Biomaterials for neurology and cardiology: lesson learned from BIONECA

Dr. Ana Paula Pêgo, on behalf of the Working Group 1 of the Bioneca COST action

i3S - Instituto de Investigação e Inovação em Saúde, Universidade do Porto, Porto, Portugal.
INEB - Instituto de Engenharia Biomédica, Universidade do Porto, Porto, Portugal.
Instituto de Ciências Biomédicas Abel Salazar (ICBAS), Universidade do Porto, Porto, Portugal.

The nervous system and the heart are very different in composition (cellular and extracellular matrix content), format and function. Nevertheless, these are two vital systems for our survival. As a result, many key aspects of these tissues are shared. One of them is their limited regenerative capacity, with the heart and the brain being, among the human tissues, with the lowest regenerative capacity. This has obvious consequences to patients that suffer any type of lesion or degenerative disease that impacts the cardiac or nervous system.

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 several cardiac and neural functions. Nevertheless, there are no biomaterials fully approved for clinical use that aim the promotion the regeneration of these tissues. In fact, 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 culture and use of stem/progenitor 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, survival of transplanted cells, tissue regeneration guidance, improve the regeneration environment).

The COST action BIONECA brought together neurologists, cardiologists, biomaterial scientists, biomedical and tissue engineers that intensively discussed the challenges foreseen for the improvement and novel design of biomaterials for application in both fields. Emphasis was given on the exchange of experiences between fields to avoid repetition of experiments and fast-forward developments in both fields.

Several topics have been identified as of relevance for sharing experiences and cross-fertilization. These are briefly summarized in the following paragraphs:

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 review prepared in the framework of BIONECA[1]):
   a) better definition of brain targets;
   b) stimulation variables;
   c) microelectrode design to ameliorate foreign body response.

Current developments include the development of flexible, viscoelastic, comformable electrodes that can be easily adaptable to the surface of viscoelastic tissues like the cardiac muscle and the brain, both for recording and stimulation purposes [2].

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 consider 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.

   Several reports, including some prepared by members of BIONECA, review the different aspects that must be taken into consideration in the context of the exploration of biomaterials as matrices for stem cell culture and/or transplantation for both applications [3-7].

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 [1],[8].

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 [9].

In conclusion, despite the many know specificities, many challenges are common for the development of biomaterials for both heart and nervous tissue regeneration. In BIONECA these have been amply explored in the projects additional work groups. Namely, for exploration of the stem cell transplantation in ALS and cardiac regeneration after myocardium infraction.

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