

EuroNanoMed

NEWSLETTER
NUMBER 1

EuroNanoMed

BASQUE REGION (SPAIN)

FRANCE

GERMANY

HUNGARY

ICELAND

ISRAEL

LATVIA

LITHUANIA

POLAND

PORTUGAL

ROMANIA

SPAIN

SWEDEN

SWITZERLAND

THE NETHERLANDS

TURKEY

VENETO REGION (ITALY)

WALLONIA (BELGIUM)

Nanomedicine is the application of nanotechnology to medicine and healthcare. The field takes advantage of the physical, chemical and biological properties of materials at the nanometer scale to be used for diagnosis, treatment and follow-up of diseases. Given the immense potential impact of nanomedicine on public wellbeing and on economic growth, the field is of considerable strategic importance for Europe.

The EuroNanoMed ERA-NET initiative comprises 24 partners from 18 countries/regions. EuroNanoMed aims at fostering the competitiveness of European nanomedicine players through the support of trans-national collaborative and multidisciplinary Research and Technology Development (RTD) projects with participants from academia, clinical/public health communities, and industry (particularly small and medium-sized enterprises).

Described below are multinational research projects of two Joint Calls which are now being funded by the partnering funding organizations.

1ST JOINT TRANSNATIONAL CALL 2009

Submitted projects	24
Partners	117
Country/Region	19
<hr/>	
Funded projects	8
Partners	40
Country/Region	14
<hr/>	
Success rate	33%
Budget (M€)	9.4

Dendrimers as nanovectors for targeted siRNA delivery in gene therapy (DENANORNA)

Project coordinator:

Ling Peng (FR)

ling.peng@univmed.fr

Project partners:

Carlo Catapano (CH)

Palma Rocchi (FR)

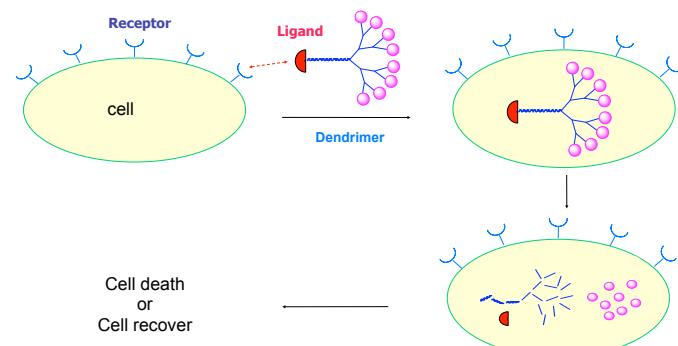
M^a Angeles Munoz-Fernandes (ES)

Sabrina Prich (IT)

Valentin Callejo Cena (ES)

Dendrimers are promising nanovectors for systemic delivery of therapeutic agents, like small interfering RNA (siRNA). In this project, we will develop, with the help of computer-modeling, biocompatible dendrimers decorated with ligands or antibodies for selective delivery of siRNA therapeutics to specific targeted cancer or HIV infected cells. The efficiency of siRNA-conjugated dendrimers will be investigated using cell cultures as well as animal models. The goal of this project is to validate the potential of dendrimer nanovectors for targeted delivery of siRNA by combining specific and complementary expertise in nanotechnology and biotechnology via transnational collaboration within Europe.

Dendrimer as nanovectors for targeted siRNA delivery in gene therapy



EU FP7 EuroNanoMed project DENANORNA

Nano-Functionalised Implants for the Regenerative Treatment of Spinal Cord and Nerve Lesions (Nano4Neuro)

Project coordinator:

Burkhard Schlosshauer (DE)

schlosshauer@nmi.de

Project partners:

Mikael Wiberg (SE)

Erhard Müller (DE)

Elias Fattal (FR)

Jorgen Kjems (DK)

Nano-medicine can potentially help with the daunting task of treating spinal cord injuries and peripheral nerve lesions. The proposed project will utilise nanostructured resorbable implant tubes, enabling us to bridge lesion gaps in nervous tissue. The implants will contain RNAi nanotherapeutics to prevent scar formation and enable axon path-finding and regeneration. Special focus will be placed on siRNA nanoparticle formation including novel cell targeting labels in conjunction with the macro-implant. The nanotherapeutics technology is a cross-sectional technology that could easily be applied to other medical indications.

LYMPHONANOCARRIERS FOR THE TREATMENT OF METASTATIC CANCER (LYMPHOTARG)

Project coordinator:

Maria José Alonso Fernández (ES)

mariaj.alonso@usc.es

Project partners:

Vincenzo Bronte (IT-V)

Rafael Lopez Lopez (ES)

Jean Pierre Benoit (FR)

Inhibiting cancer cell invasion and metastasis has become a top priority in cancer research. The lymphatic system is particularly important for the process of cancer cell dispersion. The LYPHOTARG project proposes to develop specifically targeted anticancer treatments, by associating anticancer drug to specific nanostructures composed of lipids and polymers, which have a specific affinity for the lymph nodes. In this way, we expect to prevent the process of metastatic spreading through lymphatic vessels. The final goal is to reach the preclinical evaluation stage with one of these novel nanocarrier systems.

Integrative nano-Composites And Regeneration of the Eye (I-CARE)

Project coordinator:

May Griffith (SE)

May.Griffith@liu.se

Project partners:

Lars Haag (SE)

Ramunas Valiokas (LT)

Gershon Golomb (IL)

Johannes Junger (DE)

Herpes Simplex Keratitis (HSK), caused by Herpes Simplex Virus-1, is the leading infectious cause of blindness in developed nations. Treatment is by transplantation but success rates are very low due to disease recurrence. I-CARE aims to improve transplantation rates. The first generation biosynthetic implant already developed by several members of I-CARE is the world's first corneal implant to stimulate the patient's own stem cells to regenerate corneal cells and nerves. The next generation implant will be strengthened to withstand the adverse conditions of the diseased eye and prevent HSK recurrence by incorporation of drug delivery systems.



I-CARE: Developing next-generation implants for high risk HSV cornea transplantation

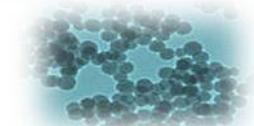


The Problem: HSV-1 infection

I-CARE Solutions in Development



Nano-architected and patterned scaffolds assembled into implants



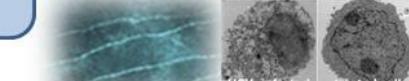
Nanoparticle delivery systems shown by electron microscopy



Anti-inflammatory nucleosides and anti-viral Peptides



Our Goal



Imaging of human corneas *in situ* and ultrastructural viral imaging

Project coordinator:

Paul Gatenholm (SE)

paul.gatenholm@chalmers.se

Project partners:

Jens Riesle (NL)

Gerjo, J.V.M Van Osch (NL)

Nicole Rotter (DE)

Ralph Müller (CH)

Anette Jork (DE)

Ear Tissue Regeneration Using Human Cells and Novel Nano-Cellulose Scaffolds (EAREG)

Auricular reconstruction remains one of the greatest challenges of reconstructive surgery. We propose using a novel nano-biomaterial, bacterial cellulose as a scaffold for ear tissue regeneration using a co-culture of human chondrocytes and stem cells. Our goal is to develop and evaluate the pre-clinical stages for auricle reconstruction therapy, and propose an entry-strategy for introducing this novel therapy to the clinic. The methods and results developed here will also be applicable for the regeneration of nose, trachea, spine and articular joint tissues.

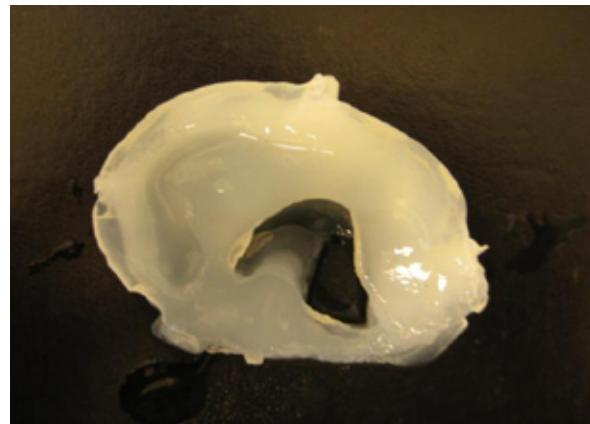
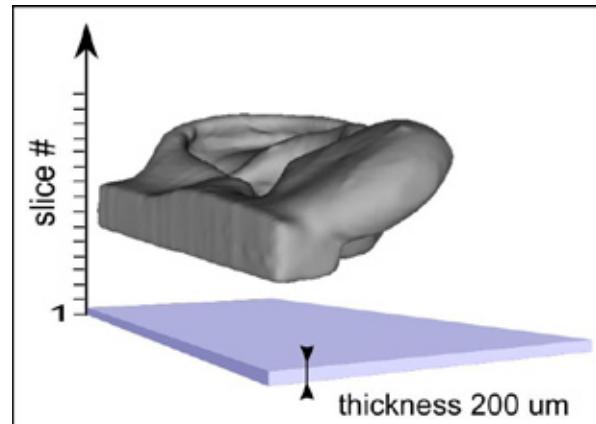


Photo Dynamic Therapy using targeted organic nano particles (TARGET-PDT)

Project coordinator:

Patrick Boisseau (FR)

patrick.boisseau@cea.fr

Project partners:

Muriel Barberi-Heyob (FR)

Bruno Fuchs (CH)

Volker Albrecht (DE)

Photodynamic therapy (PDT) is an emerging modality for the treatment of various cancers. PDT consists of a photoactive drug known as a photosensitizer, its preferential uptake and retention in malignant tissues, and its subsequent activation by a visible laser light, leading to tumor destruction. Despite its many advantages, the use of PDT has been restrained due to ineffective targeting of the photosensitizers to the tumor and potential damage to nearby healthy cells. Therefore, the project will study the delivery of photosensitizers encapsulated into lipid nano-particles that will include tumor-specific antibodies, thereby improving targeting and minimizing destruction of healthy tissue.

Project coordinator:

M^a Angeles Muñoz Fernandez (ES)

mmunoz.hgugm@salud.madrid.org

Project partners:

Jean-Pierre Majoral (FR)

Valentín Ceña (ES)

Fco. Javier de la Mata (ES)

Dietmar Appelhans (DE)

Maria Bryszewska (PL)

Peptides-associated dendrimers in dendritic cells for the development of new nano-HIV vaccines (DENPEPTHIV)

The aim of this project is to develop an effective HIV vaccine, an unattained goal so far. We will focus on dendritic cells (DCs), which are among the first HIV-1 targets due to their localization at mucosal surfaces, and their antigen-capturing proficiency. In order to target DCs for immunization, HIV-peptides would be associated with dendrimers (branched, spherical molecules, known to be versatile carriers). Our hypothesis is that the dendrimers' dendrites induce better uptake and processing of HIV antigens by DCs, leading to a better vaccine. Epitope and dendrimer optimization will also be essential for the development of an effective anti-HIV vaccine.

Project coordinator:

Simo Schwartz Jr (ES)

sschwartz@ir.vhebron.net

Project partners:

Patrick Boisseau (FR)

Rogério Gaspar (PT)

Lorea Mendoza Arteche (ES-B)

Targeting Combined Therapy to Cancer Stem Cells (NANOSTEM)

Cancer stem cells (CSCs) are responsible for initiating cancer, and are therefore highly sought for therapeutic target. Unfortunately, CSCs are a minority among tumour cells, and highly resistant to conventional treatments. Breast cancer CSCs express CD44, a unique membrane receptor, and can thus be specifically targeted. NANOSTEM will develop drug delivery systems that will specifically target CD44-expressing CSCs, enter the cells and release a chemotherapeutic drug, thus selectively killing the tumorigenic cell. The project will use model animals to evaluate the therapeutic potential and toxicity of each system.

2nd JOINT TRANSNATIONAL CALL 2010

Submitted projects	33
Partners	178
Country/Region	19
<hr/>	
Funded projects	8
Partners	46
Country/Region	10
<hr/>	
Success rate	24%
Budget (M€)	9

Delivering nanopharmaceuticals through Biological Barriers (BIBA)

Project coordinator:

Patrick Boisseau (FR)

patrick.boisseau@cea.fr

Project partners:

Caroline Maake (CH)

Pascal Van De Veire (DE)

Claus-Michael Lehr (DE)

Patrice Marche (FR)

Azucena Salas (ES)

Damian Garcia-Olmo (ES)

Inflammatory bowel disease is an increasingly prevalent condition in European countries, and is mostly treated by corticosteroids and immunosuppressants, which cannot be administered continually due to adverse events. Therefore local delivery of encapsulated corticosteroids and immunosuppressants will be investigated using two types of organic biodegradable nanocarriers to prevent side effects. The targeting strategy is based on passive targeting towards inflamed tissues. Three delivery forms will be tested in order to maximise accessibility to the gastrointestinal tract, and formulations and nanopharmaceuticals will be assayed both *in vitro* and *in vivo*.

Novel vaccines against Hepatitis C using nanotechnology (HCVAX)

Project coordinator:

Ken McCullough (CH)

Kenneth.Mccullough@ivi.admin.ch

Project partners:

Stanislas Pol (FR)

Carsten Laue (CH)

Albert Matthew (FR)

Thomas Joos (DE)

Carlos Alberto Guzman (DE)

Anti-viral treatments against hepatitis C virus (HCV) suffer from many disadvantages, and infections usually become chronic. While an efficient anti-HCV vaccine would help alleviate the problems of this disease, such a vaccine does not yet exist. This is the goal of the HCVAX consortium. The HCVAX vaccines are generated from innovative, biocompatible chitosan-based nanogels carrying RNA-replicon vaccines. The latter are modified swine fever virus genomes - incapable of infecting human cells as a biosafety measure – encoding HCV antigens, yet unable to generate infectious virus. For focussed vaccine delivery, the nanogel carrier is designed to target and introduce the RNA replicon cargo into dendritic cells, the pivotal cells for inducing efficient immune responses. Innovative adjuvants will also be screened for increasing the efficacy of these vaccines. Promising formulations will be identified through *in vitro* screening assays, and evaluated preclinically *in vivo*, to prioritize them for clinical development.

Project coordinator:

Verrier Bernard (FR)

b.verrier@ibcp.fr

Project partners:

Garcia Felipe (ES)

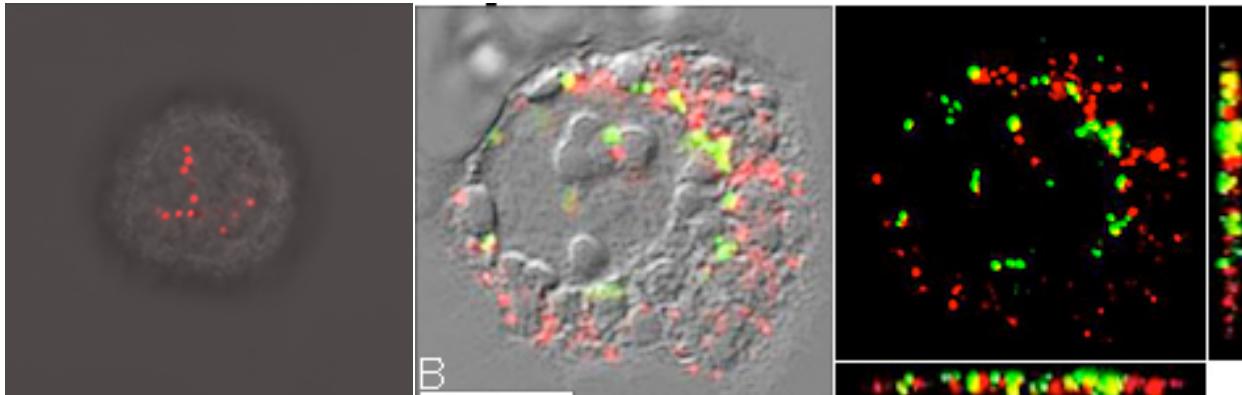
Harandi Ali (SE)

Huet Jacqueline (FR)

Le Grand Roger (FR)

Design of multifunctional nanoparticles targeting TLR or Nod receptors for dendritic cell immune therapy (iNanoDCs)

Currently, the most promising cell therapy candidates are dendritic cells (DCs), the immune sentinels of the body that orchestrate innate and adaptive immune system. Optimal education of DCs can be achieved by ex vivo loading of DCs with antigens - a laborious and expensive procedure. In order to avoid this step, the iNanoDCs project aims to develop multi-functional poly(lactic acid) nanoparticles that will assume control over intracellular DC processes and increase antigen presentation properties of DCs. This will be done by encapsulating within the nanoparticles molecules that affect the intracellular machinery and by decorating the particles with specific viral proteins.



Novel drug delivery routes mediated via nanotechnology targeting allergy vaccination (NANOASIT)

Project coordinator:

Hakan Engqvist (SE)

hakan.engqvist@angstrom.uu.se

Project partners:

Bernard Malissen (FR)

Reto Crameri (CH)

Karin Meyer Rosberg (SE)

Annika Scheynius (SE)

Conventional drug delivery techniques are characterized by sinusoidal, temporal peaks of blood drug concentration, which may lead to side effects or reduced drug efficiency. We propose to use state-of-the-art nanotechnology, including micro-nanoporation array patches (MNPs), to enable targeted and uniform drug delivery for the treatment of allergy. The project will include the design of precise pore systems with tunable pore wall interactions of the drug carrier, and will ensure that the tailored nanostructures interact favorably with the body on the macro scale.

Project coordinator:

Maya Simionescu (RO)

maya.simionescu@icbp.ro

Project partners:

Reiner Zeisig (DE)

Teodor Necsoiu (RO)

Erdal Cevher (TR)

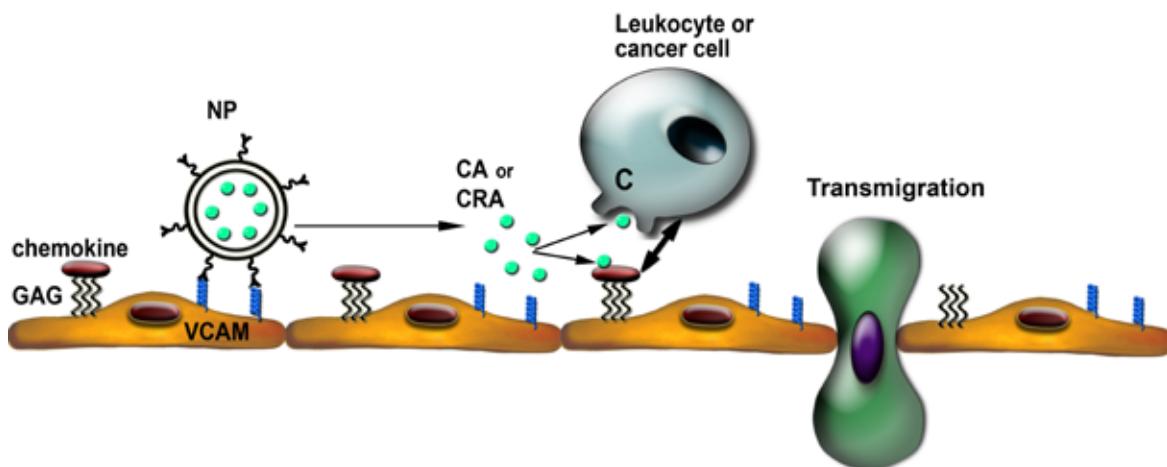
Gerd Bendas (DE)

Lubor Borsig (CH)

Marius Enachescu (RO)

Nanoparticles designed to target chemokine-related inflammatory processes in vascular diseases and cancer metastasis and implementation of a biosensor to diagnose these disorders (NANODIATER)

Inflammatory processes and endothelial expression of chemokines and cell adhesion molecules accompany atherosclerotic plaque formation and cancer cell metastasis. Therefore, therapeutic blockage and early diagnosis of inflammation may prevent these pathological events. NANODIATER proposes to design nanoparticles (NP) as "cell sensors" for tumorigenic or inflammatory cells and for targeted drug delivery to the inflammatory sites. The NP targeting exclusively activated endothelium will carry chemokine antagonists or chemokine receptor antagonists. Upon binding, the NP will release the antagonists, thus blocking downstream the inflammatory processes and preventing atheroma development or metastasis.



Project coordinator:

Christine Guenther (DE)

c.guenther@apceth.com

Project partners:

Hagen von Briesen (DE)

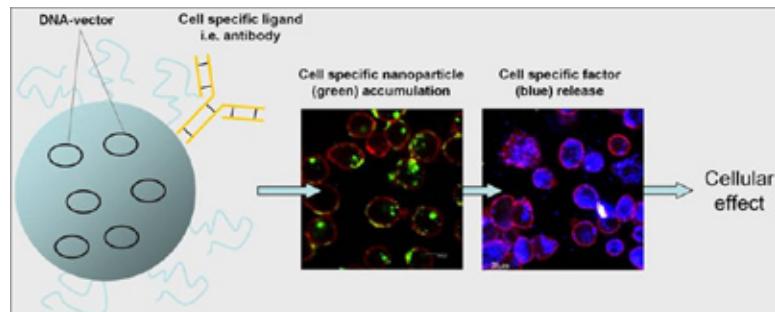
Paula Marques Alves (PT)

Felipe Prosper (ES)

Klaus Langer (DE)

Stem cell generation and manipulation by nanoparticle mediated gene transfer for the safe clinical application of gene-modified cells (NanoGene)

The NanoGene project aims to offer an alternative for the risky use of viral vectors in gene therapy. To this end, we will develop an innovative gene-transfer system based on nanoparticles for genetic modification of cells and their safe clinical application. The novel system will be used for cancer treatment by means of delivery of anti-tumor genes into mesenchymal stem cells, which possess an innate ability to migrate specifically to tumors. In addition, the novel gene transfer system will be used to generate induced pluripotent stem cells from somatic cells for future application in cell therapy.



Nanoconstructs for delivery of RNA splice-switching oligonucleotide therapeutics (NanoSplice)

Project coordinator:

Edvard Smith (SE)

edvard.smith@ki.se

Project partners:

Edward Darzynkiewicz (PL)

Roger Str (SE)

Andis Slaitas (LV)

Oligonucleotides are increasingly being researched for use in gene therapy, mainly to inactivate gene expression using the antisense or ribozyme approaches. However, this strategy suffers from limited efficacy due to inefficient uptake of the oligonucleotides by target cells. The large oligonucleotide doses that are needed induce side effects and render the treatment highly costly. Our project aims at developing nano-tools for increasing the efficacy of therapeutic nucleic acids by adding small address labels that direct them to cell nuclei, and also by changing their chemical nature, so that they more readily are taken up into cells.

Hybrid Nanostuctured Hydrogels: Bone regeneration using multifunctional injectable hydrogels (REBONE)

Project coordinator:

José Domingos Silva Santos (PT)

jdsantos@medmatinnovation.com

Project partners:

Sophie Rouif (FR)

Ana Colette Mauricio (PT)

Maria Ascensão Lopes (PT)

Javier Garcia Castro (ES)

Francisco Miguel Portela da Gama (PT)

Laurent David (FR)

The major objective of the ReBone project is the development of superior biomaterials and therapeutics for osteoregenerative medicine, in order to address the growing cumulative stress on the skeletal system due to the increase in life expectancy. We will develop injectable hydrogels incorporating self-assembled nanogels for the delivery of non-hydrophilic pharmaceuticals. The hybrid hydrogels will also provide stability to Bonelike graft granules and entrap mesenchymal stem cells. Such a system will result in a minimal invasive surgical procedure with decreased patient morbidity, lower risk of infection and reduced scar formation.

REBONE

