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Membrane-based approaches for creating multifunctional tools for Neuronal Tissue-Engineering

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Current research in neural tissue engineering is focused on the realization of *in vitro* advanced devices that enhance the neuronal growth and differentiation by mimicking specific features of the in vivo environment. Among the different devices used in neuroscience, membrane-based systems are promising approaches for culturing neuronal cells, offering a homogeneous environment in which the proper topographical, mechanical and biological conditions trigger the specific cellular organization. They offer a broad range of application in developing neuronal functional analogue or substitutes allowing cutting edge investigations in neuroscience field. Indeed, they represent both innovative devices to be used in restoring peripheral nerve damage by boosting its regeneration and valuable *in vitro* platforms for the investigation of new molecules for neurodegenerative diseases treatments.

Within this scenario, this talk will discuss the multifunctional role of biohybrid membrane systems in neuronal tissue engineering as innovative *in vitro* platforms with a well-controlled microenvironment, that enhance nervous system repair by guiding neuronal growth and differentiation. For the design of an advanced neuronal tissue-engineered constructs, membrane properties, including morphological, structural, mechanical, physicochemical, and electrical properties, are key elements in dictating cellular behavior and in controlling new tissue formation. An important challenge in neuronal tissue engineering is the optimization of the design parameters for the realization of novel instructive biomaterials able to promote neuronal outgrowth. To this purpose, different collagen-blend membranes were realized by combining collagen with chitosan (CHT) or poly (lactic-co-glycolic acid) (PLGA) to enhance their properties and thus create new biofunctional materials and permissive environment with great potential use for neuronal tissue engineering and regeneration. Collagen blending strongly affected membrane properties. It improved the surface hydrophilicity of both, pure CHT and PLGA membranes, reduced the stiffness of CHT membranes, but it did not modify the good mechanical properties of PLGA membranes.

Another challenging aspect in the field of neuronal tissue engineering is to create innovative tools capable of promoting cellular response in terms of neuronal orientation that may be used as investigational platforms for studying neurobiological events and neurodegenerative disorders. Our strategy was to develop high performing neuronal membrane bioreactors as a platform for the in vitro reconstruction of neuronal networks with defined functional, geometric, and neuroanatomical features. A novel membrane bioreactor was created to test the capacity of neuronal cells to react to topographical stimuli thus guiding their orientation and to provide a 3Dwell-controlled microenvironment for neuronal outgrowth. The peculiar component within the device namely the poly(lactic-L-acid) (PLLA) highly aligned and packed microtube array membrane, together with the perfusion system, offers a high grade of fidelity for cell growth and elongation thus leading cell polarisation and orientation. PLLA membrane bioreactor offers a continuous perfusion to the cells with oxygenated medium and removal of catabolites avoiding profile concentration and shear stress. It promotes long-term growth and differentiation of neuronal cells, and guided neurite alignment giving rise to a 3D neuronal tissue-like construct.

Our studies have provided new insights regarding the effects of membrane properties on neuronal behavior, and thus it may help to design and improve novel instructive biomaterials for neuronal tissue engineering.

Speaker Biography

Sabrina Morelli, Dr. in Animal Biology, is Researcher Scientist at the Institute on Membrane Technology of the National Research Council of Italy (ITM-CNR). She has expertise in the field of bioartificial membrane devices, especially in the realization of advanced membrane systems for creating 3D engineered tissues and organs for regenerative medicine, pharmacological screening, and as investigational platforms for studying physiological and/or pathological processes. She was scientific responsible for CNR of a PRIN project granted by Italian Ministry of Education, University and Research and she is also involved in several international projects, in the organizing committee of international conferences, in the referee pool of scientific journals. She is co-author of over 70 peer-review scientific papers published in international journals, chapters in books and encyclopedia.

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