Combined approaches of magnetic, structural, and functional tissue bioengineering

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Project description : Full organ biogenesis *in vitro* remains a yet unreachable challenge. It is however needed first to provide damaged tissue replacements for regenerative medicine, but also for drug assessments and advanced biological investigations. The common goal of all tissue bioengineering approaches is to recapitulate *in vitro* the *in vivo* tissue features. Since its inception, 3D bioprinting has clearly made significant progress towards the goal of functional tissue production. However, many efforts must still be made to properly differentiate cells and promote the tissue development and organization in printed tissues. This is particularly linked to the need to recapitulate both the extracellular structures, the intercellular organization, and the mechanical stimulation experienced in vivo, in order to finally promote a functional tissue development.

We have developed these last years a series of tools to advance these challenges. On one hand, we have introduced a magnetic tissue engineering technology, taking advantage of cell magnetization to further organize magnetic cells in 3D assemblies and stimulate them at will by means of external (electro)magnets.[1] On the other hand, thanks to microfluidic approaches, we are investigating the structural role of the 3D microenvironment to provide anisotropic cell with guidance cues or to control their biomechanical and or biochemical environment.[2]

This project aims at initiating a novel research methodology in the field of 3D bioengineering with a tuned balance between magnetic cellular component and structural components.

Both will be specifically designed towards the common goal to address the need for cellular anisotropic alignment and mechanical (compression/elongation) stimulation that is common for many types of tissues, including muscle (cardiac or skeletal) and nervous ones. It will include the use of tissue spheroids, muscle precursor cells, and induced pluripotent stem cells to force in situ their differentiation with mechanical and structural cues.

This master project will welcome candidates with background in biomedical and biomaterial science, biophysics, bioengineering, and/or nanoscience, and is expected to be continued with a PhD thesis, funded by ANR.

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[1] e.g. *High-Throughput Differentiation of Embryonic Stem Cells into Cardiomyocytes with a Microfabricated Magnetic Pattern and Cyclic Stimulation.* Advanced Functional Materials 12002541 (2020); *A 3D magnetic tissue stretcher for remote mechanical control of embryonic stem cell differentiation.* Nature Communications, 8(1), 400 (2017); *Successful chondrogenesis within scaffolds, using magnetic stem cell confinement and bioreactor maturation;* Acta Biomateriala, 37, 101 (2016); *Magnetic flattening of stem-cell spheroids indicates a size-dependent elastocapillary transition.* Phys Rev Lett, 114, 098105 (2015); *Magnetic forces promote stem cell differentiation, aggregates fusion and tissue building.* Advanced Materials, 25, 2611-2616 (2013);
[2] e.g. *Sliding walls: a new paradigm for fluidic actuation and protocol implementation in microfluidics*. Microsyst Nanoeng 6, 18 (2020); *Developing an advanced gut on chip model enabling the study of epithelial cells/fibroblasts interactions* Lab on a Chip, 06-2020-000672 (2020);