

## Exploring a tissue engineering strategy as a novel approach for haemophilic arthropathy treatment

Claudio Grandi<sup>1</sup>, Elena Stocco<sup>1</sup>, Silvia Barbon<sup>2</sup>, Senthilkumar Rajendran<sup>1</sup>, Daniele Dalzoppo<sup>1</sup>, Silvano Lora<sup>3</sup>, Maria Teresa Conconi<sup>1</sup>, Pier Paolo Parnigotto<sup>3</sup>, Veronica Macchi<sup>2</sup>, Andrea Porzionato<sup>2</sup>, Giovanna Albertin<sup>2</sup>, Raffaele De Caro<sup>2</sup>

<sup>1</sup> Department of Pharmaceutical and Pharmacological Sciences, University of Padua, Via Marzolo 5, 35131 Padua, Italy - <sup>2</sup> Section of Human Anatomy, Department of Molecular Medicine, University of Padua, Via Gabelli 65, 35121 Padua, Italy - <sup>3</sup> Foundation for Biology and Regenerative Medicine, Tissue Engineering and Signaling (TES), ONLUS, Selvazzano Dentro, 35030 Padua, Italy

Among the most disabling complications of Haemophilia, repeated and spontaneous intra-articular haemorrhages may cause irreversible damage to the joint. This leads to haemophilic arthropathy, a polyarticular disease characterized by joint stiffness, chronic pain and a severely limited range of motion. Occurrence of haemophilic arthropathy can be avoided by the prophylactic administration of clotting factors to prevent articular haemorrhages, but it can also be addressed using anti-inflammatory drugs and surgery to alleviate the effects of articular damage, up to arthroplasty as resolute option [1]. However, innovative strategies for the prevention and treatment of this common and serious complication are still required, due to some important limits of current therapies, first of all inhibitor development. In this work, we investigated a tissue engineering approach to regenerate articular focal lesions in Haemophilic patients by in vitro development of an autologous bio-hybrid prosthesis. For this purpose, we isolated articular chondrocytes from Haemophilic patients (HaeCs) and characterized them for the first time in literature, to verify whether they were altered by blood exposure. Using healthy chondrocytes as control, optical microscope morphological analysis, flow cytometry immunophenotype evaluation and gene expression study by qRT-PCR were performed. After that, an innovative composite scaffold was obtained by combining decellularized Wharton's Jelly (W's J) from human umbilical cord with a novel biodegradable polyvinyl alcohol (PVA) hydrogel [2]. Finally, we assessed HaeCs capacity to re-populate biosynthetic scaffolds by Scanning Electron Microscopy and MTT assay on cells seeded on supports. Taken together, our results contributed to define HaeCs phenotype, highlighting the possibility to use these cells for autologous implant. What is more, HaeCs capacity to growth and proliferate on composite scaffolds set the stage for planning the development of autologous tissue substitutes for haemophilic cartilage regeneration.

### References

- [1] Raffini and Manno. Modern management of haemophilic arthropathy. *Br J Haematol* 2007;136:777–87.
- [2] Stocco et al. Tailored PVA/ECM scaffolds for cartilage regeneration. *Biomed Res Int.* 2014;2014:762189.

### Keywords

Haemophilic arthropaty; articular chndrocytes; autologous prosthesis; tissue engineering.