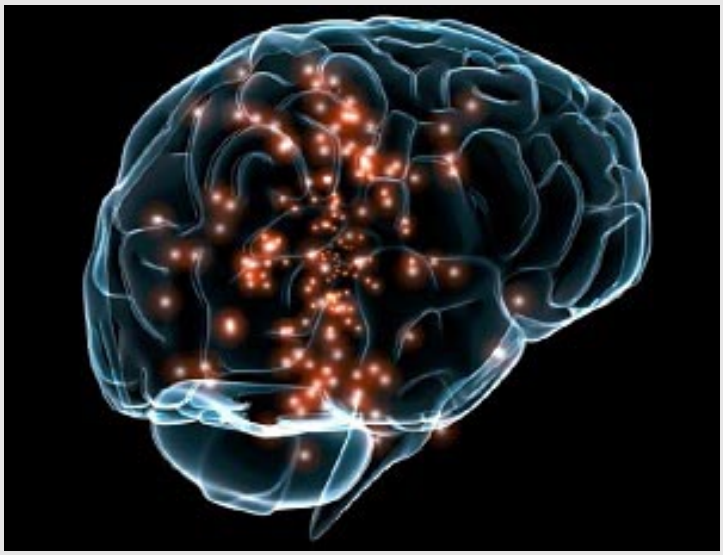
NANOMEDICINE FOR TREATING CANCER AND BRAIN DISEASES



EURONANOMED PROJECTS FOR ACTION ON NANOMEDICINE UNDER HORIZON 2020

EURO Nano Med

Nano from research to patient and industry

CINaM

8th March 2019,14:00-18:00
Salle Raymond Kern
Centre Interdisciplinaire de Nanoscience de Marseille
Campus Luminy, Marseille, France

HORIZON 2020

Welcome

We welcome you to join the symposium on “Nanomedicine for treating cancer and brain diseases”. Nanomedicine is the application of nanotechnology to achieve breakthroughs in healthcare. It exploits the distinct and often novel physical, chemical and biological properties of materials at the nanometer scale to enable and improve prevention, detection, diagnosis, treatment and follow-up of diseases. This symposium is dedicated to nanotechnology-based drug delivery to cancer and brain diseases, on occasion of the ongoing and new EU projects in nanomedicine in CINaM under the Horizon 2020 program. We hope you enjoy the science and harvest friendship during the symposium.

Dr. Ling Peng

CINaM central building

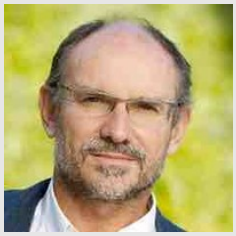
CINaM TPR1

NANOMEDICINE FOR TREATING CANCER AND BRAIN DISEASES

Prof Kazunori Kataoka

Supramolecular polymeric micelles for treating cancer and brain diseases

Innovation Center of NanoMedicine, University of Tokyo, Japan



Dr Michel Khrestchatisky

Molecular vectors for drug delivery into the brain and tumours

Institut de Neurophysiopathologie, Aix-Marseille University, France

Prof Tambet Teesalu

Homing peptides for glioma targeting

Laboratory of Cancer Biology, University of Tartu, Estonia

Dr Sinda Lepetre

Squalene-based nanomedicine for cerebral ischemia, spinal cord injury and pain

Institut Galien, Paris-Sud University, Paris, France

Contact:

Dr Dinesh DHUMAL
dhumal@cinam.univ-mrs.fr

http://www.cinam.univ-mrs.fr/site/nanomed/index.php

Program Schedule

March 8	Program details
14:00	Welcome presentation of EU project in Nanomedicine in CINaM
14:15	**Prof Kazunori Kataoka** Supramolecular polymeric micelles for treating cancer and brain diseases *Tokyo University, Japan*
15:15	**Prof Michel Khrestchatisky** Molecular vectors for drug delivery into the brain and tumors *Aix-Marseille Université, France*
16:00	**Coffee break**
16:30	**Prof Tambet Teesalu** Homing peptides for glioblastoma targeting” *University of Tartu, Estonia*
17:15	**Dr Sinda Lepetre** Squalene-based nanomedicine for cerebral ischemia, spinal cord injury and pain *Université Paris-Sud, France*
18:00	Concluding remarks
18:05	Drinks with students

Supramolecular polymeric micelle (PM) for treating cancer and brain diseases

Prof. Kazunori Kataoka

Innovation Center of NanoMedicine, Kawasaki Institute of Industrial Promotion, Kawasaki 210-0821, Japan; Policy Alternatives Research Institute, The University of Tokyo, Tokyo113-0033

Nanomedicine has received great interest for treating various diseases. Engineered polymeric nanosystems with smart functions play a key role in nanomedicine as drug carriers, gene vectors, and imaging probes. This presentation focuses present status and future trends of supramolecular nanosystems self-assembled from designed polymers for therapy and non-invasive diagnosis of intractable diseases. Most typical example is polymeric micelle (PM), which is small in size and has pH- and/or redox potential responding properties for controlled drug release, deep tissue penetrating, and reduced toxicity.[1] Five PMs developed in our group are currently in clinical trials in Asia, USA and Europe. Recently, we have also developed PM-based imaging reagents for theranostic nanomedicines[2] and PMs decorated with glucose to crossing blood-brain barrier for the treatment of neurodegenerative diseases, including Alzheimer's disease[3].

1. Y. Matsumoto, et al, *Nature Nanotech.* **11** (2016) 533-538; H. Cabral, et al, *Nature Nanotech.* **6** (2011) 815-823; K. Katsushima, et al, *Nature Commun.* **7** (2016) 13616.
2. P. Mi, et al, *Nature Nanotech.* **11** (2016) 724-730.
3. Y. Anraku et al, *Nature Commun.* **8** (2017) 1001.

Short biography

Prof. Kazunori Kataoka is the Director General of the Innovation Center of NanoMedicine (iCONM), and a Professor at the Institute for Future Initiatives, University of Tokyo, Japan. His current major research interests include supramolecular materials for nanobiotechnology, focusing on drug and gene delivery systems. Prof. Kataoka has published over 500 peer-reviewed papers (h-index 139), and has received numerous scientific awards, including the Award of the Society of Polymer Science, Japan (2000), the Clemson Award from the Society for Biomaterials, USA (2005), the Founder's Award from the Controlled Release Society (2008), the NIMS Award (2009), the Commendation for Science and Technology by the Minister of MEXT, Japan (2010), the Humboldt Research Award from the Alexander von Humboldt Foundation (2012), the Leo Esaki Prize (2012), and the Princess Takamatsu Cancer Research Fund Prize (2017).

Molecular vectors for drug delivery into the brain and tumours

Dr Michel Khrestchatisky

Institut de Neurophysiopathologie, Aix-Marseille University, France

The brain is endowed with a unique vascular system known as the blood-brain barrier (BBB) that restricts very effectively the entrance of toxic molecules and infectious agents, but also hampers drug delivery. An estimated 98% of all active drugs and virtually all biotherapeutics do not cross the BBB. The BBB thus represents a real technological barrier to treat brain diseases. Our approach is based on the principle that the BBB is not only physical barrier but also functional barrier whose natural transport mechanisms may be advantageously used for drug delivery. We focus on targeted delivery using peptide-based molecular vectors to specifically target receptors involved in Receptor Mediated Transport (RMT), a physiological process for the transport of endogenous substances into cells. We have established the proof of concept of the technology in in vitro BBB models and in vivo by vectorizing various classes of molecules including imaging agents, peptides and antibodies to tumours and into the brain.

Short biography

Michel KHRESTCHATISKY is Research Director at the CNRS, PhD in cellular and molecular biology from Marseille Luminy, specialized in neurobiology, 4 years research at the University of California Los Angeles (UCLA, USA), 10 years experience as group leader at INSERM, Paris. Director during the last 14 years of the NICN-UMR7259 neurobiology laboratory, and newly appointed since January 2018 Director of the Institute for NeuroPhysiopathology (INP) supported by the CNRS and Aix-Marseille University, leader of the BBB and Neuroinflammation group; has published over 125 peer-reviewed articles in international scientific journals, a dozen book chapters and is co-inventor in 6 families of patents with more than 70 patents delivered worldwide. Co-founder of the VECT-HORUS biotechnology company and scientific counsel of the company.

Homing peptides for glioma targeting

Prof. Tambet Teesalu

Laboratory of Cancer Biology, University of Tartu, Estonia

We perform systemic in vivo phage display screens to identify homing peptides that bind to specific targets in the tumor vasculature. Corresponding synthetic peptides are used to target drugs, biologicals, and nanoparticles into tumors to increase their therapeutic index.

I will give an overview of our approaches to mapping of vascular “ZIP codes” in normal brain and glioblastoma. I will discuss characterization and validation of candidate vascular homing peptides, and application of the peptides for precision guided delivery of therapeutic and diagnostic nanocarriers. I will provide examples of homing peptides that target malignancy-associated cell surface receptors and extracellular matrix components and discuss their applications for preclinical management of glioblastoma.

Short biography

Prof. Teesalu is working on affinity targeting of tumors with homing peptides and peptidomimetic compounds, and he heads the Laboratory of Cancer Biology at the University of Tartu since 2012. Awards and recognitions to Prof. Teesalu include the Susan G. Komen for the Cure Career Development Award (2010), an ERC grant (2010), a Wellcome Trust Senior International Fellowship (2010), an EMBO installation grant (2010), and the Estonian National Prize in Medicine (2017). He holds visiting professorships at the Center of Nanomedicine of University of California Santa Barbara (USA) and at Sanford Burnham Prebys Medical Discovery Institute, La Jolla (USA). On the non-academic side, he has founded three biotech companies, including DrugCendR Inc. (La Jolla, USA) which develops tumor-penetrating peptides for solid tumor targeting.

Squalene-based nanomedicine for cerebral ischemia, spinal cord injury and pain

Dr. Sinda Lepetre-Mouelhi
Institut Galien, Paris-Sud University, France

The "squalenoylation" approach is based on the covalent linkage between squalene, a natural and biocompatible lipid, and a drug molecule displaying serious limitations such as short biological half-life due to rapid blood metabolization and poor intracellular diffusion. Fundamentally, the dynamically folded conformation of squalene triggers the resulting squalene-drug bioconjugates to self-assemble as nanoparticles of 100–300 nm in aqueous solutions. In general, these nanoparticles showed long blood circulation times after intravenous administration and improved pharmacological activity with reduced side effects and toxicity. This squalenolytion approach has proven to be very effective against numerous diseases, including cancer, brain ischemia, spinal cord injury[1] and pain[2]. The originality of the squalene-based nanoparticles arises from the fact that they could act on the central nervous system by operating peripherally without any need to cross the blood-brain barrier.

1- A. Gaudin et al., Squalenoyl adenosine nanoparticles provide neuroprotection after stroke and spinal cord injury. Nat. Nanotechnol. 9, 1054–1062 (2014).

2- J. Feng, et al.,, A new painkiller nanomedicine to bypass the blood-brain barrier and the use of morphine. Sci. Adv. 5, eaau5148 (2019).

Short biography

Dr. Sinda Lepetre-Mouelhi is Associate Professor at Institut Galien at Paris-Sud University in Châtenay-Malabry in France. She has been working in the team of Prof. Patrick Couvreur since 2005. Her current research activity lies in the synthesis of squalene-based bioconjugates and their formulation into nanoparticles. The main fields of application include cancer, HIV, and more recently, cerebral and hepatic ischemia, as well as pain.

Era-Net EuroNanoMed II project: Target4cancer

(Nano) systems with active targeting to sensitize colorectal cancer stem cells to anti-tumoral treatment

Acronym: Target4Cancer

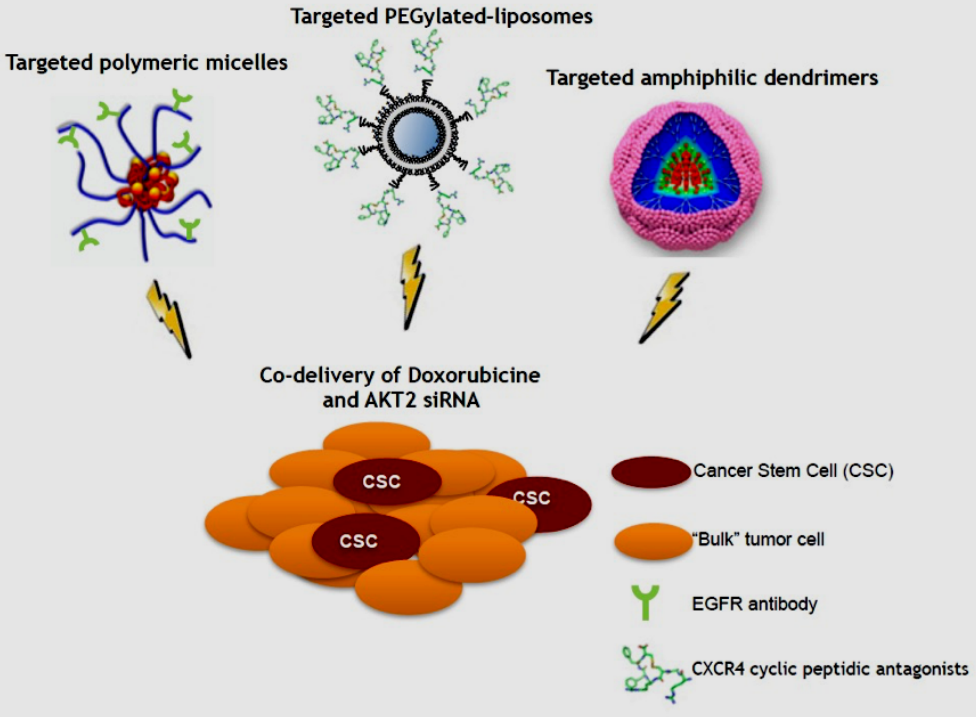
Coordinator: Simo Schwartz Jr. CIBBIM-Nanomedicine; Hospital Universitari Vall d'Hebron, Vall d'Hebron Institut de Recerca, Barcelona, Spain; simo.schwartz@vhir.org

Partners: Stefania Scala, Mafalda Videira, Ling Peng, Ming Wei

Portugal Italy France Spain

"Drug Delivery Systems targeting cancer stem cells to improve the therapeutic window"

Even though current treatments have improved the overall survival of patients with colon cancer, relapse and development of therapy-resistant metastases are still frequent. This project will develop Drug Delivery Systems targeting cancer stem cells to improve the therapeutic window of Doxorubicin and/or AKT2 siRNA against colorectal cancer. In vitro and in vivo preclinical validation will be performed to select the best performing nano-conjugate targeting for future scale-up and regulatory studies. The project is expected to produce clinical useful proof-of-concept results suitable for protection by patenting, as well as data of general scientific interest useful to the broad scientific community.



Nanoglio:
Nanotechnology based immunotherapy for glioblastoma

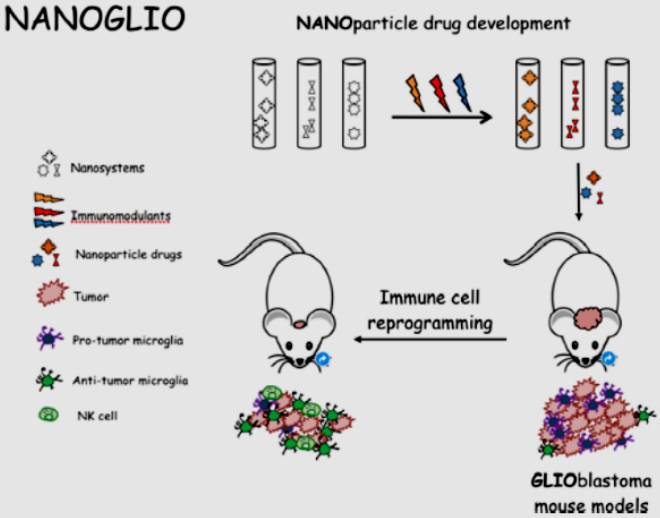
Coordinator: Angela Santoni, IRCCS Neuromed, Pozzilli , Italy, angela.santoni@uniroma1.it

Partners: Bozena Kaminska, Neurobiology Center Nencki Institute of Experimental Biology, Warsaw Poland | Ling Peng, Centre Nationale de Recherche Scientifique (CNRS), Marseille France | Mafalda Videira, University of Lisbon, Lisbon, Portugal | Costas Demetzos , University of Athens, Athens, Greece | Sabrina Pricl, University of Trieste, Trieste, Italy | Patrick March,Institut National de la Santé et de la Recherche Médicale (INSERM), La Tronche France.

Italy France Portugal Greece

"inducing a specific antitumor response by delivering immunomodulatory agents"

Glioblastoma (GBM) is a devastating brain tumor, with no efficacious therapeutic treatment. Among the factors contributing to tumor aggressiveness is a reduced immunological reaction against cancer cells. This project aims at inducing a specific antitumor response by delivering immunomodulatory agents to the tumor lesions, to re-educate the different components of the immune system to acquire an antitumor phenotype. Different nanosystems (nDDSs) constructed with lipids, polymers and dendrimers will be used to transport immunomodulators across the defective blood brain barrier, into the tumor lesions, and assess the anticancer activity using rodent models. The expectation is to identify promising anti-GBM candidates for future therapeutic implementation.



Era-Net EuroNanoMed III project: TARBRAINFEC

Jose Antonio García-Salcedo

TARBRAINFEC

Nanosystems conjugated with antibody fragments to target/treat brain infections

Coordinator:

Jose A. García-Salcedo, Instituto de Investigación Biosanitaria de Granada, Spain

Contact:

jags@genyo.es

Partners:

Ling Peng, Centre Nationale de Recherche Scientifique, Marseille, France

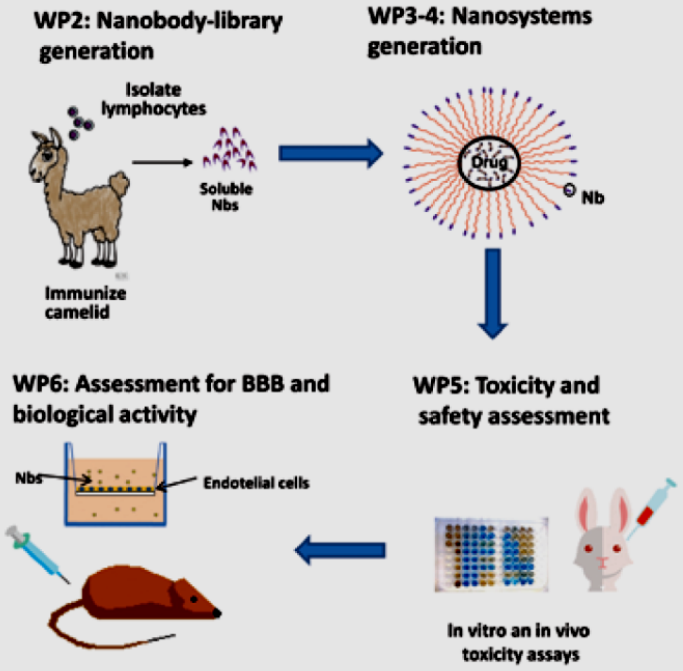
Sylwia Czarnocka-Śniadała, NanoSanguis Ltd., Warsaw, Poland

Antonio Alcamí, Centro de Biologia Molecular Severo Ochoa, Spanish Research Council, Madrid, Spain

Mangesh Bhide, Institute of Neuroimmunology, Slovak academy of Sciences, Kosice, Slovakia

Aristidis Tsatsakis, University of Crete, Athens, Greece

A major obstacle for curing brain diseases is the blood-brain barrier (BBB), which impedes therapeutic agents to reach the brain and target the related pathogens. In this project, we want to develop a drug delivery nanosystem coated with antibody fragments, called nanobodies (Nbs) as a proof of concept for targeting brain infections caused by bacteria, virus and parasite. These Nbs will be then conjugated to the drug-loaded nanoparticles constructed using polymer or dendrimer nanovectors. The success of this project will validate the proof-of-concept study to combine the nanobody technology with the nanotechnology based drug delivery for effectively overcoming BBB and targeting pathogens in brain infections. We expect to generate clinical useful pilot results for the best performing candidates for future translation, and at the same time, research data of general scientific interest useful to the broad scientific community.



COST Action 17140

Cancer nanomedicine - from the bench to the bedside (Nano2clinic)

Chair: Prof Barbara Klajnert;

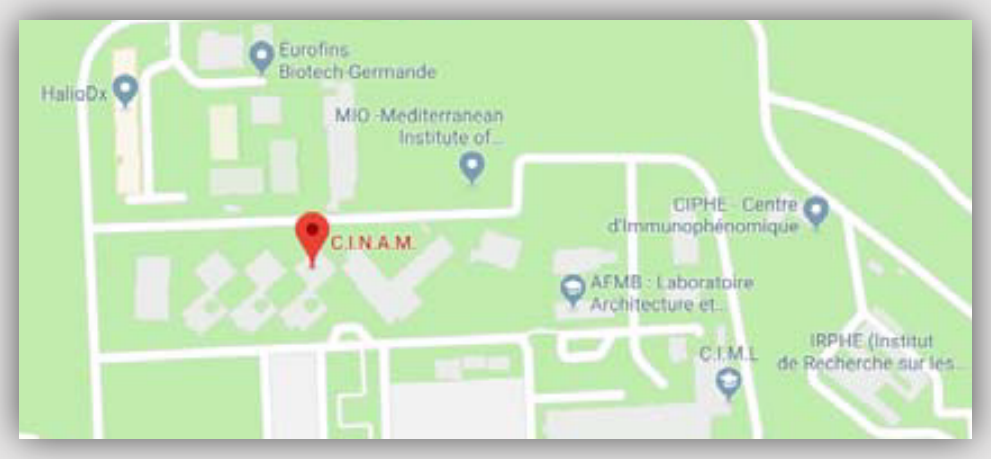
Vice-Chair: Prof Sabrina Pricl

Finding efficient cancer therapies is an urgent and still unresolved problem. Nanotherapeutics exhibit major benefits with respect to conventional anticancer drugs, including improved half-life, more efficient tumour targeting, and reduced side effects. However, only a few nanotherapeutics have reached the commercial level, most still being in the investigational phase. This Action aims at developing and strengthening industry-academia relations with an ultimate goal: fostering the clinical translation of nanomedicine from bench to bedside. This will be achieved by creating the first, pan-European interdisciplinary network of representatives from academic institutions and small and medium enterprises including clinical research organizations (CROs) devoted to the development of nanosystems carrying anticancer drugs from their initial design, preclinical testing of efficacy, pharmacokinetics and toxicity to the preparation of detailed protocols needed for the first phase of their clinical studies. By promoting scientific exchanges, technological implementation and innovative solutions, this Action will provide a timely instrument to rationalize and focus research efforts at the EU level in dealing with the grand challenge of nanomedicine translation in cancer, one of the major and societal-burdening human pathologies.

https://www.cost.eu/actions/CA17140

https://www.nano2clinic.eu/cost-action-ca17140

Way to Salle Raymond Kern



By Air : The nearest airport is Marseille-Provence airport

Public transport

Shuttle buses (Navettes) run from Marseille-Provence airport to the main railway station, Marseille-Saint Charles (SNCF lines)

Tickets are sold at the airport, close to the bus stop (8.5 € one way). There are buses every 20 min from 5:00 AM till the last flight. The journey takes about 30 min. +33 (0)4 42 14 31 27

Taxi

Ask for the scientific campus of Luminy. Once inside Luminy campus, follow directions to CINAM. Costs about 70 € (day time rate – extra night charges are applicable).
+33 (0)4 91 02 20 20 +33 (0)6 62 73 91 42 (cell phone)
+33 (0)4 91 05 80 80 +33 (0)6 11 16 60 19 (cell phone)

By train : the main SNCF railway station is Marseille-Saint Charles

Public transport :

You will need to first take the metro - line 2, direction Sainte-Marguerite and exit at « Rond-point du Prado ». Then bus B1 or Jetbus 21 (faster) to the terminus Luminy .

Tickets are available at the entrance to the metro via vending machines or at the counter. The same ticket works for both the metro and the bus at about 2 € (retain the metro ticket and reuse in the bus). ww.rtm.fr +33 (0)4 91 91 92 10

Taxi :

Ask for the scientific campus of Luminy. Once inside Luminy campus, follow directions to CINAM. Taxi to Luminy costs about 25 € (day time rate).
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+33 (0)4 91 05 80 80 +33 (0)6 11 16 60 19 (cell phone)