NEWSLETTER11

EuroNanoMed III JANUARY 2022

EuroNanoMed3

Results of the Joint Transnational call 2021

"European Innovative Research & Technological Development Projects in Nanomedicine"

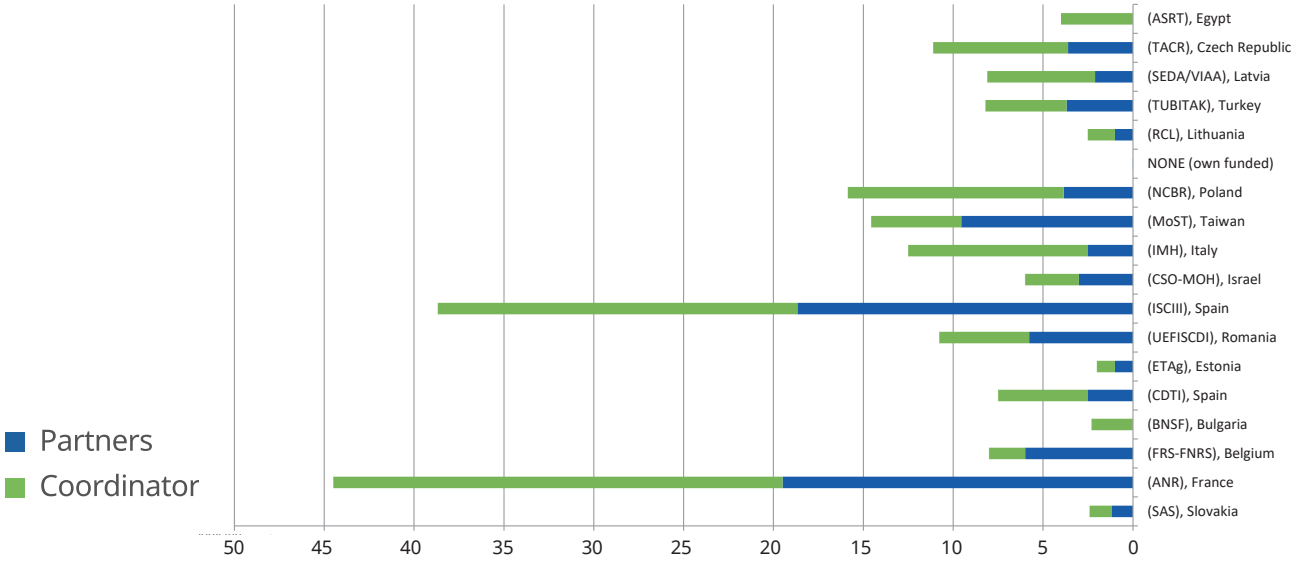
10 successful consortia are funded with a total investment of over 8.4 million € for three years

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

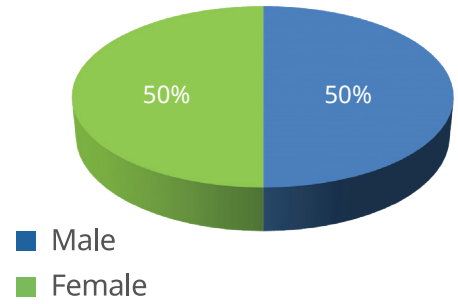
According to the new EU General Data Protection Regulation (GDPR) the ENMIII webpage informs on respective policies

euronanomed.net

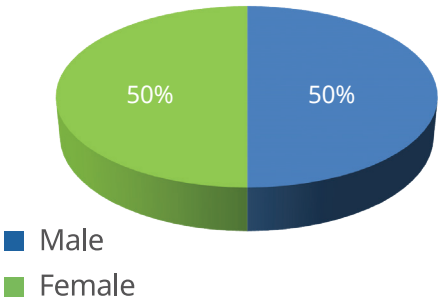
1 52 Research Groups From 14 Partner Countries.



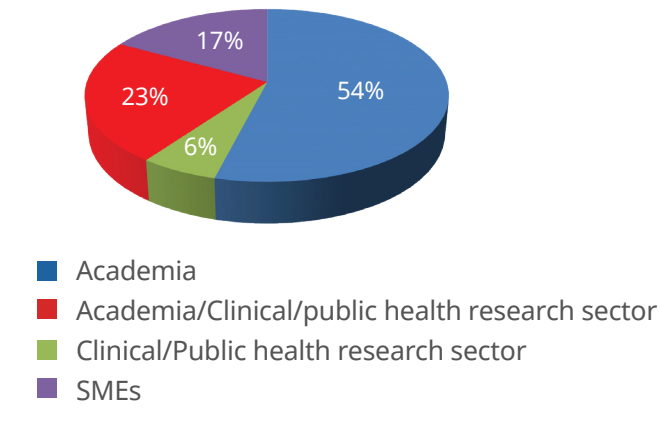
2 26 female partners (out of 52)



3 5 Female coordinators (out of 10)



4 Affiliation



Zvi Hayouka

antineuropatho

Antineuropatho novel nanopharmaceutics against bacterial infections at center nervous system

Coordinator:

Zvi Hayouka, The Hebrew University of Jerusalem, Israel

Contact:

Zvi.hayouka@mail.huji.ac.il

Partners:

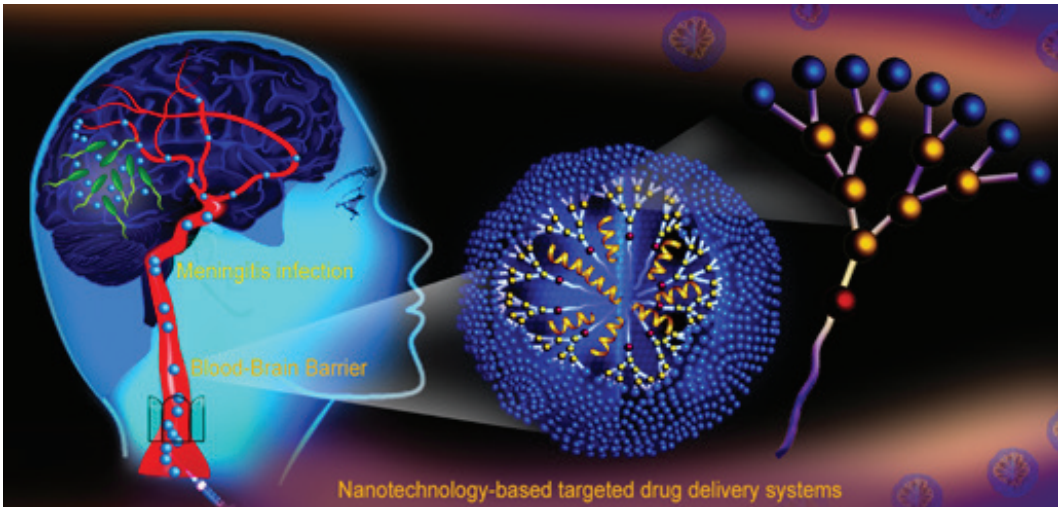
Ling Peng, Centre Nationale de Recherche Scientifique (CNRS), France

Łęczycka-Wilk Katarzyna, NanoSanguis S.A. Poland

Mangesh Bhide, Slovak Academy of Sciences (SAS), Slovakia

Cristin Coman, "Cantacuzino" National Medico-Military Institute for Research and Development, Romania

Bacterial infections affecting the center nervous system are extremely difficult to treat due to the blood-brain barrier (BBB). This project aims to develop nanotechnology-based drug delivery systems to deliver innovative antibacterial agents to the brain and to fight neuroinvasive bacterial pathogens, using bacterial meningitis as a proof-of-concept study. Promising antimicrobial peptides will be encapsulated within lipid-, polymer- and dendrimer-based nanocarriers, which will then be decorated with BBB-homing peptides. The so-obtained nanodrug candidates will be assessed for BBB crossing and antibacterial activity in vitro and in vivo using relevant models of bacterial meningitis. We expect to establish an effective strategy for identify nanodrugs to fight against bacterial infections in the brain.



Arben Merkoçi Hyka

GLEBioassay

Nano-Monitoring of Cancer Immunotherapy Efficiency: The Graphene Lateral Electrophoretic Bioassay platform

Coordinator:

Arben Merkoçi Hyka, Fundació Institut Català de Nanociència i Nanotecnologia (ICN2), Spain

Contact:

arben.merkoci@icn2.cat

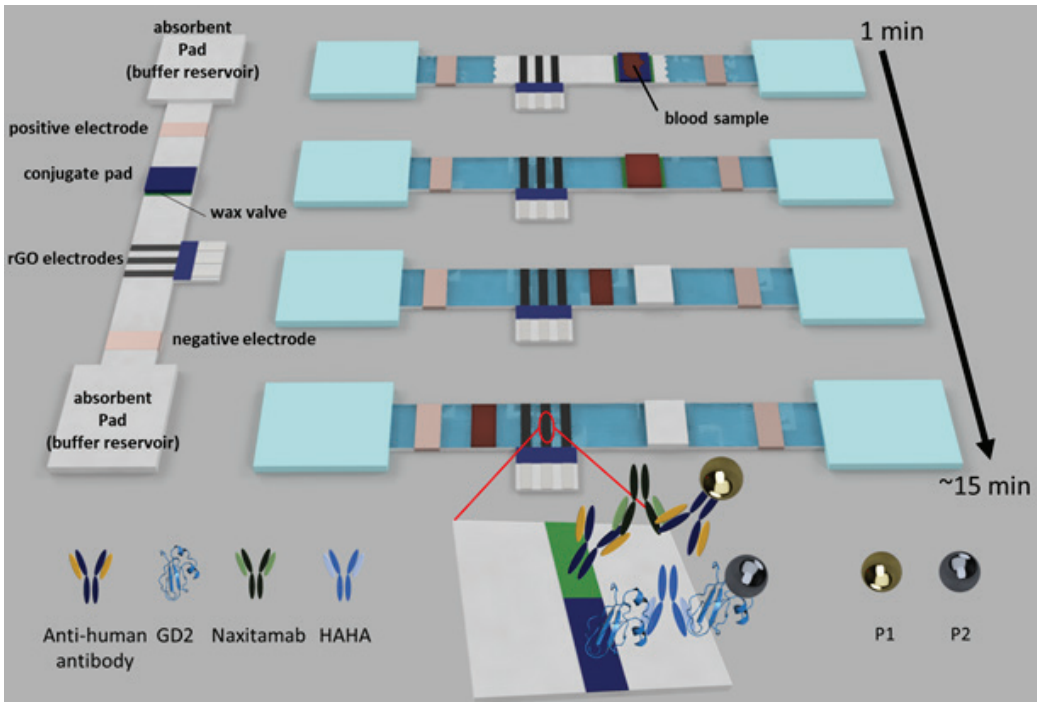
Partners:

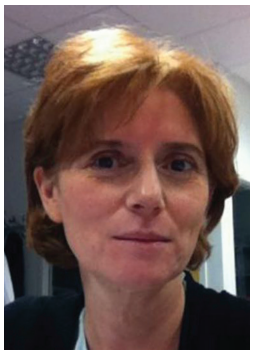
Carlos Javier Rodríguez-Hernández, Fundació Privada per a la Recerca i la Docència Sant Joan de Déu (FSJD), Spain

Serhat Sev, Nehir Biyoteknoloji Ltd. (NehitBT), Turkey

Michal Otyepka, Palacký University Olomouc (UP), Czech Republic

GLEBioassay aims to develop a multiplexed point of care nanobiosensing platform to monitor the efficiency of naxitamab-based immunotherapy in neuroblastoma. Naxitamab, a humanized anti-GD2 monoclonal, may cause some patients to develop human anti-human antibodies (HAHAs), thus provoking the deferment or suspension of the therapy. Conversely, this treatment induces in some patients a vaccine effect, when they start producing their own anti-GD2 antibodies. Currently, there is no standardized and accurate method to determine naxitamab, HAHAs and anti-GD2 in patients undergoing therapy. GLEBioassay will bring an electrophoretical paper-based portable platform with electrochemical readout to monitor the pharmacodynamics and pharmacokinetics of naxitamab in real samples. In contrast to lateral capillarity flow systems with optical detection; in our approach the mobility is driven by electrophoresis enabling a continuous flow, separating its components and cleaning the detection pad. Due to the versatility of the proposed platform, the outcome of the project can also be applied to different scenarios or other immunotherapies where a fast and efficient point of care biosensor is needed.





Nathalie Jonca

LIPARCI

Pre-clinical development of an acylceramide nanostructured delivery system to rescue the skin barrier in patients with ichthyosis

Coordinator:

Nathalie Jonca, Toulouse Institute for Infectious and Inflammatory Diseases (Infinity), Toulouse, FRANCE

Contact:

nathalie.jonca@inserm.fr

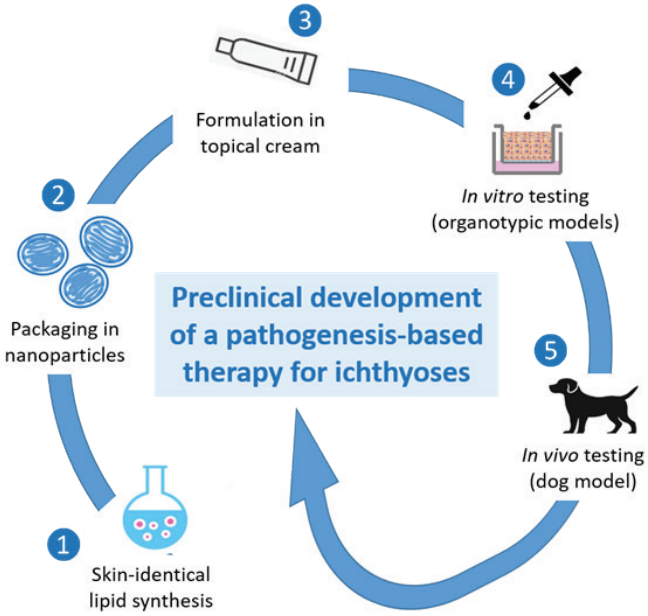
Partners:

Olga Lopez, Institute of Advanced Chemistry of Catalonia-Spanish National Research Council (IQAC-CSIC),Barcelona, SPAIN

Angela Hernandez-Martin, Hospital Infantil Niño Jesús, Madrid, SPAIN

Katerina Vavrova, Charles University, Hradec Kralove, CZECH REPUBLIC

Deniz Ceylan Tuncaboylu, Bezmialem Vakif University, Istanbul, TURKEY



Inherited ichthyoses are rare genetic diseases that occur at birth or early infancy. They cause abnormal scaling and thickening of the skin, dryness, redness, itching and pain involving life-long disfigurement and social ostracism. All forms of ichthyosis lead to a defective epidermal barrier and more than half of patients have Autosomal Recessive Congenital Ichthyosis (ARCI) in which the metabolism of ω-O-acylceramides is impaired. The lipid species of linoleic acid (LA) esterified with ω-hydroxyacyl sphingosine (CerEOS), is essential for building a healthy stratum corneum (SC), the outermost epidermal layer responsible for the skin barrier. Current treatments of the ichthyoses are mainly symptomatic, untargeted, often minimally effective and with potential serious side effects. Thus, the replacement of the missing ceramides is a promising therapeutic approach. The structure of the CerEOS quintessentially containing esterified LA seems fundamental for proper skin repair. However, the low solubility and extreme lipophilicity of CerEOS are challenging for its chemical synthesis and delivery to deeper SC to achieve its full effect. Moreover, the nanoscale organization of the SC makes the entry of substances difficult. The goal of LIPARCI is to develop an innovative lipid substitution system based on synthetic skin-identical lipids packaged in nanostructures formulated for topical skin application. These nanostructures will be validated for rescuing the damaged epidermal barrier using two pre-clinical models of ichthyosis: organotypic cultures mimicking the epidermis of patients with ichthyosis and a dog model of the disease. LIPARCI should thus allow the future development of highly efficient pathogenesis-based therapy of ichthyoses exhibiting impaired CerEOS metabolism as a primary defect.

María de la Fuente

OASIs

Targeting OsteoArthritis with Senolytic and anti-Inflammatory peptide-loaded nanopharmaceuticals

Coordinator:

María de la Fuente, Health Research Institute of Santiago de Compostela (IDIS), Servizo Galego de Saude (SERGAS), Spain

Contact:

maria.de.la.fuente.freire@sergas.es

Partners:

María Mayán, Institute for Biomedical Research of A Coruña (INIBIC). Fundación Profesor Novoa Santos (FPNS), Spain

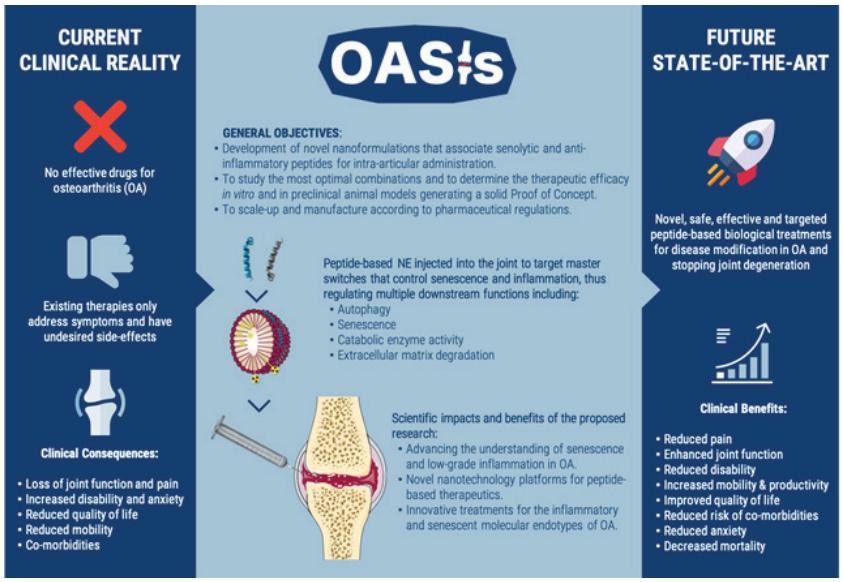
Ali Mobasheri, State Research Institute Centre for Innovative Medicine (IMC), Lithuania

Franck Pavan, V-Nano, France

Luminita Labusca, National Institute of Research and Development for Technical Physics (NIRDTP), Romania

Osteoarthritis (OA) is the most common form of arthritis and a leading cause of pain and disability worldwide. Current treatments are limited to symptomatic relief. There is an urgent need for novel therapeutics to restore joint function for the benefit of millions of people worldwide. Major limitations relate to the complexity of the underlying pathogenic mechanisms and molecular endotypes for the different clinical phenotypes, and to the need for efficient delivery strategies. OA treatment might be attained by personalizing care, accompanied by targeted therapeutics that can successfully be delivered to the affected joint using of nanotechnology.

OASIs aims to develop innovative nanopharmaceuticals based on the association of peptides that target senescence and inflammation to nanoemulsions that can safely be administered to the synovial joint via intra-articular injection, to provide sustained and long-lasting, symptom and structure modification, as OA treatment enhancement. We will develop new combinatorial targeted therapies by loading these peptides into biocompatible and biodegradable, safe-by-design and versatile, lipid nanoemulsions. Combinations will be assessed in vitro, ex vivo and in vivo. The results obtained in this proposal will help us to make state-of-the-art advances in order to successfully move towards the clinic.



Cyrille Garnier

I²PAD

Imaging and Inhibitor Probe for Alzheimer's disease Diagnostic and Treatment

Coordinator:

Cyrille GARNIER (HDR)
Inserm: Institut national de la santé et de la recherche médicale
Irset: Research Institute for Environmental and Occupational Health
Université de Rennes, France

Contact:

cyrille.garnier@univ-rennes1.fr

Partners:

Sandrine Huclier (HDR), Subatech, Université de Nantes, France

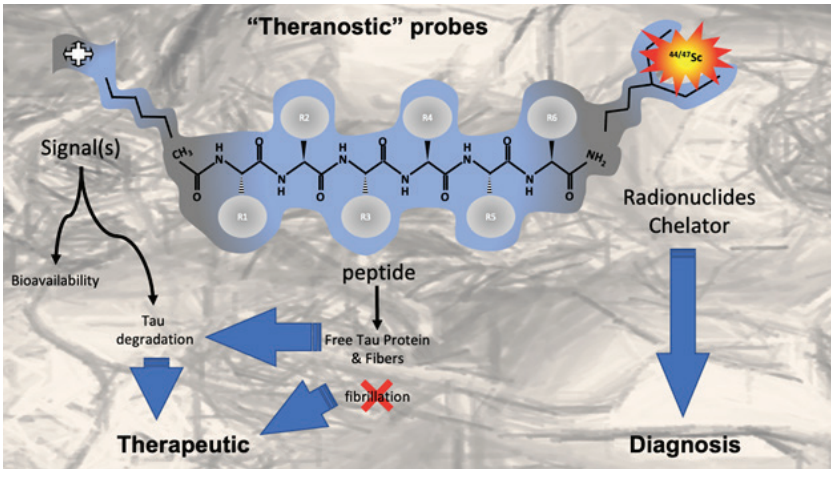
Christel Marquette, U1292 BIOsanté, DS/IRIG/DRF, Commissariat à l'Energie Atomique et aux énergies renouvelables (CEA), France

Renata Miolajczak, Radioisotope Centre POLATOM, National Centre for Nuclear Research, Poland

Dana Niculae, Radiopharmaceutical Research Centre, Horia Hulubei National Institute for Physics and Nuclear Engineering, Romania

Petr Hermann, Department of Inorganic Chemistry, Charles University (Universita Karlova), Czech Republic

Tomasz Dziel, Centrum Wysokich Technologii w Świerku Hitec Świerk Sp. Z o.o, Poland



Alzheimer's disease (AD) is a neurodegenerative disease, first described in 1906 by Aloïs Alzheimer. Today the prevalence of Alzheimer's disease is increasing mainly in developed countries and the number of cases is expected to quadruple by 2050, making it a major public health issue of € 140 billion per year. During the progression of the disease, some proteins acquire new structural properties leading to their self-assembly as amyloid fibers/plaque which progressively colonize the central nervous system and are the cause of its dysfunction. To this day, the diagnosis of the disease is established after the first clinical symptoms and is not definitive until post-mortem, and there is still no effective treatment to stop or even reverse the accumulation of protein aggregates in the brain. To overcome these shortcomings, we are developing a "theranostic" approach consisting in producing, in the same tool, molecules that can be used as a molecular probe for early diagnosis by PET imaging, before clinical presentation and the same molecule could be used later for therapeutic purposes when combined to the therapeutic radionuclide.

Brigitte Malgrange

NANOEAR

New DX243-conjugated nanoparticles as a neuroprotective drug for hearing loss

Coordinator:

Malgrange brigitte, GIGA stem cells, Université de Liège, Belgium

Contact:

bmalgrange@ulg.ac.be

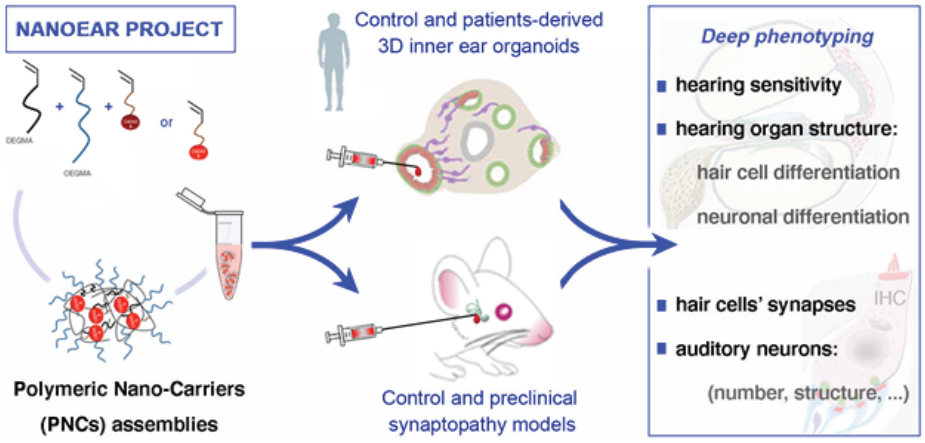
Partners:

Aziz El Amraoui - Institut Pasteur, IDA, Paris, France

José Millan, Health Research Institute La Fe, Valencia, Spain

Stéphane Silvente, Dendrogenix, Liège, Belgium

Rana Sanyal, RS Research, Istanbul, Turkey



Untreated hearing impairments have a profound negative impact on the affected individuals' quality of life, leading to social isolation, depression and reduced physical and cognitive functions. This situation is highly prevalent (5% of the population worldwide). Impaired synaptic transmission, degeneration of auditory neuron neurites, and neuronal loss characterize most of these disorders. Despite the major recent progress on hearing loss mechanisms, treatment options are mostly missing. To date, the cochlear implant, which bypasses the damaged hair cells by providing direct electrical stimulation of the primary auditory neurons, is used to restore functional hearing in many patients who were profoundly deaf. However, their beneficial outcomes vary significantly among patients, often impacted by the number and functional state of auditory neurons. A therapeutic approach that would allow the prevention or delay of degenerative processes is thus urgently needed.

We previously identified a new drug that is promising to restore cochlear synaptogenesis. Local administration of this drug through the tympanic membrane is a preferable option. Still, the efficacy of such a way of administration relies on the drug's capacity to remain long enough at the cochlear round window level. The objective of NANOEAR is to develop a novel nanoparticle-based pharmacologic strategy for treating deafness caused by auditory synaptopathy in a well-defined group of deaf patients suffering from Clarin-1 mutation.

Eva Baldrich

QUPID

Quantitative and storage-stable point-of-care diagnostic device

Coordinator:

Eva Baldrich. Vall d'Hebron Hospital Research Institute (VHIR), Spain

Contact:

eva.baldrich@vhir.org

Partners:

Joulia Larionova. Centre National de la Recherche Scientifique (CNRS), France

Una Rieksina. University of Latvia, Latvia

Sibel Ozkan. Ankara University Faculty of Pharmacy, Turkey

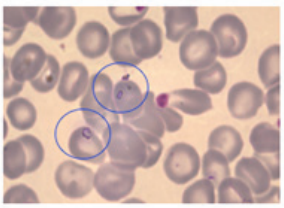
Pierre-Emmanuel Doulain. Synthesis Of Nanohybrids (SON), France

Malaria, a parasitic disease transmitted by the bite of infected Anopheles mosquitoes, is a leading cause of mortality in many developing countries. The World Health Organization (WHO) has launched an ambitious plan to eradicate malaria that will require population screening, which is not feasible with current diagnostic tools. Nowadays, malaria point-of-care (POC) testing relies on rapid diagnostic tests (RDTs), which are easy to use but display insufficient sensitivity. Other unmet needs are the generation of a quantitative response, a robust and reproducible production path, and long-term stability under a wide range of temperatures and humidity conditions.

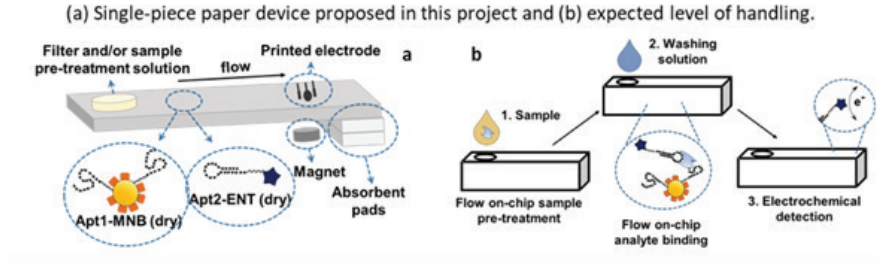
QUPID aims to develop a cost-effective analytical system that, by exploiting synthetic receptors and tags, will exhibit long-term storage stability, and fast and quantitative malaria diagnosis with minimal user intervention. Our multidisciplinary consortium will tackle this goal: Magnetic nanobeads (MNB) will be used to optimize fast and sensitive single-step bioassays, in which: i) synthetic receptors selected and produced in vitro will substitute antibodies (Ab) to improve room temperature storage stability, and ii) electroactive nanotags (ENT) will substitute enzyme labels to reduce sample matrix interference and provide rapid direct detection. Handling will be minimized by using economical paper microfluidic electrodes to automate the assay, while a customized hand-held electrochemical platform will deliver quantitative and robust results.

We expect that this system will provide a fast diagnosis from whole blood and with little user handling. Moreover, although initially oriented to malaria diagnosis, similar technology could be employed in the future in other medical fields.

Mosquito bite and *Plasmodium falciparum* inside the red blood cells of a patient with malaria.



(a) Single-piece paper device proposed in this project and (b) expected level of handling.




Sabine Szunerits

GSkin

Growth factors-rich EVs-functionalized graphene-on-hydrogel based skin bioactive regeneration scaffolds

Coordinator:
Sabine Szunerits, Centre National de la Recherche Scientifique [CNRS]

Contact:
sabine.szunerits@univ-lille.fr

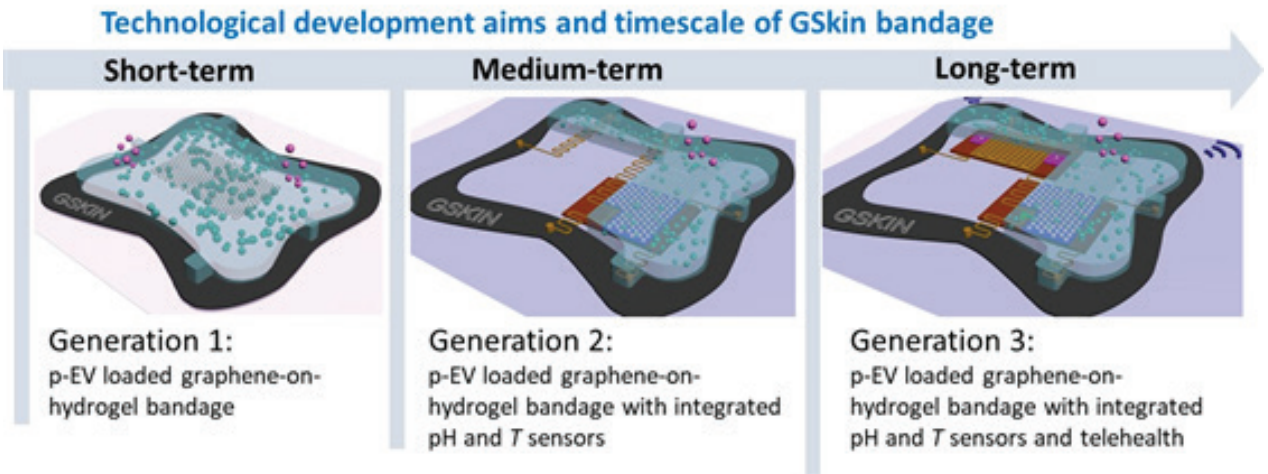
Partners:
Sorin Melinte, Université catholique de Louvain (UCLouvain)

Thierry Burnouf, Taipei Medical University (TMU)

Yuan-Sheng Tzeng, Tri-Services Hospital (TSGH)

Vincent Bouchiat, Grapheal (Grapheal)

Despite an abundant supply of wound dressings, a real need remains to improve efficiency and quality of healing in wound care management. Nanotechnology offers unique opportunities to tackle such unmet needs. The GSkin project addresses the numerous skin regeneration challenges through the development of a theranostic graphene-on-hydrogel bandage loaded with growth factors-rich extracellular vesicles (p-EVs) from platelets, the physiological healing cells of the body. Temperature (T) and pH sensors based on the sensing capability of graphene will monitor in-situ the wound healing state. Integration of electrothermal nanoactuators will allow on-demand delivery of p-EVs. This “intelligent skin bandage” is expected to enhance wound healing at early stages with a step forward in the development of advanced wound dressings for chronic wounds such as diabetic foot ulcers.



Pablo Hervella

ECM-CART

LDL-like nanoparticles for CAR-T-based glioblastoma immunotherapy

Coordinator:

Pablo Hervella, Health Research Institute of Santiago de Compostela (IDIS), Spain

Contact:

pablohervella@gmail.com

Partners:

Anat Globerson Levin, Tel Aviv Sourasky Medical Center (TAS), Israel

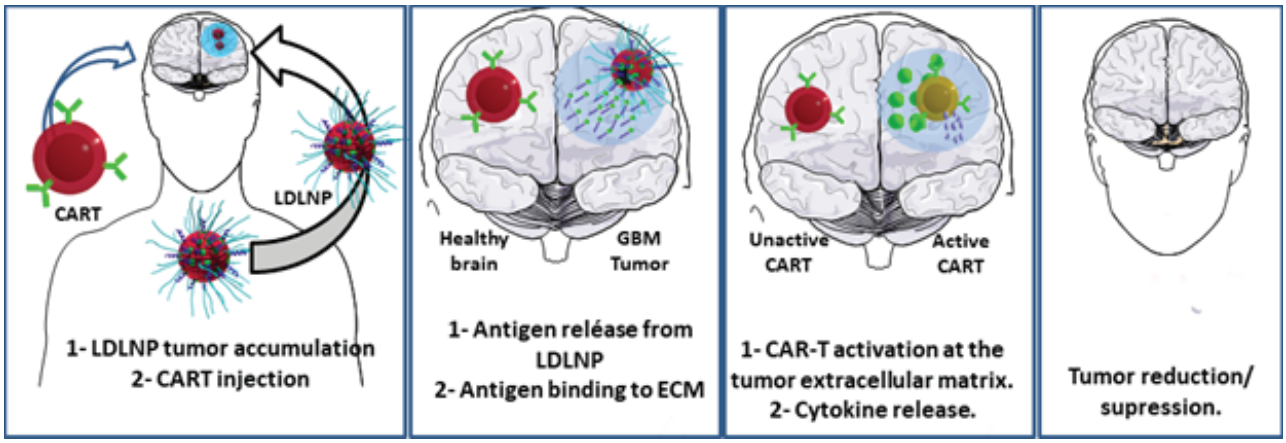
Dinorah Friedmann-Morvinski, Tel Aviv University (TAU), Israel

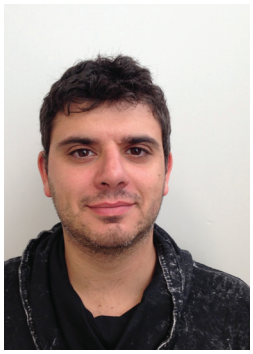
Jacobo Cruces, GalChimia S.A., Spain

Tambet Teesalu, University of Tartu, Estonia

This project aims to demonstrate that the targeted delivery of nano-formulated exogenous antigens to the extracellular matrix (ECM) of brain tumors provides a safe and specific target for chimeric antigen receptor T-cell (CART) for the treatment of glioblastoma (GBM). GBM is the most common brain tumor in adults and despite all the advances combining surgery, chemotherapy, and radiotherapy, there is still no cure for this disease. In this regard, CART therapy is one of the most promising approaches in the treatment of GBM. The main obstacle limiting CART efficacy is the scarcity of highly expressed tumor antigens in GBM.

In this project, we hypothesize that the components of the ECM could become ideal targets for CART therapy if labelled with exogenous antigens, enabling a tumor treatment using CART directed to the delivered antigens. Therefore, we propose to deliver CART antigens to the ECM by incorporating these conjugates in small nanoparticles that mimic low-density lipoproteins (LDLNP), taking advantage of the known capacity of LDL to load high amounts of hydrophobic compounds and to accumulate into brain tumors. The nanoparticle-based delivery of exogenous antigens will promote a local accumulation of antigens in the tumor while avoiding unspecific antigen build-up in healthy organs, which will result in the activation of CART preferentially at the ECM of GBM.





Marcos Garcia-Fuentes

RAIN

Radiotherapy-Activated Immunomodulating Niches

Coordinator:

Marcos Garcia-Fuentes, Instituto de Investigaciones Sanitarias de Santiago de Compostela (IDIS), Spain

Contact:

marcos.garcia@usc.es

Partners:

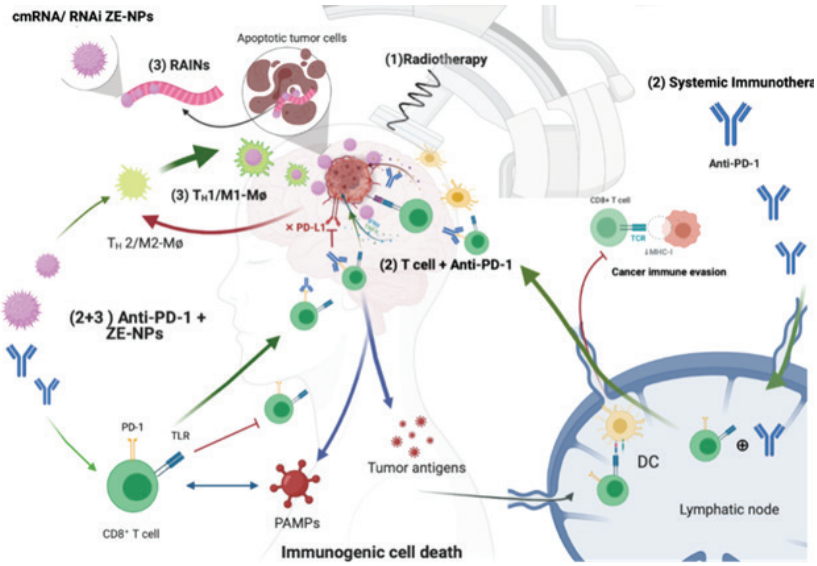
Hsieh-Chih Tsai, National Taiwan University of Science and Technology (NTUST), Taiwan

Yolanda Prezado, Institut Curie-CNRS (IC), France

Long-Sheng Lu, Taipei Medical University and Taipei Medical University Hospital (TMUH), Taiwan

Bernard Gallez, Université Catholique de Louvain (UCL), Belgium

Ilaria Marigo, Istituto Oncologico Veneto (IOV), Italy



Glioblastoma (GBM) is one of the deadliest types of cancer and new treatments in the last decades have had little impact on patient survival. Immunotherapy aims to activate the host immune system against the tumor, but unfortunately, GBM is poorly immunogenic. In addition, GBM is characterized by an immunosuppressive environment, rendering immunotherapy ineffective and highlighting the urgent need for innovative approaches. Radiotherapy, the first-line treatment for glioblastoma, has a direct immune effect cause by the release of tumor antigens in the tumor microenvironment by dying cells. This immune stimulation alone is insufficient due to the profound immunosuppression of the GBM microenvironment. RAINs are delivery systems for local implantation at the GBM resection cavity consisting of nanoparticle-delivered immune stimulating molecules and RNA inhibitors against immunosuppressive pathways aimed at boosting the antitumoral effects of radiation and immune checkpoint inhibitors. The delivery of these molecules in nanostructured formulations (a) if spread around the bloodstream, (b) they require stabilization of long-term effects and (c) they must reach intracellular targets.

The RAIN team will first identify photon radiotherapy protocols that generate the most effective immune responses and simultaneously design different types of nanomedicines for immune activation. Then, the team will study the antitumoral effect of the prototypes in combination with radiotherapy and with the immune checkpoint inhibitor anti-PD-1 in different glioblastoma models to move these nanomedicines towards clinical translation.