

# NEWSLETTER 3

## EuroNanoMed II

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EuroNanoMed 2 Joint Transnational Call for Proposals (2015): "European Innovative Research & Technological Development Projects in Nanomedicine"

Submission deadline: 03-March-2015 at 17:00 CET

Information: <http://www.euronanomed.net/>

## An Overview of 5 Transnational Joint calls

Five joint calls for proposals have been successfully launched under ERA-NET EuroNano Med I & II programs during **2009-2014**. The calls funded **40** transnational research projects in the field of nanomedicine bringing together **217** partners from **21** countries/regions. Approximately **€38** million was secured from the EuroNanoMed funding agencies and an additional **€28** million was funded by the research partners participating in the projects.

### Applicants country of origin

Altogether **914** partners from more than **21** countries in **192** project proposals were submitted to the 5 calls. As demonstrated in Figure 1, the number of applicants in each country has grown across the board over the five-year period. The data in Table 1 indicate a steady increase in the number of submitted proposals, from 24 in 2009 to 51 in 2014.

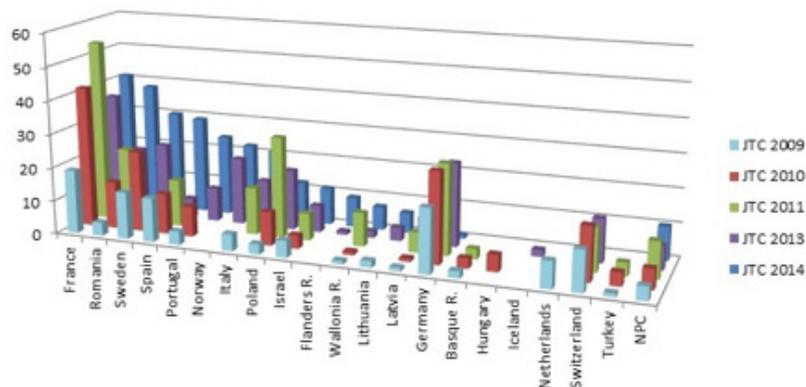


Figure 1: Number of applicants per country for the first five calls for proposals

Table 1: JTCs 2009-2014 – Select data

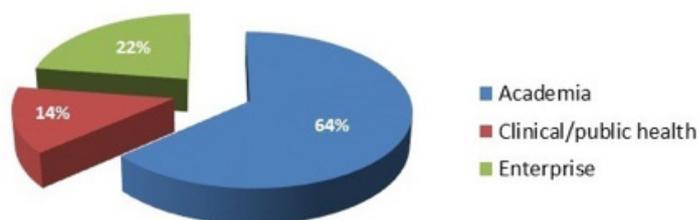
Item	JTC-2009	JTC-2010	JTC-2011	JTC-2013	JTC-2014	TOT.
Number of submitted proposals	24	33	41	43	51	192
Number of funded proposals	8	8	7	8	9	40
Total cost of funded projects (M€)	17	15,9	11,1	11,50	10,10	65,6
Total requested budget of funded projects	9,4	9	6,3	7	6	37,7
% of success rate	33%	24%	17%	19%	18%	
Number of partners in funded projects	40	46	37	42	52	217

## Participation of research organizations in translational projects in Nanomedicine

Each consortium was required to include teams from at least two of the following sectors: academia, industry, clinical research/public health organizations.

The distribution between the three sectors among funded consortia is illustrated in Figure 2 below. It is worth noting that **61%** of the funded projects included partners from all three sectors.

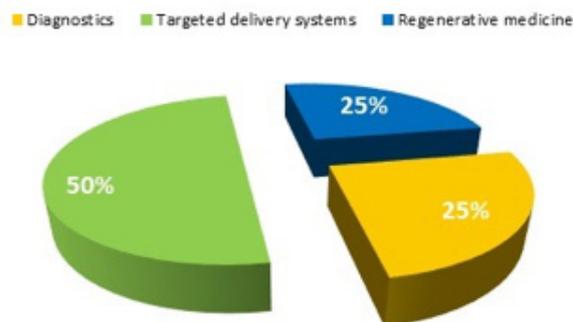
Figure 2: Type of research organizations funded through the five EuroNanoMed I & II joint calls for proposals



## Scientific / technological areas covered by funded projects

The first five calls were open to projects covering at least one of the three priority topics of the European Technology Platform on Nanomedicine: **targeted delivery systems, diagnostics, and regenerative medicine**. The distribution of these three areas of study among funded projects is presented in Figure 3.

Figure 3: Distribution of scientific areas covered by funded projects in the first five calls



## Fifth Joint Call - 2014 - Project Summaries

### ADT-COPD

Airspace Dimension Test for improved diagnosis of chronic obstructive pulmonary disease



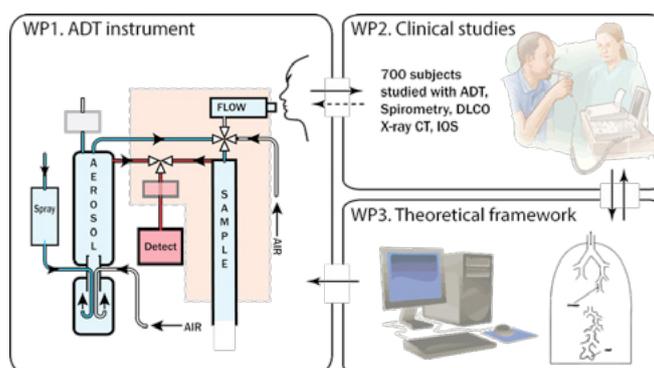
**Project coordinator:** Professor Per Wollmer, Department of Clinical Sciences, Lund University, Sweden, [per.wollmer@med.lu.se](mailto:per.wollmer@med.lu.se)

**Partner countries:**     
Sweden Israel Italy

COPD is one of the world's most common diseases. The disease entails chronic bronchitis and emphysema, affecting both the bronchi and lung tissue. In emphysema, the size of the air sacs in the periphery of the lungs increases, impairing the uptake of oxygen. The diagnosis of COPD is usually made after performing a simple spirometric breathing test. Spirometry, however, is not adequately sensitive for the detection of emphysema, which in many cases may be the first manifestation of COPD. The aim of ADT-COPD is to evaluate the Airspace Dimension Test (ADT), a novel technique for the diagnosis of emphysema. This test is based on the measurement of the retention of inhaled particles in the nanometer range. Nanoparticles are deposited in the lungs by diffusion and their retention is, therefore, sensitive to air sac size increases.

This project includes the further development of an instrument for ADT (work package 1; WP1), determination of the sensitivity and specificity of a diagnostic test for emphysema (WP2) and the development of theoretical modelling of the behaviour of nanoparticles in the human lung (WP3).

“The aim of ADT-COPD is to evaluate the Airspace Dimension Test (ADT), a novel technique for the diagnosis of emphysema”



## BRAINOMICS

### Nanoporous silicium for molecular fingerprinting in neurodegenerative disorders



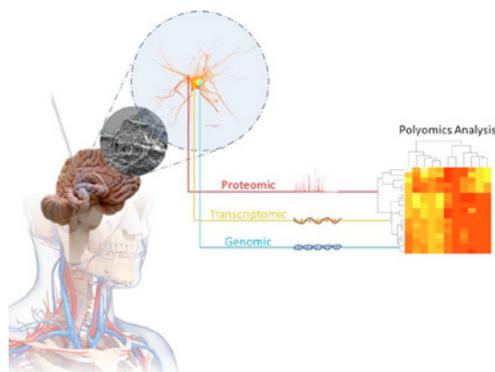
**Project coordinator:** Ali Bouamrani, CEA/LETI – CLIMATEC, France, [ali.bouamrani@cea.fr](mailto:ali.bouamrani@cea.fr)

**Partner countries:**



With the increase of life expectancy and the growth of aging populations in Western countries, neurodegenerative motor diseases will constitute a major public health challenge in the coming decades. Currently affecting some 7 million people worldwide, Parkinson's disease (PD) is principally characterized by the progressive and massive degeneration of dopaminergic neurons in substantia nigra pars compacta (SNc). To date PD is still incurable. Chemical and/or surgical symptomatic treatments are employed to alleviate the motoric symptoms (tremors, rigidity and akinesia), but do not address the disease itself. The underlying molecular events associated with PD's neuropathology remain poorly documented, since this requires accessibility to the pathological tissues. Deleterious consequences of tissue lesion in highly functional brain regions prohibit the performance of biopsies, thus restricting molecular analysis to post-mortem samples alone. Deep brain stimulation (DBS) remains the only nonlesional approach to explore various brain nuclei, and it uniquely offers temporary access to the pathological tissue in awake patients, at earlier stages of disease. Taking advantage of DBS surgery, Brainomics proposes to develop a dedicated device, based on nanoporous surfaces directly applied to the surgical instruments, to perform a nonlesional fingerprinting of brain tissue. The availability of fresh brain tissue for extensive genomic and proteomic studies will enable the deciphering of key molecular mechanisms and the identification of potential biomarkers of this complex neurodegenerative disease.

"Brainomics proposes to develop a dedicated device, based on nanoporous surfaces directly applied to the surgical instruments"



## DiamESTar

Targeted delivery of therapeutic siRNA to Ewing sarcoma junction oncogene by traceable diamond nanocrystal antibody fragment conjugate

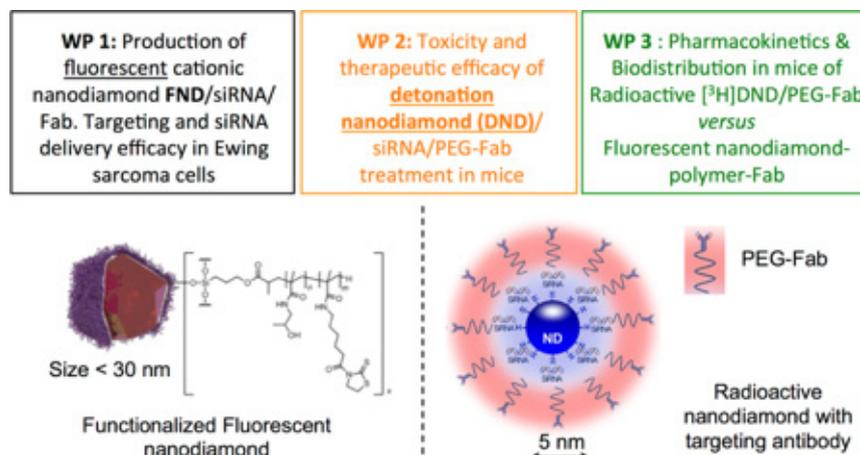


**Project coordinator:** François Treussart, CNRS / Université Paris Sud / Ecole Normale Supérieure de Cachan, Laboratoire Aimé Cotton, France, francois.treussart@ens-cachan.fr

**Partner countries:**     
France Czech Republic Spain

Ewing sarcoma (ES) is a rare, primarily pediatric bone cancer. When metastatic, the prognosis for the patient is not encouraging. We will evaluate the efficacy of a new small interfering RNA (siRNA) nanocarrier complex to treat ES metastatic tumors xenografted on mice. The siRNA inhibits the expression of the EWS-FLI1 fusion oncogene, which is considered the primary cause of Ewing sarcoma. The drug will be delivered by a fragment of antigen-binding (Fab) binding to a membrane protein overexpressed in ES cells. The nanocarrier will comprise a diamond nanocrystal core with a surface chemically modified to bind siRNA electrostatically and bear the Fab delivering the drug to the targeted cells. Nanodiamonds are compelling carriers in several respects: (i) they are chemically inert and non-toxic on cell cultures; (ii) they can be made intrinsically fluorescent or radioactive, hence traceable long-term; (iii) their surface can be modified to provide cationic or anionic charges or to covalently bind biomolecules. DiamESTar should provide the foundations for therapeutic solutions ready for preclinical development.

“DiamESTar should provide the foundations for therapeutic solutions to treat Ewing Sarcoma”



## GEMNS

Self-navigated integrin receptors seeking “thermally-smart” multifunctional few-layer graphene-encapsulated magnetic nanoparticles for molecular MRI-guided anticancer treatments in “real time” personalized nanomedicine

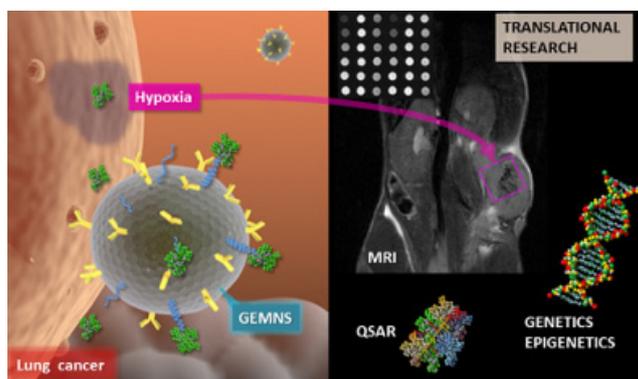


**Project coordinator:** Ireneusz P. Grudzinski, Department of Toxicology, Faculty of Pharmacy, Medical University of Warsaw, Poland, ireneusz.grudzinski@wum.edu.pl

**Partner countries:**   
Poland Norway Romania

The integration of multifunctional nanoparticles in the treatment of cancer shows great promise for the advance of personalized medicine. The GEMNS project is designed to develop novel, thermally “smart”, multifunctional, multi-layered graphene-encapsulated magnetic nanoparticles (GEMNS) for molecular MR imaging (mMRI) and anticancer treatments. The theranostic GEMNS will be bioengineered with self-assembled polymeric nano-gels and decorated with antibodies that recognize certain integrin receptors on lung cancer tissues and identify new cancer vessels. A chosen enzyme will be adsorbed onto the GEMNS and released in a controllable and fully predictable manner in order to promote anticancer activity, creating a “Trojan-horse” effect. The release of the enzyme triggers “on-off” hypoxia states at the molecular level in lung cancer cells and tissues. After several courses of such enzymatic-based molecular pre-sensing, mMRI-guided targeted X-ray radiotherapy will be applied to target lung cancer in preclinical animal models. A new nanosafety paradigm for the PRE-FIM strategy will also be developed using comprehensive QSAR, microfluidic, and genetic/epigenetic approaches to characterize the GEMNS theranostic contrast/drug candidates compliant with regulatory requirements.

“The theranostic GEMNS will be bioengineered with self-assembled polymeric nano-gels and decorated with antibodies that lung cancer tissue”



*A schematic presentation of GEMNS recognizing and releasing a thermostable enzyme into lung cancer cells (left), T2-weighted images of solid cancer in mice (right) and cancer cells (insert, right) using a 7T system (Grudzinski IP et al.). The nanosafety paradigm for the PRE-FIM strategy is listed (right).*



## naNOals

### Nanoparticle delivery system for neurodegenerative disorders

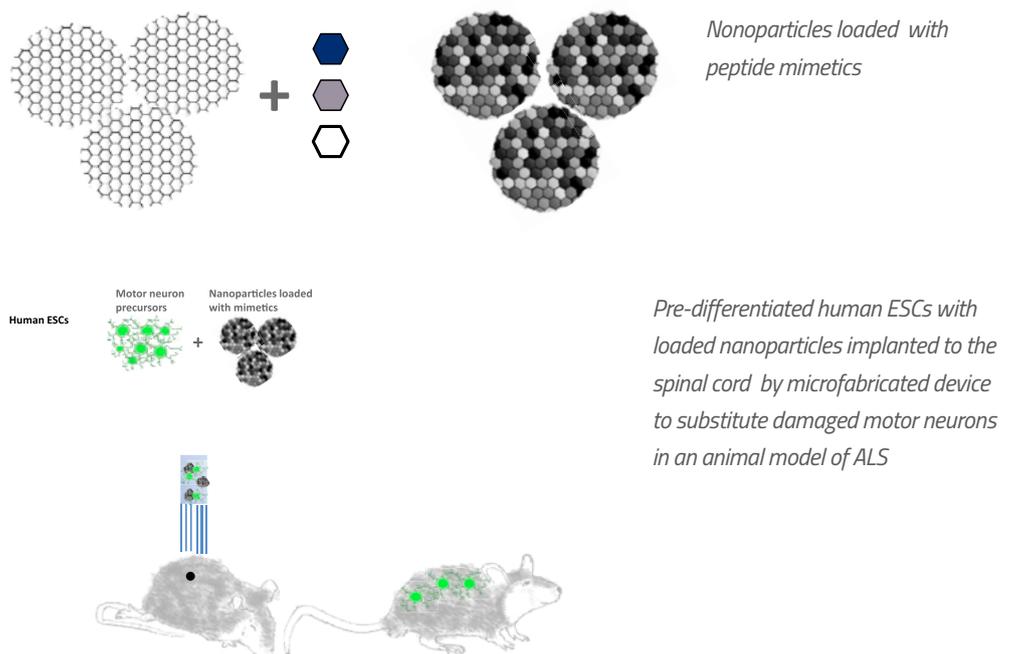
**Project coordinator:** Elena N Kozlova, Uppsala University, Sweden, [elena.kozlova@neuro.uu.se](mailto:elena.kozlova@neuro.uu.se)

**Partner countries:**



As a translational project, naNOals addresses the pressing need for improved treatment of ALS. The primary objective of the project is to develop a new therapeutic approach to treat early-stage ALS using nanoparticles loaded with mimetics to support motor neuron survival and antagonize the toxic effects of abnormal forms of the Cu/Zn superoxide dismutase 1 enzyme, which is implicated as a driving force in the progression of ALS. The generation of precursors of human motor neurons from human embryonic stem cells and their subsequent transplantation to the spinal cord, (where they are induced to differentiate to fully functional motor neurons and replace lost cells), will be tested for late stages of the disease. For transplantation, a special delivery device with multiple microfabricated needles will be used. We anticipate that the results of our studies can be translated to pre-clinical investigations preceding clinical trials. Utilizing nanomaterial-based research, this project provides a foundation for a combined therapeutic strategy, which independently tackles fundamental elements in the progression of ALS.

"This project provides a foundation for a combined therapeutic strategy, which independently tackles fundamental elements in the progression of ALS"



## NanoDiaBac

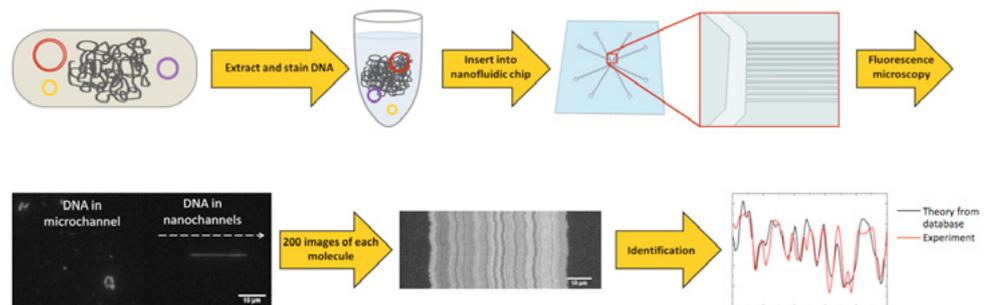
Nanofluidics for ultrafast diagnosis of bacterial infections

**Project coordinator:** Prof. Fredrik Westerlund, Chalmers University of Technology, Department of Biology and Biological Engineering, Sweden, [fredrik.westerlund@chalmers.se](mailto:fredrik.westerlund@chalmers.se)

**Partner countries:**     
Sweden Spain Portugal



The overall goal of the NanoDiaBac project is to develop new nanofluidic tools for the fast identification of bacterial infections and characterization of antibiotic resistance. The development of the toolbox is based on obtaining coarse-grained sequence information from individual DNA molecules extracted from bacteria. The molecules are stretched in nanofluidic channels and visualized with a fluorescence microscope. Traditional diagnostic techniques are based on bacteria cultivation, time-consuming process. The NanoDiaBac technique, in contrast, is based on examining a small number of single DNA molecules, a process which requires only an extremely small sample. It obviates time-consuming cultivation and reduces diagnostic time to hours rather than days. Fast diagnosis is beneficial to the patient by facilitating early and optimal treatment. It is also beneficial to society since it minimizes the spread of infectious bacteria and antibiotic resistance.



“The NanoDiaBac technique is based on examining a small number of single DNA molecules, a process which requires only an extremely small sample”

## Photobrain

AGuIX® theranostic nanoparticles for vascular-targeted interstitial photodynamic therapy of brain tumors

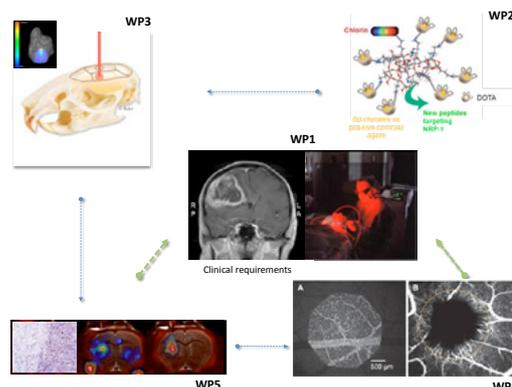


**Project coordinator:** Muriel Barberi-Heyob, Centre National de la Recherche Scientifique (CNRS), France, [muriel.barberi@univ-lorraine.fr](mailto:muriel.barberi@univ-lorraine.fr)

**Partner countries:**   
France Poland Sweden

Photodynamic therapy (PDT) for brain tumors appears to complement conventional treatments. Photobrain aims to functionalize nanoparticles called AGuIX®, consisting of a surface-localized tumor vasculature targeting neuropilin-1 peptide, encapsulated photosensitizer and magnetic resonance imaging (MRI) contrast agents, for the interstitial PDT (iPDT) of brain tumors guided by real-time imaging. In vivo experiments will be performed in rats bearing an orthotopic glioblastoma multiforme (GBM) tumor. MRI-guided implantation of the optical fiber will be performed prior to iPDT. This procedure will demonstrate the relevance of targeting the tumor neovasculature to enhance the selectivity and efficiency of iPDT for GBM. We will characterize the treatment-induced vascular effects by quantification of vessel architecture and density. The combination of non-invasive positron emission tomography with computed tomography and magnetic resonance spectroscopy will facilitate therapeutic monitoring. By performing short and long-term non-invasive imaging, characterization of the leukocyte infiltrate as well as molecular monitoring of angiogenic and inflammatory cytokines and vascular adhesion molecules, we will enhance insight into the mechanisms of the immune reactions. This understanding can facilitate the real-time control of inflammation. A combination of both explicit and implicit parameters, monitored during iPDT are potentially valuable tools in the treatment of brain tumors.

“Photobrain aims to functionalize nanoparticles called AGuIX for the interstitial PDT (iPDT) of brain tumors guided by real time imaging”



## POStURE

### PhOtocrosslinked hydrogels for guided periodontal TissUe Regeneration

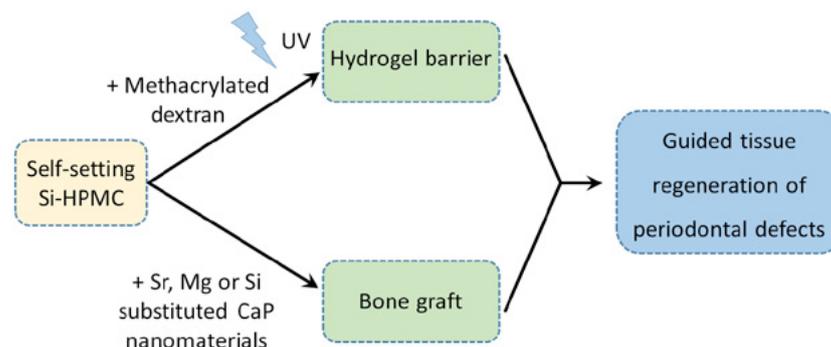


**Project coordinator:** Catherine Le Visage, Inserm U791, Center for OsteoArticular and Dental Tissue Engineering, University of Nantes, France, [catherine.levisage@inserm.fr](mailto:catherine.levisage@inserm.fr)

**Partner countries:**  France Portugal Latvia Italy

Periodontitis, a recognized disease worldwide, is a serious gum infection that damages soft tissue and results in loss of tooth-supporting alveolar bone. Regenerative periodontal procedures aim to reverse this damage by using both a bone graft and a membrane to obtain complete tissue reconstruction. The multidisciplinary POStURE project aims to develop an innovative periodontal regeneration device based on: (i) a self-setting injectable bone grafting material containing Sr, Mg or Si substituted CaP nanoparticles with enhanced bioactivity and (ii) a photo-cross-linked interpenetrating polymer network based on UV photosensitive methacrylated dextran that will be applied as a viscous solution and cured in situ with UV light, as a membrane to prevent excessive proliferation of gingival tissue.

“The multidisciplinary POStURE project aims to develop an innovative periodontal regeneration device”



## REGENERATE

### REGENERATE - REGENERATING the cornea



**Project coordinator:** Marie-Jose Tassignon, Laboratory of Ophthalmology, Centre for Cell Therapy and Regenerative Medicine, University of Antwerp, Belgium,

[Marie-jose.tassignon@uza.be](mailto:Marie-jose.tassignon@uza.be)

**Partner countries:**



The human cornea is transparent and relies on this property to enable vision. Damage to the stem cells that maintains the cornea surface results in Limbal Epithelial Stem Cells Deficiency (LSCD), causing conjunctival encroachment over the cornea with scarring, corneal neovascularisation and opacification, pain reduced visual acuity and photophobia. The surgical transplantation of large segments of donor-excised limbal tissue is effective, but carries a high risk of complications. Recent research has demonstrated the benefit and feasibility of small limbal grafts cultured on biological scaffolds. These, however, are optically deficient, difficult to standardise and engender health risks. Employing a multidisciplinary approach, the objective of REGENERATE is to develop a synthetic alternative with superior cell-interactive properties, which circumvent the problems encountered with current limbal stem cell delivery scaffolds. Our research strategy is to exploit the recent introduction of human recombinant collagen to develop transparent, mechanically stable and peptide-enhanced nano-implants, which mimic the corneal collagen alignment observed in normal, healthy corneas. We will bring the nano-corneal scaffold to the stage of proof-of-principle in animal models of limbal stem cell deficiency. The data acquired from this research will help us better understand the role that collagen nano-fibre alignment and surface nano-patterning plays in improving implant integration and survival.

“Our anticipated results include the development of new scaffolds for stem cell delivery, which could have a significant impact on healthcare, in particular ophthalmology”

Coming soon: a review seminar and a training workshop on Unique Ethical issues in Nanomedicine, December 3, 2014, Oslo, Norway.  
For details please visit our webpages:  
<http://www.euronanomed.net/>

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