



Cover Story

Injectable hyaluronic acid hydrogel for bone augmentation

Bone augmentation techniques are commonly employed in orthopedics, neurosurgery as well as oral and maxillofacial surgery. One common approach is autologous bone graft surgery which requires expensive invasive procedures, is often painful, and can cause donor site morbidity. Furthermore, the availability of transplantable bone is extremely limited. Thus, it is highly attractive to develop a biomaterial system that is readily available, easily applicable by minimally-invasive technique, and able to release an osteoinductive growth factor. Such a system will be able to engineer new bone formation locally at the site of injection.

In an article published in this issue, Dr. Varghese's team has developed new chemistry to synthesize hyaluronic acid (HA) aldehyde under mild conditions and utilized it for hydrazone crosslinked hydrogel preparation [1]. This injectable material has been used in vivo, as a depot for bone morphogenetic protein-2 (BMP-2), the protein known for differentiation of mesenchymal stem cells and progenitor cells towards bone. This material with different concentrations of BMP-2 (0, 5, and 150 $\mu\text{g}/\text{mL}$) was injected with a minimal skin incision below the periosteum, the membrane which separates bone from the surrounding tissue. After injection, the hydrogel provided a 3D space beneath the periosteum which resulted in stem cell migration and differentiation which eventually lead to mature bone formation after 8 weeks. This engineered bone integrated with the native bone as evaluated by peripheral Quantitative Computed Tomography (pQCT), histology, and immunohistochemistry. The volume of the newly formed bone was correlated with the amount of BMP-2 loaded in the hydrogel. Furthermore, authors demonstrated the significance of subperiosteal implantation by

comparing subcutaneous injection of the same hydrogel. They clearly showed a crucial role of the periosteum, a mesenchymal layer rich in pluripotent cells covering the bone, for the process of osteogenesis. Moreover, they elucidated the mechanism of in vivo bone formation through in vitro experiments showing controlled release of active rhBMP-2 from the hydrogels for 28 days. As expected, the hydrogel formulation lacks cytotoxicity.

This article shows that clinically relevant calvarial bone augmentation can be achieved by minimal injection of the BMP-2 containing HA hydrogel. This new drug delivery system and its application procedure may present an attractive clinical alternative to current approaches for bone augmentation in terms of increased simplicity, reduced trauma, and potentially lower cost. The osteogenic potential of this HA hydrogel can be exploited not only for repairing bone defects but also for providing transplantable bone for the reconstruction of a variety of bone defects.

Reference

- [1] E. Martínez-Sanz, D.A. Ossipov, J. Hilborn, S. Larsson, K.B. Jonsson, O.P. Varghese, Bone reservoir: injectable hyaluronic acid hydrogel for minimal invasive bone augmentation, *J. Control. Release* 152 (2011) 233–241.

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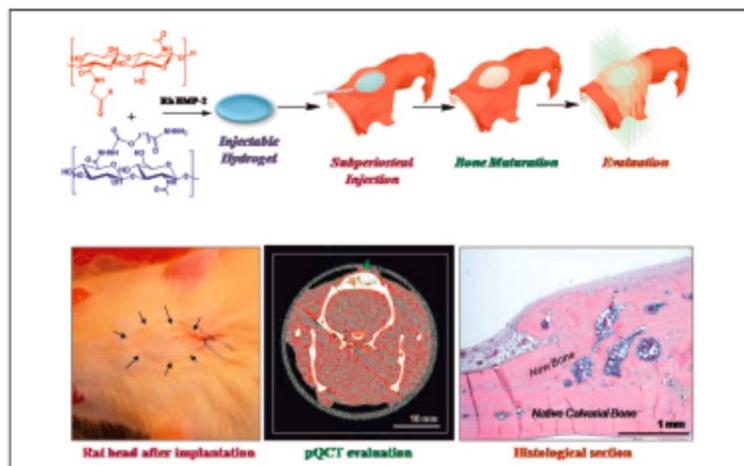


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