ENCAPSULATION PROCESS OF MUSCLE STEM CELLS IN ALGINATE MATRICES TO ENHANCE THEIR *IN VIVO* POST-TRANSPLANT PROPERTIES

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Identification of a stem cell population derived from human muscle (hMuStem) and the demonstration of its regenerative potential have led to new cell therapy proposals for muscle diseases [1]. However, the ability of these adult stem cells to survive and integrate into the host tissue is a limiting factor with regard to their overall therapeutic impact. Emergence of tissue biomimetic approaches based on encapsulating cells in biocompatible and biodegradable biomaterials offers new opportunities to overcome the limitations of cell therapy in terms of viability and potentiation of effects. Initial *in vitro* results have enabled us to validate the possibility of encapsulating hMuStem cells in alginate matrices without altering the biological properties associated with their commitment in the myogenic program [2]. It was shown that macroscopic hydrogels obtained by molding methods possess mechanical, structural and diffusion properties compatible with hMuStem cells. However, their large size limits their therapeutic applications to subcutaneous implants. For this reason, transposition of the encapsulation method to microfluidic approaches seems essential to achieve micrometric matrices more suitable with transplantation protocols [3]. To improve the efficiency of hMuStem cell delivery, we have developed a microfluidic chip enabling the efficient encapsulation of cells in micrometer-scale alginate matrices. In parallel, we assessed the impact of this encapsulation process on the morphology and viability of hMuStem cells.

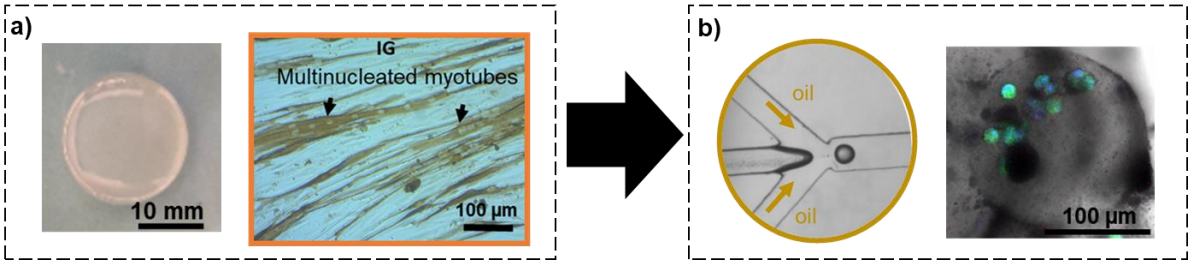

Figure 1. (a) Conservation of biological activities of hMuStem cells inside calcium-alginate macrogels mimicking muscle elastic modulus (12 kPa). (b) Scaling up by transposition to droplet microfluidic approaches to open up application for cell transplantation-based therapy.

References:
1. J. Lorant, C. Saury, C. Schleder, F. Robriquet, B. Lieubeau, E. Négroni, I. Leroux, L. Chabrand, S. Viau, C. Babarit, M. Ledevin, L. Dubreil, A. Hamel, A. Magot, C. Thorin, L. Guevel, B. Delorme, Y. Péréon, G. Butler-Browne, V. Mouly, K. Rouger, *Molecular Therapy*. **2018**, 26, 2; 618-633.
2. M. Marquis, A. Zykwinska, B. Novales, I. Leroux, C. Schleder, J. Pichon, S. Cuenot, K. Rouger, *International Journal of Biological Macromolecules*. **2024**, 266, 130823
3. A. S. Mao, B. Özkale, N. J. Shah, K. H. Vining, T. Descombes, L. Zhang, C. M. Tringides, S-W. Wong, J-W Shinh, D. T. Scadden, D. A. Weitz, D. J. Mooney, *PNAS*. **2019**, 116, 31, 1592-1597.