



Biomaterials and advanced physical techniques for regenerative cardiology and neurology

Current state of the art in Biomaterials in neurology and cardiology

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The application of biomaterials in the cardiology and neurology fields have given so far, a substantial contribute to the development of implantable and interfaceable devices dedicated to the restoration of a number of cardiac and neural functions. But the use of biomaterials in the context of cardiac or nervous system regenerative medicine is still in its infancy with expected impact both in the framework of tissue engineering, drug delivery and imaging approaches. In parallel with amazing progress in cultivation and use of stem cells, modern biotechnology brings the possibility to obtain numerous types of materials which can support stem cells and help to overcome some major obstacles in the field (e.g. 3D cultures, tissue regeneration guidance, improve the regeneration environment).

During the last two years, in all the events organized in the framework of BIONECCA, as well as in the different STSM supported by the action, neurologists, cardiologists, biomaterial scientists, biomedical and tissue engineers intensively discussed the challenges foreseen for the improvement and novel design of biomaterials for application in both fields. Particular emphasis was given on the exchange of experiences between fields to avoid repetition of experiments and fast-forward developments in both fields.

In particular the following topics were considered as fields for cross-fertilization:

- 1) Materials/devices for electrical stimulation (microelectrodes). In both areas of medicine, electrical stimulation plays an important role in the treatment options offered to patients (e.g. cardiac and cerebral pacemakers). Lessons can be learned from years of use of the cardiac pacemaker and can be extrapolated in terms of material design for the development of the cerebral pacemaker. Although well established and approved for some diseases, current caveats of the latter include (see submitted review¹):
 - a) better definition of brain targets;
 - b) stimulation variables;
 - c) microelectrode design in order to ameliorate foreign body response.
- 2) Transplantation of the stem cells. Within biological systems, cells reside in the extracellular matrix (ECM), a complex and highly dynamic microenvironment that provides structural, mechanical, and biochemical support to cells, ultimately determining their behavior, function and fate. In this sense, and to improve the efficacy of cell transplantation therapies, biomaterial-based matrices mimicking the ECM are being designed to be used as vehicles for cell delivery. The goal is to

create a permissive niche for the transplanted cells, promoting cell survival, proliferation, differentiation, and integration within the host tissue. One of the major challenges one faces when designing a cell compatible matrix is the recapitulation of the instructive cellular niches of natural tissues and the control of the bidirectional interaction between cells and the surrounding microenvironment. The design of such matrices must take into account a number of biological and physical criteria, as follows:

- a) Biocompatibility. The selected matrix should be able to perform its function without causing any toxic or undesirable effects.
 - b) Mechanical properties. The matrix mechanical properties should closely match those of the target tissue, since these will impact cell behavior and, consequently, determine the therapeutic efficacy of the transplanted cells.
 - c) Permeability. The matrix should allow the continuous exchange of gases, ions, nutrients and metabolites with the surrounding microenvironment, which is vital for the survival and proliferation of transplanted/encapsulated cells.
 - d) Degradation. Envisaging an application in the context of tissue repair/regeneration a degradable matrix
- 3) Development of new platforms to study mechanisms of disease and assess novel therapies in neurology and cardiology; here biomaterials are playing a key role as matrices for the development of this in vitro testing platforms. See submitted review¹.
 - 4) Novel bioimaging tools; these include the use of biomaterials as new tools in bioimaging as for example the exploration of nanodiamonds for fluorescence imaging.

[1] M Gulino; K Donghoon; S Pané; SD Santos; AP Pêgo "Tissue response to neural implants: the use of model systems towards new design solutions of implantable microelectrodes" Frontiers in Neuroscience (under review).