Docket #: S13-081

Crosslinked chitosan-lactide matrices for the controlled delivery of therapeutic agents

Researchers at Stanford have developed methods for preparing photo-, and chemical-, cross-linkable three-dimensional matrices for the controlled delivery of bioactive molecules for therapeutic applications. The matrices can be used for growth factor delivery and for cell delivery. The chitosan-lactide hydrogel combines excellent biocompatibility, protein affinity, and degradability from hydrophilic chitosan, and tunable physical and mechanical properties from hydrophobic lactide. Simple manipulation of chitosan-lactide ratio, UV irradiation time or catalyst concentration can be used to regulate hydrogel properties such as swelling behavior, degradation rate, and spatial as well as temporal distribution of released proteins. The material can be applied to the targeted area as a preformed matrix and also can be gelled in situ via UV light exposure. The technology is currently available for licensing for non-otolaryngology applications only.

In a rat critical size bone defect model, the chitosan-lactide matrix has clearly shown dose dependent efficacy in delivering bone promoting growth factors such as bone morphogenetic protein-2 (BMP-2). When compared to commercially available BMP products, the same dose BMP-2 containing chitosan-lactide matrix demonstrated significantly improved bone healing (85% vs. 50%) due to controlled sustained release of bioagent and improved structural guidance.

Applications

- Medical device for regeneration of hard and soft tissues
- Enabling and promoting bone healing in critical-size defects in combination with bone generating growth factors (functional bone substitute)

- Delivery of antibiotics to treat bone infection in combination with various growth factors
- Delivery of analgesic for pain management
- Basic science related to cancer and angiogenesis

Advantages

- Easy fabrication at low cost
- Easy implementation by applying aqueous formula to the targeted area with any shape and gelling via UV exposure
- Enables easy surgical handling and stable fixation at the site of defect
- Easy manipulation of the properties of hydrogels by simply adjusting chitosan-lactide ratio, UV irradiation time and catalyst concentration according to applications
- Applicable to many different medical devices due to its excellent biocompatibility, biodegradability, protein affinity, and tunable mechanical properties

Publications

- Kim, S; Kawai, T; Yang Y, Engineering a Dual-Layer Chitosan-Lactide Hydrogel To Create Endothelial Cell Aggregate-Induced Microvascular Networks In Vitro and Increase Blood Perfusion In Vivo,ACS Appl Matter Interfaces, 2016 Aug 3;8(30):19245-55. doi: 10.1021/acsami.6b04431. Epub 2016 Jul 22.
- S Kim, K Bedigrew, T Guda, WJ Maloney, S Park, JC Wenke, YP Yang, Novel osteoinductive photo-cross-linkable chitosan-lactide-fibrinogen,Acta Biomaterialia, 2014 Dec;10(12):5021-33. doi: 10.1016/j.actbio.2014.08.028. Epub 2014 Aug 28.
- S Kim, Y Kang, AEM Pagán, WJ Maloney, YP Yang, In vitro evaluation of photo-cross-linkable chitosan-lactide hydrogels for bone tissue engineering, Journal of Biomedical Materials Research Part B - Applied Biomaterials; 2014 Oct;102(7):1393-406. doi: 10.1002/jbm.b.33118. Epub 2014 Feb 6.

Patents

- Published Application: WO2014169045
- Published Application: 20160058867
- Issued: 9,814,779 (USA)

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