



New PLGA-P188-PLGA matrix enhances TGF- β 3 release from pharmacologically active microcarriers and promotes chondrogenesis of mesenchymal stem cells

Submitted by Claudia Montero... on Mon, 06/29/2015 - 15:36

Titre	New PLGA-P188-PLGA matrix enhances TGF- β 3 release from pharmacologically active microcarriers and promotes chondrogenesis of mesenchymal stem cells
Type de publication	Article de revue
Auteur	Morille, Marie [1], Tran, Van-Thanh [2], Garric, Xavier [3], Cayon, Jérôme [4], Coudane, Jean [5], Noël, Danièle [6], Venier-Julienne, Marie-Claire [7], Montero-Menei, Claudia [8]
Pays	Pays-Bas
Editeur	Elsevier
Ville	Amsterdam
Type	Article scientifique dans une revue à comité de lecture
Année	2013
Langue	Anglais
Date	2013 Aug 28
Numéro	1
Pagination	99-110
Volume	170
Titre de la revue	Journal of Controlled Release
ISSN	1873-4995
Mots-clés	Alkaline phosphatase [9], Animals [10], Cell Adhesion [11], Cell Survival [12], Cells, Cultured [13], Chondrogenesis [14], Drug Carriers [15], fibroblasts [16], Humans [17], Lactic Acid [18], Mesenchymal Stromal Cells [19], Mice [20], Mice, Knockout [21], Muramidase [22], Poloxamer [23], Polyglycolic Acid [24], Transforming Growth Factor beta3 [25]

Résumé en
anglais

The use of injectable scaffolding materials for in vivo tissue regeneration has raised great interest in various clinical applications because it allows cell implantation through minimally invasive surgical procedures. In case of cartilage repair, a tissue engineered construct should provide a support for the cell and allow sustained in situ delivery of bioactive factors capable of inducing cell differentiation into chondrocytes. Pharmacologically active microcarriers (PAMs), made of biodegradable poly(d,l-lactide-co-glycolide acid) (PLGA), are a unique system, which combines these properties in an adaptable and simple microdevice. However, a limitation of such scaffold is low and incomplete protein release that occurs using the hydrophobic PLGA based microspheres. To circumvent this problem, we developed a novel formulation of polymeric PAMs containing a P188 poloxamer, which protects the protein from denaturation and may positively affect chondrogenesis. This poloxamer was added as a free additive for protein complexation and as a component of the scaffold covalently linked to PLGA. This procedure allows getting a more hydrophilic scaffold but also retaining the protective polymer inside the microcarriers during their degradation. The novel PLGA-P188-PLGA PAMs presenting a fibronectin-covered surface allowed enhanced MSC survival and proliferation. When engineered with TGF β 3, they allowed the sustained release of 70% of the incorporated TGF- β 3 over time. Importantly, they exerted superior chondrogenic differentiation potential compared to previous FN-PAM-PLGA-TGF- β 3, as shown by an increased expression of specific cartilage markers such as cartilage type II, aggrecan and COMP. Therefore, this microdevice represents an efficient easy-to-handle and injectable tool for cartilage repair.

URL de la notice <http://okina.univ-angers.fr/publications/ua13186> [26]
DOI 10.1016/j.jconrel.2013.04.017 [27]
Titre abrégé J Control Release
Identifiant (ID) PubMed 23648834 [28]

Liens

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- [27] <http://dx.doi.org/10.1016/j.jconrel.2013.04.017>
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Publié sur *Okina* (<http://okina.univ-angers.fr>)