that the scaffold-based system for BMP-2 and BMP-7 cmRNA delivery significantly accelerated osteogenesis and mineralization of human mesenchymal stem cells (hMSCs) in vitro.

The innovative approach developed within this project showed great promise for gene therapy in regenerative medicine, particularly in treating large-volume bone defects. It has the potential to

revolutionize current clinical practices for bone regeneration, offering a safer, more affordable, and effective method.

The findings from this study have significant implications for the field of bone tissue engineering and regenerative medicine. The research paves the way for the development of more effective treatments for bone defects and injuries, potentially improving patient outcomes in orthopaedics and related medical fields.

**Plans for continuing collaboration:**

As mentioned, the in vivo study is scheduled to be finalised in December, with the analysis of the data planned for the first and second quarters of 2024. This analysis will encompass comprehensive procedures, including histological staining, ELISA, oxygen consumption rate (OCR), and micro-computed tomography (µCT) analysis. The primary objective of these analyses is to ascertain whether the scaffolds delivering chemically modified RNA (cmRNA) can effectively induce bone formation in vivo. This ongoing collaboration remains critical for the successful completion and evaluation of our research, promising to contribute significantly to the field of bone tissue engineering and regenerative medicine.

We plan to continue the collaboration with the MERLN Institute at Maastricht University. We anticipate two publications from the project and two international talks. The results obtained through the project and incorporated into the publication and provide a strong background for applications for grants from national and international agencies, including the SFI-IRC Pathway, Health Research Board Emerging Investigator Awards, and ERC Starting Grant. Furthermore, we also plan to apply for collaborative grants to foster knowledge exchange. The grants include COST Actions or MSCA Innovative Training Networks.

**Additional Collaboration:**

I am currently part of a research team for the project WoundActiv (PI: Prof. Fergal O'Brien, Royal College of Surgeons in Ireland). This collaboration includes academic partner Prof. Helen McCarthy from Queen's University Belfast. Additionally, I am currently a part of COST Action PlasTHER, which investigates the therapeutic applications of cold plasmas. This action is led by Prof. Cristina Canal from Universitat Politècnica de Catalunya. I act as the leader of Working Group 5 (Combination Therapies and am a member of the committee representing Ireland. The COST Action gathers over 100 scientists (national and international partners) from more than 25 countries. The full list of collaborators and participants can be found on the website: https://www.plasther.eu/.

**Publications associated with this project that you have been involved in:**

The project will result in two publications:

'Transcript Activated Matrices with Chemically Modified mRNA Coding for BMP-2 and BMP-7 Accelerates Osteogenesis'; Claudia Del Toro Runzer, Joanna M. Sadowska, Christian Plank, Fergal J. O'Brien, Martijn van Griensven, and Elizabeth R. Balmayor. Targeted journal: Advanced Functional Materials – The manuscript is currently under internal review.

'The Effect of Scaffolds Delivering Chemically Modified mRNA Coding for BMP-2 and BMP-7 on Bone Formation In Vivo'; Claudia Del Toro Runzer, Joanna M. Sadowska, Christian Plank, Fergal J. O'Brien,

Martijn van Griensven, and Elizabeth R. Balmayor. Targeted journal: Advanced Materials – The manuscript will be completed after finalising the analysis of the in vivo results.

**Dissemination and plans for future dissemination:**

We anticipate two communications at international conferences in 2024. The targeted conferences are the European Orthopaedic Research Society Annual Meeting (Aalborg, September 2024) and the Tissue Engineering and Regenerative Medicine World Meeting (Seattle, June 2024).

**Outreach and engagement activities:**

During my scientific career, I have been actively engaging with the general community to disseminate my science and outreach. In previous years, I gave several invited talks either in person or online which were open to the public. This includes:

1. J.M. Sadowska, 'Development of Biomaterial Scaffolds Delivering microRNAs for Bone Repair', TERMIS Virtual Seminar Series, 23 March 2021.

2. J.M. Sadowska, 'Delivering microRNAs on Biomaterial Scaffold for Bone Repair (Oral Communication), Virtual Seminars in Biomedical Science, 23 July 2020, online content: https://www.youtube.com/watch?v=gxSHoEXHsKA.

In 2023, I shifted my public engagement to online platforms including my Twitter account *(@jmsadowska,* 661 followers) and my LinkedIn account (https://www.linkedin.com/in/joanna-sadowska-phd/, 4.3k followers). On my LinkedIn profile, I publish regularly (twice per week) posts regarding cell and gene therapy, regenerative medicine, and tissue engineering.