PhD in Bioengineering and Medical-Surgical Sciences

Research Title: Synergistic combination of stem cell-based approach and automated controlled dynamic culture for advanced dental tissue engineering

Dental tissue engineering combined approach

Funded by	Politecnico di Torino (Polito^{BIO}Med Lab, Dipartimento di Ingegneria Meccanica e Aerospaziale) and Università degli Studi di Torino (Dipartimento di Scienze Chirurgiche)
Supervisors	Prof. Alberto Audenino (alberto.audenino@polito.it) Prof. Federico Mussano (federico.mussano@unito.it) Prof. Diana Nada Caterina Massai (diana.massai@polito.it)
Contacts	http://www.dimeas.polito.it/la_ricerca/gruppi/biomeccanica_dei_solidi_e_dei_fluidi https://www.polito.it/ricerca/centri/index.php?lang=en Bone and dental tissue engineering laboratory, CIR Dental School, University of Turin: http://www.surgicalexcellence.unito.it/it/hp_training_dd
Context of the research activity	In regenerative medicine, where the ultimate goal is to replace or restore damaged or diseased tissues, the combination and integration of medical, biotechnological, and bioengineering competences is essential for both understanding cell and tissue behavior to advance basic knowledge and for supporting the development of advanced therapeutic strategies. With a view to generating *in vitro* dental engineered tissues characterized by native-like biological, mechanical, and functional properties, the development of advanced solutions combining stem cell-based constructs cultured under dynamic biomimetic conditions is crucial. Indeed, dental/oral tissues are emerging as promising cellular sources of human mesenchymal stem cells, and recently dental tissue-derived cells have been used clinically due to their great potential and easy accessibility. In parallel, *in vivo* biophysical stimuli regulate cell response, promote tissue regeneration, and direct development of tissues and pathologies. Thus, culturing *in*

	vitro dental tissue models (i.e., alveolar bone, peri-implant defects, temporo-mandibular joint tissues, periodontal ligament…) under monitored, controlled, and automated biomimetic dental physical loads (e.g., compression, traction, shear stress) will allow obtaining functional substitutes and understanding the role played by physical stimuli on soft and hard dental tissues in healthy and pathological conditions. The research activity will be focused on the following main tasks: 1) Development of dental tissue models based on dental/oral stem cells and biofabrication techniques; 2) Design and development of bioreactors for automated controlled biomimetic dynamic culture; 3) Definition of *in vitro* tissue investigation and culture protocols; 4) Multiscale mechanical characterization of native and engineered tissues. The PhD programme activities will be performed in the context of the Laboratory of Bone and dental tissue engineering at the Università di Torino and the PoliTo^{BIO}Med Lab at Politecnico di Torino. The research will rely on a wide range of cross-sectoral facilities, including a cell and tissue culture lab equipped with a 3D bioprinter and a state-of-the-art flow-cytometer, a bioreactor lab and a biomechanics lab, provided with rapid prototyping technologies, electronics workbench, and multiscale testing and analysis machines (uniaxial/biaxial static/dynamics), including nanoindentation facilities for both hard and soft tissues. Moreover, a high performance cluster will be available for the computational tasks supporting both the bioreactor design phase and the *in silico* assessment of the engineered tissues.

Objectives	This PhD programme will focus on the development of advanced solutions for dental regenerative medicine based on the combination of stem cell-based constructs and controlled dynamic culture conditions. Multisectoral experimental and computational methodologies will be synergistically adopted to perform the following research goals: 1) Development of dental tissue models (i.e. alveolar bone, peri-implant defects, temporo-mandibular joint tissues, periodontal ligament), involving dental/oral stem cell sources from healthy and pathological patients, and using natural scaffolds (e.g., decellularized derma) or biofabrication approach. 2) Design and development of bioreactors for automated and controlled biomimetic dynamic culture, to be used as powerful investigation and culture platforms. Bioreactors will provide combined physical stimuli (e.g., compression, traction, shear stress) mimicking the physical conditions acting *in vivo* for studying the precise combination of physical parameters needed to reach a desired biological effect. Moreover, automation will lead to increased process efficiency and reproducibility.

	3) Definition of *in vitro* tissue investigation and culture protocols, for testing, validating, and producing the proposed dental tissue models with the use of the developed bioreactors. 4) Multiscale mechanical characterization of native and engineered tissues. A multiscale approach will be adopted and experimental characterization will be based on mechanical tests at the macro (e.g., uniaxial/biaxial tensile testing) and microscale (e.g., nanoindentation), in order to capture the typical features of native and engineered tissues under investigation. The final aim will be to provide guidelines for several issues related to the mechanical testing of soft tissues and to identify standardized testing methods. Adopting an iterative process of design, modelling, prototyping, and testing, the proposed solutions will be optimized and validated. The final aim will be to define the culture protocols and guidelines and to develop dedicated bioreactor prototypes for producing advanced dental regenerative medicine solutions.

Skills and competencies for the development of the activity	We are looking for a talented and motivated candidate, preferably with skills/experience in: Bioreactor design and development; Multiphysics computational modelling; Electronics and sensors; Technical drawing; Computer programming; Data acquisition systems; Data processing; Simulink/Matlab; Cell and tissue culture. The candidate should be characterized by strong aptitude for teamworking and problem solving, open and able to work in multidisciplinary teams and having good communication skills, with a good proficiency level in both written and spoken English.