Du 21 au 23 juin 2021

Book of Abstracts

France : *16h - 17h30*

Canada : *10h - 11h30*

LUNDI 21

Session 1 : **Les associations Biomatériaux, France – Canada** *(Didier Letourneur, Sébastien Meghezi)*

Session 2 : **Reconstruction of Segmental Mandibular Defect: a preclinical pilot study in sheep**
(Baptiste Charbonnier)

The reconstruction of segmental mandibular bone defects (SMD), resulting from high-energy trauma, congenital deformity, infection or tumor resection, still remains challenging. The failure to repair SMD may be profound, including esthetic deformities and a significant functional disability leading to negative psychological consequences and long term socioeconomic burden.

Vascularized bone graft (VBG) is the current gold standard for the treatment of large SMD. However, harvesting otherwise healthy bone from patients already affected from a severe medical condition may be highly detrimental to their well-being and recovery process. Furthermore anatomical mismatch between the VBG and recipient site often hinder the restoration of normal function.

Alternatives, based on tissue engineering strategies have demonstrated interesting potential in preclinical models. Nonetheless, their translation to clinical settings is hindered by the inability to keep the cells alive and functional in a non-physiological and compromised environment (e.g., hypoxia, nutriments depletion) and by the lack of control over bioactive substances release.

The proposed study addresses this unmet clinical need, by implanting in a relevant SMD model, a tailored 3D printed bioceramics with an innovative architecture, loaded with total bone marrow, and perfused by an arteriovenous loop. If successful, this represents a proof of concept that may be easily transposable from bench to bedside.

MARDI 22

Session 1 : **Développement d'un biomatériau fonctionnalisé par des vésicules extracellulaires pour le traitement de l'insuffisance cardiaque** *(Chloé Pezzana)*

Les vésicules extracellulaires (VE) sont une population hétérogène de nanoparticules sécrétées par toutes les cellules de l'organisme et à l'origine de leurs effets paracrines. Leur utilisation en médecine régénératrice cardiaque a été démontrée comme une alternative intéressante à la transplantation de cellules. En vue d'applications cliniques, la recherche translationnelle se concentre sur leur caractérisation, la sélection des cellules parentes, leur production à grande échelle et leur voie d'administration.

Maximiser la distribution des VE au cœur pour potentialiser leur effet thérapeutique est l'objectif de ce projet. Des VE issues de cellules stromales mésenchymateuses de cordon ombilical (hUC-MSC) ont donc été incorporées à un biomatériau, sous la forme d'un hydrogel injectable d'acide hyaluronique, afin qu'elles soient maintenues dans le tissu cible pendant une période suffisante et libérées de manière contrôlée.

Les VE et le biomatériau ont été produits et étudiés in vitro pour évaluer respectivement leur potentiel cardioréparateur (caractérisation, test de bioactivité) et la faisabilité de son injection intramyocardique pour la libération contrôlée de VE (rhéologie, profil de libération, répartition des VE dans le gel). In vivo, sur un modèle d'insuffisance cardiaque chronique induit par ischémie-reperfusion du myocarde chez le rat, l'effet thérapeutique des VE, injectées en suspension ou contenues dans le biomatériau, a été évalué par échocardiographies.

Session 2 : **Development of biomimetic surfaces: Towards the next generation of stents** *(Sergio Diaz)*

The rapid endothelialisation of bare metal stents (BMS) is counterbalanced by inflammation-induced neointimal growth. Drug-eluting stents (DES) prevent leukocyte activation but impair endothelialisation, delaying effective device integration into arterial walls. A strategy to overcome these side effects is the use of vascular receptors, such as CD31, which have been demonstrated to be crucial for endothelial and leukocyte homeostasis and arterial healing.

A biomimetic surface on cobalt chromium (CoCr) stents was developed using a soluble peptide P8RI, a CD31 agonist. In vitro and in vivotesting demonstrated that this biomimetic surface promoted a rapid endothelialisation whilst preventing in-stent restenosis and thrombosis up to 28 days after implantation. These results suggest an increased biocompatibility of the cardiovascular device.

This CD31 surface might constitute a promising alternative to current stents on the market, as it presents the advantages of both BMS and DES favouring CoCr stent integration while promoting arterial wall healing around stent struts without the characteristic adverse effects of these stents.

Session 3 : **Kalego & BONE 3D, histoires de Start-up** *(Jacopo Profili, Jeremy Adam)*

MERCREDI 23

Session 1 : **A 3D-printed hybrid hydrogel-nanoparticle formulation as a localized delivery system for cervical cancer therapy** *(Mariia Kiseleva)*

Cervical cancer is the second most common malignancy among women. Due to the easy access to the cervix, localized delivery plays an important role in its treatment. Among the delivery systems, gels are known to be tolerated better by patients. However, conventional gel formulations are associated with several drawbacks including loss of the significant amount of encapsulated therapeutics upon the administration.

These drawbacks could be attenuated by using anatomically relevant 3D-printed hydrogels that can be securely fixed at the cervix wall upon implantation. As an emerging technology, 3D printing provides an opportunity for personalized medicine, not only in the possibility to customize the doses but also in the fabrication of delivery systems with specific geometry according to the patient's needs.

The main aim of the present study was to develop a localized delivery system composed of a 3D-printed gel containing gold nanoparticles (AuNPs) for the treatment of cervical cancer. AuNPs were chosen because of their therapeutic potential as radiosensitizers in radiotherapy. The applicability of the developed hybrid formulation for intravaginal applications was demonstrated by studying the following parameters: 1) printability of a hydrogel ink and its geometrical resolution; 2) in vitro and in vivo hydrogel degradation and AuNPs release; 3) mucoadhesive properties of the delivery system; 4) biocompatibility. The results of these experiments will be summarized and discussed.

Session 2 : **Design of innovative injectable and porous hydrogels and their potential for skeletal muscle tissue engineering** *(Louise Griveau)*

Injectable hydrogels are promising therapeutic candidates for the treatment of volumetric muscle loss (VML) but often rely on the presence of a porosity to allow cell infiltration. Here we aimed (1) to create injectable and porous hydrogels based on poly-lysine dendrimers (DGL)/NHS-polyethylene-glycol (PEG) through an effervescent approach (2) to then evaluate their ability to sustain muscle cells differentiation for muscle regeneration.We found that hydrogels of modular mechanical properties could be rendered porous by dissolving effervescent porogens to DGL and PEG solutions, to create a spontaneous, homogeneous, and interconnected porosity, remnant of stabilized CO2 bubbles in the polymer network. The use of sole precursor solutions is compatible with porous hydrogels injection through dual-chamber syringes, which allowed to prove their biocompatibility by subcutaneous injection in mice.

Interestingly, primary human myoblasts seeded into 3D hydrogels showed extensive myotube formation, visible striation, and spontaneous contractions 6 days post differentiation. The presence of quiescent satellite cells inside 3D hydrogels was confirmed with Pax7 expression, consolidating their potential to maintain a pool of muscle stem cells.

In conclusion, we describe a novel porous hydrogel able to provide an optimal support for muscle cells to differentiate into contractile myotubes with potential as scalable solution for VML treatments within a swift injectable delivery.

Session 3 : **Interviews croisées de collaborations France – Canada** *(Sergio Diaz, Alex Destrieux, Quentin Muller)*

Thésez-vous ? *(Raphaëlle Coté-Parent)*