NEWSLETTER 7
EuroNanoMed III

EuroNanoMed3

EuroNanoMed III Results of the Cofunded Call 2017

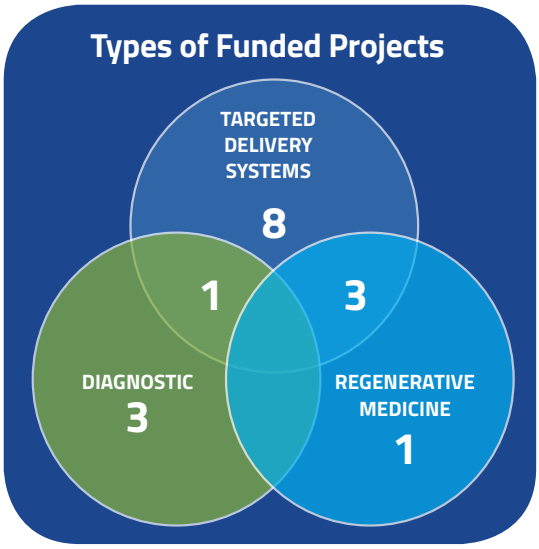
"European Innovative Research & Technological Development Projects in Nanomedicine"

16 successful consortia are funded with a total investment of about 14 million € for three years

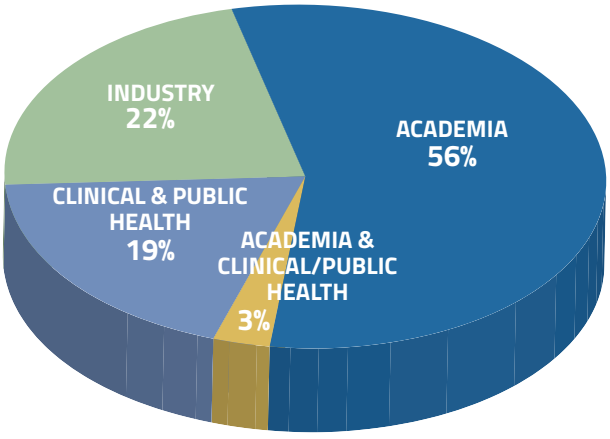
EuroNanoMed III is funded under the ERA-NET Cofund scheme of the Horizon 2020 Research and Innovation Framework Programme of the European Commission Research Directorate-General, Grant Agreement No. 723770

ENMIII Joint Transnational Call (JTC2017)

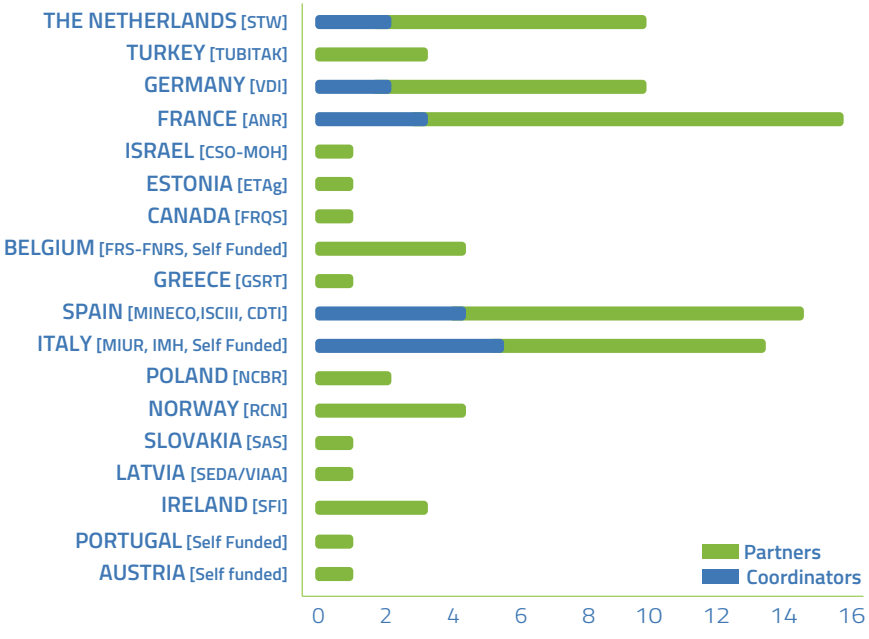
COFUNDED CALL ON TRANSNATIONAL RESEARCH PROJECTS ON NANOMEDICINE



82 Research Groups participate in 16 Funded Projects



Research Groups from Participating Countries



14 million€
Investment in total

Including 3,3 million€ from the European Commission

4NanoEARDRM

NANOFABRICATED NANOCOMPOSITE NANOBIOACTIVE AND NANOFUNCTIONAL REPLACEMENTS OF TYMPANIC MEMBRANE AS ADVANCED DRUG DELIVERY AND REGENERATIVE PLATFORMS

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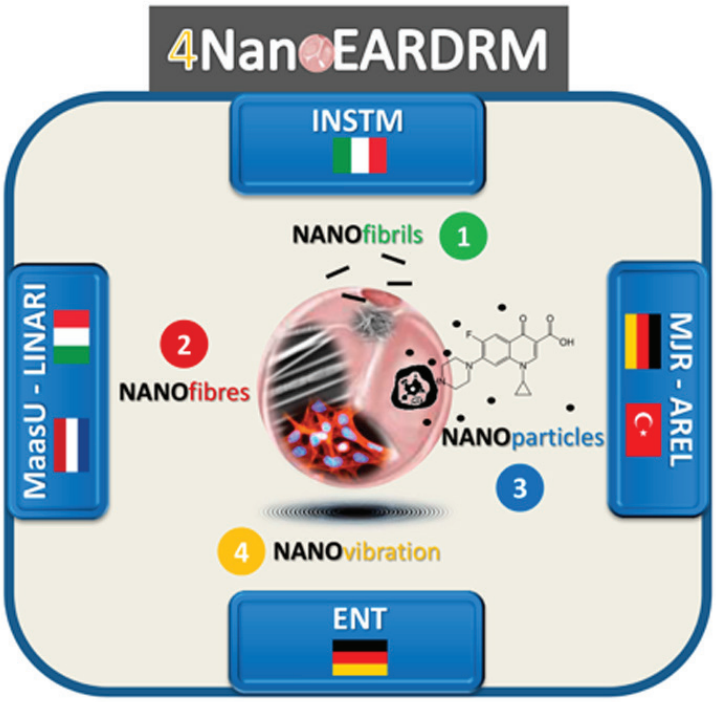
'4NanoEARDRM aims at filling an exposed gap in COM treatment by providing biomimetic, reliable and highly performant eardrum devices'

Tympanic membrane (or eardrum) is provided by nature with unique anatomic features that ultimately allow a superb physiologic performance in varying frequency ranges. Several pathologies damage this tissue, including chronic otitis media (COM), which ultimately bring to deafness. Current approaches used for eardrum repair or replacement show sub-optimal hearing outcomes. 4NanoEARDRM aims at filling an exposed gap in COM treatment by providing biomimetic, reliable and highly performant eardrum devices provided with targeted drug delivery and anti-inflammatory activity, finally enabling in situ tympanic membrane regeneration with optimal acoustics. The 4NanoEARDRM device is conceived to be "4 times" "nano", as it will have nanofibres supportive for cell repopulation, immunomodulatory nanofibrils, drug-delivery nanoparticles, and nanoscale vibration.

At the same time, it will be "for" "Nano", namely, for enabling exploitable nanotechnologies and nanomedicine products in otologic surgery.



AMI

ANTIDRUG-ANTIBODY AND DRUG MOLECULAR DETECTION IN INFLAMMATORY DISEASES WITH ORGANIC ELECTRONICS PLATFORM

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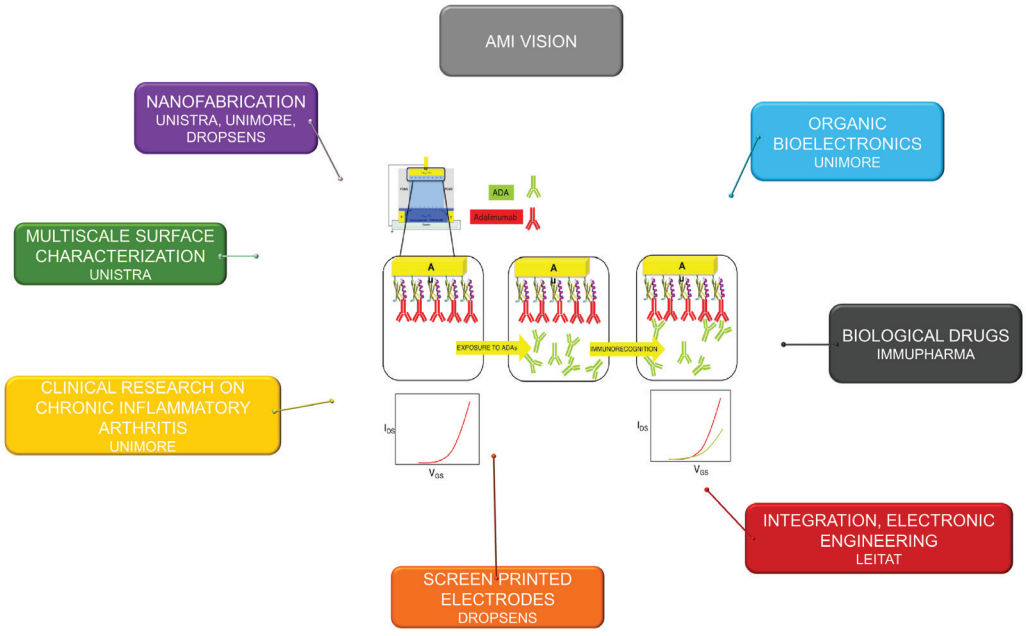
'The vision of AMI is a nanoscalea platform for the assessment of the immune reaction against biologicals targeted at inflammatory pathologies.'

For an increasingly large number of pathologies, state-of-the-art therapies rely on the use of biologicals. These drugs are very effective on some patients, whereas exhibit no effect on others due to the production of antidrug-antibodies (ADAs), hence rendering it critical to diagnose their immunogenic response, in view of a personalized therapy. The vision of AMI is a nanoscale platform for the assessment of the immune reaction against biologicals targeted at inflammatory pathologies. Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) will be used as prototype diseases. The technological platform envisioned is made of organic bioelectronic units, namely, arrays of label-free electrolyte gated organic field effect transistors with multiple functionalized gates. The driving and readout will be done through an in-home multiplexer, operated by a customizable, user-friendly interface. Prospected end-users are clinicians at a Point-of-Care for RA, and drug design companies developing peptides against SLE. Thus, engineering the device for non-specialists is an important objective beyond the mere proof-of-concept.



ARROW NANO

NEW APPROACHES TO RARE RESPIRATORY ORPHAN FIBROTIC DISEASES WITH LOCALLY ADMINISTERED TARGETED NANOPARTICLES

"we aim in this project to engineer novel, fully biocompatible, targeted nano-vectors made of lipids (liposomes) that would be safely and repeatedly administered by inhalation"

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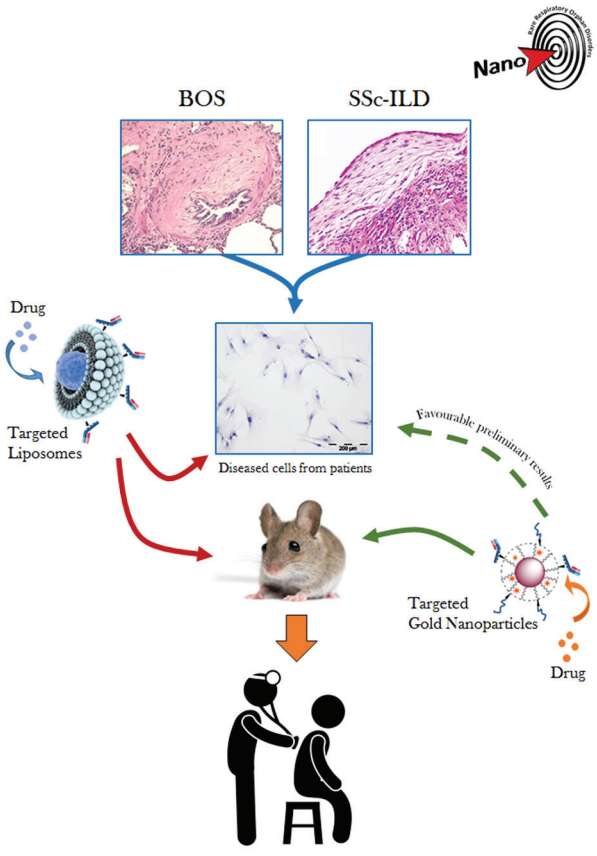
Conventional treatments for bronchiolitis obliterans syndrome (BOS) and systemic sclerosis associated interstitial lung disease (SSC-ILD) are poorly effective due to insufficient drug accumulation into the lung, limited efficacy and high toxicity. We have already demonstrated in vitro that drugs loaded into specifically targeted gold nanoparticles (GNP), coated with an antibody which recognizes diseased cells, were more effective in inhibiting their target cells in vitro and did not affect normal airway epithelial cells. The same GNPs administered to normal mice by inhalation, were selectively localized in the lungs with no toxicity to any other organs. When we tested GNPs on a mouse model of pulmonary fibrosis by local delivery, these nano-vectors were effective in preventing pulmonary fibrosis. However, long-term treatment may result in accumulation of GNPs in lung macrophages, suggesting that chronic administration may cause excessive storage of gold in the alveoli. Therefore, we aim in this project to engineer novel, fully biocompatible, targeted nano-vectors made of lipids (liposomes) that would be safely and repeatedly administered by inhalation.



EXIT

EXosomes Isolation Tool with Nanofluidic Concentration Device

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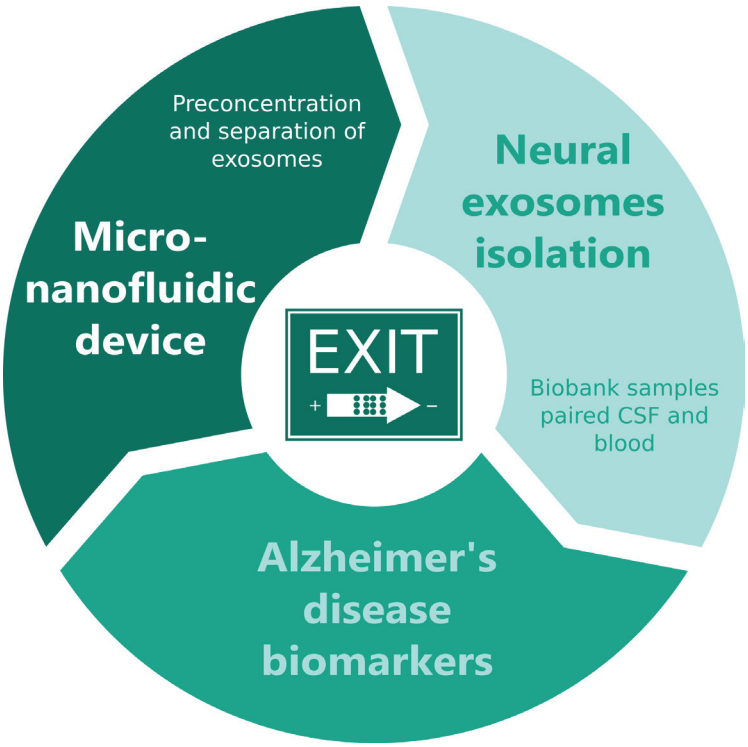
"EXIT aims to develop a state-of-the-art, nanotechnologically driven, analytical platform for the isolation of exosomes from bodily fluids, designed to investigate changes in Alzheimer's disease."

At present there is no effective therapy to Alzheimer's disease and the mechanism of the disease is not fully understood. Recently, exosomes – nanosize membrane vesicles that are present in all bodily fluids – have been shown to play an important role in the remote communication between cells and to be able to pass the blood-brain barrier. EXIT aims to develop a state-of-the-art, nanotechnologically driven, analytical platform for the isolation of exosomes from bodily fluids, designed to investigate metabolic, proteomic, immunologic and transcriptional changes in Alzheimer's disease. The basis of this platform is a novel electro-driven separation and concentration method. EXIT will integrate nanotechnology, transcriptomics, genetics and metabolomics with large existing EU biobanks, enabling the investigation of large sample cohorts of paired cerebrospinal fluid and blood. Within EXIT nanotechnologists, analytical chemists, biologists, geneticists, epidemiologists and clinicians will work together to make the long-awaited breakthrough in exosome isolation and rapidly translate this breakthrough into etiologic, preventive and therapeutic applications.



GLIOGEL

PREVENTION OF GLIOBLASTOMA RECURRENCE BY INJECTION IN THE RESECTION CAVITY OF A HYDROGEL FORMED BY TARGETED LIPID NANOCAPSULES LOADED WITH ANTICANCER DRUGS

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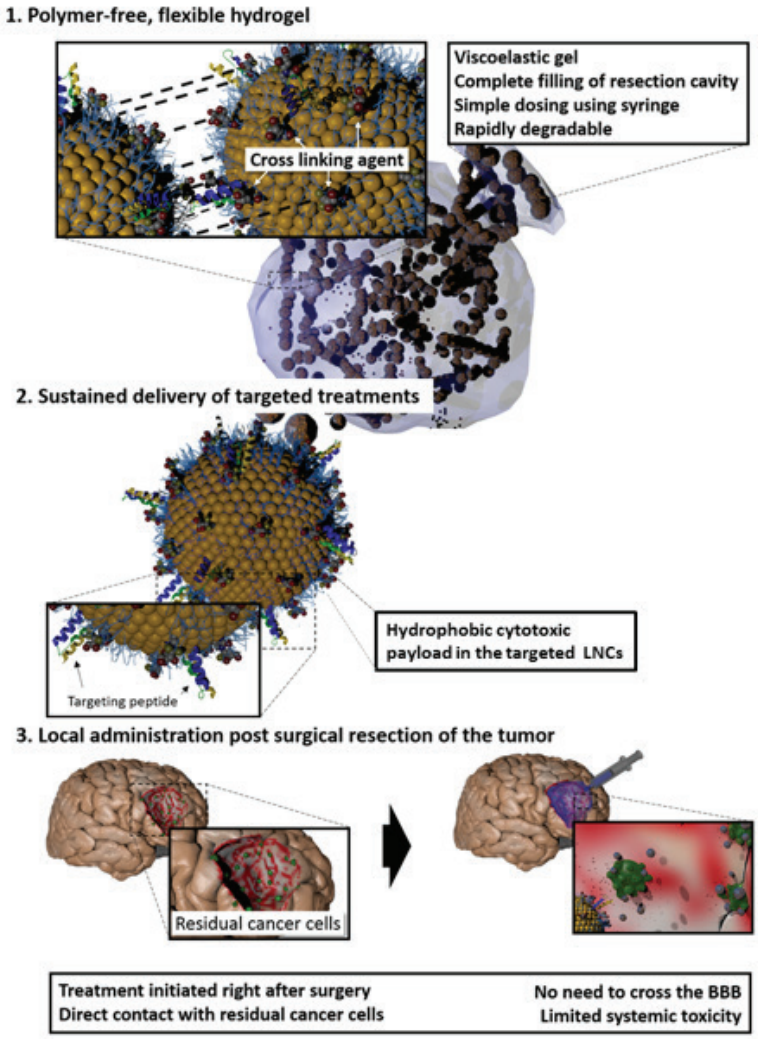
Nicolas Bertrand, CHU de Québec Research Center, Canada
Claire Lépinoux-Chambaud, GLIOCURE SAS IBS-CHU, France

'The objective of the GLIOGEL project is to develop an implantable polymer-free hydrogel, based on self-associated lipid nanocapsules, acting as a sustained-release matrix'

Glioblastoma is a malignant brain tumor with high morbidity and mortality. With the current standard of care (surgical resection combined with adjuvant radiotherapy and/or chemotherapy), the median survival is only 14 months due to recurrences from infiltrating glioblastoma cells at the border of resection. The objective of the GLIOGEL project is to develop an implantable polymer-free hydrogel, based on self-associated lipid nanocapsules, acting as a sustained-release matrix to deliver targeted therapeutic nanoparticles specifically to cancer cells. This technology, which will bridge the current therapeutic needs between surgical resection and initiation of systemic regimens, is expected to limit GBM recurrences by i) maintaining therapeutic concentrations of anticancer drugs at the resection border (without the necessity of crossing the blood-brain barrier) and ii) targeting GBM cells specifically using targeting peptides at the lipid nanocapsule surface.



INAT

INHALED NANOCARRIERS WITH ANTISENSE THERAPY FOR LUNG FIBROSIS

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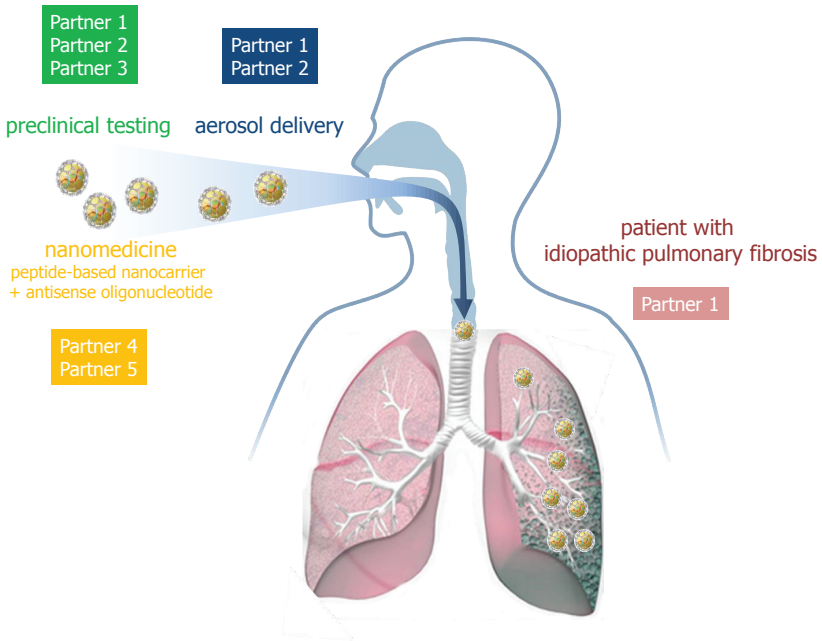
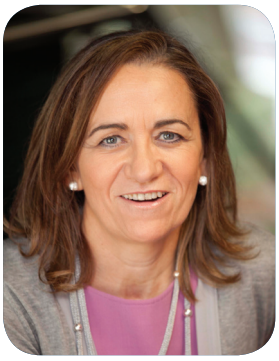
Gilles Divita, DIV'INCELL. , France
Jonas Renz, Secarna Parmaceuticals GmbH & Co. KG. , Germany

"The INAT project aims to develop a novel nanomedicine, to be delivered locally and non-invasively, through aerosols into the lungs, to improve its therapeutic index."

Idiopathic pulmonary fibrosis (IPF) is a rare, not curable, chronic lung disease. The INAT project aims to develop a novel nanomedicine, to be delivered locally and non-invasively via aerosols into the lungs to improve its therapeutic index (high efficacy, low side effects). This nanomedicine combines an innovative nanoparticle patented by Partner 5, which is biodegradable and highly effective and an oligonucleotide produced by Partner 4, to target a profibrosis mediator discovered by Partner 1. The nanomedicine will be formulated for inhalation in humans and its toxicity and efficacy tested pre-clinically by Partners 1-3.

The INAT consortium synergistically combines the efforts of 3 academic labs with complementary expertise in aerosolized medicine and 2 industry partners, whose platform technologies will be merged. This will allow us to develop a novel nanomedicine for inhalation in humans and to achieve its robust preclinical evaluation for the treatment of IPF.





INTRATARGET

NANO-IMMUNOTHERAPY: INTRACELLULAR TARGETING OF CANCER CELLS AND TAMS

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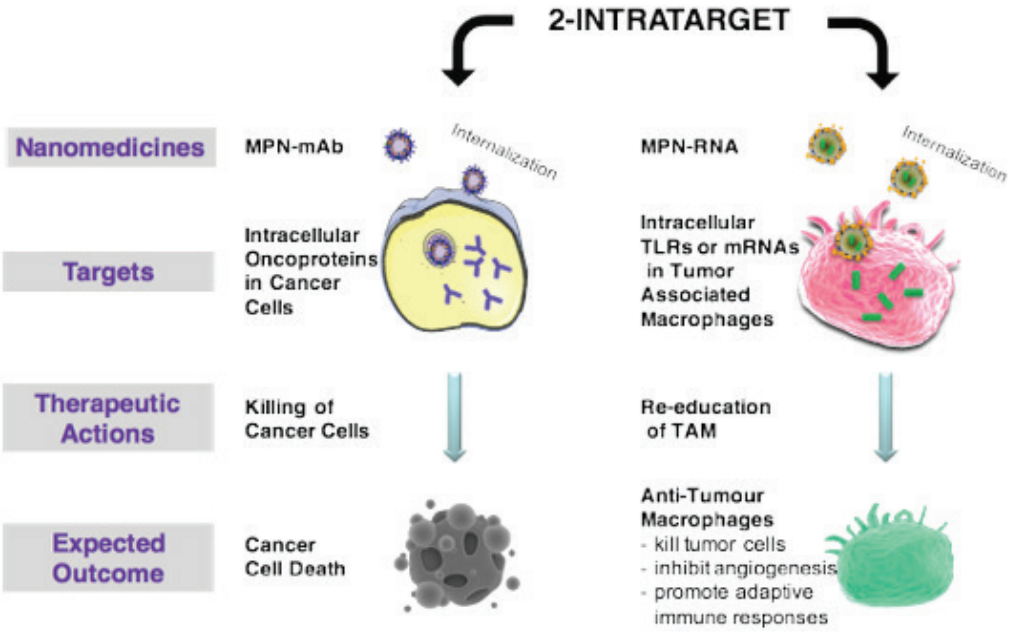
"The main goal of 2-INTRATARGET is to improve delivery mechanisms of the novel immunotherapies toward their targets inside cancer or immune cells."

Scientific research in the field of cancer immunology has led to the development of new potential cancer immunotherapies, such as monoclonal antibodies (mAb) or polynucleotides (RNA-based therapies), which are designed to act inside cancer cells, but also inside immune cells. Despite their huge potential, these therapies suffer of limited access to their target cells (cancer and immune cells) and tissue (primary tumor site and metastatic niches) , often resulting in poor efficacy/toxicity balance.

The main goal of 2-INTRATARGET is to improve delivery mechanisms of the novel immunotherapies toward their targets inside cancer or immune cells. In our consortium, 5 European Partners, with complementary expertise in the fields of Nanomedicine and Cancer Immunotherapy plan to engineer multifunctional nanocarriers aimed to deliver: 1) monoclonal antibodies (mAb) into cancer cells, thereby targeting intracellular oncoproteins, and 2) RNA molecules into the Tumor Associated Macrophages (TAM), in order to re-educate them and switch the tumor microenvironment to one that kills tumor cells.



MAGBBRIS

NEW MAGNETIC BIOMATERIALS FOR BRAIN REPAIR AND IMAGING AFTER STROKE

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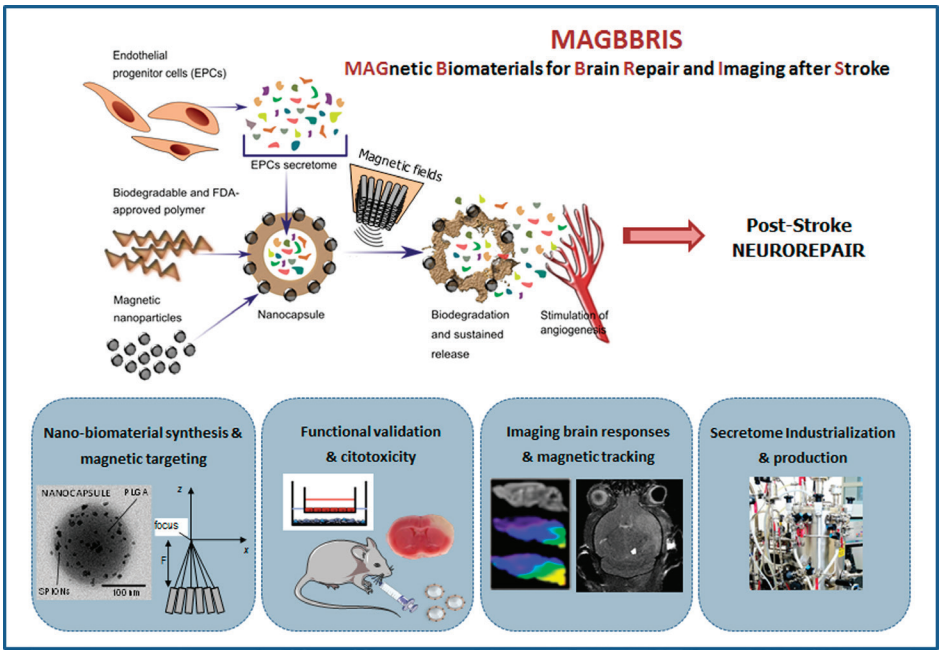
Fabien Gosselet, University of Artois, France
Maria Picchio, Ospedale San Raffaele IRCCS, Italy
Filip Jelen, Pure Biologics Ltd., Poland
Peter Kopcansky, Institute of experimental physics, SAS, Slovakia

"By engineering novel magnetic nano-biomaterials, we will achieve tissue repair in the event of an ischemic attack."

According to the World Health Organization data, 15 million people worldwide experience a stroke each year. Neuro-repair treatments offer the opportunity to treat stroke patients by extending the therapeutic time window. By engineering novel magnetic nano-biomaterials, we will achieve tissue repair in the event of an ischemic attack. We will take advantage of nanotechnology to deliver therapeutic growth factors secreted by progenitor cells into the injured brain. MAGBBRIS will demonstrate that growth factors secreted by endothelial progenitor cells, having proven potential to induce tissue repair, can be encapsulated in magnetic biomaterials and successfully and safely transplanted into mice brains, with the guidance of magnetic fields, to induce tissue repair.

MAGBBRIS consortium is made up of a highly multidisciplinary, materials-science, biomedical and clinical research and industrial partnership. The project will provide a new medicinal product, ready to be tested in a preclinical multicenter study.



MAGneTISe

MAGNETIC PARTICLE IMAGING FOR THE TREATMENT AND IMAGING OF STROKE

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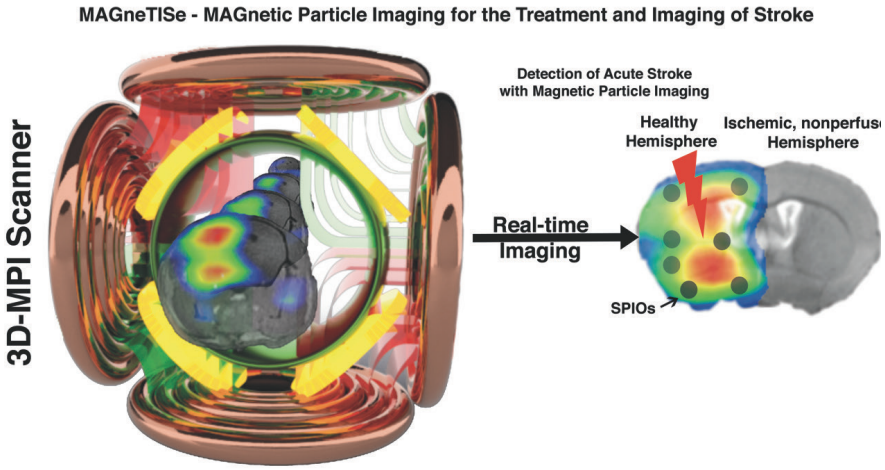
Mauro Magnani, University of Urbino, Italy
Emine Ulku Saritas, Bilkent University, Turkey
Yan Yan, University College Dublin, Ireland

"MAGneTISe aims to develop a new, two-pronged approach by combining the therapy and monitoring of stroke patients with Magnetic Particle Imaging."

Despite 20 years of experience with thrombolysis of cerebral blood clots with tissue-type plasminogen activator (rt-PA), fifty percent of patients remain disabled for life. A narrow therapeutic time window, insufficient thrombolysis rates, serious side effects, and time-consuming imaging techniques decrease the efficacy of stroke treatment. MAGneTISe aims to develop a new, two-pronged approach by combining the therapy and monitoring of stroke patients with Magnetic Particle Imaging (MPI).

This new imaging technique enables rapid assessment of cerebral perfusion (real-time-MPI), as well as the steering of superparamagnetic iron oxide nanoparticles (SPIO) by magnetic fields (force-MPI). We will develop strategies for continuous bedside cerebral perfusion monitoring, using red blood cells (RBC) as a biomimetic tracer-delivery system for the SPIOs, which otherwise would have been quickly eliminated. This method will enable rapid diagnosis of stroke or bleeding and facilitate faster treatment and better patient outcomes. Using the magnetic fields of the MPI system, we will trap the coupled nanoparticles in the occluded vessel, which will locally increase the amount of active enzyme, resulting in an increased rate of successful revascularization while decreasing systemic side effects.



NanoGSkin

TRANSVERSAL TISSUE ENGINEERING AND NANOMEDICINE APPROACH TOWARDS AN IMPROVED CHRONIC WOUND THERAPY

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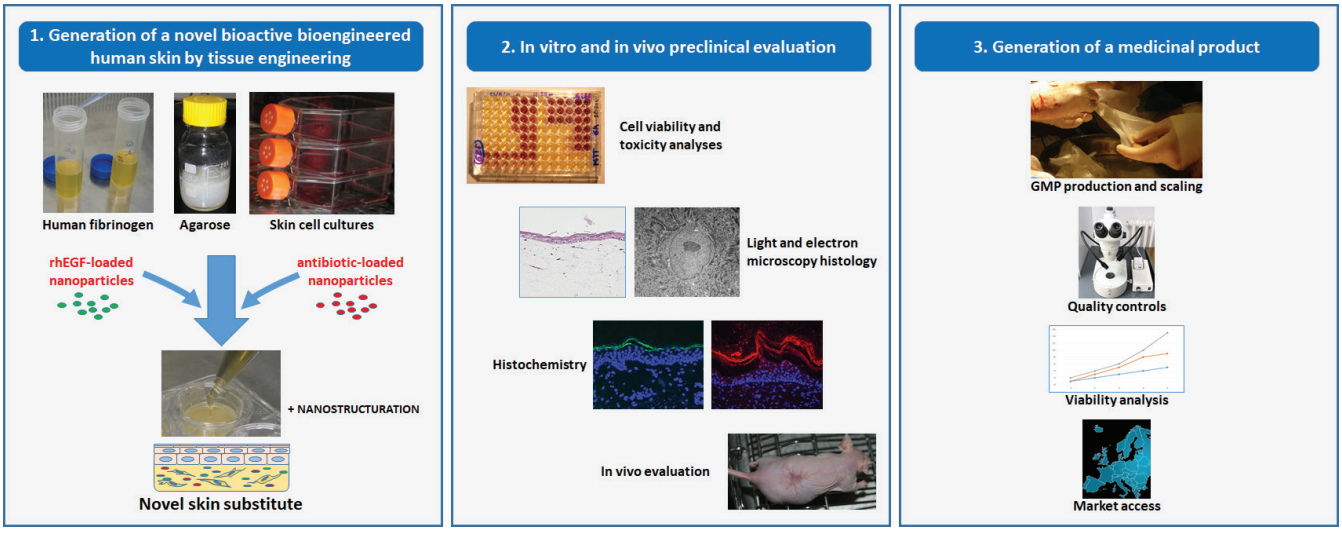
Abhay Pandit, National University of Ireland (NUIG), Ireland

"NanoGrowSkin is a novel therapeutic tool for patients with chronic wounds aimed towards the generation of bioactive human artificial skin substitutes."

Severe chronic wounds are a therapeutic challenge in medicine, and curative treatment is not available in most cases. NanoGrowSkin is a novel therapeutic tool for patients with chronic wounds aimed towards the generation of bioactive human artificial skin substitutes. This tool will overcome the side-effects associated with currently available therapeutic approaches. We propose a multidisciplinary healthcare approach, combining tissue engineering methods with growth factors and antibiotic-loaded nanoparticles (NPs), concluded in the fabrication of a novel, advanced medicinal product for efficient treatment of chronic wounds. We expect this novel product will have increased growth and development properties and antibacterial activity resulting in a more efficient clinical result.



NANOpheles

DEVELOPMENT OF NANOVECTORS FOR THE TARGETED DELIVERY IN ANOPHELES MOSQUITOES OF AGENTS BLOCKING TRANSMISSION OF PLASMODIUM PARASITES

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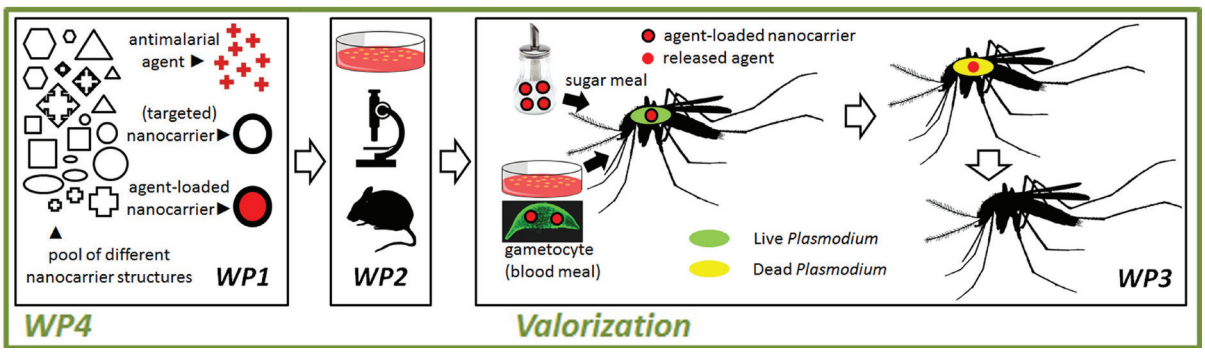
Krijn Paaijmans, Barcelona Institute for Global Health (ISGlobal), Spain
Inga Siden-Kiamos, Foundation for Research and Technology– Hellas (FORTH), Greece
Fatima Nogueira, Universidade Nova de Lisboa, Portugal

"The objective of NANOpheles is to design polymeric nanovectors for the delivery of antimalarial agents to Plasmodium stages in the mosquito.'

The unmet medical and patient need of malaria eradication will not be achieved unless the targeted delivery of new drugs is vastly improved. The objective of NANOpheles is to design polymeric nanovectors for the delivery of antimalarial agents to Plasmodium stages in the mosquito, and to characterise the efficacy of nanovectors and antimalarial agents to reduce mosquito infectiousness. This objective will be achieved through (i) synthesis of nanocarriers capable of encapsulating antimalarials and preventing their degradation in storage conditions, (ii) engineering targeted nanovectors capable of delivering their antimalarial contents to Plasmodium stages in the Anopheles mosquito, and (iii) evaluating the effect of selected nanovectors (loaded with antimalarial agents) on the mosquito stages of Plasmodium and their transmission capacity in a murine model of malaria. NANOpheles unites leading laboratories with expertise in nanoparticle synthesis, targeted drug delivery to Plasmodium-infected cells, molecular and cell biology of malaria, mouse models and mosquito vectors of malaria and clinical aspects of malaria.

NANOpheles



NANO-SCORES

NANOSTRUCTURED OSTEOCHONDRAL SCAFFOLD: NOVEL BIOMIMETIC TRIGGERS FOR ENHANCED BONE REGENERATION

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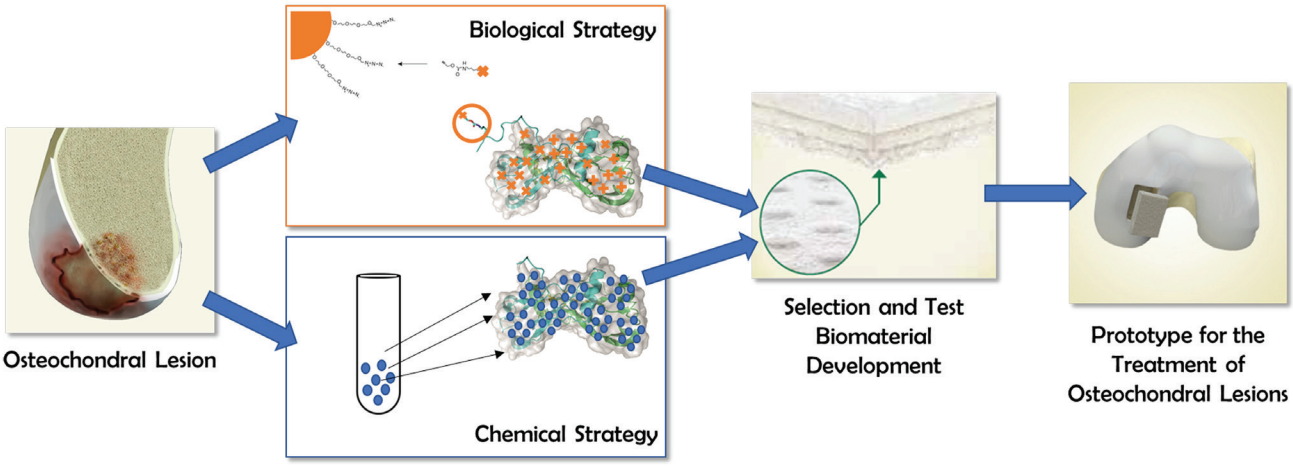
Locs Janis - Riga Technical University, Latvia
Brama Pieter - University College Dublin, Ireland
Harmand Marie Francois - Laboratoire d'Evaluation des Matériels Implantables, France
Figallo Elisa - Fin-ceramica Faenza S.p.A., Italy

" This project aims to revolutionize osteochondral regeneration by developing new nano-strategies to trigger and sustain subchondral bone regeneration.'

Degeneration of the articular osteochondral tissues causes pain and decreased function leading to osteoarthritis (OA), one of the most globally widespread diseases with a huge impact on society. OA development and progression could be prevented by regenerating the osteochondral unit. Until now, the regeneration of the subchondral bone remains a critical aspect, dooming most patients to prosthetic implants. This project aims to revolutionize osteochondral regeneration by developing new nano-strategies to trigger and sustain subchondral bone regeneration. The first strategy will chemically improve the bone layer of an osteochondral scaffold through nanostructured "ion banks". The second strategy will biologically improve the new nanostructured material through bioactive and bioconjugated peptides for osteoprogenitor cells homing and stimulating bone formation.

The most promising strategy will be evaluated with a translational approach up to a model closely resembling the human application, developing a successful regenerative prototype for the treatment of osteochondral lesions and the prevention of OA.



NSC4DIPG

NANOSONOCHEMOTHERAPY FOR DIFFUSE INTRINSIC PONTINE GLIOMA

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Dannis van Vuurden, VU University Medical Center, The Netherlands
Chrit Moonen, University Medical Center Utrecht, The Netherlands
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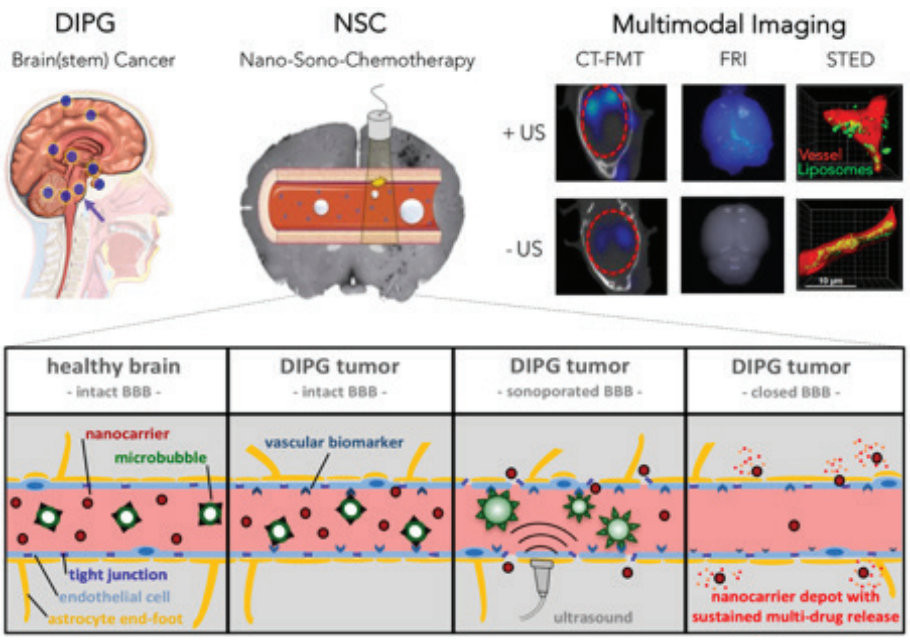
"In the NSC4DIPG project, we will employ ultrasound and microbubbles to create a temporally and spatially controlled sonoporation-window, during which drug delivery systems loaded with optimized combinations of two different drugs can be shuttled across the BBB."

Diffuse Intrinsic Pontine Gliomas (DIPG) are highly aggressive brain tumors which affect hundreds of children in Europe every year. No curative treatments are available for DIPG. Anticancer agents fail because the blood-brain barrier (BBB) prevents drugs and drug delivery systems from reaching the pathological site. In the NSC4DIPG project, we will employ ultrasound and microbubbles to create a temporally and spatially controlled sonoporation-window, during which drug delivery systems loaded with optimized combinations of two different drugs can be shuttled across the BBB. Multiple clinically relevant nanocarrier materials will be used, including 10 nm linear polymers, 50 nm micelles, 100 nm liposomes and 150 nm PACA nanoparticles. Engineered protein capsules with a size of 30-40 nm and an intrinsic ability to cross the BBB will also be employed. These efforts will contribute to the development of novel (nano-) drugs and treatment protocols for (pediatric) patients suffering from brain cancer.



RESOLVE

SUPPRESSION OF IMMUNOPATHOLOGY BY NANOPARTICLE DELIVERY OF MRNA TO MONOCYTES

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Vincenzo Bronte, University of Verona, Italy
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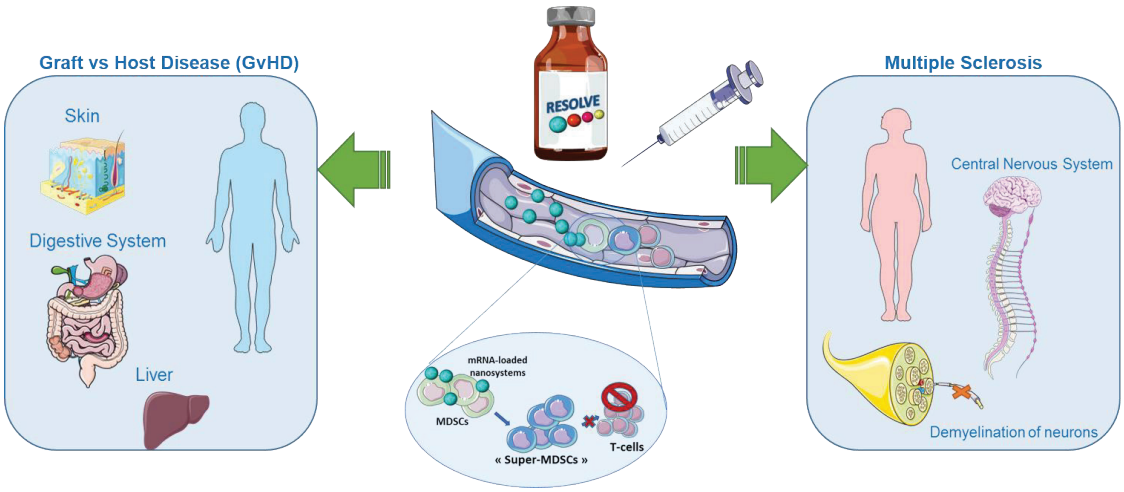
Ugur Sahin, BioNTech RNA Pharmaceuticals, Germany

"The RESOLVE project aims to develop novel therapeutic approaches based on the engineering of nanomedicine, to limit the immune reactivity against host self-antigens in the course of bone marrow transplantation and autoimmune diseases'

The RESOLVE project aims to develop novel therapeutic approaches based on the engineering of nanomedicine, to limit the immune reactivity against host self-antigens in the course of bone marrow transplantation (graft versus host disease, GvHD) and autoimmune diseases (multiple sclerosis, MS).

Currently, therapy for these pathologies is based on either systemic or local immunosuppression, which eliminate or suppress polyclonal, autoreactive T-cell specificities while compromising the entire systemic immunity to various side effects, sometimes life threatening.

The most promising up and coming strategies are represented by either restoration or de novo induction of cells capable of inducing tolerance, such as the monocytic myeloid-derived suppressor cells (MO-MDSCs). Their immunosuppressive activity, and, consequently, their tolerogenic ability, can be enhanced by increasing the cellular level of a protein involved in apoptosis regulation, CFLAR. Over the course of the present project, new nanosystems will be designed to specifically target in vivo the MO-MDSCs, and efficiently deliver mRNAs to produce CFLAR.



SPEEDY

SURFACE-ENHANCED RAMAN SCATTERING WITH NANOPHOTONIC AND BIOMEDICAL AMPLIFYING SYSTEMS FOR AN EARLY DIAGNOSIS OF ALZHEIMER'S DISEASE PATHOLOGY

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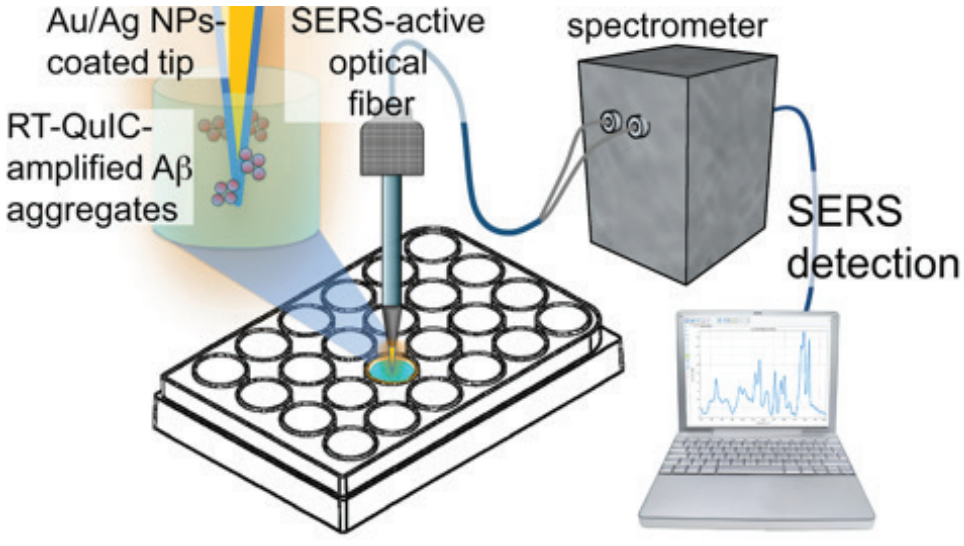
"The aim of this project is to set-up a nanotechnology-inspired method for early detection of misfolded Aβ in peripheral tissues of Alzheimer's patients."

A definitive diagnosis of Alzheimer's disease (AD) can be made only through autopsy after death, due to the fact that beta-amyloid (Aß) aggregates, a main AD biomarker, can be detected only in the central nervous system. However, recent evidence indicates that trace-amount of misfolded Aβcan migrate into peripheral tissues of AD patients. The aim of this project is to set-up a nanotechnology-inspired method for early detection of misfolded Aß in peripheral tissues of Alzheimer's patients versus controls, which meets the needs of reliability, ultrasensitivity, effectiveness and low cost. This will be obtained by a Surface-Enhanced Raman Spectroscopy (SERS) system combined with a misfolded protein amplification assay, known as Real-Time Quaking-Induced Conversion (RT-QuIC) assay, which will enable detection of Aβtraces in cerebrospinal fluid and olfactory mucosa samples. A nanoparticle-decorated optical fiber, generating huge electromagnetic fields concentrated at the plasmonic nanostructures covering the fiber tip, will be developed and tested for rapid, simple and reproducible multisampling analysis.



TEMPEAT

TEMPERATURE-RESPONSIVE POLYPEPTIDE NANOCARRIERS FOR ABDOMINAL THERAPIES

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" The particles are injected in the peritoneum and then irradiated with light, which leads to creation of oxygen radicals that kill selectively the cancer cells.'

In 75% of women, the first diagnosis of ovarian cancer is made at an advanced stage with the tumor already metastasized to the peritoneum. Once metastasized, response to chemotherapy is poor and therefore, fatal. There is an urgent need to develop more effective therapies for this type of cancer.

In the TEMPEAT project we aim to develop protein-based nanoparticles that carry anticancer drugs and light-sensitive molecules. They are furthermore decorated with homing devices (nanobodies) that can recognize the specific tumor cells. The particles are injected in the peritoneum and then irradiated with light, which leads to creation of oxygen radicals that kill selectively the cancer cells. Upon washing the peritoneum with a slightly cooled solution, the particles open up and release the anticancer drugs, killing the remaining cancer cells.