Accepted Manuscript

Full length article

Accepted Date:

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PII:	S1742-7061(18)30343-X
DOI:	https://doi.org/10.1016/j.actbio.2018.06.007
Reference:	ACTBIO 5517
To appear in:	Acta Biomaterialia
Received Date:	9 February 2018
Revised Date:	1 June 2018

4 June 2018

Please cite this article as: Nguyen, M.K., Jeon, O., Dang, P.N., Huynh, C.T., Varghai, D., Riazi, H., McMillan, A., Herberg, S., Alsberg, E., RNA interfering molecule delivery from *in situ* forming biodegradable hydrogels for enhancement of bone formation in rat calvarial bone defects, *Acta Biomaterialia* (2018), doi: https://doi.org/10.1016/j.actbio.2018.06.007

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ACCEPTED MANUSCRIPT

RNA Interfering Molecule Delivery from *in situ* Forming Biodegradable Hydrogels for Enhancement of Bone Formation in Rat Calvarial Bone Defects

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Abstract:

RNA interference (RNAi) may be an effective and valuable tool for promoting the growth of functional tissue, as short interfering RNA (siRNA) and microRNA (miRNA) can block the expression of genes that have negative effects on tissue regeneration. Our group has recently reported that the localized and sustained presentation of siRNA against noggin (siNoggin) and miRNA-20a from *in situ* forming poly(ethylene glycol) (PEG) hydrogels enhanced osteogenic differentiation of encapsulated human bone marrow-derived mesenchymal stem cells (hMSCs). Here, the capacity of the hydrogel system to accelerate bone formation in a rat calvarial bone defect model is presented. After 12 weeks post-implantation, the hydrogels containing encapsulated hMSCs and miRNA-20a resulted in more bone formation in the defects than the hydrogels containing hMSCs without siRNA or with negative control siRNA. This localized and sustained RNA interfering molecule delivery system may provide an excellent platform for healing bony defects and other tissues.

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