Thesis subject: Multi-scale analysis of multi-layered tissues constructs: interfaces in the musculo-skeletal system based on tissue engineered myotendinous and osteotendinous junctions

PhD Advisors:

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Context of the thesis:

The thesis is part of the project activities of the Laboratory of Excellence (LABEX) at the Université de Technologie de Compiègne (UTC) in France on the Control of Technological Systems of Systems (MS2T) (www.utc.fr/labexms2t). It is more specifically part of the Research topic 3: Optimized design of technological SoSs.

The system of systems (SoS) of interest is a tissue engineered muscle-tendon-bone continuum, in which it is planned to pay more specific attention to interfaces between these different structures that are highly interdependent to promote motion. Tissue engineering consists in cultivating human cells in a polymeric artificial or natural scaffold, usually using external stimuli such as biochemical factors and/or mechanical constraints in order to obtain a final construct mimicking the native organ or tissue. Recent progresses led to independent tissue engineered constructs that are now recognized as Advanced Therapies Medicinal Products (ATMP) and are coming close to clinical application. However, up to now, there is almost no focus on the interfaces between different reconstructed or native tissues, to promote their further integration and most of all to reach full functions of the replacement system. These interfaces should be defined and modeled at different scales: from the cell-materials interactions to the whole tissue, taking into account the bilateral actions between biological and artificial components leading to changes in their mechanical properties and physiological functions. This is a crucial aspect highlighted by surgeons, in case of maxilla-facial or orthopedic surgery. This is also a key issue in reparation programs performed by physiotherapists, in case of rupture of the tendon, for instance.

In collaboration with the maxillofacial surgery service and the stem cell unit of Amiens Hospital, we thus plan to address this question for further application in a specific model of defect.

PhD thesis description :

After a previous project dedicated to mono-layered bone tissue engineering, the present PhD thesis aims at simultaneously reconstructing two adjacent tissues (eg. tendon-muscle or tendon-bone) ensuring cohesive interfaces during and beyond the cell culture process. After a bibliographical analysis of the composition of native structures, the tendon will be reconstructed based on bi-layered electrospun materials mimicking the collagen structure, seeded with fibroblasts or mesenchymal stem cells provided by Amiens Hospital under different densities. Mechanical stress field will be used as differentiation stimulator during the cell culture phase. The mechanical stimulation will be monitored by using Bose Biodynamic Bioreactor, available on the BMBI's cell culture platform. The changes of both the mechanical properties (using adequate mechanical tests) and the cell differentiation (based on histological and immunostaining studies) will be followed up according to the culture conditions.

Depending on the reconstructed tissues, bone-tendon or tendon-muscle, two approaches will be adopted. The interface bone-tendon will be mimicked, to obtain tissue densification at the interface, thanks to materials (electrospinning of a much denser layer) or to mechanical stimuli (leading the fibroblasts to produce more of type I collagen). Both approaches are strongly interconnected. For the tendon-muscle configuration, the interface (tendon-muscle) will be simulated, with close analysis of the morphological and biochemical interactions between collagen microfibrills and transmembrane proteins of the myoblasts (muscular cells).

Candidate's profile:

This project is highly interdisciplinary. Therefore, we are looking either for a Master student in Mechanical Engineering (specialized in Materials and Polymer Science) attracted by biomedical applications, and willing to be trained in cell culture or for a Master student in Biomedical or Biological Engineering willing to be trained in Materials Science.

Some part of the work could be achieved with other partners either in Germany or the USA, therefore a good level in English is expected.

Finally, the candidate should be ready to integrate a multi-disciplinary team in close contact with cell biologists, polymer scientists, biomechanical and mechanical engineers and researchers, and to work in collaboration with the clinical units in Amiens University Hospital.

Documents required to apply:

Send to cecile.legallais@utc.fr and fahmi.bedoui@utc.fr

- Curriculum vitae
- Motivation letter
- At least two references and/or recommendation letters
- A statement of research experience and interests

Location:

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