


nanoTBtech





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# The nanoTBtech project

Nanoparticles-based 2D thermal bioimaging technologies



## Our Project

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This project has received funding from the European Union's Horizon 2020 FET Open programme under grant agreement No 801305.

# PROJECT

Temperature measurements are crucial in countless technological developments, accounting for 80% of the sensor market throughout the world. The pitfalls of temperature readouts at the biomedical battleground are mostly represented by the currently achievable spatial resolution. To address key issues, such as intracellular temperature fluctuations and in vivo thermal transients, a technique able to go clearly below 1  $\mu\text{m}$  is highly and urgently needed, as the traditional contact-based sensors and near infrared thermometers are not suitable for measurements at that tight spatial range. To overcome these limitations requires a non-contact thermometry approach granted with sub-micrometer resolution, also providing real-time high relative thermal sensitivity values.

The goal of NanoTBTech is to develop a 2-D thermal bioimaging technology featuring sub-microscale resolution, based on nanothermometers and heater-thermometer nanostructures. We will design, synthesize, and bio-functionalize nontoxic luminescent nanostructures, operating essentially beyond 1000 nm, for in vivo nanothermometry and nanoheating.

Furthermore, to monitor the temperature-dependent nanostructures' luminescence we will develop a novel imaging system. The effective delivery of that major advance in 2-D thermal bioimaging will be implemented through two impactful biomedical showcases: highly spatially-modulated intracellular magnetic/optical hyperthermia and in vivo detection and tracking of cancer. In the long-term, we foresee our technology having a broad impact on non-invasive clinical imaging and theranostics. For instance, the accurate measurement of temperature gradients' sources will be an invaluable tool for real-time control of thermal therapies, thus making them harmless for the patient.

Multiple conceptual breakthroughs can be further envisaged from the proposed 2D-thermal imaging system, credibly spreading its impact towards non-biomedical technological areas.

## OBJECTIVES

### 1. Self-monitored nanothermometers and heater-thermometer nanostructures

Design and fabrication of NIR emitting NPs and heater-thermometer nanostructures with  $S_r > 1\%K^{-1}$ , resolution  $< 0.1$  K and efficiency of light-(or magnetic field) to-heat conversion  $> 50\%$  (figures of merit well above the currently achieved values).

### 2. Modelling the predesigned structures

Understanding the parameters of the nanothermometers and heater-thermometer nanostructures for objectives 3-5, e.g., brightness,  $S_r$ , heating conversion efficiency, and heat producing/diffusion mechanisms.

### 3. Biofunctionalization and toxicity assessment

Optimization and in vitro/in vivo incorporation of luminescent, nontoxic, long-term biodegradable, long-circulating, tumour-targeted, heating/sensing nanoplatfoms linked to specific therapeutic antibodies.

### 4. Magneto-thermal 2D luminescent thermometry for local hyperthermia

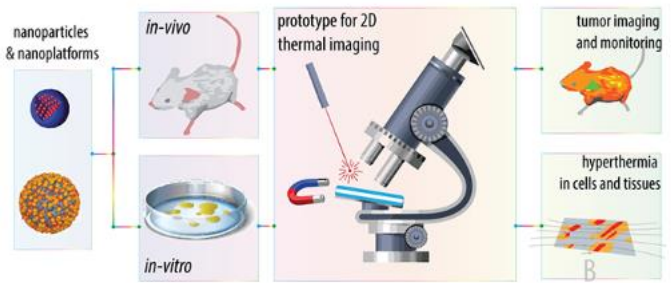
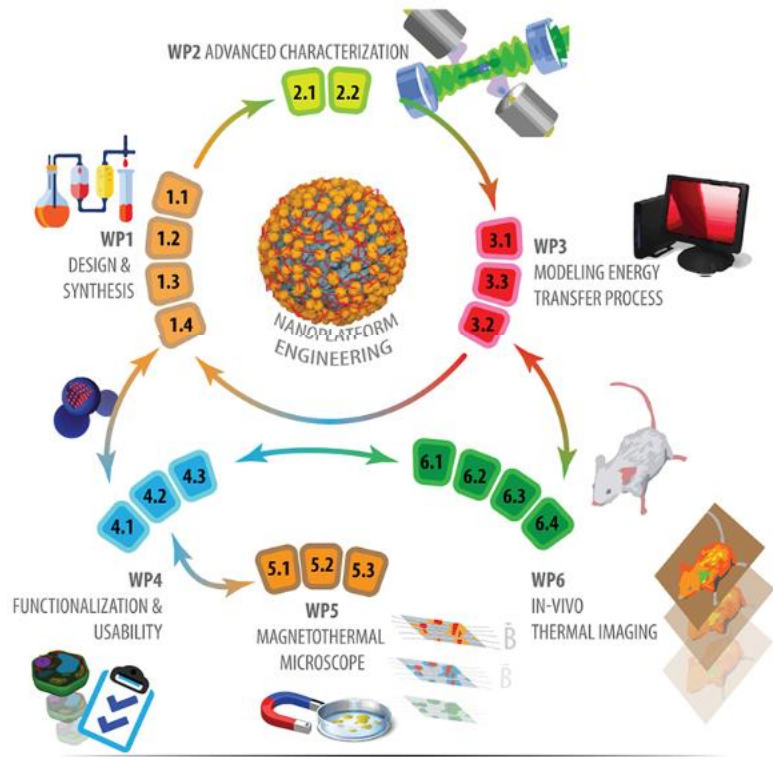
Developing a new technology for in vitro and in vivo simultaneous luminescent 2D thermal imaging and optical microscopy imaging for localized controlled hyperthermia in cancer cells and tumour microenvironment.

### 5. Time-resolved in vivo thermal images in BW-II and BW-III for tumour detection and dynamical monitoring

Explore in vivo time-gated and 2D magnetic- or optical-gated thermal transient thermometry.

# WORK PACKAGES

Since the materials selection criteria rely on numerous factors (size and toxicity of the NPs, its brightness and q values, the light- and magnetic field-to-heat conversion efficiency, etc.) the feedback between the WPs dealing with 2D thermal imaging applications (WP5, 6) will be provided by the materials (WP1), characterisation (WP2), modelling (WP3) and functionalization (WP4) WPs to select the best candidate materials for in vitro and in vivo studies. Moreover, the frequency and content of the intra- and inter-WPs coordination/monitoring meetings between consortium members will be varied following the "flexible response" principle throughout the development of the project (monitored by WP7 - Management).



# COMMITTEES

## STEERING COMMITTEE

Luis D. Carlos	Coordinator
Miroslav Dramičanin	(WP1)
Artur Bednarkiewicz	(WP2)
Andries Meijerink	(WP3)
Florence Gazeau	(WP4)
Angel Millán	(WP5)
Daniel Jaque	(WP6)
Rute Ferreira André	(WP7)

## EXPLOITATION COMMITTEE

UATEC (UAVR)  
IRYCIS business development office  
NIT  
BIOSPACE

## EXTERNAL ADVISORY BOARD

### **Giovanni Migliaccio**

Scientific director of EATRIS, the European infrastructure for translational medicine



### **John Capobianco**

Concordia University, Canada



### **Xiaogang Liu**

NUS, Singapore







## PARTNERS

### UNIVERSIDADE DE AVEIRO (UAVR), PORTUGAL

CICECO - Aveiro Institute of Materials  
Photonic Hybrids and Nanomaterials Group, Phantom-g  
Luís D. Carlos  
Maria Rute Sá Ferreira  
António Benayas Hernandez  
Carlos D. S. Brites  
Justyna Zeler



Scientific Staff Management  
Eliana Cavaleiro (*project manager*)  
Tatiana Costa

### FUNDACION PARA LA INVESTIGACION BIOMEDICA DEL HOSPITAL UNIVERSITARIO RAMON Y CAJAL (FIBIRYCIS), SPAIN

Fluorescence Imaging Group  
Alfredo Carrato Mena (MD)  
Daniel Jaque  
José Garcia Solé  
Nuria Fernandez  
Laura García-Bermejo



### CENTRE NATIONAL DE LA RECHERCHE SCIENTIFIQUE (CNRS), FRANCE

MSC, UMR CNRS 7057  
Florence Gazeau  
Amanda Silva  
Nathalie Luciani



LCMCP UMR CNRS 7574  
Corinne Chanéac

UTCBS UMR CNRS 8258 Unit  
Cyrille Richard  
Johanne Seguin

IRCP UMR-CNRS 8247 Unit

**AGENCIA ESTATAL CONSEJO SUPERIOR DE INVESTIGACIONES CIENTIFICAS (CSIC), SPAIN**

Instituto de Ciencia de Materiales de Aragón, University of Zaragoza  
Groups M4 and NAP, Department of Multifunctional Materials and Biomaterials  
Angel Millan  
Valeria Grazu



**INSTITUT ZA NUKLEARNE NAUKE VINCA (VINCA), SERBIA**

Department of Radiation Chemistry and Physics  
Optical Materials & Spectroscopy Group, Vinca Institute of Nuclear Sciences, University of Belgrade  
Miroslav Dramićanin  
Dragana Jovanović



Institut za nuklearne nauke Vinča

**INSTYTUT NISKICH TEMPERATUR I BADAN STRUKTURALNYCH IM. WLODZIMIERZA TRZEBIATOWSKIEGO POLSKIEJ AKADEMII NAUK (WPAS), POLAND**

Excited State Spectroscopy  
Artur Bednarkiewicz  
Lukasz Marciniak



**UNIVERSITEIT UTRECHT (UU), THE NETHERLANDS**

Condensed Matter and Interfaces Group  
Andries Meijerink



Universiteit Utrecht

**NANOIMMUNOTECH SL (NIT), SPAIN**

Christian Sánchez Espinel  
Daniel Pérez Estévez  
Amanda Gallego Suárez  
Tamara Lozano Fernández



**BIOSPACE LAB SA (BIOSPACE LAB), FRANCE**

Nicolas Carvou  
Lise Laumonier  
Rémi Laumonier  
Anikitos Garofalakis



## COORDINATOR

**LUÍS DIAS CARLOS**

Luís António Dias Carlos got his Ph.D. in physics from the University of Évora, Portugal, in 1995 working on photoluminescence of polymer electrolytes incorporating lanthanide salts. Currently, he is Full Professor in the Department of Physics at the University of Aveiro and vice-director of the CICECO-Aveiro Institute of Materials (Portugal). He is member of the Lisbon Academy of Sciences and of the Brazilian Academy of Sciences. His current research interests include luminescent nanothermometers, luminescent solar concentrators, organic-inorganic hybrids for green photonics (solid-state lighting and integrated optics), and luminescent/magnetic nanoparticles, as new probes for multimodal imaging. He has published around 420 papers and 4 international patents, which have received ca. 14850 citations (Hirsch' index h of 61), and co-guest editor of a RSC book on Nanoscale Thermometry (Nanoscience & Nanotechnology series) and special issues of the Journal of Sol-Gel Science and Technology (2010) and of the Journal of Luminescence (2015 and 2018). He is editor of Physica B – Condensed Matter, speciality chief editor of Frontiers in Chemistry (Inorganic Chemistry), associate editor of the Journal of Luminescence and member of the editorial board of the Journal of Coordination Chemistry, Journal of Sol-Gel Science and Technology and Journal of Rare Earths.



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## WORK PACKAGES LEADERS

### MIROSLAV DRAMIĆANIN WP1

Miroslav Dramićanin is research Professor at Vinča Institute of Nuclear Sciences and Full Professor at Faculty of Physics, University of Belgrade, Serbia. He obtained his PhD in Engineering Physics at University of Belgrade in 1998, working on the analysis of nonlinear effects in photoacoustic spectroscopy. Since 2006, he is the Head of Laboratory for Radiation Physics and Chemistry, Vinča Institute of Nuclear Sciences, University of Belgrade. He has published 1 book (Luminescence Thermometry: Methods, Materials, and Applications, Woodhead Publishing; ISBN: 9780081020296), 9 book chapters, and more than 230 papers in international journals which have been cited for about 5000 times (according to Google Scholar). He acts as an associate editor of the Optical Materials journal and is one chairpersons of the International Conference on the Physics of Optical Materials and Devices (ICOM) – [www.icomonline.org](http://www.icomonline.org). He is an adjunct senior scientist in the Houston Center for Biomaterials and Biomimetics at The University of Texas, Houston, USA, and Distinguished Foreign Professor of the Physics and Materials Science and Engineering Subjects at the School of Science, Chongqing University of Posts and Telecommunications (CQUPT), PR China. He is member of the Steering Committee of the Association of Italian and Serbian Scientists and Scholars - [www.ais3.rs](http://www.ais3.rs) and member of the National Board for Physics of the Republic of Serbia. His participation and management experience includes coordinating of 8 Serbian national projects and 17 international (IAEA and European) projects. He has mentorship in 11 doctoral dissertations and trainings of young researchers.

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### ARTUR BEDNARKIEWICZ WP2

Professor Artur Bednarkiewicz received his PhD and habilitation in physics from the Institute of Low Temperature and Structure Research, Polish Academy of Sciences, in 2003 and 2013 respectively. After 4 year lasting postdoctoral research in the European Commission Joint Research Centre, Italy, he returned to ILT&SR PAS in December 2008 and simultaneously established an interdisciplinary team NAOMIS with the Wrocław Research Centre EIT+ focusing on Nanoparticle Assisted Molecular Imaging and Sensing (NAOMIS). Together with prof. Lukasz Marciniak, they established also one another research group and lab, i.e. Luminescent nanoparticle Assisted Sensing and Imaging (LuNASI) Group, dedicated for luminescence thermometry/optical heating topic.

His current interdisciplinary research focuses on optical (bio)spectroscopy, novel designs of lanthanide doped nanoparticles and quantum dot biolabels, optical and spatial light modulation engineering, as well as on pure physics, spectroscopy and chemistry of lanthanide doped materials. Since 2015 he is an associated professor at Institute of Low Temperature and Structure Research, PAS, Poland. He is a co-author of over 90 publications (H-index =22, cited>1300, sum IF>150), he is an author of 4 patents and 3 patents applications. In the course of his research he has received numerous prizes (stipends from Ministry of Education, FNP Starting grant, Brussels Eureca). He has a broad experience as researcher (3 research grants as PI), scientific reviewer and grant evaluator, scientific supervisor of M.Sc. and PhDs students, entrepreneur. Since 2014, he is also a member of Young Academy of Science, where he is engaged in widening European participation of new EU member countries. He is also Polish representative and active participant and collaborator of COST CM1403 European Upconversion Network.

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### ANDRIES MEIJERINK WP3

Andries Meijerink received his MSc and PhD degree in Chemistry at Utrecht University. After a post-doc in Madison (University of Wisconsin) he returned to Utrecht in 1991. In 1996, at the age of 32, he was appointed at the chair of Solid State Chemistry in the Debye Institute of Utrecht University where he leads an active group in the field of luminescence spectroscopy of quantum dots and lanthanide ions.

In the field of lanthanide ions his work involves fundamental research on the energy level structure of both 4f<sub>n</sub> and 4f<sub>n</sub>-15d states and finding new concepts related to applications in solar cells, LEDs and scintillators. His research on quantum dots is aimed at unraveling the influence of quantum confinement and surface effects on the electronic structure and exciton dynamics of quantum dots through optical spectroscopy and using the quantum dots as labels in bio-imaging. Research on luminescence of doped nanocrystals integrates the two themes. Recent work has resulted in a better fundamental understanding of photonic effects on optical processes, insight in energy transfer processes and application of luminescent nanocrystals as temperature probes. The work has resulted in over 350 publications and 10 patents and is highly cited. For his research Andries Meijerink received

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Dr. Florence Gazeau, senior CNRS researcher, deputy director of MSC lab, 48 years old, obtained her Ph.D. in solid state physics in 1997, focusing on the magnetic and hydrodynamic properties of ferrofluids. She joined the CNRS as a staff scientist in 1998, when she broadened her research on biomedical applications of magnetic nanoparticles. Her current research interests focus on the physics of nanomagnetism applied to nanomedicine, cell-nanoparticles interactions, cellular MRI, nanoparticles-mediated magnetic hyperthermia and photothermia for cancer therapy, mechanobiology of cancer, magnetic targeting, nanoparticles behavior, biodegradation and long term in vivo fate and nanotoxicology applied to metallic nanoparticles and carbon nanostructures, extracellular vesicles as drug delivery system and mediators for regenerative medicine. She is participating to the NOCANTHER H2020 project applying magnetic hyperthermia as adjuvant therapy for pancreatic cancer. She was animator of the group Nanomedicine at the French observatoire de micro and nanotechnology. She is author of more than 140 publications, 5 patents, 8000+ citations with an H-index of 46.

MSC (Matière et Systèmes Complexes) is a joint laboratory from CNRS and University Paris Diderot, dedicated to physics of soft matter, turbulence, nanomaterials and living systems. The interdisciplinary Biother team (<http://biother.net/>) has internationally renowned expertise in nanomedicine and biophysics, particularly nanotechnology and nanomagnetism applied to cancer therapy, drug delivery and regenerative medicine in collaboration with clinician groups. In the NanoTBTech, MSC will provide expertise in thermal therapy using nanoparticle-mediated hyperthermia under optical or magnetic remote excitation, in the follow-up of cancer microenvironment and in the molecular and physical mechanisms leading to cell death. MSC will also provide expertise in evaluating the nanoparticle/cell interactions, toxicology and long term fate of the nanoparticles in the body.


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#### CORINNE CHANÉAC

WP4

Corinne Chanéac is full professor at Sorbonne University (Paris, France) in Chemistry department since 2009. She received her PhD degree in Materials Chemistry on magnetic nanoparticles at University Pierre and Marie Curie in 1996. Currently, she is working in the Laboratory Chimie de la Matière Condensée de Paris (LCMCP) as senior scientist at the head of Functional nanomaterials design group. LCMCP has been a pioneer in the field of sol-gel processes. Her research focusses the synthesis of original nanomaterials, based on oxides (metallic and hybrid organic-inorganic). She develops some strategies based on her knowledge of nucleation and growth steps to controlled chemical composition, crystalline structure, morphology and size of nanoparticles. She also works on the design of nanostructures and nanocomposites evolving surface functionalization of particles. Since 2004, she strongly involved in development of persistent luminescent nanoparticles (NPs) as optical imaging nanoprobes and nanothermometers. She has published more than 120 papers (> 5000 citations, h index = 39 Google Scholar) and 6 international patents. Invested in the networking in Nanosciences and nanotechnology, she is director of the Steering Committee of the Centre of Competences in NanoSciences, C'Nano, a national network for nanoscience emergence. This centre was created in 2007 by the CNRS to federate research in nanoscience and to lead an interdisciplinary scientific community.


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Dr Angel Millán got his Ph.D. in chemistry in 1990 on the "theoretical and analytical aspects of Calcium Oxalate Urolithiasis". His research experience comprises stays in: University of Balearic Islands (5 years), University College London (2 months), Institute of Inorganic Chemistry of Czechoslovakia (4 months), University of Nijmegen (4 years), IMP-CNRS Perpignan (1 year), and from 1996 in the ICMA-CSIC/University of Zaragoza, where he is actually a tenure researcher. His research activities have spread over a variety of fields: urolithiasis, crystal growth, photographic emulsions, solid-gas reactions, thin films, semiconductor and superconductor materials, molecular magnets, magnetic nanoparticles, etc. Actually, his main research interests are synthesis, characterization and performance of multifunctional nanoplatforms for therapy. He has published 93 papers (3000 citations, h=24), 6 book chapters, 3 international patents, and 4 Spanish patents. His management experience includes coordinating 3 Spanish national projects and 8 international projects. He has also participated in 32 national and International Research Projects as co-investigator.


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Daniel Jaque (PhD in Physics, '99) is currently Associate (tenured) Professor in the Department of Material Physics at Autonomous University of Madrid (UAM, acronym in Spanish), co-director of the Fluorescence Imaging Group FIG at UAM, and Director of the Nanobiology Group at "Ramón y Cajal" Health Research Institute (IRICYS). Nowadays, his main research focus lies in multimodal in vivo imaging and sensing bioapplications of hyperspectral microscopy. He has published around 350 peer-reviewed papers in international journals (>10.900 citations, h-index=51, Google Scholar, Oct. 2018) and 2 patents. He presented over 35 plenary and invited lectures at international conferences, (over 130 communications of all kinds accepted in international forums). Prof. Jaque is a recognized pioneer and worldwide renowned authority in the field of luminescent nanothermometry, especially regarding biomedical implementation of this fast-growing research field.

He has been Associate Editor of Optics Express and he just recently ended his tenure as Associate editor of Optical Materials. He is co-author of the teaching book entitled "An introduction to the Optical Spectroscopy of Inorganic Solids" (Wiley 2005). Prof. Daniel Jaque was awarded with the European Association for the Study of Rare Earths and Actinides Young Researcher Prize in 2006. Since 2011, he is a correspondent member of the International Conference of Luminescence Committee. His management experience includes coordinating 13 national Spanish research projects and participating in 3 European projects and networks. He also acted during two years as vice-dean of the Faculty of Sciences of UAM.


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Alfredo Carrato is Professor of Medical Oncology at Alcalá University and Director of the Medical Oncology Department at Ramon y Cajal University Hospital in Madrid, Spain. He is presently serving as Director of the Ramon y Cajal Institute for Health Research IRYCIS.

He was President of the National Advisory Commission of Medical Oncology at the Spanish Ministries of Health and Education from 2003 until November 2014, and was the past President of the Spanish Society of Cancer Research (ASEICA) and the Spanish Federation of Oncologic Societies (FESEO), from January 2013 until 2015. He was President of the Spanish Society of Medical Oncology (SEOM) from 2005 to 2007.

Dr Carrato is involved in translational research projects, including the molecular epidemiology and biology of solid tumors such as pancreatic and urothelial cancer. His clinical research mainly focuses on digestive tract cancer. Since 1992, he is member of the executive committee of the Spanish Cooperative Group for the Treatment of Digestive Tumors (TTD).

Dr Carrato has served as a member of the editorial board for several international journals (Journal of Clinical Oncology, among others), as a reviewer for national and international research projects, and has contributed to more than 250 publications in peer-reviewed journals, 80 chapters in medical books and 500 abstracts at medical congresses. He is also an active member of the European Society of Medical Oncology (ESMO), the American Society of Clinical Oncology (ASCO) and the European Association for Cancer Research (EACR).


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### RUTE ANDRÉ

WP7

Rute AS Ferreira (born 1974) got her Ph.D. in Physics from the University of Aveiro, Portugal, in 2002 and the Agregação in Physics in 2012, from University of Aveiro. Currently, she is an Associated Professor at Department of Physics (University of Aveiro), coordinates the research Line "Information and Communication technology" of CICECO – Aveiro Institute of materials and she is member of the Scientific Council for Exact Sciences and Engineering of the Portuguese Science Foundation (FCT).

She has published over 310 SCI papers and 5 book chapters, with ca. 8,800 citations (h-index 46). She has supervised 7 post-doctoral associates, 9 Ph.D., 18 M.Sc. and 20 undergraduate students.

Her scientific interests include are focused on the optoelectronic studies on sol-gel derived organic/inorganic hybrids without metal activator centres and doped with lanthanide ions, processed as bulk and nanostructured monoliths and thin films and to crystalline and amorphous nanoparticles of semiconductors. She has hands-on experience on the optical (photoluminescence in steady-state, time resolved modes, and quantum yield, as well as UV/Vis/NIR spectroscopy) and structural (XRD, SAXS, NMR, Raman, and Fourier-transform infrared spectroscopies) characterization of these materials. She has also expertise on the characterization of waveguiding performance of organic-inorganic hybrids and on spectroscopic ellipsometry, including optimization of modelling algorithms. Her research aims at the interpretation of the photophysical behaviour of these materials that is determined by synthesis and processing, foreseeing applications in the fields of optoelectronics and photonics (solid-state lighting, integrated optics and sensing) and photovoltaics (luminescent solar concentrators and down-shifting layers).


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### NANOTBTECH KICK-OFF MEETING

September 2018

NanoTBTech's kick-off meeting was held in University of Aveiro on September 24<sup>th</sup>, 2018.

From bottom to the top: Eliana Cavaleiro (UAVR), Tatiana Costa (UAVR), Nuria Fernandez (UAM), Laura Bermejo (IRYCIS), Rute Ferreira (UAVR), Amanda Suarez (NIT), José Garcia Solé (UAM), Zeljka Antic (VINCA), Bruno Viana (CNRS), Vesna Djordjevic (VINCA), Florence Gazeau (CNRS), Lise Laumonier (BIOSPACE), Corine Chanéac (CNRS), Artur Bednarkiewicz (WPAS), Luis Carlos Santos (UAVR), Daniel Estévez (NIT), Carlos Justyna Zelar (UAVR), Antonio Benayas (UAVR), Anikitos Garofalakis (BIOSPACE), Angel Millan (CSIC)

### NANOTBTECH LOGO

October 2018

NanoTBTech's logo.



### NANOTBTECH WEBSITE LAUNCHED

October 2018

NanoTBTech's website was launched. Twitter and linked-in accounts are also activated.



## MEETINGS

Under construction

## CONTACT

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