

## Regeneration of the intervertebral disc

Joana Silva-Correia, Diana R. Pereira, Sebastião van Uden, Joaquim M. Oliveira and  
Rui L. Reis

*3B's Research Group - Biomaterials, Biodegradables and Biomimetics, University of Minho, Headquarters of the European Institute of Excellence on Tissue Engineering and Regenerative Medicine, AvePark, S. Cláudio de Barco, 4806-909 Taipas, Guimarães, Portugal*

*ICVS/3B's – PT Government Associate Laboratory, Braga/Guimarães, Portugal*

Degeneration of intervertebral disc (IVD) seems to be one of the main causes associated to lower back pain (LBP), one of the most common painful conditions that lead to work absenteeism, medical visits, and hospitalization in actual society [1,2]. This complex fibro-cartilaginous structure is composed by two structures, an outer multilayer fiber structure (annulus fibrosus, AF) and a gel-like inner core (nucleus pulposus, NP), which are sandwiched in part between two cartilage endplates (CEP) [1]. Existing conservative and surgical treatments for LBP are directed to pain relief and do not adequately restore disc structure and mechanical function [2]. In the last years, several studies have been focusing on the development of tissue engineering (TE) approaches aiming to substitute/regenerate the AF or NP, or both by developing an artificial disc that could be implanted in the body thus replacing the damaged disc [3]. TE strategies aiming to regenerate NP tissue often rely on the use of natural hydrogels, due to the number of advantages that these highly hydrated networks can offer. Nevertheless, several of the hydrogel systems developed still present numerous problems, such as variability of production, and inappropriate mechanical and degradation behaviour. Recently, our group has proposed the use of gellan gum (GG) and its derivatives, namely the ionic- and photo-crosslinked methacrylated gellan gum (GG-MA) hydrogels, as potential injectable scaffolds for IVD regeneration [4,5]. Work has been conducted regarding the improvement of GG mechanical properties either by chemically modifying the polymer (allowing to better control *in situ* gelation and hydrogel stability) [4] or by reinforcing it with biocompatible and biodegradable GG microparticles (enabling the control of degradation rate and cell distribution) [5]. Another strategy currently under

investigation relies on the development of a biphasic scaffold that mimics the total disc by using a reverse engineering approach.

[1] Richardson SM, Mobasher A, Freemont AJ, Hoyland JA. Intervertebral disc biology, degeneration and novel tissue engineering and regenerative medicine therapies. *Histol Histopathol* 2007;22:1033-41.

[2] Kalson NS, Richardson S, Hoyland JA. Strategies for regeneration of the intervertebral disc. *Regen Med* 2008;3:717-29.

[3] Silva-Correia J, Correia SS, Pereira H, Espregueira-Mendes J, Oliveira JM and Reis RL. Tissue engineering strategies applied in the regeneration of the human intervertebral disc. *Biotechnol Adv* (*accepted for publication*).

[4] Silva-Correia J, Oliveira JM, Caridade SG, Oliveira JT, Sousa RA, Mano JF, et al. Gellan gum-based hydrogels for intervertebral disc tissue-engineering applications. *J Tissue Eng Regen Med* 2011;5:e97-e107.

[5] Pereira DR, Silva-Correia J, Caridade SG, Oliveira JM, Salgado AJ, Sousa N, et al. Development of Gellan gum-based microparticles/hydrogel matrices for application in the intervertebral disc regeneration. *Tissue Eng Part C* 2011;17:961-72.