Open Call oc-2013-1 | Proposal Reference oc-2013-1-15511

Main Proposer Details

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General Features

Title: **BIOMATERIALS AND ADVANCED PHYSICAL TECHNIQUES FOR REGENERATIVE CARDIOLOGY AND NEUROLOGY**

Acronym: **BIONECA**

Initial Idea:

Cardiovascular diseases are the leading cause of death in the western world. Moreover, a progressively ageing population is increasingly affected by neurological diseases, like Parkinson's disease, stroke, amyotrophic lateral sclerosis, Alzheimer's disease or multiple sclerosis, with a large impact on European economies due to huge rehabilitation costs. In the last decade, advanced experimentations involving stem cells were carried out for the treatment of cardiovascular and neurologic diseases, including clinical trials. Many of these studies were based on the employment of new biomaterials and technologies and on the use of advanced characterization techniques. In this context, regenerative medicine requires a multidisciplinary approach involving

basic scientific knowledge on material sciences, stem cell biology, advanced physical techniques for stem cells tracking at 3D level. The main aim of BIONECA is to establish an intensive interaction among top-level scientists of the following scientific disciplines involved in this very ambitious challenge: physics, chemistry, material science, material engineering, rapid prototyping, computational modelling, advanced imaging technologies, stem-cell biology, regenerative cardiology and regenerative neurology. The networking action will include scientific and technical meetings, website, workshops and seminars, STSMs, training schools and common publications. The participants will be organized according to the following four Working Groups: *1) biomaterials processing; 2) characterization; 3) modelling; 4) stem cells, regenerative cardiology and regenerative neurology*. The value of exchanging information at an intra-working group level is obvious. However, the main goal of the action is to stimulate the inter-working group interaction maximally and to implement strong feedback processes.

Expertise needed for evaluation:
1.3 Physical Sciences: Biophysics
1.6 Biological sciences: Stem cell biology
2.6 Medical engineering: Databases, data mining, data curation, computational modelling
2.5 Materials engineering: Biomaterials, metals, ceramics, polymers, composites
2.10 Nano-technology: Nano-materials and nano-structures

Keywords:
cardiovascular and neurological diseases;biomaterials;advanced characterization techniques; stem cell tracking;regenerative cardiology and neurology

Field(s) of application:
Health

Affiliations *:

Number of COST Country Institutions: 14
Number of COST International Partners: 0

Other Institutions (International Organisations, European Institutions and Agencies, European RTD Organisations): 0

**Calculations performed as per TDP Pilot Guidelines and based on users' e-COST profiles and COST Affiliation Categories*

Strategy

Objective 1 (A.3) - Type:Coordination of experimentation or testing

1. Science and Technology Event or Meeting, Action Workshop.
2. Science and Technology Coordination, Short-Term Scientific Missions (STSM).
3. Action Science and Technology Meeting, Working Group.

Objective 2 (A.5) - Type:Development of knowledge needing international coordination: new or improved theory/model/scenario/projection/simulation/narrative/methodology/technology/technique

1. Science and Technology Event or Meeting, Action Workshop.
2. Science and Technology Coordination, Short-Term Scientific Missions (STSM).
3. Science and Technology Event or Meeting, Training School.

Objective 3 (A.6) - Type:Achievement of a specific tangible output that cannot be achieved without international coordination (e.g. due to practical issues such as database availability, language barriers, availability of infrastructure or know-how, etc.)

1. Science and Technology Coordination, Application for Funding to Intergovernmental Programs or Agencies.
2. Science and Technology Coordination, Application for Funding to National Programs or Agencies.
3. Contacts with Stakeholders, Input for the Formulation of Framework Programme Calls.
4. Joint peer-reviewed publication , open access.
5. Science and Technology Coordination, Application for Framework Programme Funding.
6. Internal and External Communication, Production of dissemination material for distribution.
7. Internal and External Communication, Website.
8. Science and Technology Coordination, Short-Term Scientific Missions (STSM).

Objective 4 (B.13) - Type:Bridging separate fields of science/disciplines to achieve breakthroughs that require an interdisciplinary approach

1. Joint peer-reviewed publication , open access.
2. Science and Technology Event or Meeting, Action Workshop.
3. Science and Technology Coordination, Short-Term Scientific Missions (STSM).
4. Science and Technology Event or Meeting, Training School.
5. Internal and External Communication, Participation to Activities of Other Networks.
6. Action Science and Technology Meeting, Working Group.

A. Challenge

Describe the challenge you would like to meet by creating a COST Action and explain why you consider it important (i.e. relevance and timeliness). The challenge is about:

a. *Explaining the problems you want to solve: the content of the challenge falls within one or more of the categories of Action objectives you selected. Any background information needed to explain or to make a convincing case for the challenge you propose needs to be given here.*
b. *Explaining why solving the proposed challenge(s) has an impact: the envisaged impact can be either on codified and tacit knowledge (for definitions see Guidelines for Proposers) or on society. Unless you selected category 6 (Achievement of a specific tangible output…), explain exclusively the content of the challenge (e.g. if you selected 'new model' explain what the model is about and why it is needed), not the form that the solution will take (e.g. a co-authored peer-reviewed publication where the new model will be presented).*

General background

The leading causes of death in western world are cardiovascular diseases (CVDs), in particular the myocardial infarction [1] and neurological diseases (NDs), especially stroke. Moreover, neurovascular and neurodegenerative diseases (Alzheimer's disease, Parkinson's disease, multiple sclerosis) are the leading cause of long lasting impairment and a serious burden to European economies, due to extremely high rehabilitation costs.

Unfortunately, there is a huge disproportion between costs of those diseases and current investment to improve such a situation. For example, the cost for treatment and rehabilitation of neurological patients in

Europe is around 800 billion euros/year, while research investments are around 7 billion euros/year, meaning that less than 1% of costs are invested in new protocols and innovative approach in treatment.

One of the most important reasons for such discrepancy is **a lack of interdisciplinary approach**. Pharmaceutical companies and university research centres do not invest in the interconnection of researchers and knowledge from completely different fields, although it has become obvious that only a coordinated work of different scientific fields will bring real benefit for such complex diseases.

CVDs are also projected to remain the single leading cause of death; it is estimated that the number of people who die from CVDs, will increase, worldwide, to reach 23.3 million by 2030.

The WHO report, *Neurological disorders: Public health challenges*, revealed that one billion people are affected worldwide by neurological disorders (24 million of them suffer from Alzheimer and other dementias), irrespective of age, sex, education or income.

Conventional therapy approaches to CVDs and NDs present several problems, mainly linked to the restricted intrinsic regeneration capacity of heart and neurons and lack of organs for transplantation. Therefore, nowadays, many researchers in various fields including surgery, internal medicine, pharmacology, medical device technology, chemistry, and cell biology, are actively attempting to find solutions, establishing new therapies for curing severe cardiac and neurological diseases.

Recently, cell-based regenerative medicine has appeared as one of the most promising approaches for treating cardiac and neurological diseases. Regenerative therapy by the direct injection of dissociated cells has been performed in the clinic, but only modest therapeutic benefits were confirmed by several published works [2-6].Tissue engineering is currently based on the concept that a three-dimensional (3D) scaffold is used as an alternative for extracellular matrix (ECM), and cells are seeded into the scaffolds [7].

In this field, unfortunately, the official spokespersons of major discoveries and cutting-edge researches are from North American and selected Asiatic Countries (Japan and China) [8].

The situation in Europe is significantly different because most part of the research contributions arise from single excellent institutions or universities in a sort of “spotted experiences”, not supported by strong European networks that could facilitate and greatly enhance the results.

In this context, **the principal BIONECA challenge is to establish an intensive interaction among top-level researchers of the different European scientific communities involved in this very ambitious enterprise, in particular, material scientists, engineers, cells biologists, cardiologists and neurologists.** Each of these communities is actually organized within national and international associations that exchange information in specialized conferences, but interact with each other sporadically.

Therefore we firmly believe that a **COST Action is the optimal tool to face these communication problems**, **by creating an efficient pan-European team among scientists having different cultures, languages, methodologies (Action Objective 5)**. The close cooperation of these scientists, that needs to be intended at international level because it aims to collect and merge the excellent experiences in Europe, is necessary in order to be successful in achieving the final ambitious and extremely difficult goal of producing tangible advancements in the diagnosis and treatment in the two addressed medical areas, as simply expressed by Rita Levi-Montalcini, winner of the Nobel Prize in Medicine, speaking on NDs: "The burden of neurological disorders is reaching a significant proportion in countries with a growing percentage of the population over 65 years."

The BIONECA COST envisions establishing intensive interaction between top-level European Institutions of different scientific communities. More generally, the Action will enhance the cooperation between materials

COST is supported by the EU Framework Programme Horizon 2020

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scientists and engineers and establish a link with partners active in stem-cell research and medicine (cardiovascular and neurology). To our knowledge, such a deeper link has never been achieved so far in Europe. This is motivated by **the priority need of experimentation and testing coordination (Action Objective 3),** in order to drive the European contribution in Regenerative Cardiology and Neurology to establish and consolidate a pan-European scientific community, bridging separate fields of disciplines and bringing together the current isolated approaches. This is why COST is a potential optimal tool to induce the proposed scientific and technological networking (based on an efficient interaction between engineering/materials science, biology and medicine) **to pilot an innovative and multidisciplinary research activity with a consequent expected benefit (Action Objective B13),** producing a faster progress in all the involved disciplines.

Practically the Action will achieve the above mentioned general goals, **by setting-up a series of concrete instruments as specified below (Action Objective 6).**

a) Short-Term Scientific Missions (STSM). Interdisciplinary STSM will be encouraged in which a young scientist belonging to a given research area will visit an institution of complementary interest (for instance a physicist visiting neurologists), as it will be explained in more detail in section B. Several tens of STSMs are foreseen each year, including some reserved to senior scientists, who have a broad experience and knowledge of the capacities of their laboratories.

b) The most tangible outputs of the action, are the joint peer-reviewed scientific publications, most of which will be of interdisciplinary nature. The interdisciplinarity of the publications, their quality, their quantity and their biomedical implications, will be a concrete instrument for evaluating if the ambitious goals of the action will be reached and, synthetically, to assess the extent of the success of the action.

c) In order to contribute to a rational exchange of information among the partners, a website will be set-up and continuously updated.

d) Production of dissemination materials like posters, leaflets, DVDs is foreseen, for advertising the Action in the scientific community and to continuously attract new members of outstanding scientific level during the course of the action.

e) On the basis of the newly developed interdisciplinary cooperation, applications for Framework Programs funding will be submitted, as well as for Intergovernmental or National Programs.

f) The interdisciplinary community resulted from the proposed action will be able to formulate qualified and sound inputs for the Framework Programme Calls.

Current state of knowledge

A primarily important challenge for medicine is the development of novel techniques for diagnosis and treatment of cardiovascular and neurological pathologies, in order to improve the quality of life of the corresponding patients and to contribute in an appreciable way to the extension of human life-expectancy, which was accrued by 10 years in the last 40 years [9]. This improvement is one of the reasons why progressively ageing populations will likely be affected at some point by some of the above mentioned diseases.

Recently, in several fields of medicine, stem cells have been used in different therapeutic strategies for tissue and organ regeneration, as an alternative to more conventional therapeutic approaches.

In particular, in the last decade experimentations of this kind were carried out also for the treatment of

cardiovascular and neurological diseases, including clinical trials.

For instance, experimental and clinical observations on the plasticity of adult stem cells has provided new tools in understanding the pathophysiology of cardiac diseases opening new strategies for the treatment of heart failure. Recent published reports [10-13] have contributed to identify the possible approaches of cellular therapy to generate new myocardium [14], involving systemic and local mobilization of progenitor cells. Moreover, different laboratories [15-19] have recently made available the unequivocal documentation of the existence, in the adult murine and human heart, of primitive cells able to generate all the different component structures of the myocardium.

The first attempt to treat a central nervous system (CNS) disorder with cell transplantation took place three decades ago [20]. In this study, autologous adrenal medulla cells were implanted into the striatum of Parkinson's disease (PD) patients, but the beneficial effects were minimal. Since then, many patients have received stem-cell transplants from different sources, with variable outcome.

Stem-cell research and its application are opening great opportunities in the treatment of neurodegenerative disease based on the idea of transplanting stem cells into the patients to ameliorate/slow the disease course and possibly restore target organ functionality. Transplantation experiments in animal models of neurodegenerative diseases have revealed that neural stem cells (NSCs) are able to survive, migrate, and integrate into the host brain. Recent transplantation studies, performed in animal models of amyotrophic lateral sclerosis (ALS) [21, 22] and other neurodegenerative diseases [23] have demonstrated the ability of NSCs to respond to inflammation/degeneration factors released by damaged tissue, migrate and exert a plethora of detoxifying/trophic actions. Today, it seems also possible to generate in vitro neurons from a variety of stem cells including embryonic or fetal stem cells as well as induced pluripotent stem cells. Such cells allow for extensive in vitro and in vivo testing as well as "good manufacturing production," reducing the risks in clinical application [24]. Another type of adult stem cells, mesenchymal stem cells (MSC), show great promise as an alternative approach to therapy in neurological diseases, controlling inflammatory activity leading to neurodegeneration and promoting repair of CNS tissue. MSC, which are easily isolated from bone marrow and other tissues, have now been tested in phase I and II clinical trials for quite a number of neurodegenerative diseases of various etiology, including ALS, Huntington's, Alzheimer's and PD, as well as spinal cord injury, stroke, and multiple sclerosis. Rather than through differentiation into cells of the relevant tissue, MSC appear to exert their therapeutic effect more through the ability to release therapeutic molecules upon sensing the host environment, providing neuroprotection and promoting regenerative mechanisms in the CNS [25].

Polymers are the major type of materials used in cardiac tissue engineering. Collagen, fibrin, gelatin and alginate have been extensively investigated for myocardial tissue engineering [26]. Although naturally occurring polymers possess the above-mentioned advantages, their poor mechanical properties and variable physical properties have hampered the progress of alternative approaches. It has become widely realized that an ideal tissue engineered substitute should be made from a synthetic scaffold. Among them, aliphatic polyesters (PLA, PGA, and PCL) have widely been applied as scaffolding materials for 3D tissue engineering constructs.

Regarding **drugs delivery into the CNS**, the main obstacle is the presence of the blood-brain barrier (BBB), which forms a physiological and pharmacological barrier to the entry of therapeutic agents from the blood stream [27-29]. To circumvent the BBB, various drug carrier systems have been developed. The promising drug carriers that have been investigated in systemic delivery systems include liposomes, polymeric nucleus pulpous, polymeric micelles, ceramic NPs and dendrimers [30-34]. However, only liposomes and polymeric NPs have been widely exploited in brain drug delivery. To reduce systemic side effects and increase the therapeutic effectiveness, local administration of the therapeutic agents from a biocompatible polymeric delivery system implanted at the target site provides a promising strategy [35]. This approach avoids the difficulty of penetration through the BBB, systemic side effects and toxicity, peripheral drug inactivation and necessity for modification of the carrier surface [36-37]. The disadvantages

of local delivery are that the dosage cannot be adjusted after implantation, the rate of drug release typically decreases with time, repeated implantation may be required for long-term release and the implantation surgery is invasive [38-39].

Other attractive **scaffolds for improved tissue regeneration and CNS repair are the hydrogels**, owing to their tissue-like mechanical abilities conformable to the soft CNS tissue; porous structure allowing cell infiltration, transplantation and axon outgrowth; potential to attach adhesion; capacity for drug/gene incorporation and delivery.

At tissue level of organization, microscopy techniques attempting to visualize the tissue rebuilding process, such as light, fluorescence, scanning and transmission electron microscopy are limited to two-dimensional local information or, otherwise, require laborious three-dimensional reconstruction of serial sections. In-vivo imaging methods, including MRI, PET and micro-CT, have the potential to play a major role in the setting attempting to allow quantification of the rebuilding process, including longitudinal cell tracking [40-44]. On the other hand, current radiologic 3D-methods, possess intrinsic limitations to identify the localization and fate of the injected cells in both clinical [45] and experimental [46-47] settings. All these contentions related to cell tracking methodologies, at least for myocardial regeneration, have been elegantly described [48]. Micro-CT was used for detection of rat Cardiac Progenitor Cells (CPCs), previously labeled with iron oxide nanoparticles, inside the infarcted rat heart, one week after injection and in ex-vivo conditions [49]. This experiment contributes to understand how and to which extent the injected cells are able to migrate and regenerate the damaged myocardium.

Recently, a new approach to deliver differentiating factors to the transplanted stem cells with mesoporous silica was developed. Thus mesoporous silica particles loaded with CNTF and GDNF peptide mimetics and transplanted together with motor neuron precursors resulted in a 10-fold increased survival, specific motor neuron differentiation and functional activity of transplanted stem cells compare to cells transplanted alone [50]. Further utility of mesoporous silica loaded with differentiation factors was tested on recently developed dorsal root avulsion model [51].

Reasons for the Action

In spite of several important positive results obtained so far, a lot of work remains to be done in order to adopt safe clinical protocols (the so-called good manufacturing practice – GMP) [52] for cardiovascular and neurological pathologies.

Despite major efforts in basic and clinical research, there is still no clinically competitive cell therapy for neurodegenerative disorders. The reasons for this failure reside in the lack of reliable animal models, the clinical heterogeneity, the absence of biomarkers, the progressive course of the diseases. Moreover a major problem is the insufficient communication between basic researchers and clinicians. In 2008, the International Society for Stem Cell Research released a set of recommended guidelines for the development of stem cell-based treatments [53]. These recommendations include the use of experts in stem cells ranging from preclinical to clinical research and new oversight criteria for medical innovative care. The construction of a road map to the clinic, taking into account the critical scientific, clinical, regulatory, and ethical issues, defined by basic scientists and clinicians together could lead to the definition of efficient translational clinical protocols.

In this context, a developing GMP-coded stem cell technology for NSCs represents a prime research challenge. Indeed, while MSC used in clinical trials for neurological diseases are expanded from autologous tissue (e.g. bone marrow), the hNSCs to be used in ongoing (EudraCT 2009-014484-39 see also www.clinicaltrial.gov) and future clinical trials will be derived from stable primary human NSCs lines, under GMP conditions.

In terms of advanced characterization of stem cells, in vitro and in vivo high-resolution imaging techniques would help to understand specific-tissue cells fate in many species, including humans. This constitutes another challenge because real time in-vivo imaging is not possible with the current state-of-the-art, unless active control of ventilation – that requires complex intubation of the patient/animal model – is performed.

This situation highly motivates a multidisciplinary approach involving fundamental scientific knowledge in the fields of material sciences (including processing, characterization and modeling), stem cell biology, advanced physical techniques for tracking the stem cells fate at 3D level, regenerative cardiology and neurology.

The proposed action is expected to have a very important impact on the European Society, because it will improve the mutual interaction and therefore the overall scientific output of several categories of scientists, who are pursuing the common goal of defeating several cardiological and neurological diseases which are major causes of death among the European society. The action ranging over four years will surely contribute to a major progress in the two medical areas, having as a main consequence the prolongation of the human life expectancy. That will have not only an obvious and high-relevance positive social impact, but will also lead to important economic benefits by reducing the more and more increasing costs related to the treatments of the considered diseases, especially of those of neurological character, such as Alzheimer's disease. For instance, about 35.6 million people worldwide live with some type of dementia — about four times the population of Sweden. Considering the current medical curing capacities, the caseload will increase to 65.7 million by 2030 and to 115.4 million by 2050. Globally, $604 billion is spent per year on dementia care – this represents 1% of the world's GDP [61].

The saved financial resources could be further invested in research, with a consequent improvement of the welfare, in a virtuous process of dynamical feedback.

Complementarity with other research programmes

Being stressed that the COST Actions funds do not cover research activities, it is reported below that research funding of the partners is guaranteed through the following current National, European and Transnational research projects. From the name of the various projects, it is clear that all these projects deal with subjects related to our proposed COST action. The obtained expertise will be disseminated via this Action.

"Combining Stem Cells and Biomaterials for Brain Repair - Unlocking the Potential of the Existing Brain Research through Innovative In Vivo Molecular Imaging"- Glowbrain (FP7)

"Biohybrid templates for peripheral nerve regeneration"- BioHybrid (FP7-IP)

"Multi-scale Biological Modalities for Physiological Human Articulation" - MultiScaleHuman (FP7- Marie Curie RTN)

"Mastering sweet cell-instructive biosystems by copycat nano-interaction of cells with natural surfaces for biotechnological applications" - FIND & BIND (FP7)

"Sponge Enzymes and Cells for Innovative Applications" - SPECIAL (FP7)

"Unlocking the research potential of 3Bs Group, University of Minho, in Nanomedicine field to stengthen its competitive position at the European level" - POLARIS (FP7-REGPOT)

"Regeneration of Cardiac Tissue Assisted by Bioactive Implants"- RECATABI (FP7)

“The trafficking of hematopoietic stem cells and their bone marrow homing as the prerequisites to improve the outcome of transplant”, Italian Ministry of Health RF-LIG-2008-1221276

“Mesenchymal Stem cells for Multiple Sclerosis (MESEMS), phase I/II clinical trial for the treatment of multiple sclerosis with mesenchymal stem cells”, FISM 2012/S/3

“Clinical trial for the treatment of multiple sclerosis with mesenchymal stem cells”, Carige Foundation

“Establishment of a functional nano-biointerface between neurons and semiconductor nanowires for real-time sensing” - InterfaceFund (Medicine/SOTON)

“Bio-active nanoparticles for treatment of Neurons” (SOTON/PGR Scheme)

“Nanosystems for early diagnosis of neurodegenerative diseases” - NADINE (FP7)

“Tools for minimally invasive diagnostics” - DIATOOLS (FP7)

"TargetBraIn", 5 year program on the role of inflammation in stem cell mediated stroke regeneration (FP7)

"BrainPath", 5 year program on multimodal methodologies and approaches for optical imaging (Marie Curie IAPP)

Biomarkers of Brain Ageing", funded by German Ministry of Education and Research

Furthermore, this Action will take advantage of the results of the on-going projects in a way that these are integrated and further used to add maximum value to researchers, cardiologists and neurologists in the European context. Moreover, the proposed Action will coordinate efforts towards future research projects focused on research gaps and needs. Therefore, this COST Action will not only be complementary to, but also highly synergistic with the future activities in this challenging area.

B. Added Value of Networking

Explain exactly and in practical terms why and how the pan-European coordination provided by COST would leverage non-COST funded human and physical resources (e.g. employee time; infrastructures). Explain why the same challenges could not be met at all or at the same level (in terms of scope, scale or quality) without a pan-European network.

Faced with the enormous problem of lack of treatment for brain diseases, EU proclaimed May 2013 to be a Month of the brain and 2014 as the Year of the brain. During a final May conference in Dublin, one of the

main problems in the current treatment of both brain and cardiovascular diseases has emerged: all pharmaceutical companies and the majority of Research University centres faced disproportionally high investments with respected to the limited outcomes. For example, out of more than 1 million compounds tested in the last year, only 8 reached serious level of clinical trials. This fact brought both industry and researchers to the edge: many projects are being ceased because of too large complexity of the problem. One point has been recognized as highly probable cause that requires an urgent corrective: the limited multidisciplinary approaches of such researches. This fact, that was also recognized as possible reason of the ineffectual investments, should trigger EU to better redistribute funds to industries and research centres in order to establish innovative and multidisciplinary networks for knowledge exchange, keeping in mind the cutting-edge interdisciplinary research experiences from North American, Japan or China.

BIONECA was intended to be an Action facing the previously mentioned limitation, providing a platform for exchange of expertise, data and personnel and stimulating interactions between researchers of different disciplines, with the great ambition to defeat many of the most dangerous and fatal diseases menacing our society.

In particular, the aim of this Action is to give a boost to the European scientific and technological advance by overcoming the fragmentation of research activities, methodologies and knowledge belonging to scientists involved in different disciplines such as physics, chemistry, material science, material engineering, rapid prototyping, informatics, advanced imaging technologies, cell biology #□□ □□□□□□□□□□□□□□□□□
cell biology), molecular biology, regenerative cardiology, regenerative neurology.

Efficient transfer of knowledge between such numerous and sometimes distant disciplines will be obtained through this pan-European network in a much faster and low-cost way, as compared to current individual and sporadic efforts. This would be mainly achieved by exposing participants of different disciplines #□□ □□ □□□ t
complementary disciplines. In fact, without the proposed networking Action, researchers normally interact with colleagues of the same or close disciplines. This happens for several reasons such as common scientific language, narrow specialization, lack of transdisciplinary conferences, etc., with the consolidated tendency to attend several events offered in one given discipline. Moreover, the proposed Action can help to overcome the conservative attitude of avoiding the non-negligible efforts necessary to get through different professional, cultural and methodological barriers.Without the proposed COST Action, young researchers, when involved in personnel exchange, will usually go to laboratories of colleagues of their professors, active in the same disciplinary areas, for instance a young neurologist will be sent to visit an established professor of neurology in another university. And similarly, the same will happen for cardiologists, biologists, physicists and so on. This is, of course, very important and necessary, corresponding to a very long and fruitful European scientific tradition. But in modern times this necessary condition is not anymore sufficient to cope with the need of interdisciplinary, for achieving very ambitious scientific and technological goals like defeating critical pathologies, due to their enormous complexity.

With the use of large public funds, several large scale facilities #□□ □□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□□
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physicists but are normally exploited just for interesting and challenging scientific issues in physics. Their application in chemistry are limited and only rarely these advanced techniques are involved for solving biological problems with clinical impact. Examples of these rare multidisciplinary approaches are the use of the Nuclear Magnetic Resonance - from nuclear spin studies to chemical analytics and finally biological and established medical imaging applications - and of the X-ray diffraction, that was in the beginning of 20th century used only by physicists, followed by chemists and only after World War II the biological and medical applications emerged culminating with the discovery of the DNA structure. Indeed, the discovery of DNA structure would have not been possible without the close cooperation of biologists led by Watson and Crick on one side and the team of physicists, experts in x-ray diffraction interpretation, led by Wilkins, on the other side.

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With the proposed Cost Action young researchers will have the opportunity to make Short Term Scientific Missions in an institution of complementary nature. For instance, a physicist could visit a group of biologists, neurologists or cardiologists in order to discuss their research challenges and set-up a road map to provide help to address them. Furthermore, a physicist could eventually take part in the preparation of biological samples to be investigated later by advanced physical techniques. Additionally, an experienced physicist could present a seminar illustrating the scientific opportunities offered by the most innovative and advanced characterization techniques. The biomedical colleagues, following common scientific discussions, could suggest new experiments, in which the physical techniques can provide precious complementary information to the classical techniques, which are peculiar for a given biomedical group. For example, the cardiologists and neurologists could foresee the use of X-ray micro-CT in order to obtain 3-dimensional complex structural and morphological information, complementary to the 2-dimensional information obtainable by histology. The complementary use of the two above mentioned techniques were recently greatly appreciated by orthopaedists and dentists, producing tissue engineered bone by using stem cells.

Without the Cost Action, young researchers would attend Training Schools of the same disciplinary area in which they are active #
cardiology, material scientists subjects of material science, and so on#
upgrading the knowledge of an individual young researcher, owing to the velocity of new discoveries, but it is not anymore sufficient when dealing with very ambitious and complex goals, as those aiming to fight cardiovascular or neurological diseases. The proposed Action will offer in addition to young researchers the possibility to attend Training Schools of interdisciplinarity level in which teachers belong to different disciplinary areas included in the Action itself. For instance, in a single School, young researchers will attend lectures on biomaterials production and modelling, on stem cell biological properties, on advanced techniques of imaging at 3-D level and tracking of stem cells, available at European large scale facilities like synchrotrons, on the last progresses in cardiology and neurology, especially the ones obtained with the help of the scientists belonging to the mentioned areas of basic natural sciences.

Additionally, students of these interdisciplinary courses will obtain another crucial added value, namely the possibility to interact scientifically during several days with students of different disciplines and to establish fruitful links, very precious for developing future interdisciplinary cooperation. In order to enhance and optimize this added value, the Action foresees that the first part of the first day of each School will be devoted to short presentations given by each student regarding their own scientific activity and the research interests of their institutions.

A good analogy can be made between the interdisciplinarity research and a beautiful orchestra. Individual training of each orchestra member is important, so each one can perform well his own instrument. But for the creation of a beautiful composition, an interaction is needed. Musicians must understand enough about his colleagues' instruments to join them in harmony. Each orchestra member can solo, but together they produce more than any one alone.

It is expected that, by the BIONECA Action, a faster interdisciplinary knowledge growth will occur, producing large benefits due to finding new solutions against brain and cardiovascular diseases. Keeping in mind the figures presented in Section A, a simple calculation shows that each 1% in the improvement of the current situation implies a cost reduction of about 8 billion euros/year. This means that the international coordination in the field of cardiovascular and neurological research proposed by the BIONECA COST Action, is expected to give an appreciable economical advantage for the EU, which will definitely overcome by a large factor the public funds invested in the Action itself.

It must be also mentioned that the quick spreading of the knowledge produced in the basic scientific areas, like for instance the development of new advanced physical characterization techniques and the

progresses in understanding phenomena occurring at biological level in stem cells, will not only be beneficial to medical areas, but also for several other ones. This statement is based on the experience of the proposers and on the fact that basic sciences advancement can always find several applications, some of them initially unexpected.

Long-held biases, beliefs, educational practices, and research funding mechanisms have created a system in which it is easier to conduct unidisciplinary than multidisciplinary work. Creation of environments in which interdisciplinary research and training occur requires multiple integrated approaches and substantial efforts. Although it might be difficult, it is well worth the try because many of today's disciplines #□□ □□□□□□□□□□□□□□□□□□□ biochemistry#□□ □□□ tomorrow's disciplines. BIONECA aims at this goal.

"The seeds of progress germinate, and the shape of the future unfolds in our conviviality, at the convergence of all our different paths. It is in this gradual cross-fertilization that the future of knowledge - and indeed of the world – resides."

Federico Mayor

(Director-General of UNESCO from 1987 to 1999)

C. Milestones and Deliverables: contents and time frames

Describe the specific form of the activities (milestones and deliverables) needed to meet the challenge and selected as relevant to each objective: specify clearly the outputs corresponding to the achievement of your objectives and to the solution of the challenge proposed.For the main outputs, specify:

- *The means to achieve them;*
- *Their envisaged time frames.*

All milestones and deliverables should be:

- *Achievable within an Action's lifetime;*
- *Feasible in terms of content;*
- *Realistic in terms of time frame.*

At this stage, a few examples per objective (minimum 1) are sufficient, as work plans are finalized only once the COST Action starts.

Milestone MS1: Appointment of the Action managing structures: Management Committee (MC), Chair and a Vice Chair, four WG leader, Dissemination and STSM coordinators and Steering Committee (SC). This Milestone will be reached during the Kick-off Meeting, in the first month of the Action and has the crucial role to ensure the well-functioning of the Action

Milestone MS2: Creation of a dedicated website that aims to maintain and enhance communication among the partners and to disseminate the results obtained in the different WGs towards the general public, in order to raise public awareness of the BIONECA Action and on the efforts that cardiologists and neurologists, with the help of scientists from different fields, make in

order to improve the life quality of the population. The website will also contain a restricted access area for registered participants of the COST Action in order to give access to relevant restricted information, tools and databases.

This Milestone will be achieved by the third month of the Action. The Dissemination coordinator will be in charge of developing and updating the website, in close cooperation with the WG leaders who will provide the news, results and planned activities within their WG.

Deliverable D1 (month 3) is the website itself, an essential tool for meeting the A.6 objective, as it can put together and make available to all the Action members and partially also to the large public (depending on information confidentiality) the available infrastructure and knowhow of the partners and all the output of the Action.

Milestone MS3: Science & Technology Meetings. These Meetings will consist in WG Meetings and other horizontal Meetings between Action members. The purpose of WG Meetings consists in discussing the results obtained in pre-funded research and the progress made within the WG and to identify future common activities to be performed with the aim of reaching specific scientific goals, difficult or impossible to be achieved without a common effort of members from the same WG or from different WGs. BIONECA Action will hold an annual three-day meeting for each WG at different partner locations. The first day of such meetings will allow exchange of specific information and ideas related to the WGs topics and encourage collaborations between scientists and institutions, stimulating the planning of joint experimental work and translational activities. The second day will include a combined session with the other WGs. This would enhance integration of activities from the different fields and promote interface between WGs. For example, feedback from the characterization (WG2) is important for the processing activities (WG1). Data and results exchange is foreseen also between WG2 and WG3 - Modelling, while biologists, cardiologist and neurologists from WG4 will use the output from the other WGs and will give back essential feedback. The final day will involve the planning of exchanges of young researchers, planning of a program of training schools, preparation of materials for distribution to other WGs via the website. This will further enhance the exchange of ideas between the different WGs.

The horizontal Meetings between partners from different WGs can be organized together with the WG leaders as often as needed, for discussing a specific collaboration or preparing an application for Framework Programme funding, Intergovernmental or National Programs or Agencies.

These Meetings will be mainly organized using the online communication facilities (online conferences), for cost effective reasons.

All these activities clearly address the objectives A.3, the coordination of experimentation or testing and B.13 by bridging separate fields of science/disciplines to achieve breakthroughs that require an interdisciplinary approach.

The MS3 milestone will be achieved in month 33, when the last WG Meeting is foreseen, where

last common scientific activities and possible future collaborations, after the end of the project, will be planned.

Deliverable D2 (months 12, 24 and 33) will consist in reports containing the main ideas and actions discussed or decided during the Meetings and will be send to each partner via Newsletter and will also be uploaded in a specific section of the Action website. **Deliverable D3** (months 12, 24 and 36) will contain a list with the names of the approved national or international research projects, together with the names of the Action's partners involved, projects resulting from common applications established during the COST Action.

Milestone MS4: Action Workshops. WGs Workshops will inform interested scientists, but also the general public about the results of the project and about new technologies and knowhow developed throughout the project. Unlike Science & Technology meetings, that are foreseen to be held only among Action members, the Workshops will be opened to scientists from different fields and to the general public. Thus, it will contribute to the A.5 objective by creating an efficient pan-European team among scientists having different cultures, languages, methodologiesand, especially, to the B.13 objective, giving the possibility of widening the community of people interested in the regenerative cardiology and neurology. The Workshops will be organised in different geographic regions to allow participants from across Europe to gain access to the leading European expertise in the field of cardiologic and neurologic therapies using stem cells, with all the related research aspects: processing, characterization, modelling.

One Workshop will be organized each year, so by month 36 of the Action, the milestone MS4 will be achieved. The MC will nominate an Organizing Committee (the WGs leaders will be part of it), which is responsible for the organization of the Workshops. As it will be opened to the wider community, the announcement will be extensively disseminated at least 3 months before using different media channels, the Action website, flyers and/or posters.

Deliverable D4 (months 12, 24 and 36) will consist in three reports, corresponding to the three Workshops that will be made available on the Action website.

Milestone MS5: Training Schools. The purpose of a Training School is to disseminate knowledge developed within the Action to targeted groups, mainly young researchers, but also researchers that want to enrich their knowledge in a certain domain. Without the COST Action, young researchers will attend Training Schools of the same disciplinary area in which they are active. The proposed Action will offer in addition to young researchers the possibility to attend Training Schools of interdisciplinary level in which teachers belong to different disciplinary area considered in the Action itself. For instance, in a single School there will be given lectures on biomaterials processing and modelling, on stem cells biological properties, on advanced techniques of 3D imaging and tracking of stem cells, on the last progresses in cardiology and neurology, especially the ones obtained with the help of the scientists belonging to the mentioned areas of basic natural

sciences.

Additionally, the students of these interdisciplinary courses, will have the possibility to interact scientifically during several days with students of different disciplines and to establish fruitful links, very precious for developing future interdisciplinary cooperation.

The Training Schools directly address objectives A.5 and B.13 through the pan-European interdisciplinary approach.

Three Training Schools, one per year, will be organized by the different partners, under the supervision of the Steering Committee. Thus, Milestone MS5 will be achieved in month 36, while **Deliverable D5** (months 12, 24, 36) will consist in the Training Schools proceedings that will collect the lectures and will be available on the Action's website, in a specific section.

Milestone MS6: Short-Term Scientific Missions (STSMs). In general, STSMs aim at allowing a grantee to learn a new technique or gain access to specific instruments and/or methods not available in their own institution. Normally, young researchers, when doing scientific visits, will go to laboratories of colleagues of their professors, active in the same disciplinary areas. This is, of course, very important and necessary, corresponding to a very long and fruitful European scientific tradition. But in modern times this necessary condition is not anymore sufficient to cope with the need of interdisciplinary, for achieving very ambitious scientific and technological goals like defeating critical pathologies, due to their large complexity. With the proposed Cost Action young researchers will have the opportunity to make a STSM in an institution of complementary nature. For instance, a physicist could visit a group of biologists, neurologists or cardiologists in order to discuss their research difficulties and set-up a road map to provide help to address them. Furthermore, a physicist could eventually take part in the preparation of biological samples to be investigated later by advanced physical techniques.

The STSMs are addressing all four Action objectives in a very direct way, being one of the main sources of knowledge transfer, enhancing the interdisciplinarity of the Action and being a key factor in strengthening the existing collaborations between different partners and establishing new ones.

The STSMs will be organized under the supervision of the STSM Coordinator, who will perform the primary evaluation of the STSMs, before the final judgment is made by the MC. Three different calls for STSMs are foreseen, at months 3, 15 and 27 and the beneficiaries of the STSMs will have 6 months' time to visit the requested partner and 1 month time to deliver a report on it. The time length of a STSM will be between 1 week and 1 month. The total number of STSMs is foreseen to be about 60, 20 for each STSM call, as the number of partners in the Action will be about 20, so one person from each institution will have the opportunity to perform a STSM each year.

The Milestone MS6 will be achieved at the end of the project (month 36), when the last STSM reports will arrive to the STSM Coordinator and to the MC.

Deliverable D6 (months 12, 24, 36) After receiving all the reports and after their approval by the MC (within one month), the STSM Coordinator will upload all the reports in a specific section of the Action's website.

Milestone MS7: Joint peer-reviewed Publications between Action participants. One of the most tangible outputs of the Action are the joint peer-reviewed scientific Publications, most of which will be of interdisciplinary nature. The interdisciplinarity of the Publications, their quality, their quantity and their biomedical implications, will be a concrete instrument for evaluating if the ambitious goals of the Action are reached and, synthetically, to assess the extent of the success of the Action. In this context, the Publications written by researchers from at least 2 different institutions will address both A.5 and B.13 objectives.

Milestone MS7 will be achieved at the end of the Action (month 36) and even further on, when all the results born from the interactions among partners during the Action will be published in peer-reviewed journals.

Deliverable D7 (month 36) will consist in the published articles, which the Dissemination Coordinator will send to all the partners and will upload on the Action's website.

D. Action structure and participation – Working Groups, management, internal procedures

Describe the Action organization in terms of Working Groups and management structure that would best help the Action meet the proposed challenge. Bear in mind that the proposed Action organization and management structure must respect COST rules. In particular:

- *Management Committee Members are nominated by the COST National Coordinators*
- *Working Group Members and Occasional Participants are decided directly by the Management Committee, but their reimbursement is constrained by budget availability*
- *Working Groups and management can be adapted by the Management Committee of the Action during an Action's lifetime.*

In order to achieve the Action objectives, four different Working Groups (WGs) will be established, as described below, with a strong interconnection between them.

WG1: Processing

The aim within this WG is to process higher quality biomaterials, involving stem cells, to be used in specific applications by cardiologists and neurologists. Silk-based hydrogels or decellularized human myocardial sheets are currently used for pre-clinical and clinical studies for enhancing stem

cell function in the heart and treating myocardial infarction, while single-walled carbon nanotubes are successfully used in experiments in which mouse embryonic neural stem cells are differentiated in neurons. Further development of these or similar biomaterials will be one of the objectives of the Processing WG.

WG2: Biomaterial characterization

Besides classical techniques such as micro/nanostructural characterization and phase identification by advanced electron microscopy and spectroscopy (SEM, TEM/HRTEM, FIB, STEM/EDS) or X-ray diffraction, new advanced physical characterization techniques are emerging: synchrotron radiation micro-CT and holotomography, able to visualize in 3D, at micron or submicron resolution, blood vessels without any contrast agent or follow human stem cells migration in infarcted hearts. Synchrotron microbeam x-ray micro-fluorescence can be used for topography and quantitative analysis of selected metals ions; their accumulations within neurons is supposed to be at the origin of Parkinson's disease and amyotrophic lateral sclerosis.

WG3: Modelling

Characterization data obtained from partners in WG2 can be used to develop and validate mathematical models based on multiscale fluid and solid mechanics concepts including transport phenomena and bio-chemical kinetics of scaffold-cell-growth factor interactions. Model input regarding chemical composition and microstructure can be collected from SEM, XRD or micro-CT experiments. The use of novel biomaterial-tissue simulation tools in Finite Element Analysis of organ-implant structures will give access to unparalleled insight into the functionality of the scaffolds and will open new perspectives for their optimization.

WG4: Stem cells, cardiology and neurology

This working group will consists of cell biologists, cardiologists and neurologists, carrying out research activities related to cells properties and regenerative medicine in the areas considered by the proposed action.

Cardiologists and neurologists will take advantage from the new materials processed within WG1 and characterized by WG2, will benefit from the modeling performed by WG3 and will use the discoveries of the cell biologists in order to improve the quality of their results. One example of research to be addressed by an interdisciplinary approach is finding means to deliver MSC-secreted molecules to the brain by overriding the blood-brain barrier. Biologists need to work together with scientists experts in nanotechnology for finding the proper carriers, with physicists dealing with cutting edge imaging technology to monitor delivery and neurologists who assess the results.

Management structure

The Action organization will follow the general COST rules described in the "Rules and Procedures for Implementing COST Actions". The Management Committee (MC) will be convened by representatives of the participating countries as described in the COST guidelines. The MC will elect a Chair and a Vice Chair by majority vote.

The MC will be charged with:

- promoting collaborations and exchange of data, tools and results across WGs, maximizing interactions among partners;
- monitoring and assessing the different activities (meetings, scientific exchanges, training schools, website, publications) to ensure they meet the objectives defined for this COST Action;
- eventually propose changes of activities in order to better fulfil the objectives;
- preparation of the annual and final reports;
- ensuring that milestones and deliverables are due in time.

The following positions will be created and named at the first MC meeting during the Kick-off Meeting:

1. Four WG leaders, each corresponding to the four scientific WGs. They will plan the details of the Science & Technology meetings and Training schools within their WG, will coordinate the activities within their WG to meet the COST Action objectives, will promote the exchange of information between tasks of the same WG and across WGs.

2. A STSM Coordinator, responsible for organization and primary evaluation of the STSMs, before the final judgment by the MC.

3. A Dissemination Coordinator, who will take care of publicizing the results of the Action through its website, will be responsible for the production of dissemination materials like posters, leaflets, DVDs.

4. For a dynamic management, a Steering Committee (SC), comprising members of the MC, Chair, Vice-Chair, WG leaders, STSM and Dissemination Coordinators, will be established. It will coordinate events such as Workshops, Training Schools, interactions with other networks. Regular meetings of the SC will be held on Internet basis for an efficient inexpensive management. In any

case, major issues will be handled directly by the MC at its annual meeting.

A Kick-off meeting will be held at the beginning of the Action in order to crystallize Action details, publicize the Action and call for new members to join the defined WGs. A first MC meeting will then be held to elect the MC Chair, Vice-Chair, WG leaders, STSM and Dissemination Coordinators. MC will meet at least once per year, with a second virtual meeting that can be organized using modern online communication methods.

Meetings of the WGs will be held on an annual basis at different partner locations. BIONECA will hold an annual three-day meeting for each WG, that will allow exchange of specific information and ideas within and between the WGs and encourage collaborations between scientists and institutions. For example, feedback from the characterization (WG2) is important for the processing activities (WG1). Data and results exchange is foreseen also between WG2 and WG3 - Modelling, while WG4 will use the output from the other WGs and will give back essential feedback. The final day will involve the planning of exchanges of young researchers for the following year, planning of a programme of training schools, implementation of web site tools and databases, preparation of reports and materials for distribution to other WGs via the website. This will further enhance the exchange of ideas between the different WGs.

Gender and age balance will be sought in every organization aspect of the Action, while keeping emphasis on excellence.

Network of Proposers - Features

Countries*:

14 COST Country Institutions

- Italy
- Spain
- Croatia
- Germany
- Czech Republic
- Austria
- Portugal
- France
- United Kingdom
- Ireland
- Slovenia
- Slovakia
- Serbia

Romania

0 Near-Neighbour Country Institutions

0 COST International Partners

0 European Commission and EU Agencies

0 European RTD Organisations

0 International Organisations

** This section lists the countries of the institutions with which Proposers are affiliated. Proposers affiliated with more than one institution are asked to choose the institution that is most relevant to the Proposal. Independents are not eligible to be Proposers, as specified in the COST Guidelines for TDP Pilot.*

Number of Proposers: 20

Gender Distribution of Network of Proposers: Males 55.0%; Females: 45.0%

Average number of years elapsed since PhD graduation of Proposers***: 19.0

****This figure takes into account only those Proposers who reported holding a doctoral degree, i.e. of all Proposers. The calculation is based on the month and year in which the last doctoral degree was obtained by each Proposer.*

Number of Early Stage Researchers****: 4

*****This figure takes into account only those Proposers who reported holding a doctoral degree, for whom a maximum of 8 years elapsed between the date of in which their PhD was awarded and the date of submission of this Proposal.*

Core Expertise of Proposers: Distribution by Sub-Field of Science****:

25.0% Materials engineering
15.0% Basic medicine
15.0% Clinical medicine
15.0% Medical biotechnology
10.0% Chemical sciences
20% Other

*****The Core Expertise is defined by each Proposer at registration and it is the sub-field of science corresponding to the first research exertise area selected.*

Institutional distribution of Network of Proposers*****:

90.0% Higher Education & Associated Organisations
5.0% Business enterprise
5.0% Government/Intergovernmental Organisations except Higher Education

Higher Education & Associated Organisations: 18

Number by Field of Science of Department/Faculty of Affiliation:

- Interdisciplinary : 2
- Materials engineering : 3
- Clinical medicine : 4
- Basic medicine : 2
- Medical engineering : 1
- Medical biotechnology : 1
- Physical Sciences : 1
- Other medical sciences : 1
- Other engineering and technologies : 1
- Electrical engineering, electronic engineering, Information engineering : 1
- Biological sciences : 1

Number by Type:

- Education Oriented : 8
- Research Oriented : 10

Number by Ownership:

- Fully or mostly public : 16
- Fully or mostly private : 1
- 50-50 Public and Private : 1

Business enterprise: 1

Number by Market sector of unit of affiliation:

- Professional, Scientific And Technical Activities : 1

Number by Type:

- Private enterprises : 1

Number by Ownership and International Status:

- Independent Enterprise : 1

Number by Size:

- SME (EU Definition provided underneath after selection) : 1

Government/Intergovernmental Organisations except Higher Education: 1

Number by Level:

- Local government : 1

Number by Type:

- Other Public Non-Profit Institution : 1

***** *Based on contractual relationship deemed as most relevant to the Proposal by each Proposer.*

Bibliographical References

You are free to provide bibliographic references. This section is shown to evaluators but it is optional and is not necessarily taken into account for evaluation purposes.

[1] WHO Library, Global status report on noncommunicable diseases(2010)

[2] G. Ibarretxe et al. Stem Cells International(2012)

[3] M. Corselli et al. Arterioscler Thromb Vasc Biol 30(2010)

[4] S. Roura et al. PLOS ONE 7(2012)

[5] US. Neill. June, J Clin Invest(2012)

[6] A. Alvarez et al. Neuroscience & Medicine 1(2010)

[7] J. Leor et al. Pharmacology & Therapeutics 105(2005)

[8] http://www.eurostemcell.org/story/clinical-trials-news-january-2012-update

[9] Journal of Sports Science & Medicine,Vol.8(2009)

[10] Leri A et al. Curr Probl Cardiol 33(2008)

[11] Wollert KC. et al. Lancet 364(2004)

[12] Balsam LB. et al. Nature 428(2004)

[13] Orlic D et al. Nature 410(2001)

[14] Matsuura K et al. Biochemical Biophysical Research Communications 425(2012)

[15] Beltrami AP. et al. Cell 114(2003)

[16] Barile L. et al. Nat Clin Pract Cardiovasc Med 4(2007)

[17] Oyama,T. et al. J Cell Biology 176(2007)

[18] Oh H. et al. Proc Natl Acad Sci USA 100(2003)

[19] Matsuura K.et al. J Biol Chem 279(2004)

[20] Backlund, EO et al. J Neurosurg 62(1985).

[21] Xu et al. Transplantation 82(2006).

[22] Corti et al. Brain 130(2007).

[23] Pluchino et al. Nature 436(2005).

[24] Schwarz SC. J Lab Clin Med 156(2010)

[25] Uccelli et al. Lancet Neurol, 10(2011)

[26] WH. Zimmermann et al. Biomaterials 25(2004)

COST is supported by the EU Framework Programme Horizon 2020

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[27] Wang, P.et al. Adv Drug Deliv Rev 54(2002)

[28] Misra, A. et al. J Pharm Pharmacol Sci 6(2003)

[29] Garcia-Garcia et al. Int J Pharm 298(2005)

[30] Cherian, AK. et al. Drug Dev Ind Pharm 26(2000)

[31] Lian, T. et al. J Pharm Sci 90(2001)

[32] Adams, ML. et al. J Pharm Sci 92(2003)

[33] Kaur, IP. et al. J Control Rel 127(2008)

[34] Oliveira M. et al. Progress in Polymer Science 35(2010)

[35] Jain, A. et al. Biomaterials 27(2006)

[36] Domb, A. J Mol Med Today1(1995)

[37] Begley, D. J Pharmacol Ther 104(2004)

[38] Meilander, N. et al. J Control Re l71(2001)

[39] Saltzman, W. et al. Nat Rev Drug Discov1(2002)

[40] Badea CT. et al. Med Phys 31(2004)

[41] Badea CT. et al. Molecular Imaging 4(2005)

[42] Badea CT. et al. Toxicologic Pathology 34(2006)

[43] De Vries IJM. et al. Nature Biotechnology 23(2005)

[44] Dhodapkar MV et al. J Exp Med193(2001)

[45] Frangioni JV. et al. Circulation110(2004)

[46] Li Z. et al. J Am Coll Cardiol53(2009)

[47] Schelbert HR. et al. J Nucl Cardiol10(2003)

[48] Terrovitis JV. et al. Circ Res106(2010)

[49] Giuliani, A. et al. J Tissue Eng Regen Med5(2011)

[50] Alfonso Garcia-Bennett et al. Stem Cells Translational Medicine(2013)

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[51] Konig et al. TERM(2013)

[52] http://ec.europa.eu/health/documents/eudralex/vol-4/

[53] Hyun et al. Cell Stem Cell 3:607–609 (2008)

[54] http://healthland.time.com/2010/09/23/the-impact-of-alzheimers-disease-by-the-very-scary-numbers/#ixzz2V9i3A2sB

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