



Secteur des Sciences  
et Technologies

Invitation à la soutenance publique de thèse de  
**Monsieur Mirasbek KUTERBEKOV**

Master ingénieur civil en chimie et science des matériaux

Pour l'obtention du grade de Docteur en sciences de l'ingénieur et  
technologie

« Polymeric microcarriers with bioactive coatings for the osteogenic  
differentiation of human adipose stromal cells »

qui se déroulera  
**le lundi 06 mai 2019 à 14h**  
**Amphi Z108 – Grenoble INP Phelma**  
**Parvis Louis Néel, 3**  
**38000 Grenoble, France**

Membres du jury :

Prof. Karine Glinel (UCLouvain), promotrice et secrétaire  
Prof. Catherine Picart (Grenoble INP, France), promotrice  
Prof. Alain Jonas (UCLouvain), président  
Prof. Philippe Laval (INSERM, Strasbourg, France)  
Prof. Daniel Noël (INSERM, Montpellier, France)  
Prof. Susanna Miettinen (U Tampere, Finlande)



 **UCLouvain**

The regeneration of critical-sized bone defects remains a major healthcare challenge. The limits of tissue grafting prompted us to develop a synthetic alternative based on biomaterial constructs, osteoinductive factors and stromal/stem cells. For biomaterial constructs, we focused on porous polymeric microcarriers as they support large-scale cell expansion and modular tissue assembly, circumventing two crucial bottlenecks for clinical translation. To insure industrial supply and regulatory approval, we designed a solvent-free method for their fabrication based on the spherulitic crystallization of poly(L-lactide) (PLLA) in its blends with polyethylene glycol (PEG). The PLLA spherulites were easily recovered as microcarriers by rinsing away the water-soluble PEG. Their size and porosity could be independently controlled by tuning the PLLA/PEG ratio and crystallization temperature. The biocompatibility and osteoconductivity of PLLA microcarriers were confirmed through the expansion and osteogenic differentiation of human adipose stromal cells (hASCs). Because the latter hASC function is sensitive to different culture parameters, we then used the Design of Experiments for their rapid screening. In combination with high-throughput analysis, we identified a strong effect of serum, hASC process, ascorbate and bone morphogenetic protein 9 (BMP-9) on the osteogenic differentiation of hASCs. Finally, to deliver osteoinductive factors, we elaborated polyelectrolyte multilayers (PEMs) based on biocompatible poly(L-ornithine) and hyaluronic acid. These PEMs were characterized in terms of their growth, morphology, the ability to incorporate different BMPs and to function as coatings on PLLA microcarriers. Our preliminary results showed that the incorporation of BMPs inside PEMs had a strong effect on hASC adhesion. While further studies are needed, PLLA microcarriers coated with BMP-loaded PEMs and seeded with hASCs could be a promising synthetic implant for bone regeneration.