Sugar-based supramolecular gelators as scaffolds for 3D-neuronal cell growth

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INTRODUCTION

Finding optimal scaffolds for 3D-cell growth remains one of the most active topic in tissue engineering notably for brain tissue regeneration after traumatic brain injury or neurodegenerative diseases. Currently, most of the scaffolds used are based on synthetic or natural polymers. Another kind of soft materials, the low molecular weight (LMW) supramolecular gelators which are not polymeric, are currently emerging in this field. It has been recently reviewed[1,2]. LMW gels, depending on their molecular structure, display a variety of supporting fibers morphologies, from nanometric to micrometric fibers with various shapes, helicity, rugosity, local stiffness and cross-links topology (Fig A-B). The impact of the fibers morphology and topology of LMW gels on the cell growth is nearly unexplored. Yet they differ from polymer scaffolds since many of them do not provide a large and stiff substrate at the microscale, but rather a network of nanoscaled macromolecules. The aim of this work is thus to explore the impact of these specificities on cell growth and to develop new tissue engineering approaches for neuronal cell development based on the use of sugar-based supramolecular gelators.

EXPERIMENTAL METHODS

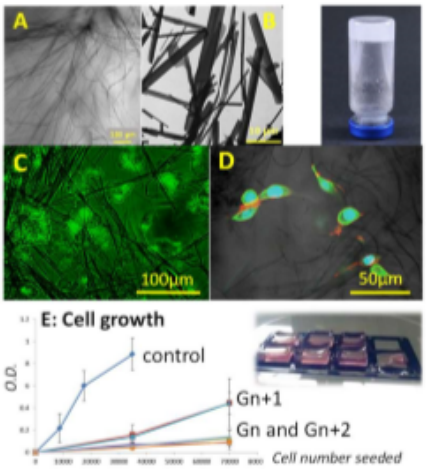
Three sugar-based supramolecular gelators (Gn, Gn+1, Gn+2) differing only by a one-carbon increment on their alkyl chain length (n, n+1 or n+2 carbons) have been prepared[3]. Gels have been prepared by heating-cooling cycles. They have been analysed by optical confocal, electronic microscopy and compared using ImageJ and OrientationJ softwares (Fig. A-B-C-D). The biocompatibility with a neuronal cell line of the different gelators was studied using a cell viability kit or a MTT assay for cell growth study (Fig. C-E). Immunostaining combined with optical microscopy or confocal microscopy were also performed to study cell adhesion, morphology, and 3D-spreading of the cells with the different gelators (Fig. D).

RESULTS AND DISCUSSION

The three LMW gelators studied provided gels with remarkable different morphologies, despite their tiny chemical structure difference. The 1-carbone increment affected strongly the fibers width, length, and curvature. Besides, fast-cooled gels appeared more heterogeneous and fragile compared with slow-cooled gels, which is related to the physical cross-linking density.

Neuronal cells have been grown on these scaffolds. Significant differences in growing have been observed depending on the gelator. Only the gel displaying the larger and straigther fibers enabled a reproducible and important growth of the cells (Fig. E). This difference illustrates the high sensitivity of the cell growth to scaffold stiffness and local topology.

Interestingly, the growth of the cells in 3D has been observed by confocal microscopy directly or after fluorescent immunolabelling (Fig D).



CONCLUSION

These results are introducing the use of simple sugar-based supramolecular gelators as promising scaffolds for the growth of neuronal cells in 3D. From a more fundamental point of view, they highlighted how a tiny difference in chemical structure (a one-carbon length difference) can have a strong impact on the scaffold morphology at the mesoscale, the cell viability and the 3D growth. Work is currently in progress to develop further this new tissue engineering approach.

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