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Evaluation of therapeutical efficacy of heparin-conjugated fibrin hydrogel containing bone morphogenic proteins and periosteum derived stem cells in critical size rabbit ulna defect

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Critical size bone defects caused by severe trauma or tumor resection are still a major problem in orthopaedics and traumatology. In this regard, application of tissue engeneering approach based on fibrin hydrogel, bone morphogenic proteins (BMPs) and osteogenic stem cells could be an effective treatment strategy to restore damaged bone tissues. The purpose of this study was to develop and evaluate the therapeutic efficacy of heparin-conjugated fibrin (HCF) hydrogel containing recombinant bone morphogenic factors (BMPs) and autologous periosteum derived stem cells (PDSCs) in rabbit critical size bone defect model. In this study, PDSCs were isolated from Flemish Giant rabbits and expanded *in vitro*. HCF was prepared by conjugating heparin to fibrinogen and subsequently mixing with thrombin and then used as an injectable hydrogel for delivery of PDSCs, BMP-2 and BMP-7. The kinetics of BMP-2 and BMP-7 release from HCF hydrogel was determined with ELISA. The therapeutic efficacy of HCF hydrogels containing PDSCs (3×10^6 cells) and/or BMPs (400 ng) was evaluated on critical size segmental bone defect in the rabbit ulna using X-ray tomography and histology within 12 weeks. The results of our work showed that fabricated HCF hydrogels are biocompatible for rabbit PDSCs and can maintain a sustained release of BMP-2 and BMP-7 compared with fibrin hydrogel within 14 days. *In vivo* study revealed that both PDSCs encapsulated in HCF hydrogel and HCF containing BMP-2 and BMP-7 can promote regeneration of critical size bone defects in the rabbit ulna. However, greatest therapeutic effect was observed at combined application of HCF hydrogel containing PDSCs and BMPs which resulted in complete restoration bone defects within 9 weeks after hydrogel implantation. In the current study, we conclude that HCF hydrogel containing PDSCs and BMPs will be a promising tissue engineering technique by which bone regeneration can be significantly promoted.

Biography

Vyacheslav Ogay has completed his PhD from Pushchino State University and Post-doctoral studies from Seoul National University School of Natural Sciences. He is the Head of Stem Cell Laboratory at National Center for Biotechnology. He has published more than 40 papers in peer reviewed journals on biotechnology and biomedicine.

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