IPBS
Institut de Pharmacologie et de Biologie Structurale

Institute of Pharmacology and Structural Biology

Research & cutting-edge technological facilities in life science

cnrs

UNIVERSITÉ TOULOUSE III PAUL SABATIER

New group leaders at the IPBS Institute, Toulouse, France

Founded in 1996, the Institute of Pharmacology and Structural Biology (IPBS) is a leading research institute of the French National Centre for Scientific Research (CNRS) and the University of Toulouse. Located on the main Campus of the *Université Toulouse III-Paul Sabatier* in Toulouse, southwest France, the IPBS offers multidisciplinary education in the fields of Science, Health, Engineering and Technology, developing one of the most important scientific research clusters in France.

Our Institute is a world leader in the discovery, characterization and validation of novel important pathways and pharmacological targets in the fields of cancer and infectious diseases, through the use of molecular and cellular biology approaches, together with in vivo experiments. It conducts state-of-the-art research in structural biology, proteomics, biophysics, cancerology, immunology and microbiology (http://www.ipbs.fr). The IPBS brings together more than 250 scientists and supporting staffs, including more than 60 national and international postdoctoral fellows and PhD students. The IPBS offers outstanding scientific and stimulating research environment and several cutting-edge core facilities with highly qualified staff. These include mass spectrometry and proteomics, macromolecular crystallography, liquid- and solid-state NMR, biophysical characterization of proteins and complexes, virtual screening, whole body, tissue and cellular imaging, flow cytometry and cell sorting in standard or BSL3 environments, single particle tracking and tethered particle motion analysis, and animal facilities.

In order to reinforce its research endeavors in an inspiring, collaborative and cutting-edge environment, **the IPBS is seeking new talented junior group leaders** addressing fundamental questions within the spectrum of its research fields. Young scientists of any nationality, at junior or midcareer level, and with an excellent track record of publications in internationally recognized journals, are encouraged to apply. International experience as well as capacity to interact with other research groups within the institute are highly recommended.

Successful candidate(s) will be provided laboratory and office space for 5-8 people, a technical personnel and free access to the institute's core facilities for a period of 2 years, together with a starting package for basic equipment and consumables. In addition, strong support will be provided from the IPBS to obtain tenured positions at CNRS, INSERM or the University of Toulouse. Outstanding candidates are expected to establish independent and vigorous national and international extramurally-funded research programs (ANR, ERC, *etc.*) that fit at least with one of the priority topics listed below. Researchers already holding a permanent position are also welcome to apply.

IPBS PRIORITY TOPICS

See full details for each topic at: http://www.ipbs.fr/call2017

- **Tumor microenvironment – Cancer immunology** - Interactions of immune cells with stromal cells, the extracellular matrix and/or other immune cells; immune response to cancer.
- **DNA repair/chromatin remodeling in cancer** - DNA damage response (DDR) in connection with cancer through epigenetics, transcriptional regulation, DNA repair pathologies, chromosomal translocations, DDR-based drug discovery, or tumor resistance to clastogenic agents.
- **Pulmonary infections** - Biology of bacterial respiratory pathogens, with a strong focus on mechanisms underlying pathogen's persistence, drug resistance or tolerance within the host.
- **Drug discovery & structural biology** - Development of biological and chemical drugs of the future, with the aim of strengthening the pharmacological aspects of the IPBS research framework; characterization of drug-target interactions and mechanism of action; "hit to lead" strategies and new approaches for drug target deconvolution or vectorization will be favored. A particular attention will be given to candidates willing to create a group in biological NMR.

PROCEDURE & CALENDAR

Application (about 5 pages in English) should include a cover letter describing previous research experience, an outline of the future research project, motivation for joining the institute and names and e-mail address of 3 referees, together with an updated CV (including a complete list of publications). Application should be sent to recruit@ipbs.fr in a single PDF file named LASTNAME_FIRSTNAME_IPBS2017.pdf. Other formats will not be considered.

Pre-selection: September 2017
Interviews: Mid-October 2017
Result: Early November 2017
New groups are expected to open in fall 2018 (National selection process for tenured positions will take place between January and April 2018)

Application deadline: July 15, 2017

The University of Toulouse and the IPBS value diversity and are committed to equal opportunities. The institute has the responsibility to ensure that all employees are eligible to live and work in France. Toulouse is at the heart of the southwest France, with a very large and dynamic community of students and scientists, several international-level research and clinical centers, and has been ranked among the first cities in France for its quality of life.

www.ipbs.fr

Tumor microenvironment – Cancer immunology

Deciphering the influence of different cellular components of the tumor microenvironment, such as high endothelial venules (HEVs), which are portals of entry for lymphocytes into tumor tissues, mature adipocytes, dendritic cells and macrophages, on tumor progression is one of the major topics developed at IPBS. In addition, molecular aspects of cell migration and integration of biophysical parameters (such as matrix stiffness) are also studied. These projects benefit from cutting-edge technological facilities for whole body, tissue and cellular imaging (including intravital microscopy), flow cytometry and cell sorting, DONALD super-resolution microscope) and mass-spectrometry. In order to strengthen this topic, we are looking for a junior group leader with a genuine interest in studying immune components of the cancer microenvironment. Projects dealing with the followings will be favored: interaction of immune cells with stromal cells, the extracellular matrix and/or other immune cells; immune response to cancer.

Selected publications from our research teams

• Bouissou *et al.* (2017) Podosome force generation machinery: a local balance between protrusion at the core and traction at the ring. ***ACS Nano***

• Laurent *et al.* (2016) Periprostatic adipose tissue acts as a driving force for the local invasion of prostate cancer in obesity: role of the CCR3/CCL7 axis. ***Nat Commun***

• Lafouresse *et al.* (2015) L-selectin controls trafficking of chronic lymphocytic leukemia cells in lymph node high endothelial venules *in vivo*. ***Blood***

• Lazar *et al.* (2016) Adipocyte exosomes promote melanoma aggressiveness through fatty acid oxidation: a novel mechanism linking obesity and cancer. ***Cancer Res***

• Proag *et al.* (2015) Working together: Spatial synchrony in the force and actin dynamics of podosome first neighbors. ***ACS Nano***

• Labernadie *et al.* (2014) Protrusion force microscopy reveals oscillatory force generation and mechanosensing activity of human macrophage podosomes. ***Nat Commun***

• Lamsoul *et al.* (2013) ASB2αregulates migration of immature dendritic cells ***Blood***

• Bochet *et al.* (2013) Adipocyte-Derived Fibroblasts promote tumor progression and contribute to desmoplastic reaction in breast cancer. ***Cancer Res***

• Girard *et al.* (2012) HEVs, lymphatics and homeostatic immune cell trafficking in lymph nodes. ***Nat Rev Immunol***

• Dirat *et al.* (2011) Cancer-associated adipocytes exhibit an activated phenotype and contribute to breast cancer invasion. ***Cancer Res***

• Martinet *et al.* (2011) Human solid tumors contain high endothelial venules (HEV): association with T and B lymphocyte infiltration and favorable prognosis in breast cancer. ***Cancer Res***

• Moussion & Girard (2011) Dendritic cells control lymphocyte entry to lymph nodes via high endothelial venules ***Nature***

DNA repair or chromatin remodeling in cancer

Two teams, among the groups working on cancer at IPBS, investigate DNA transactions in pathological (ionizing radiations and clastogenic chemotherapeutic drugs) and physiological settings (antigen receptor rearrangements). Their respective projects highly benefit from collaborations with other IPBS teams specialized in NMR, structural biology and computer simulation, and from in-house core facilities such as proteomics, advanced light microscopy (two-photon microscopy), and animal facilities. In order to strengthen this research topic at IPBS, we are looking for a junior group leader using cutting-edge approaches in the DNA damage response (DDR) area, connected with cancer through epigenetics, transcriptional regulation, DNA repair pathologies, chromosomal translocations, DDR-based drug discovery, or tumor resistance to clastogenic agents.

Selected publications from our research teams

• Braikia *et al.* (2017) An inducible CTCF insulator delays the IgH 3' regulatory region-mediated activation of germline promoters and alters class switching. ***PNAS***

• Chanut, Britton *et al.* (2016) Coordinated nuclease activities release Ku from single-ended DNA double strand breaks. ***Nat Commun***

• Menchon *et al.* (2016) Structure-based virtual ligand screening on the XRCC4/DNA ligase IV interface. ***Sci Rep***

• Britton, Dernoncourt *et al.* (2014) DNA damage triggers SAF-A and RNA biogenesis factors exclusion from chromatin coupled to R-loops removal. ***Nucleic Acids Res***

• Yuan, Britton *et al.* (2015) Single-stranded DNA oligomers stimulate error-prone alternative repair of DNA double-strand breaks through hijacking Ku protein. ***Nucleic Acids Res***

• Braikia *et al.* (2015) Developmental switch in the transcriptional activity of a long-range regulatory element. ***Mol Cell Biol***

• Puget *et al.* (2015) Insertion of an imprinted insulator into the IgH locus reveals developmentally regulated, transcription-dependent control of V(D)J recombination. ***Mol Cell Biol***

• Cottarel *et al.* (2013) A noncatalytic function of the ligation complex during nonhomologous end joining. ***J Cell Biol***

• Haddad *et al.* (2011) Sense transcription through the S region is essential for immunoglobulin class switch recombination. ***EMBO J***

• Cheng *et al.* (2011) Ku counteracts mobilization of PARP1 and MRN in chromatin damaged with DNA double-strand breaks. ***Nucleic Acids Res***

• Bombarde *et al.* (2010) TRF2/RAP1 and DNA-PK mediate a double protection against joining at telomeric ends. ***EMBO J***

Pulmonary infections

A large part of the IPBS research activity is dedicated to studying various aspects of tuberculosis and other lung infections. This includes lipid biochemistry and biogenesis of the mycobacterial cell envelope, virulence mechanisms and host-pathogen interactions, and immunity to mycobacteria and other lung pathogens. We are looking for a junior group leader in the field of pulmonary bacterial infection, with a strong focus on the biology of pathogens. Topics related to the followings will be favored: mechanisms underlying pathogen's persistence, drug resistance or tolerance within the host. Deciphering the mechanisms of bacteria adaptation to their microenvironment will be a central question, and will benefit from state-of-the art approaches including, but not restricted to, single cell analysis, omics, microscopy and structural biology. In particular, our BSL3 animal facilities are fully equipped tissue and cellular imaging (including multiphoton intravital microscopy) and flow cytometry and cell sorting.

Selected publications from our research teams

- Carel *et al.* (2017) Identification of specific posttranslational O-mycoloylations mediating protein targeting to the mycomembrane. ***PNAS***
- Troegeler *et al.* (2017) C-type lectin receptor DCIR modulates immunity to tuberculosis by sustaining type I interferon signaling in dendritic cells. ***PNAS***
- Decout *et al.* (2017) Rational design of adjuvants targeting the C-type lectin Mincle. ***PNAS***
- Boritsch *et al.* (2016) pks5-recombination-mediated surface remodelling in *Mycobacterium tuberculosis* emergence. ***Nat Microbiol***
- Lastrucci *et al.* (2015) Tuberculosis is associated with expansion of a motile, permissive and immunomodulatory CD16+ monocyte population via the IL-10/STAT3 axis. ***Cell Res***
- Gonzalo-Asensio *et al.* (2014) Evolutionary history of tuberculosis shaped by conserved mutations in the PhoPR virulence regulator. ***PNAS***
- Gouzy *et al.* (2014) Nitrogen metabolism in *Mycobacterium tuberculosis* physiology and virulence. ***Nat Rev Microbiol***
- Gavalda *et al.* (2014) The polyketide synthase Pks13 catalyzes a novel mechanism of lipid transfer in mycobacteria. ***Chem Biol***
- Blattes *et al.* (2013) Mannodendrimers prevent acute lung inflammation by inhibiting neutrophil recruitment. ***PNAS***
- Gouzy *et al.* (2013) *Mycobacterium tuberculosis* nitrogen assimilation and host colonization require aspartate. ***Nat Chem Biol***
- Liu *et al.* (2013) Bacterial protein-O-mannosylating enzyme is crucial for virulence of *Mycobacterium tuberculosis*. ***PNAS***
- Botella *et al.* (2011) Mycobacterial P1-type ATPases mediate resistance to zinc poisoning in human macrophages. ***Cell Host Microbe***

Drug discovery & structural biology

We are looking for a junior group leader in areas complementary to our current research portfolio, and with a significant synergistic effect towards the existing IPBS research teams. The objective is to further nurture our genuine commitment to novel drugs identification and development against cancer and infectious diseases. We encourage applications addressing dynamic aspects of interactions and networks at the molecular and cellular levels, with a strong ambition to develop the drugs of the future and to strengthen the pharmacological aspects of the IPBS research framework. Topics related to structural biology, "hit to lead" strategies and new approaches for drug target deconvolution or vectorization will be favored. A particular attention will be given to candidates willing to create a group in biological NMR (in liquid- or solid-state NMR).

Selected publications from our research teams

- Saurel *et al.* (2017) Local and global dynamics in *Klebsiella pneumoniae* outer membrane protein a in lipid bilayers probed at atomic resolution. ***J Am Chem Soc***
- O'Connor *et al.* (2015) NMR structure and dynamics of the agonist dynorphin peptide bound to the human kappa opioid receptor. ***PNAS***
- Brunet *et al.* (2015) Probing a label-free local bend in DNA by single molecule tethered particle motion. ***Nucleic Acids Res***
- Fabre *et al.* (2015) Deciphering preferential interactions within supramolecular protein complexes: the proteasome case. ***Mol Syst Biol***
- Plénat *et al.* (2012) High-throughput single-molecule analysis of DNA-protein interactions by tethered particle motion. ***Nucleic Acids Res***
- Guillet *et al.* (2011) Crystal structure of gamma-tubulin complex protein GCP4 provides insight into microtubule nucleation. ***Nat Struct Mol Biol***
- Garcia-Alles *et al.* (2011) Structural reorganization of the antigen-binding groove of human CD1b for presentation of mycobacterial sulfoglycolipids. ***PNAS***
- Garcia-Alles *et al.* (2011) The crystal structure of CD1e reveals a groove suited for lipid exchange processes. ***PNAS***
- Kollmann *et al.* (2011). Microtubule nucleation by gamma-tubulin complexes. ***Nat Rev Mol Cell Biol***
- Paganin-Gioanni *et al.* (2011) Direct visualization at the single-cell level of siRNA electrotransfer into cancer cells. ***PNAS***