Gellan Gum-Hyaluronate Spongy-like Hydrogels Promote Angiogenesis in Hindlimb Ischemia

<u>Lucília P. da Silva</u>^{1,2}, Mariana T. Cerqueira^{1,2}, Rogério P. Pirraco^{1,2}, Tírcia C. Santos^{1,2}, Rui L. Reis^{1,2}, Vitor M. Correlo^{1,2}, Alexandra P. Marques^{1,2}

1- 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, 4806-909 Taipas, Guimarães, Portugal 2- ICVS/3B's - PT Government Associate Laboratory, Braga/Guimarães, Portugal

Gellan gum (GG) spongy-like hydrogels are highly attractive materials for Tissue Engineering applications once they present hydrogel main properties and are capable to promote cell adhesion. Considering the inefficient vascularization of thick 3D constructs, we hypothesised that GG spongy-like hydrogels containing hyaluronate (HA) would promote the recruitment of endothelial cells upon degradation, due to the angiogenic nature of the released HA fragments.

GGHA spongy-like hydrogels (1% and 2%, w/v) were prepared as previously described 1,2 . The susceptibility of the materials to hyaluronidase degradation was demonstrated *in vitro* by the increased amount of reducing sugars (DNS assay) and low molecular weight HA fragments released up to 28 days (GPC). After implantation in an ischemia hindlimb mouse model, increased blood perfusion, in comparison to the control, was observed in the presence of GGHA materials. Furthermore, blood vessels density was higher in the presence of the materials, 1% (5.5±1.5) and 2% (6.0±1.6), relatively to the control (4.5±1.5). To understand vascular network maturation and stability, α -SMA positive vessels were quantified and showed a higher percentage in the presence of GGHA 1%. Based on the degradation results these differences seem to be related to the faster GGHA 1% degradation rate.

GGHA spongy-like hydrogels, combining specific intrinsic features with the biorecognition of HA, are potential materials to be used in acellular and cellular approaches to improve neotissue vascularization.

1.da Silva LP et al. WO2014167513, 2013.2.da Silva LP et al. Acta Biomater 10,4787, 2014.

SFRH/BD/78025/2011 (FCT), POPH/FSE and RL1-ABMR-NORTE-01-0124-FEDER-000016.

No conflict of interest to declare.