CDD Biomedical Engineer –Biomaterials – nov 2018-2021

CDD Biomedical Engineer:
Osteoinductive coatings: translation toward the clinics

Scientific context

To date, the repair of critical sized bone defects remains a clinical unmet need. Autograft, the current gold standard, presents several drawbacks justifying safer strategies. “Orthobiologics” products that combine synthetic grafts, mostly collagen sponges and ceramics, and bioactive molecules such as growth factors, are appealing since they actively trigger stem cell differentiation in situ to form new bone. Inductos ® is the most widely used, delivering BMP-2 combined with collagen. It presented adverse effects due the too high dose of BMP-2 delivered and extensive off-label use [1]. Being able to reduce the dose of BMP-2 and to confine it locally in an appropriate material carrier, in order to deliver it with improved safety and efficacy, would considerably broaden the perspectives of its clinical use.
We have engineered a biomimetic coating that delivers BMP-2 locally [2] from the surface of any type of implants, whatever their chemistry (ceramics, metals and polymers) and shape. We have already proved that film-coated implants are osteinductive in small animal models [3, 4] and that it is possible to repair a 3D volumetric bone defect via the osteoinductive coating of a hollow cylinder made a PLGA [5], a widely clinically used synthetic polymer. The regenerated bone, composed of cortical and trabecular bone, was also vascularized. The translation of this **innovative nanocoating toward the clinics** requires to further prove the **efficacy** of the osteoinductive film to repair a critical size defect in large animals and its **safety.**
The ANR project OBOE aims to advance the pre-clinical translation of this innovative orthobiologics. Our goal is to repair a large bone defect in large animals by controlling independently the 3D architecture of the implant and the dose of BMP-2 delivered via the osteoinductive coating. We have selected synthetic polymers as 3D architectured scaffolds in view of their versatility and adaptability to advanced printing techniques.
OBOE is organized in 3 workpackages: In WP1, we will design and test the architecture of a 3D polymeric implant and will optimize the biomimetic film coating. In WP2, we will evaluate the safety (biocompatibility and biodegradability) of the osteoinductive coating following the regulatory requirements. In WP3, we will evaluate the efficacy of the film-coated implant for the repair of a critical-size defect in a large animal model (sheep).
OBOE gathers 4 partner labs (LMGP and IAB in Grenoble, CIC-IT in Bordeaux and B20A in Paris) in a multidisciplinary network that leverages expertise in biomaterials, in vivo imaging and small animal models, regulatory affairs, bone tissue engineering and in vivo pre-clinical trials in large animals. We will take benefit from the key technical expertise of the team members and using several technical platforms for biotechnologies and the imaging of small animals in Grenoble, for technical medical innovation in Bordeaux (CIC-IT) and for experiments in large animals in Maisons-Alfort.

Project on OsteoinductiveCoatings: translation toward the clinics in the framework of ANR OBOE.
We aim to translate the osteoinductive nanocoatings toward the clinics. To this end, we will test 3D architectured polymeric implants and optimize the biomimetic film coating, in collaboration with IAB in Grenoble for small animal experiments. In collaboration with CIC-IT Bordeaux, we will design and perform safety and biodegradability tests. To this end, the biomimetic films will be prepared in cell culture microplates using a liquid handling robot [6] in order to perform cell experiments at high throughput. Finally, we will prepare samples for experiments in large animals that will be done at the B2OA in Paris in collaboration with Maisons Alfort Veterinary school.
Techniques: biomaterials/bioengineering, automated deposit of biomimetic films using a robot, 3D printing techniques, optical microscopies and spectroscopies including confocal microscopy; electron microscopy, stem cell culture and biological assays;. State-of-the art technologies are available in the neighboring technical platforms (CIME biotechnologies, IAB…).

Bibliographic References

[1] Carragee EJ, Hurwitz EL, Weiner BK. A critical review of recombinant human bone morphogenetic protein-2 trials in spinal surgery: emerging safety concerns and lessons learned. Spine J. 2011;11:471-91.
[2] Crouzier T, Ren K, Nicolas C, Roy C, Picart C. Layer-by-Layer films as a biomimetic reservoir for rhBMP-2 delivery: controlled differentiation of myoblasts to osteoblasts. Small. 2009;5:598-608.
[3] Crouzier T, Sailhan F, Becquart P, Guillot R, Logeart-Avramoglou D, Picart C. The performance of BMP-2 loaded TCP/HAP porous ceramics with a polyelectrolyte multilayer film coating. Biomaterials. 2011;32:7543-54.
[4] Guillot R, Gilde F, Becquart P, Sailhan F, Lapeyrere A, Logeart-Avramoglou D, Picart C. The stability of BMP loaded polyelectrolyte multilayer coatings on titanium. Biomaterials. 2013;34:5737-46.
[5] Bouyer M, Guillot R, Lavaud J, Plettinx C, Olivier C, Curry V, Boutonnat J, Coll JL, Peyrin F, Josserand V, Bettega G, Picart C. Surface delivery of tunable doses of BMP-2 from an adaptable polymeric scaffold induces volumetric bone regeneration. Biomaterials. 2016;104:168-81.

[6] Machillot P, Quintal, C., Dalonneau, F., Hermant, L., Monnot, P., Matthews, K., Fitzpatrick, V., Liu, J., Pignot-Paintrand, I., Picart, C. Automated buildup of biomimetic films in cell culture microplates for high throughput screening of cellular behaviors Adv Mater. 2018;e1801097.

Location

The candidate will be working in MINATEC (scientific Polygone Grenoble) in the « Interfaces between Materials and Biological Matter » IMBM team (C Picart), a team supported by Fondation Recherche Medicale, ERC and ANR, in close collaboration the Institute of Advanced Biosciences (Prof Bettega CHR Annecy, V. Josserand, JL Coll), the B2OA in Paris (D Logeart-Avramoglou, V. Viateau at the Maisons Alfort Veterinary school) and CIC-IT Bordeaux (L. Bordenave, M Durand). The creation of a start-up company on this project is envisioned by 2020.
Grenoble offers a high quality of life and lots of opportunities for those who like outdoor activities and mountains.
Web Site: http://www.lmgp.grenoble-inp.fr/

Profile & requested skills

Engineer in biomaterials science/bioengineering who is open to multidisciplinary work on a collaborative project. Team work and oral/written expression in French and in English will be highly appreciated. The candidate should be willing to work in the collaboration with the partner labs. There is a possibility to register a PhD thesis during the contract.

Application: (as soon as possible, no later than Sept 29Th 2018)

Please send your CV, a motivation letter as well as 2 names of referees + the transcript of your grades for the two last years of study (2016/2017 and 2017/2018) to Catherine.Picart@grenoble-inp.fr

Supervisor

Catherine Picart; Catherine.Picart@grenoble-inp.fr ; Grenoble Institute of Technology, MINATEC