

## Université de technologie de Compiègne – Thesis proposal

| <b>Part 1: Scientific sheet</b> |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
|---------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Thesis proposal title           | Tendon organoid for drug screening studies                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| PhD grant                       | Thesis funded by ANR TENORS (PI C. Legallais)                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Research laboratory             | <ul style="list-style-type: none"> <li>Lab of Biomechanics and Bioengineering BMBI UMR CNRS 7338, UTC.</li> </ul> Website: <a href="https://bmbi.utc.fr/">https://bmbi.utc.fr/</a>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          |
| Thesis supervisor(s)            | Cécile Legallais, DR CNRS, and Sandrine Morandat, MCF HDR at BMBI                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Scientific domain(s)            | Biology, biomedical and health sciences, biochemistry<br>Science and technology                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             |
| Research work                   | <p>Up to now, tendon engineering has been developed in the framework of regenerative medicine, but not applied to preclinical drug screening. Evaluate the side effects of drugs on this specific tissue is thus very original. Together with partners at IBPS (Sorbonne Université) and EFS Créteil, we propose an ambitious program to design and characterize healthy or altered tendon organoids and to evaluate the effects of drugs on these engineered tissues.</p> <p>The first goal of this PhD will be to generate a tendon organoid by the culture of tendon progenitor cells on electrospun matrix made of polycaprolactone (PCL) under static and dynamic conditions, in the bioreactor system (T6 CellScale), based on the previous studies performed at BMBI (Garcia Garcia et al). This organoid will be characterized regarding its biochemical, biological and mechanical properties. More precisely, tendon ECM composition and spatial organization will be assessed with immunohistochemistry, in collaboration with IBPS. Focus will be made on type I collagen the functional component of tendon. The expression, the location and the orientation of Type I collagen fibers will be analyzed. Recognized tendon associated ECM's proteoglycans, such as decorin and fibromodulin, will also be considered. The local Young modulus of each scaffold will be measured with a Chiaro nanoindenter system (Optics 11) mounted on an optical microscope. AFM measurements will also be performed to determine elastic and viscoelastic properties of the native and biohybrid materials at the fiber scale. In a second period, a reconstructed muscle patch will be co-cultured with the tendon organoid to better mimic the <i>in vivo</i> situation. In both configurations, once an extracellular matrix will be neosynthesized, different biochemical pathways leading to an alteration will be investigated. Finally, once the organoids will be well characterized, specific drugs well known to generate tendinopathies will be tested to evaluate the alterations of the tissue.</p> <p>This validation step should lead to a new <i>in vitro</i> evaluation tool as an alternative method to animal trials.</p> <p>Ref : Garcia Garcia A, Perot JB, Beldjilali-Labro M, Dermigny Q, Naudot M, Le Ricousse S, Legallais C, Bedoui F. Monitoring mechanical stimulation for optimal tendon tissue engineering: a mechanical and biological multiscale study. JBMR Part A (2021), 109(10), 1881-1892. <a href="http://doi.org/10.1002/jbm.a.37180">http://doi.org/10.1002/jbm.a.37180</a> .</p> |
| Key words                       | Electrospinning, extracellular matrix, stem cells, glycation                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Requirements                    | Candidate's experience: either a MS degree in cell biology, with basic knowledge in biomaterials and biochemistry, or a MS degree in biomaterials/biomechanics with basic knowledge in cell biology/biochemistry, or an engineering diploma in biomechanics, biomaterials, or bioengineering.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Starting time                   | October 1st, 2022                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |

|          |                                                                                                                                                          |
|----------|----------------------------------------------------------------------------------------------------------------------------------------------------------|
| Location | Most of the work will be performed at UTC Centre de recherche. Some experiments will be performed at IPBS (Jussieu campus Sorbonne University) in Paris. |
|----------|----------------------------------------------------------------------------------------------------------------------------------------------------------|

| Part 2: Job description                 |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
|-----------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Duration                                | 36 months                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Additional missions available           | Teaching activities, (hands-on, practical work) could be performed in 2 <sup>nd</sup> and 3 <sup>rd</sup> year.                                                                                                                                                                                                                                                                                                                                                                            |
| Research laboratory                     | <b>The laboratory of Biomechanics and Bioengineering</b> (a joint CNRS-UTC research Lab) covers a broad scope in the field of biomechanics and bioengineering. The multidisciplinary nature of the unit brings international expertise in biomedical engineering, tissue engineering and multiscale modeling and characterization of the muscle-skeletal system. The PhD thesis project is included in a larger research project in which the teams CBB and C2MUST from BMBI are involved. |
| Material resources                      | Fully equipped platforms for cell culture and characterization of the reconstructed tissues, personal laptop.                                                                                                                                                                                                                                                                                                                                                                              |
| Human resources                         | At BMBI: 35 permanent staff (including 14 technical staff), 28 PhD, 7 postdocs, distributed in 3 teams                                                                                                                                                                                                                                                                                                                                                                                     |
| Financial resources                     | Financial support will be provided in the framework of the ANR TENORS.                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Working conditions                      | The candidate should be able to interact with the other teams involved in TENORS, i.e. the LBD led by Dr Delphine DUPREZ at IBPS, and the team of Dr H el ene ROUARD at IRMB. A degree of autonomy is therefore expected. Interactions with other PhDs, post-doc students and technical staff are also to be considered.                                                                                                                                                                   |
| Research project                        | ANR TENORS <a href="https://anr.fr/Project-ANR-21-CE18-0035">https://anr.fr/Project-ANR-21-CE18-0035</a>                                                                                                                                                                                                                                                                                                                                                                                   |
| National collaborations                 | Mentioned above                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| International collaborations            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| International cosupervision (cotutelle) |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            |
| Contact                                 | <b>LEGALLAIS C ecile (DR1 CNRS)</b> <a href="mailto:cecile.legallais@utc.fr">cecile.legallais@utc.fr</a><br><b>MORANDAT Sandrine (MCF HDR)</b> <a href="mailto:sandrine.morandat@utc.fr">sandrine.morandat@utc.fr</a>                                                                                                                                                                                                                                                                      |

**Please contact first the thesis supervisor** before applying online on <https://webapplis.utc.fr/admissions/doctorants/accueil.jsf>