**Thursday 18 - Friday 26 of October 2012 |**

**University of Angers |**

# 1st NanoFar Autumn School

## NanoFar

**European Doctorate in nanomedicine and pharmaceutical innovation**

**Associate partners**

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Atlanpôle Biotherapies
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NanoFar

European Doctorate
in nanomedicine and
pharmaceutical innovation

# 1st NanoFar Autumn School

## October 22-26, 2012 |
## University of Angers, School of Medicine

# Program

| **Monday, 22 October 2012** | | |
|---|---|---|
| **Time** | **Item** | **Speaker** |
| **08:30 - 10:00** | Welcome and opening ceremony | |
| **10:30 - 12:00** | Formulation, Challenges and Opportunities in Nanomedicine | Prof. Jean-Pierre Benoît |
| **12:00 - 14:00** | **LUNCH BREAK** | |
| **14:00 - 15:30** | Development of bopolymer-based matrices for controlled release of molecules with high toxicity | Prof. Guillermo Castro |
| **16:00 - 17:30** | Surface modification and self-assembly of cellulose nanoparticles | Dr Ir. Wim Thielemans |
| **Tuesday, 23 October 2012** | | |
| **Time** | **Item** | **Speaker** |
| **08:30 - 10:00** | Nanoparticle Delivery systems for Site Specific Delivery | Dr Martin Garnett |
| **10:30 - 12:00** | Imaging biological systems by mass spectrometry | Prof. Edwin De Pauw |
| **12:00 - 14:00** | **LUNCH BREAK** | |
| **14:00 - 15:30** | Responsive polymers-applications in controlled and site-specific drug delivery | Prof. Cameron Alexander |
| **16:00 - 17:30** | Pulmonary delivery of nanomedicines | Prof. Rita Vanbever |
| **Wednesday, 24 October 2012** | | |
| **Time** | **Item** | **Speaker** |
| **08:30 - 10:00** | Challenges in Cell delivery | Prof. Kevin Shakesheff |
| **10:30 - 12:00** | Nano medicines, an essential component of tissue engineering strategies | Anne des Rieux |
| **12:00 - 14:00** | **LUNCH BREAK** | |
| **14:00 - 15:30** | Polymeric nanostructures for nasal drug delivery | Prof. Noemi Csaba |
| **16:00 - 17:30** | Engineering proteins for targeted DDS | Prof. Moreno Galleni |

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| Tuesday, 25 October 2012 | | |
|---|---|---|
| **Time** | **Item** | **Speaker** |
| **08:30 - 10:00** | PEG-dendritic block copolymers for biomedical applications | Prof. Eduardo Fernandez-Megia |
| **10:30 - 12:00** | Nanomedicine for gene delivery | Prof. Bruno Pitard |
| **12:00 - 14:00** | **LUNCH BREAK** | |
| **14:00 - 15:30** | Development and applications of radiopharmaceuticals | Prof. Jacques Barbet |
| **16:00 - 17:30** | Targeted radiotherapy: recent advances | Dr François Hindré |
| **Friday, 26 October 2012** | | |
| **Time** | **Item** | **Speaker** |
| **08:30 - 10:00** | Presentation of thesis projects by the NanoFar PhD students - | |
| **10:30 - 12:00** | Presentation of thesis projects by the NanoFar PhD students - Result of the poster exhibition | |
| **12:00 - 14:00** | **LUNCH BREAK** | |
| **Afternoon** | Facultative visit | |

## Details:

| | |
|---|---|
| Place | University of Angers, France<br>Health Campus - School of Medecine<br>rue Haute de Reculée- 49000 Angers |
| Rooms | On Monday morning: **Amphi 200**<br>From Monday afternoon to Friday: **rooms ED7 and ED9** |
| Nearest tram station | Capucins |

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# Prof. Jean-Pierre Benoît
# (Université d'Angers – INSERM U 1066)

## Position

Unit director

## Research interests

His research, at the frontiers of physical chemistry, pharmaceutical technology, and biology, concerns both the development of new encapsulation methods for active ingredients without recourse to organic solvents, and drug targeting in tumours, particularly in the brain and the lungs.

## Biography

**QUALIFICATIONS**

- Master thesis, Macromolecular Organic Chemistry, with distinction, University of Le Mans, 1979.
- PhD in Pharmacy, with distinction, University of Paris-Sud, 1983.
  (Title: 'Preparation and characterisation of biodegradable microspheres for chemo-embolisation' Co-ordinator: Pr F. Puisieux).
- Accreditation to supervise research, University of Paris-Sud, 1987.

**PRIZES**

- 1993: Prize of the Baxter Dubernard Hospital Foundation for Research and Innovation in Hospital Pharmacy. *(Intracerebral implantation of microspheres containing anticancer drugs. New local drug delivery systems).*
- 1994: AAPS Fellow *(American Association of Pharmaceutical Scientists)*
- 2002: INPI Trophy for innovation *(regional prizewinner)*
- 2004: Award of the European Journal of Pharmaceutics and Biopharmaceutics for the best research paper in 2003
- 2010 : Lauréat du Concours National de la Création des Jeunes Entreprises Innovantes (projet Carlina)
- 2010 : FIP (Fédération Internationale de la Pharmacie) – PSWC Research Achievement Award (Pharmaceutical Sciences World Congress)
- 2011 : Prize of Notoriety from the French National Academy of Pharmacy

**ACADEMIC FUNCTIONS**

- Assistant professor, Pharmaceutical Technology: University of Paris-Sud. *1982-1988.*
- Professor, Pharmaceutical Technology: University of Angers. *1988- present*
- Director of INSERM U 646: University of Angers. *2001-present*

## Title and summary of the course

**Formulation, Challenges and Opportunities in Nanomedicine**

## Prof. Guillermo Raul Castro
## (Universidad Nacional de La Plata - CONICET)

**Position** Professor - Principal Investigator

### Research interests

Drug delivery using natural and chemically-enzymatically modified biopolymers

### Biography

MSc & PhD degrees from School of Sciences, University of Buenos Aires, Argentina.

Postodc studies at Dept. Chem., Massachusetts Institute of Technology (USA, 1996- 98), and later at Dept of Biomedical Eng., Tufts University (2000-2), later incorporated as Research Associate (2003-5) , and Adjunct Prof. (2006-11) of the same University. Present positions: Adjunct Prof. at School of Sciences, Universidad Nacional de La Plata (Argentina), and Principal Investigator from the National Research Council for Science and Technology (CONICET, Argentina).

He is the Director of Nanobiotechnology Lab. at CINDEFI (UNLP-CONICET). He has more than 180 scientific presentations in scientific meetings and conferences including more than 70 peer-reviewed international publications.

### Title and summary of the course

**Development of bopolymer-based matrices for controlled release of molecules with high toxiciy**

The aim of my lectures is to show novel strategies for the development of biopolymer matrix gels, films and microspheres, for control release. The strategies include studies on coacervates, blends, coating and emulsification procedures, to provide appropriate support for the cargo molecules. Interactions of the cargo molecule with the matrix by spectroscopies, microscopies and rheology techniques will be analyzed. Effect of environmental and kinetic parameters, matrix stabilities will be considered.

## Dr. Ir. Wim Thielemans
## (University of Nottingham)

**Position** Lecturer in Chemistry and Chemical Engineering

### Research interests

Renewable materials based on cellulose, starch, lignin and chitin. Surface modification and self-assembly of polysaccharide nanoparticles for use in drug delivery, supercapacitors, water treatment, electrochemical (bio)sensors, and electronic materials.

### Biography

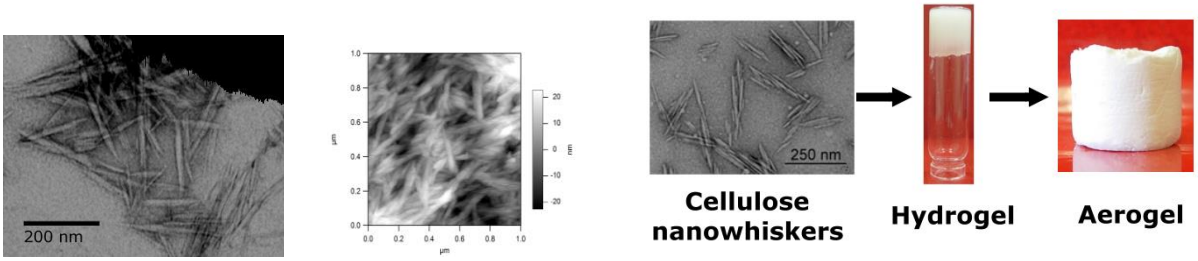
Dr. Ir. Wim Thielemans is leader of a 10 member team centred on the development of materials from renewable resources, and in particular the surface modification of self-assembly of polysaccharide nanoparticles.
He obtained is PhD in 2004 from the University of Delaware (USA) and was a Marie Curie research fellow at the National Polytechnic Institute of Grenoble (France). Wim is a member of the Royal Society of Chemistry and sits on the scientific advisory board of the journal Industrial Crops and Products (Elsevier).
He has over 50 publications and 1 patent. In 2007, he won the Silver Award for his research in 2007 at the UK House of Commons Set for Britain event, and in 2008, received the Green Chemistry Prize for Innovative Science at the Gordon Research Conference for Green Chemistry. In 2011 he held a Science Communication Fellowship from Advancing Green Chemistry and Environmental Health Sciences to interact with the media to prepare scientifically accurate articles which were also inderstandable by the general public.
He is currently also involved in a current drive to develop a general platform for toxicological and endocrinological testing of new chemicals which are proposed to replace existing and proven endocrine disruptors or toxins.

### Title and summary of the course

**Surface modification and self-assembly of cellulose nanoparticles**

Humanity is under increased pressure to reduce energy consumption, reduce waste disposal and increase the use of renewable materials. The development of functional nanomaterials based renewable resources has the potential to deliver a holistic solution by increasing activity, reducing the use of depletable resources, reduction in $CO_2$ emissions, and reducing the waste at end-of-life. In our group we are developing a renewable nanoparticle technology platform based on cellulose nanowhiskers, rigid-rodlike single-crystal nanoparticles derived from native cellulose. We investigate a range of surface functionalisation pathways such as introduction of ionic groups and pH-sensitive fluorophores as well as surface-initiated polymerisation, and metal nanoparticle immobilisation. In addition, we also study their self-assembly into higher order structures such as membranes, hydrogels and aerogels. The combination of virtually unlimited surface functionality which can be introduced with our expertise in nanoparticle self-assembly enables the design and manufacture of highly functional structures with applications in for example separations, ad/absorption materials, and catalysis.

During this course I will focus on medical applications of our work such as drug delivery, biofilm destruction, biosensor development and toxiology of nanoparticles.



# Dr. Martin Garnett
# (University of Nottingham)

**Position** Associate Professor

## Research interests

Drug delivery using polymer nanoparticles for small molecule drugs, proteins and nucleic acids. Development of new polymers, physicochemical and biological characterisation of nanoparticles. Development of 3-D cell models to investigate uptake and transport of nanoparticles.

## Biography

Dr Martin Garnett obtained his BSc in biochemistry and 1974 and was awarded his Ph.D based on studies on oxygen toxicity in 1981. Martin then spent 10 years at Nottingham University developing antibody drug conjugates before joining the School of Pharmacy at Nottingham in 1991. Martin is currently an associate Professor in Drug Delivery and teaches on a number of modules involved with biopharmaceutics and advanced drug delivery. Martin's research involves a broad portfolio of drug delivery work based on two different polymers. The first involves the novel biodegradable polymers based on poly(glycerol adipate) for drug delivery applications and the second the development of nucleic acid delivery systems using linear poly(amidoamines).

Linear poly(glycerol adipate) was developed as a new polymer for matrix nanoparticles for drug delivery. Work on PGA nanoparticles has included physicochemical investigation on the incorporation and release of a variety of drug molecules and the relationship between these parameters and the physicochemical properties of the polymers. Extensive work has also been carried out on the uptake of these particles into cells and their metabolism within cells including use of organotypic 3-D cell culture systems. Using an in vitro 3-D co-culture system, nanoparticles made from PGA have been shown to be taken up selectively by cancer cells. The application of these polymer nanoparticles are currently being investigated in a variety of diseases including viral disease, cancer, and osteoarthritis.

The nucleic acid delivery work has involved collaboration with Prof Paolo Ferruti from Milan providing novel linear polyamidoamines and PEG polyamidoamine copolymers for this work. New methodology has been developed to produce well defined PEGylated polyplexes and to assess and characterise them. Novel polyamidoamine derivatives were also developed to stabilize these particles by a reversible cross-linking reaction. These polyplexes are currently being developed for applications involving both DNA and SiRNA.

## Title and summary of the course

**Nanoparticle Delivery systems for Site Specific Delivery**

This lecture will focus on many of the physiological aspects of how nanosized medical formulations are handled by the body. In particular it will emphasize the need to understand the anatomy and relevant physiological processes in the body. This will give a basic understanding on what is possible with nanosized delivery systems and also highlight how various of these mechanisms can be exploited to achieve site specific delivery with whatever delivery system you are working on.

The difference between passive accumulation and active targeting will be defined and the barriers which can prevent site specific accumulation will be discussed. The importance of size of nanoparticles will be explained with a brief reference to the different types of nanosized formulations available. The role of macrophages and the immune system of the body will be outlined together with their role of eliminating circulating particulates, the mechanisms by which this occurs and how this can be avoided.

The limitations on how nanoparticles circulating in the body can exit blood to reach tissues will be covered. Also the way that certain pathology can affect the physiological barriers and an explanation of the enhanced permeability and retention effect. The pathways for accumulation of nanoparticles within cells by the various vesicular intracellular pathways will be briefly outlined and the role that biological ligands can play, will be explained. The evidence for accumulation of nanoparticles in various normal tissues within the body will be reviewed.

The principles discussed in this lectures will be illustrated from studies carried out both in studies on nanoparticulates at Nottingham and also examples of site specific delivery using nanoparticles from the scientific literature.

## Prof. Edwin De Pauw
## (Université de Liège)

**Position** Director of the Laboratory of Mass Spectrometry,
Chairman of the department of chemistry

## Research interests

**Research activities: at the interface between chemistry, physics and biology**

*Molecular biophysical Chemistry and Bioanalytical Chemistry*

Mass spectrometry Imaging
Kinetics and energetics of ion emission from condensed phases (ESI, MALDI)
Molecular dynamics of complex ions in the gas phase
Molecular recognition and non covalent interactions
Methods development and applications of proteomics in analytical chemistry
*New strategies for trace analysis*

*Applied research*

Development of analytical methods for food security and epidemiology
Development of intelligent nano-materials for biomedical applications
Development oh high throughput screening methods in venoms analysis (FP7)

**Current granted international projects**

WP leader proteomics, FP7 project VENOMICS
Member of COST actions

| | |
|---|---|
| COST FA1002 | Farm animl proteomics |
| COST BM 1104 | Mass Spectrometry Imaging |
| COST TD1003 | Bioinspired nanotech |
| COST MP1001 \| IOTA | Ion Traps for tomorrow's Applications |

## Biography

**Current position**

- Research assistant Liege University: 1974-1985
- Post-doctoral fellowship Alexander von Humblodt fellowship, Bonn University: 1982/83
- Permanent Research Scientist Liege University 1986
- Group leader (on mission from Liege University), European Union JRC Environment Institute 1988-1990 Ispra, Italy
- Administrator, European union, DGXIII: research valorization 1990-1991
- Associate professor 1994
- Full Professor (Professeur ordinaire), chair of Physical Chemistry, January 2003
- Vice President of the chemistry department October 2005
- President of the Chemistry Department (October 2007….)
- Member of the research council, ULg, 2006-2009
- Member of the Science and Techniques research council, ULg 2010-…
- Member of the University Research council, ULg, 2010…
- President of the Science and Techniques research council ULg (January 2011-)

**Publications (more than 200)**

See list at the official ULg site: http://orbi.ulg.ac.be/

**Web site**

www.giga.ulg.ac.be/jcms/prod_183306/laboratoire-de-spectrometrie-de-masse

## Title of the course

**Contribution of mass spectrometry imaging in the elaboration of new drugs and delivery systems**

# Prof. Cameron Alexander
# (University of Nottingham)

**Position** EPSRC Leadership Fellow & Professor of Polymer Therapeutics

## Research interests

Polymer therapeutics, responsive materials and advanced drug, gene and cell delivery systems.

## Biography

Cameron Alexander is Professor of Polymer Therapeutics and Head of the Division of Drug Delivery and Tissue Engineering in the School of Pharmacy at the University of Nottingham. He was awarded BSc and PhD degrees in Chemistry at the University of Durham, UK and conducted post-doctoral work at the Melville Laboratory for Polymer Synthesis, University of Cambridge. He is a Fellow of the Royal Society of Chemistry, a member of the editorial board of the new RSC journal Biomaterials Science, and has published more than 120 refereed articles. Research centres on responsive/'smart' materials, drug, gene and cell delivery, and developing materials for synthetic biology. Professor Alexander was awarded a five-year EPSRC Leadership Fellowship in 2009 for research in the area of personalised medicines.

## Title of the course

**Bioresponsive drug delivery systems**

# Prof. Rita Vanbever
# (Université catholique de Louvain)

**Position** FNRS Senior Research, Professor

## Research interests

Pulmonary delivery of nanomedicines for the treatment of severe lung diseases

## Biography

Rita Vanbever is Professor at the Louvain Drug Research Institute of the Université catholique de Louvain (UCL), Brussels, Belgium. She received a Pharmacist Degree in 1992 and a Ph.D. in Pharmaceutical Sciences in 1997, both from UCL. From 1997 to 1998, she was a Fulbright post-doctoral fellow at the Massachusetts Institute of Technology in Boston, USA. Since 1998, she leads research on pulmonary drug delivery at the Louvain Drug Research Institute. In 2001, she was given tenure by the Belgian Fund for Scientific Research. She has co-authored more than 50 publications and is co-inventor in 8 patent applications. She lectures on Pharmaceutical Technology at UCL

## Title of the course

**Pulmonary delivery of nanomedicines**

## Prof. Anne Des Rieux
## (Université catholique de Louvain)

**Position** FNRS Senior Research

### Research interests

The research aims at developing 3D implants (hydrogels, polymeric scaffolds) delivering growth factors, gene therapy, drugs and/or cells that provide sustained delivery factors, support survival, infiltration and proliferation of cells for tissue engineering applications, in particular spinal cord injury.

### Biography

Anne des Rieux performed her PhD at the Louvain Drug Research Institute between 2002 and 2006. She studied M cells as a useful tool to study nanoparticle transport across the intestinal epithelium and developed and in vitro model of human M cells. She performed her post-doctoral stay as a BAEF fellow at the Northwestern University, Chicago, on spinal cord regeneration. she obtained a “chargée de recherche” position form the FNRS for 4 years and now she is supported by a permanent position of the FNRS. She is leading, within the Pharmaceutics and Drug Delivery Unit, a starting group focused on drug delivery in tissue engineering.

### Title and summary of the course

**Nanomedicines, a essential component of tissue engineering strategies**

The courses will be composed of 3 main parts. The first one will introduce the field of tissue engineering, its requirements and constrains. The second part will deal with the role of nanomedicines in tissue engineering and the third part will be about the use of nanomedicines for tissue engineering applications.

**Dr Noemi Csaba**
**(Universidade de Santiago de Compostela)**

## Position

Assistant professor

## Research interests

- Nanotechnologies applied to biomaterials of pharmaceutical and biomedical interest.
- Design of nanostructures as carriers across biological barriers.
- Design of nanostructures for the targeting of antitumoral drugs.
- Advanced delivery systems for drugs and vaccines.

## Biography

Noemi Csaba has over 10 years of experience in the design of delivery systems for biomacromolecules. She obtained her Ph.D. degree at the University of Santiago de Compostela in the field of nanomedicine and nanotechnology (2005). She worked as a post-doctoral research fellow at the Swiss Federal Institute of Technology (ETH Zurich) at the Department of Chemistry and Applied Biosciences (2005-2007). She currently holds a research and teaching position at the University of Santiago de Compostela at the Department of Pharmaceutical Technology, Nanobiofar Group. Noemi is the author of more than 20 scientific articles published in internationally recognized journals, several book chapters, one national and two international patents and she is the co-editor of the book "Nanostructured biomaterials for overcoming biological barriers" published by the Royal Society of Chemistry (2012). She has also authored more than 30 presentations at international symposia. During the last years she has been participating in a number of national and international research projects on nanotechnology applied to nanomedicine, such as the FP7 projects “Lymphotarg” on targeted cancer therapy and "TransInt" on oral peptide delivery.

## Title of the course

**Polymeric nanostructures for nasal drug delivery**

## Prof. Eduardo Fernandez-Megia
## (Universidade de Santiago de Compostela)

### Position
Professor

### Research interests

The interface between organic and polymer chemistry with emphasis on the preparation of well-defined polymeric nanostructures for biomedical applications and the development of NMR tools for their characterization.

### Biography

Eduardo Fernandez-Megia completed a PhD in Chemistry in 1995 at the University of Santiago de Compostela (USC) under the supervision of Prof. F. J. Sardina. After a postdoctoral stay with Prof. Steven V. Ley at the University of Cambridge (1997-1999), he returned to USC as a Marie Curie Fellow and Prof. Asociado. Thereafter he became a Ramon y Cajal Fellow (2003), and was appointed Prof. Contratado Doctor (2008) and Profesor Titular (2009) at the Department of Organic Chemistry, USC. In 2011 he moved to the Center for Research in Biological Chemistry and Molecular Materials (CIQUS) at the USC.

### Title and summary of the course

**PEG-dendritic block copolymers for biomedical applications**

The incorporation of poly(ethylene glycol) (PEG) chains at the focal point of dendrimers results in customizable platforms where the careful selection of the PEG length, the nature of the peripheral groups, and the structure and generation of the dendritic block entail materials for specific applications in the biomedical field. In this presentation, the synthesis, properties, and biomedical applications of PEG-dendritic block copolymers will be discussed with examples in drug and gene delivery, tissue repair, and diagnosis.

**Dr Oscar Crasson**
**(Université de Liège)**

## Position

Research Associate

## Research interests

Protein Enginnering – carbohydrate binding domain

## Title and summary of the course

**Engineering proteins for targeted DDS**

Since 2000, our laboratory developed a new strategy based on the insertion of protein motif into a carrier protein. We used two different protein scaffolds: the class A beta-lactamase BlaP produced by *Bacillus licheniformis* and the inactivated form of the α-hemolysin ICHA from *Staphylococcus aureus*. The advantages of the two scaffolds are that they are easily produced and purified as soluble proteins. In addition, they exhibit a high stability towards proteolysis.

Our approach was divided in three aims:

- Firstly, we characterized the position of permissive sites in both proteins by molecular modeling and random mutagenesis.
- Secondly, we investigate the use of BlaP as reporter system. In that case, we inserted a chitin binding domain (ChBD) into BlaP. We could show that the corresponding hybrid protein conserved the properties of both domains. In addition, this protein can be used as tools to study and characterize the interaction between ChBD and different carbohydrates.
- Thirdly, ICHA was used as carrier of polyepitopes. We evaluated the use of this carrier in the development of new recombinant vaccines against *S. aureus*.

**Dr Bruno Pitard**
**(Université de Nantes)**

## Position

Research director

## Research interests

Physico chemistry of synthetic vectors. Gene Transfer. Macromolecular drugs delivery.

## Biography

Bruno Pitard, Physicochemist, graduated from the University of Paris in 1991.

He is Director of Research CNRS (Nantes, France). He started his carrer in 1995 at Rhône-Poulenc Rorer (currently Sanofi-Aventis). Then, he worked at Sanofi Pasteur for the DNA vaccine program. Bruno Pitard has a long history of successful research that has led to the identification of breakthrough technologies to delivery nucleic acids molecules including DNA and siRNA, in cells either in vitro but most importantly in vivo after local or systemic administrations. These new classes of synthetic vectors are very promising and allow today to consider their future application in human.

The team of Bruno Pitard is also pursuing highly promising projects in the field of DNA-based therapeutic and prophylactic vaccines, with successful studies in animal models of cancers and infectious diseases. With on-going R&D programmes in the fields of oncology, as well as cardiovascular and infectious diseases, Bruno Pitard's team also works very actively in the field of development of RNAi therapeutic products for interference with the expression of targeted disease-associated genes. Bruno Pitard is authors of more than 60 publications and 10 patents on nucleic acids and protein formulations.

## Title and summary of the course

**Nanomedicine in gene delivery**

Intramuscular (i.m.) DNA vaccination induces strong cellular immune responses in the mouse, but only at DNA doses that cannot be achieved in humans. Current gene delivery systems either viral or nonviral need to be improved in terms of efficiency and safety. Since antigen expression is weak after naked DNA injection, we recently reported that nanospheres hold promise as non viral vector for DNA vaccination as they are able to enhance DNA vaccination using a galactosidase (Gal) encoding plasmid, pCMBGal, or other plasmids encoding other antigens, as immunogens.

More importantly, nanospheres allowed significant reductions in the dose of antigen encoding plasmid. A single injection of 1 µg pCMVGal with nanospheres gave humoral and ELISPOT responses equivalent to those obtained with 100µg naked DNA, and conferred protection in tumor and prophylactic vaccination models. Considering that naked DNA vaccination failed to induce protection in human clinical trials and that nanospheres-mediated vaccination involves different mechanism while allowing use of low DNA dose, we conclude that nanospheres are highly promising vectors for human DNA vaccination.

# Dr Jacques Barbet
# (Université de Nantes)

## Position

Exceptional class research director

## Research interests

Targeted radionuclide therapy and molecular imaging in oncology. Cyclotron production of radionuclides, preclinical and clinical development of innovative radiopharmaceuticals including antibody-pretargeted peptides and liposomes, pharmacokinetics

## Biography

### CAREER HISTORY

Trained as an engineer at the Ecole Polytechnique in Paris, Jacques Barbet received his PhD degree in organic chemistry from the Paris University in 1978 for his work on bivalent DNA intercalating drugs. He then moved to the Centre d'Immunologie Inserm-CNRS de Marseille-Luminy to work on radioimmunoassay development, antibodies, drug targeting and anti-cancer drug pharmacokinetics. He spent years 1984 and 1985 in John Weinstein's laboratory at NIH to work on antibody-mediated radionuclide delivery. From 1987 to 1997, Jacques Barbet headed the Imaging and Therapeutics department of Immunotech in Marseille that developed the Affinity Enhancement System, a pretargeting approach, which is under development in the clinic for cancer radioimmunotherapy. Since 2001, in the Nantes-Angers Cancer Research Center, he was the leader of a research team that focuses on pretargeted radioimmunotherapy and alpha-immunotherapy.

### PRESENT WORK

Jacques Barbet is, with Jean-François Chatal, Jacques Martino and Yves Thomas, one of the scientists who promoted the installation in Nantes of ARRONAX, a high-energy high-intensity cyclotron dedicated to nuclear medicine and radiochemistry research. ARRONAX has been in operation since October 2010. Since April 2010, Jacques Barbet is the director of ARRONAX.

## Title and summary of the course

### Development and applications of radiopharmaceuticals

Both molecular imaging and targeted radionuclide therapy use radiopharmaceuticals. Molecular imaging is useful in most medical domains, particularly cardiology, neurology and oncology. Obviously targeted radionuclide therapy mostly deal with oncology. Imaging is made possible by using radionuclides emitting gamma rays (scintigraphy) or positrons that decay into a pair of gamma rays upon annihilation. Appropriate cameras (Auger cameras for single photon imaging, PET scanners) allow whole body imaging and tomographic imaging. They are generally coupled to a CT scanner that allows image fusion for improved morphologic localization of activity uptake. Quantification of the activity is possible. For single photon imaging, technetium-99m is the most frequently used radionuclide, but indium-111, iodine-123 and, in cardiology, thallium-201 are among the many radionuclides that can be used. Iodine-131, mostly used in thyroid cancer can be imaged and used to kill thrydoid cancer cells. For PET, fluorine-18 is by far the most often used radionuclide, mostly as $^{18}$F-FDG, but new tracers are being developed. New positron-emitting radionuclides are now considered, such as gallium-68, product of a germanium-68/gallium-68 generator, or copper-64. In cardiac imaging, rubidium-82, product of strontium-82/rubidium-82 generators commercialized in the US, has demonstrated advantages over existing technicium-labeled products and thallium-201. For therapy, electron-emitting radionuclides have been used for years: iodine-131 for thyroid cancer, iodine-131 and yttrium-90 coupled to antibodies for the treatment of B-cell lymphomas. Peptides (somatostatin analogues) and antibodies are also used for therapy labeled with yttrium-90 and lutetium-177. Rhenium-188 and rhenium-186 are other radionuclides of interest for therapy. Their use to label nanocapsules will be described in other sessions. Pairs of radionuclides, one for PET imaging, one for therapy, such as copper-64 and copper-67 or scandium-44 and scandium-47, are also studied because quantitative imaging affords valuable information for dosimetry of therapeutic radiopharmaceuticals. Alpha-emitting radionuclides are also promising for therapeutic applications. Radium-223 targets bones and increase survival in metastatic prostate cancer. Antibodies and peptides are used in preclinical and clinical studies to target bismuth-213 or statine-211. They are proposed to treat residual disseminated disease to kill highly resistant tumor cells.

The first step in designing new radiopharmaceuticals is the selection of appropriate radionuclides, their mode of production, charged particle bombardment in accelerators or neutron activation in nuclear reactors. The physical properties (emission type, energy of emitted particles and half-life) must be matched with the application (imaging or therapy), the nature of targets and the biological properties of the vector. Indeed, if some radionuclides may be used as simple salts, e.g. fluoride for bone PET, iodide for thyroid cancer, rubidium chloride for cardiac imaging, in the vast majority of cases the radionuclide must be attached to a vector. This is the radiolabeling process, which may be applied to small organic molecules, peptides, antibodies or nanoparticles. These vectors may have very fast kinetics in vivo (small molecules, peptides) or very slow kinetics (antibodies).

The development of radiopharmaceuticals thus involves a very multidisciplinary approach, from physics and chemistry, to the clinic. Animal models of the diseases are used to demonstrate efficacy and to predict toxicity. The use of radioactive compounds facilitates pharmacokinetic and biodistribution studies that assess the targeting of the radioactivity, which in turn allows an estimation of target to non target contrast ratios, central for imaging, or the calculation of absorbed irradiation doses to normal and pathologic tissues, central for therapy. Specialized cameras, micro-SPECT and micro-PET, are available to this effect. Clinical studies follow, which are very similar to those of classical drugs, but also involve imaging for both imaging radiopharmaceuticals and therapeutic radiopharmaceuticals.

These aspects will be illustrated by a few examples of recent developments.

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# TRANSPORT IN ANGERS

The best way to move in Angers is to use the tram.

There is one line available in Angers, serving the train station (tram stop ***Les Gares*****,** and the Health Campus (tram stop ***Capucins***).

You can buy tickets at each station, and this is below a complete description of the tram line:


**For more information:** [bustram.irigo.fr](bustram.irigo.fr)

# CONTACT


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European Doctorate
in nanomedicine and
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# 1st NanoFar Autumn School

## October 22-26, 2012 | University of Angers, School of Medicine


For their support on the creation and organization of the NanoFar Erasmus Mundus Doctorate and the first NanoFar Autumn School, we would like to thank

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