CALL FOR APPLICATION

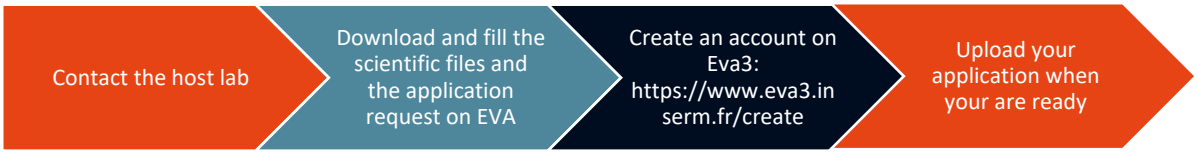
INSERM CHAIR Recruitment

Bioengineering for therapeutics

The Inserm chair recruitments opened to Inserm are intended for researchers with strong potential to manage and lead research teams and participate in national, European or international projects.

This recruitment, based on research and teaching projects, is aimed at researchers with a doctorate or equivalent and a first post-doctoral experience. The position is offered on a fixed-term contract (CDD) with a view to tenure in the Inserm Research Directors personnel at the end of the contract.

Application on EVA: https://eva3-accueil.inserm.fr/sites/eva/chaires/2024/Pages/default.aspx



Supporting institution:	Inserm : Institut national de la Santé et de la recherche médicale
Name of the head of the institution:	Pr. Didier Samuel
Academic region:	Grand ouest - Pays de la Loire
Location/ Site concerned:	Nantes and 3 distinct host laboratories : U1089 or U1229 or U1307
Partner institutions:	Nantes Université, CNRS, Arronax
Research contact: **Administrative contact:**	Omeya ADJALI : oumeya.adjali@inserm.fr Jérôme GUICHEUX : jerome.guicheux@inserm.fr Philippe JUIN : philippe.juin@inserm.fr chaires-professeur-junior@inserm.fr
Research fields EURAXESS :	Medical sciences
Keywords:	biomedical engineering, viral vectors, gene therapy, biomaterials, bioengineering, regenerative medicine, alpha-therapies, internal radiotherapies

Job title to be filled:	Chaire - Bioengineering for therapeutics
Body after tenure:	Research Director
Anticipated duration of the contract:	5 years
Scientific domains/fields:	Biomedical engineering and technology for health

Corresponding specialized scientific commissions (CSS):	CSS7 – Health technologies CSS2 – Cancer, genetic diseases CSS3 – Physiology and pathophysiology of major systems
Project name:	Bioengineering for therapeutics

Remuneration package	3 500€ - 5 000€ according to research experience
Quota	Full Time

Strategy of the host institution:

In synergy with the national priority research program (PEPR) "Biotherapies and bioproduction of innovative therapies" (BBTI), Inserm proposes to open a Inserm Chair position to develop innovative bioengineering approaches for key technologies associated with one of the following three therapeutic approaches: viral vectors for gene therapy, bioengineering for biomaterials or regenerative medicine approaches, and the biology/bioengineering interface for alpha-therapy using vectorized internal radiotherapy. Those bioengineering approaches are also supported by the Nantes Université notably in the framework of its recently launched I-SITE project NExT, winner of the Investments for the Future (PIA) program's IDEX/I-SITE call for applications. Nantes Université proposes a new university model in France by bringing together a university (Université de Nantes), a university hospital (CHU de Nantes), an Institute for Technological Research (IRT Jules Verne), the National Institute of Health and Medical Research (Inserm) and several *grandes écoles* (Centrale Nantes, École des Beaux-Arts Nantes Saint-Nazaire, École d'Architecture de Nantes) as full members. All of these stakeholders have combined their efforts to develop Nantes areas of excellence in research, and to design and build the health and industry of the future.
Proposed Host laboratories are:
- UMR 1089 : TARGET, Translational Research in Gene Therapy
- UMR 1229 : RMeS, Regenerative Medicine and skeleton
- UMR 1307 – CNRS UMR6075 : CRCI²NA - Nantes - Angers Cancer and Immunology Research Center

Strategy of the host laboratory:

TARGET (70 employees, https://umr1089.univ-nantes.fr/) covers the entire translational gene therapy development path from low TRL innovative projects, proofs-of-concept (POC), vector manufacturing to the accomplishment of Phase I/II trials, by putting together a large number of scientific and technological interdisciplinary skilled expertises. To advance gene therapy developments using viral vectors, in particular Adeno-Associated Virus-derived vectors (AAV), TaRGeT has a particular interest in chemical and molecular vector engineering, preclinical developements for neuromuscular and retinal diseases, vector immunogenicity and immunomodulation, disease modelling using new organoid models and large scale bioproduction. In this context, the translational vector core (CPV for "Centre de Production des Vecteurs") with its activities in process and analytical developments for AAV vectors is one among the 8 national "Intégrateurs en Biothérapies et Bioproduction" Industriels" of the national biotherapy strategy. Since 2004, the whole laboratory activities are performed under ISO 9001:2015 quality system.

RMeS (130 employees, 2 teams REJOINT and REGOS) supports basic, translational and clinical research related to 4R medicine (ie. Replace, Repair, Regenerate and Reprogram) dedicated to skeleton diseases and aging (osteoporosis, osteoarthritis, discarthrosis, periodontitis, rheumatoid arthritis and tendinopathies). We are notably interested in the use of stem cells, calcium phosphate biomaterials and hydrogels for the development of regenerative therapeutics. Recently we also develop bioinks, organoids, and organ on chip technologies by bioprinting to model skeletal diseases and discover new therapeutics. By formalizing an

interdisciplinary approach, RMeS offers a strong support and stimulating environment for exploring the limit of knowledge in skeleton-related 4R medicine.

CRCI²NA is composed of 12 research teams dedicated to the analysis of tumors as ecosystems composed of distinct cell types, linked by cooperative or competitive relationships. The overall project of the CRCI²NA is to explore the interactions and dynamic changes of tumor ecosystems during tumor progression as well as the mechanisms of dissemination in response to treatments. Inside the CRCI²NA, the Nuclear Oncology research team is a pluri-disciplinary gathering more than 60 researchers in nuclear medicine, chemistry, radiopharmacy, pharmacology, biology and physics. The aim of the team is to develop imaging and therapy of refractory tumors using nuclear medicine approaches.

Summary of the scientific project:

Context

In synergy with the national priority research program (PEPR) "Biotherapies and bioproduction of innovative therapies" (BBTI), It is proposed to open an Inserm Chair to develop innovative bioengineering approaches for key technologies associated with one of the following three therapeutic approaches: viral vectors for gene therapy (TARGET), bioengineering for biomaterials or regenerative medicine approaches (RMeS), and the biology/bioengineering interface for alpha-therapy using vectorized internal radiotherapy (CRCI2NA).

TARGET: Neuromuscular diseases (NMDs) are mostly genetic diseases affecting the muscles and central nervous system (CNS) system. The societal burden of these diseases is huge and many NMDs remain without therapeutic options. Gene therapy using adeno-associated virus (AAV) has shown great promises in patients but still have several limitations to unlock. For conventional gene replacement strategies, there is a need of more potent AAV vectors and/or route of deliveries to efficiently target the CNS and/or skeletal muscle tissues and so on reduce the injected doses. In addition, there is a need for new generation gene transfer strategies able to correct, edit or silence genes as most NMDs transgenes have complex genetics with genes exceeding the packaging capacity of AAV, DNA repeat expansions or dominant mutants (for instance, Duchenne myopathy, myotonic dystrophy, Steinert, Huntington, hereditary ALS, Friedreich, Rett syndrom…). In this context, the goal of this proposed position is to develop advanced molecular AAV-based gene therapy strategies for such complex genetic pathologies using different advanced gene therapy technologies such as exon skipping, pre-mRNA and RNA splicing, gene editing, prime and base editing or gene-regulated silencing. *In vitro* models based on muscular and neuronal organoïds for NMDs of interest will be developed and characterized and then used to evaluate the new gene therapy strategies. For a translational perspective, *in vivo* proofs of concept (POC) and dose finding studies will be performed when animal models of the disease of interest are available to move forward the therapeutic strategy from bench to bedside.

RMeS Musculoskeletal conditions affect the joints, bones, muscles, tendons, and ligaments and are the leading causes of disability worldwide. Engineering in vitro models of development and diseases are an essential step toward tissue and organ regeneration. Among these models, organoids have notably gained significant attention for modeling complex healthy or diseased organs, notably because of their ability to foster and accelerate the large screening of therapeutic molecules without the need for ethically controversial animal experiments. In this context, the goal of this proposed position is to develop in vitro bioengineered musculoskeletal tissues using a panel of complementary expertise encompassing stem cell biology, biofabrication technologies and biomaterial sciences. From a translational point of view, the ultimate goals of this proposed position are to contribute to the identification of novel pathogenic actors and screening of a large number of therapeutic strategies ranging from cell and cell-derived biologics-based therapies to nucleic acids, chemicals or proteins-based therapeutics. On a more basic level, we also aim to better understand the interactions between cells and their microenvironment in particular the surrounding extracellular matrix and associated mechanical and physicochemical properties (stiffness, topography..), before translating this knowledge into practical regenerative medicine strategies.

CRCI2NA Targeted Radionuclide therapy (TRT) has come "to a clinical age" in the last years with the approval of two radiopharmaceuticals (RP) against neuroendocrine metastatic castration-resistant prostate tumors. In this context, the use of alpha-emitters is seen as very promising and targeted alpha therapy (TAT) is already present in clinics with one approved RP and more than 60 ongoing clinical trials worldwide, including three of them in which the Nantes CHU/Cancer center nuclear medicine (NM) department is currently enrolling patients. The clinical impact of these new NM treatments has recently fostered the development of hundreds of new vectors for newly identified targets (e.g. PSMA and FAP). In clinics, TRT is now, for some indications, an important treatment option among immunotherapy, chemotherapy even though its position in the treatment line should be refined to increase patient's survival. The aim of this proposed position is to develop a holistic, multi-scale methodology for treatment and patient selections (i.e. to identify the best RP or cocktail of RP for each patient), for treatment personalization (i.e. to define the optimal amount of vector and activity to inject) and for treatment regimen optimization (i.e. to define the best injection schedule for each patient). To reach these purposes, multi-modal imaging, mathematical models of the radiopharmaceutical distribution and of the biological response to alpha-particles, biological biomarkers of toxicity and of potential immune response will be used in combination with the purpose of improving patient's care. To support early human trials, preclinical studies will be needed to better understand efficacy and toxicity mechanisms of TAT, by analyzing at the cellular scale the distribution and the effect of alpha-particles.

Summary of the teaching project:

The teaching objectives of the recruited researcher will be directly related to the graduate programs of the Health Science and Technology Graduate School. She/he will join the teaching team of the graduate programs M4R for which TaRGeT and RMeS labs are associated (4R (Repair, Replace, Regenerate, Reprogram) Medicine) and/or OHNU (Oncology, Hematology, and Nuclear Medicine) of which CRCI2NA is the exclusive host laboratory. The recruited researcher will therefore not only take part in the teaching activities, but he/she will also be involved in its management and coordination, particularly within the themes of the M4R or OHNU graduate programs, in line with his/her scientific expertise. In addition, she/he will be called upon to support students in the advancement of their career plans, guiding them in their immersion in the internship laboratories and advising them in the construction of their career path. The recruited researcher will also be heavily involved in the organization of the Nuclear Medicine Summer Schools. For the GP OHNU, she/he will also be responsible for teaching and organizing 2 masters courses related to nuclear medicine:
M2 SIBM *(https://sciences-techniques.univ-nantes.fr/formations/masters/m2-sibm-master-biologie-sante)* and M2 RIA *(https://sciences-techniques.univ-nantes.fr/formations/masters/master-physique-fondamentale-et-applications).*

National Research Agency package:

200k€

Other package:

	RHU Operandi (2024)	60 k€
CRCI2NA	Labex IRON (2024)	100 k€
	LabCom AidaLab	360 k€
TARGET	Infrastructures ligériennes (investissement, organoïdes)	100 k€
	ANR TRITDMD (2024, myopathie de Duchenne)	50 k€

Scientific communication and dissemination, Science and society:

Scientific communication and dissemination:
The policy of the NU/Inserm associated labs is to publish in the best journals and conferences in our discipline. The recruited researcher is expected to publish regularly as principal author but also as co-author. Several presentations at key international conferences in Biomedical engineering and specific technologies related to his/her research will be part of the expected contributions. It is also expected that he/she will participate in the organization and animation of scientific events in France and abroad. To do this, he/she will rely on the partnerships already in place between the NU/Inserm and prestigious centers in biomedical engineering. He/she will also develop new international partnerships in the field of therapeutic bioengineering.

Open Science:
In view of the industrial potential of these therapeutic bioengineering approaches, major innovations will systematically combine patent filling followed by scientific publications. All published articles will be on HAL in their integral version. As for the data collected and prepared for research, they will be made available to the community as soon as possible, after a possible embargo period
The recruited researcher will scrupulously comply with Open Access (OA) practices. In particular, She/e will bhe committed to publishing results in peer-reviewed journals using OA and will deposit data and manuscripts in preprint repositories as early as possible. She/he will manage research data in line with the FAIR principles through the use of a data management plan (DMP). She/he will comply with the principle “as open as possible, as closed as necessary”, including access to information about the research tools and instruments needed to validate or re-use our data.

Science and society:
Dissemination to the general public will be continuous, through both actions of communication and participation in local or national events as well as the use of INSERM and NU social network.
NU participates every year in the Fête de la Science and the Nuit des Chercheurs. The recruited researcher will be expected to actively participate in these events and communicate with the general public. Thanks to the close links between NantesU/Inserm members and the communication services at INSERM and Nantes Université, the awardee’s main scientific discoveries and medical advances will be regularly taken up by the local and national media

Indicators:

Teaching
The recruited researcher will contribute to the new international program project led by NU with Master’s level courses in his/her domain of expertise in English and potential participation in the organizational basis of the courses.
Classical indicators as follows will also be used to assess the teaching activities of the awardee:
- Success rate of tutored Masters and Ph.D. students
- Student assessment of teaching methods

- Degree of involvement in the organization of Biomedical engineering courses

Research

Regular publication and co-publication of research and participation in professional international conferences and scientific organizations and expertise will be fostered and expected to ensure that the recruited researcher attains the level of scientific recognition associated with an Inserm DR. Active initiation of new projects and search for independent funding is expected. The recruited researcher is expected, in particular, to apply ambitiously for high level funding such as (but not limited to) ERC grants or ANR. In these efforts, the researcher will be well guided and oriented by members of the NU who already have obtained such funding.
Classical indicators as follows will also be used to assess the Research activities of the awardee:

- Publications in peer-reviewed journals and Research grants
- Adequacy between the research carried out by the chair holder and Inserm/NU scientific policy

Knowledge transfer

Classical indicators as follows will also be used to assess the Knowledge transfer activities of the awardee:

- Collaborative research with public findings
- Research projects with public/private partners
- Participation in national and international scientific meetings

Selection of candidates:

It is expected the recruited researcher to become rapidly a group leader in the GAD team. So the candidate should demonstrate ability to supervise Ph.D students, post-doctoral fellow and technical support staff. She/he should have the capacity to obtain competitive funding to manage her/his group.

Successful candidates are chosen by a selection commission composed of six to ten members, the majority of whom are specialists in the fields of research concerned.

The commission carries out an initial examination of the applications, focused in particular on candidate experience and skills relative to the research and teaching project presented above. A shortlist of candidates is then selected for interview.
Only candidates selected by the selection committee on the basis of their applications will be invited to interview.

The interviews are followed by a deliberation during which selection commission will discuss the quality, originality and, where appropriate, the interdisciplinarity of the research and teaching projects presented by the candidates, their motivation and their scientific and teaching supervision capacity.

The candidates selected at the end of the selection process will be offered a researcher contract, following approval from the President and CEO of Inserm.

Required profile:

Education Level **: Phd**

Researcher Profile : R3/R4

R3 Established researcher A stage in a researcher's career describing those who have developed a level of independence and can described as an established researcher
R4 Leading Research A stage in a researcher's career where they can be termed a 'leading researcher'. This would include the team leader of a research group or head of an industry R&D laboratory.

Your application will be evaluated according to the following criteria :

- Relevance and originality of the project related to the research field
- International exposure in research projects
- Your ability to raise funds
- Participation in editorial and reviewing activities
- Your teaching experience
- Your ability to lead a team…

Application instruction:

Applications can be submitted online at EVA.
Deadline application: first quarter 2024

Please complete the scientific file in English.

It is imperative to contact the laboratory corresponding to the Chair you have applied for in order to build the project with them.

Position also open to 'Bénéficiaires de l'Obligation d'Emploi' (disabled persons), as defined in article 27 of law no. 84-16 of January 11, 1984 on statutory provisions for the civil service.