Enhanced Efficacy of Osteogenic Growth Factors with Heparin Binding Domain by Polyelectrolyte Complex in Small and Large Animal Spinal Fusion Model

Ming Wang[1], Raymond Lam[1], Tao Hu[1], Chia Soo[2], Kang Ting[2], James Goh[3], Hee Kit Wong[1]

[1]University Orthopaedics, Hand and Reconstructive Microsurgery Cluster, National University Health System, Singapore [2]Department of Orthopaedic Surgery and the Orthopaedic Hospital Research Center, UCLA and Orthopaedic Hospital, University of California Los Angeles, California, USA [3]Department of Bioengineering, Faculty of Engineering, National University of Singapore, Singapore

Objective: To investigate whether a new heparin based microsphere system, polyelectrolyte complex (PEC), could enhance the efficacy of osteogenic growth factors (OGF) with heparin binding domain such as BMP-2 and Nell-1.

Materials and Methods: The control release profile of BMP-2 and Nell-1 from PEC was assessed by confocal microscopy and accumulative release method. The osteogenic profile of BMP-2 delivered by PEC or absorbable collagen sponge (ACS) was assessed in the porcine spinal fusion model. The osteogenic profile of Nell-1 delivered by PEC combined with bone marrow aspirates (BMA) was assessed in rabbit spinal fusion model. Spinal fusion was assessed by Micro-CT and histology.

Results: In vitro study showed only 17.0±2.6% of BMP-2 and 14±4.4% of Nell-1 loaded onto PEC was released in the initial phase and controlled release was observed after that. Low dose of BMP-2 delivered by PEC was able to induce solid spinal fusion with reduced complications and improved microarchitecture of the newly formed bone compared to ACS. In preliminary results of rabbit spinal fusion model, Nell-1 carried by PEC with BMA was able to induce successful fusion.

Conclusion: PEC has successfully enhanced the efficacy and safety profile of BMP-2. Nell-1, a new OGF under investigation, is more specific in bone regeneration than BMP-2 as it is downstream mediator of Runx-2. However Nell-1 is not as potent as BMP-2 in osteoinduction and lacks an ideal carrier. In this study, we used PEC to improve the release profile of Nell-1 and BMC to enhance its osteogenic effect.