Data in Brief 10 (2017) 202–209

Contents lists available at ScienceDirect

Data in Brief

journal homepage: www.elsevier.com/locate/dib

Data Article

Engineered HA hydrogel for stem cell transplantation in the brain: Biocompatibility data using a design of experiment approach

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ARTICLE INFO

Article history:
Received 27 July 2016
Received in revised form
20 October 2016
Accepted 17 November 2016
Available online 24 November 2016

Keywords:
Hydrogel
Hyaluronic acid
Hyaluronan
Brain
Brain repair
Stroke
Ischemia
Design of experiment
DOE
Biocompatibility
Toxicity
Stem cell transplantation
Neural stem cell

ABSTRACT

This article presents data related to the research article "Systematic optimization of an engineered hydrogel allows for selective control of human neural stem cell survival and differentiation after transplantation in the stroke brain" (P. Moshayedi, L.R. Nih, I.L. Llorente, A.R. Berg, J. Cinkornpumin, W.E. Lowry et al., 2016) [1] and focuses on the biocompatibility aspects of the hydrogel, including its stiffness and the inflammatory response of the transplanted organ. We have developed an injectable hyaluronic acid (HA)-based hydrogel for stem cell culture and transplantation, to promote brain tissue repair after stroke. This 3D biomaterial was engineered to bind bioactive signals such as adhesive motifs, as well as releasing growth factors while supporting cell growth and tissue infiltration. We used a Design of Experiment approach to create a complex matrix environment *in vitro* by keeping the hydrogel platform and cell type constant across conditions while systematically varying peptide motifs and growth factors. The optimized HA hydrogel promoted survival of encapsulated human induced pluripotent stem cell derived-neural progenitor cells (iPS-NPCs) after transplantation into the stroke cavity and differentially tuned transplanted cell fate

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http://dx.doi.org/10.1016/j.dib.2016.11.069

NPC
Astrocytic scar
Heparin
RGD
YIGSR
IKVAV
BDNF
BMP-4
Brain derived-neurotrophic factor
Bone-morphogenic protein-4

through the promotion of glial, neuronal or immature/progenitor states. The highlights of this article include: (1) Data of cell and bioactive signals addition on the hydrogel mechanical properties and growth factor diffusion, (2) the use of a design of Experiment (DOE) approach (M.W. 2 Weible and T. Chan-Ling, 2007) [2] to select multi-factorial experimental conditions, and (3) Inflammatory response and cell survival after transplantation.

Specifications Table

Subject area	Stem cell, Biology, Engineering, Material Sciences
More specific subject area	Biomaterial, Stem cell transplantation, brain repair
Type of data	Graph, figure, table
How data was acquired	Rheology, Elisa, Microscopy
Data format	Analyzed
Experimental factors	Cell encapsulation in hydrogel before transplantation
Experimental features	Human neural progenitor cell, 3D culture and brain transplantation
Data source location	Los Angeles, California, USA
Data accessibility	Data is provided in the article

Value of the data

- This work brings a deeper understanding on the influence of cell encapsulation and bioactive signal addition on the mechanical properties of the transplanted hydrogel and its growth factor diffusion.
- The data in this article show how a design of experiment (DOE) approach can be used to selectively choose multiple conditions in a multi-factorial experimental system.
- The *in vivo* data in this article highlight the influence of the different combinations of hydrogels on the brain inflammatory response and survival of encapsulated neural progenitor cells.

1. Data

A hyaluronic acid hydrogel crosslinked *in situ* via thiol/acrylate Michael type addition, was used for human induced pluripotent neural precursor (iPS-NPC) 3D culture *in vitro,* and for a direct brain transplantation *in vivo, within the site of ischemic damage as previously described* [3]. Fig. 1 shows data related to the influence of heparin addition on mechanical properties, on cell toxicity and cell survival *in vitro*, while Fig. 2 presents dataset related to the *in vivo* transplantation of the cell and heparin-encapsulated hydrogel in stroked mice brain.

The gel was loaded with RGD and heparin both chemically modified to contain thiol groups and bind the HA backbone (Fig. 1A). In order to match the mechanical properties of brain cortex, the thiol/acrylate ratio as well as the HA weight % were modified to obtain a storage modulus of 350–400 Pa [4].

In this article, the influence of heparin addition on gel stiffness was evaluated on increasing concentrations of heparin, showing a significant increase of the storage modulus at a concentration of 0.3 mg/mL while higher concentrations of heparin were associated with a decreased storage modulus (Fig. 1B). Similarly, the influence of adhesion motifs on gel stiffness was evaluated on gels containing or not 0.3 mg/mL of heparin. The data show no significant difference between groups. Heparin addition on growth factor diffusion was then evaluated on HA hydrogels containing RGD and one of the neural growth factor brain derived-neurotrophic factor (BDNF) or bone-morphogenic protein-4 (BMP-4), showing a slower diffusion with the addition of heparin (Fig. 1C).