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Hydrogel scaffolds in tissue engineering of the enteric nervous system

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The enteric nervous system (ENS) is the complex network of neurons and glial cellsembedded within the gut wall that autonomously regulates most gastrointestinal functions. In the ENS, distinct neuronal sub-populations encode excitatory and inhibitory neurotransmitters. Indeed, interruptions in the neuronal network and derangement in the architecture of the myenteric ganglia have been linked to gastrointestinal dysmotility and visceral sensory disorders. Since the extracellular matrix proteins have been long known to provide cues for migration and regeneration of neuronal cells, in this study we designed novel hydrogel scaffolds for intestinal tissue engineering. Peptides mimicking the extracellular matrix of the ENS were synthesized by Fmoc chemistry and differently conjugated. Enteric neurons were isolated from the longitudinal muscle myenteric plexus of young mice and seeded onto different decorated scaffolds. After 5 days on culture, cell adhesion, neuronal marker expression and neurochemical coding were evaluatedby confocal microscopy and quantitative RT-PCR. Hydrogels containing laminin adhesive motif greatly promoted adhesion of neuronal cells relatively to other cells of the myenteric ganglia. Arg-Gly-Asp (RGD) motif supported the adhesion of glial cells and also induced expression of mRNA specific for neurotrophin-3, a soluble factor involved in neurogenesis. Ionic-complementary peptide EAbuK fostered axonal outgrowth. Finally, conjugation of RGD and laminin enhanced the expression of choline acetyltransferase thus inducing cholinergic neurons. In conclusion, our study demonstrated that neuronal subpopulations are modulated by varying the composition of scaffolds. These observations will be helpful in the designed of engineered scaffolds personalized for the treatment of defects of the ENS.

Biography

Paola Brun is an Assistant Professor at the Department of Molecular Medicine, University of Padova. She obtained her PhD in 2005. Her scientific research activity covers a range of multidisciplinary topics mainly focused on cell biology, bioengineering and molecular medicine. She actively collaborates with the Departments of Industrial Engineering and Physics to find out innovative materials and techniques able to promote proliferation and differentiation of different cell populations. She has published 55 papers in peer-reviewed journals and she is an Editorial Board Member of seven scientific journals.

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