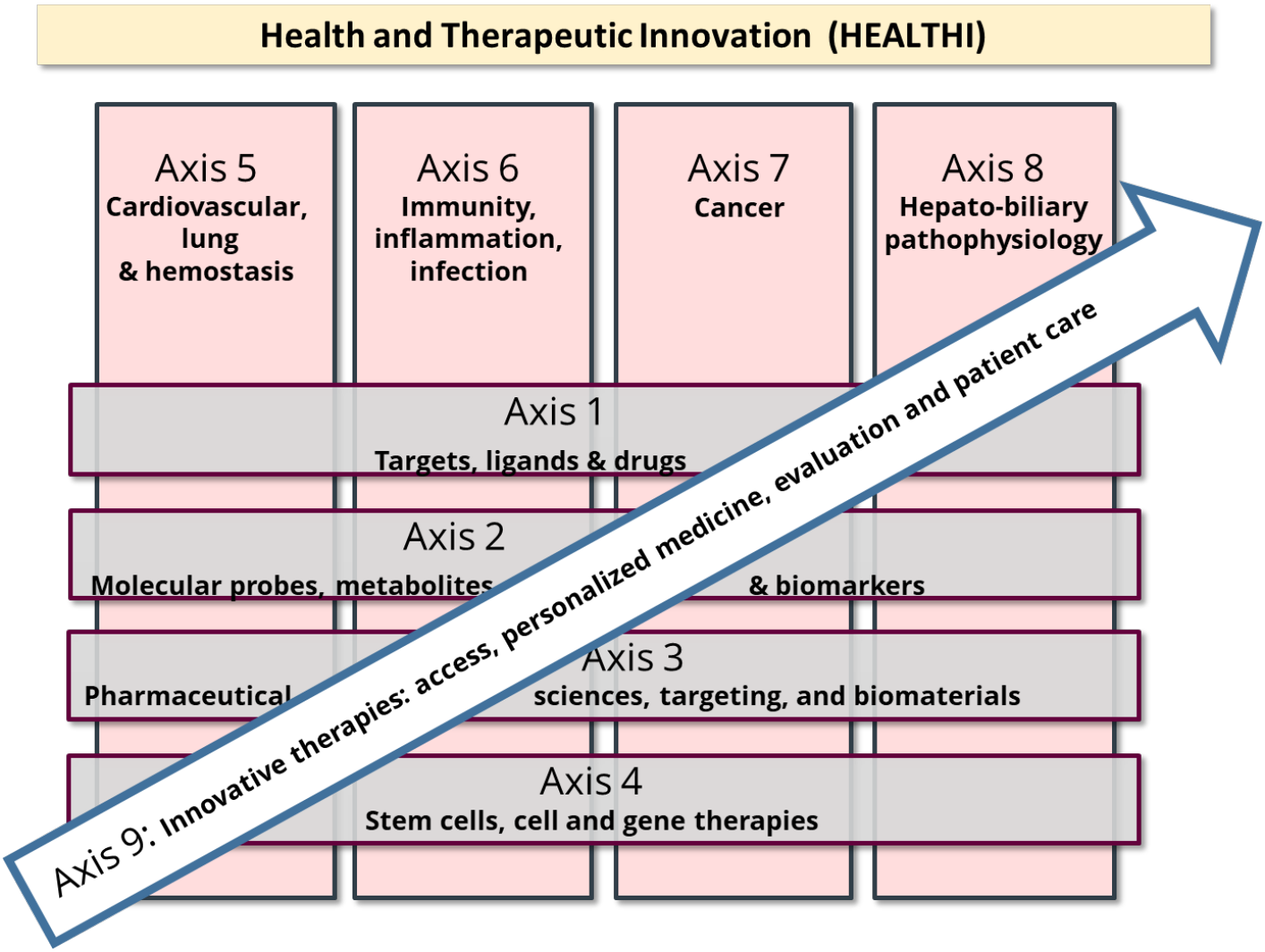
université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Appendix 1: Presentation of the different axes of HEALTHI



université PARIS-SACLAY GRADUATE SCHOOL Life Sciences and Health

université PARIS-SACLAY GRADUATE SCHOOL Life Sciences and Health

université PARIS-SACLAY GRADUATE SCHOOL Chimie

université PARIS-SACLAY GRADUATE SCHOOL Santé publique

université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 1: Targets, ligands & drugs

Coordinators :

- Delphine JOSEPH (Université Paris-Saclay, Châtenay-Malabry): delphine.joseph@universite-paris-saclay.fr
- Carine VAN HEIJENOORT (CNRS, ICSN, Gif-sur-Yvette): carine.van-heijenoort@cnrs.fr
- David BONNAFFE (Université Paris-Saclay, Orsay): david.bonnaffe@universite-paris-saclay.fr

This first thematic axis federates the complementary skills and expertise of biochemists, structural biologists, pharmacologists, physico-chemists, medicinal and organic chemists, bio- and chemo-informaticians. Its main objective is to design and to discover new therapeutics, diagnostics or theragnostic agents through:

(i) **the identification of new therapeutic targets and the understanding of the dynamic mechanisms of their cellular and molecular function:**

One of the critical challenges is to identify and validate new therapeutic targets involved in pathological pathways. For this purpose, it is essential to better understand and to spatiotemporally control the structure-dynamic-function relationships of bio(macro)molecules and the drug-target interactions by developing analytical, biophysical and biochemical methods in conjunction with advanced computational and data sciences.

(ii) **the identification of small bioactive molecules and the full characterization of their on-target and off-target effects and the understanding of their mechanisms-of-action:**

The identification of new bioactive molecules is based on a network of virtual and biological high-throughput screening platforms as well as on libraries of synthetic and natural compounds and natural product crude extracts offering an extended chemical space to explore. The latter benefit from innovative synthesis and extraction methods (diversity-oriented synthesis, multicomponent reactions, biomimetic chemistry, synthetic biology or biocatalysis) with the support of chemo- and bio-informaticians. Similarly, the discovery of drug-like candidates takes advantage of these multidisciplinary expertise and the development of computer-based predictive models for the early optimization of hit-molecules physicochemical properties concomitantly to the improvement of the on-target effects and the reduction of off-target ones.

(iii) **the development of innovative drug discovery strategies including data mining and artificial intelligence approaches:**

université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

High attrition rate as well as costly and time-consuming development processes of drug candidates currently represent serious impediments in drug development. Cross-fertilization of innovations from pharmaceutical sciences including physics, chemistry and biology with technological advancement in computational and data sciences represents a unique opportunity to better handle optimization and pre-development of drug candidates (hit-to-lead, structure-activity relationship, druggability, ADMET preliminary studies).

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 2: Molecular probes, metabolites & biomarkers

Coordinators :

- Boris VAUZEILLES (CNRS, ICSN, Gif-sur-Yvette) : Boris.VAUZEILLES@cnrs.fr
- Florence MAHUTEAU-BETZER (CNRS, Université Paris-Saclay, Curie, Orsay) : florence.mahuteau@curie.fr
- Claire SMADJA (Université Paris-Saclay, Châtenay-Malabry) : claire.smadja@universite-paris-saclay.fr

This axis aims to develop original methods based on chemistry, from synthesis to bioanalysis to study biological processes, identify new biological and therapeutic targets as well as molecular biomarkers of pathologies. The goals are: (i) to improve the understanding of biological / physiological phenomena, (ii) to develop molecules for diagnostic, therapeutic and / or theranostic purposes, (iii) to provide diagnostic tools. This axis will help to improve the following issues: development of new labeling strategies and new therapeutics, processing of sample from complex media, bioanalysis and "omics".

This axis will benefit from the complementary expertise of the all teams. These are based on one hand on the design and synthesis of new molecules (ligands, fluorescent probes) and on the study of new reactions that can be performed *in situ* in complex biological media to monitor intracellular metabolism. This will allow the development of new molecules to improve the understanding of the physiopathological mechanisms and to develop new therapeutics. The use of bio-engineering sensors relying on fluorescent proteins such as GFP, combined with spectro-microscopy techniques, will provide a comprehensive monitoring of cell signaling. This understanding of pathological phenomena will be reinforced by teams with strong expertise on analytical chemistry focusing their research activity on the microscale analysis of biological macromolecules (e.g. proteins) as well as in the development of analytical tools (mass spectrometry, immunoanalysis, molecular biology: qPCR, volatolomics), dedicated on the identification of new biomarkers using the “omics” approach and/or alternative biological fluids (e.g. exosomes). This concept can be applied to different types of pathologies: cancer, infectious, cardiovascular and pulmonary diseases.

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 3: Pharmaceutical sciences, targeting, biomaterials

Coordinators :

- Nicolas TSAPIS (Université Paris-Saclay, Châtenay-Malabry) : nicolas.tsapis@universite-paris-saclay.fr
- Eric DORIS (CEA, Université Paris-Saclay, Saclay) : eric.doris@cea.fr
- Nathalie JARROUX (Université Evry Val d'Essonne, Evry) : nathalie.jarrouxblachere@univ-evry.fr

The scientific objectives of the formulation cluster are to develop new therapeutic strategies based on innovative forms of administration of drugs and contrast agents for medical imaging. Indeed, the efficacy of a drug depends on a large number of parameters, including the crossing of biological barriers that separate the administration site from the tissue, cell or subcellular site of action. It is therefore necessary to protect the drug from enzymatic or chemical activity to enable it to reach its site of action intact. At this site of action, selective distribution is also a factor that contributes to the efficacy of the drug. In fact, many molecules which clinical application possess physico-chemical characteristics (hydrophilicity, molar mass) that are unfavorable to the crossing of biological barriers. Many are characterized by a non-selective distribution, as the therapeutic activity can only be obtained at the cost of a loss to cells or tissues not involved in the therapeutic activity, resulting in toxic effects.

The teams of the formulation cluster aim to solve these problems. This involves the development of novel and original drug delivery and transport systems (micro and nanotechnologies for delivery and controlled release systems), in particular through the synthesis and characterization of new biocompatible materials for encapsulation and transport. The development of these therapeutic innovations also involves the use of biomimetic systems to promote understanding the role of different molecules or recognition sites in the administration, migration, targeting and diffusion of drugs. The problems of bioavailability presented exist for small molecules resulting from chemical synthesis, but also for recombinant proteins or nucleic acids resulting from biotechnologies that are probably the basis of tomorrow's drugs (cf. messenger RNA vaccines). However, the physicochemical and biomimetic characteristics of these molecules make them difficult to administer because they are poorly absorbed at the cellular/tissue level and fragile with respect to degradation and metabolization. These limitations represent the main hurdle to their development as drugs. Finally, it should be noted that the barriers to be crossed are complex systems involving several "layers" (epithelium, endothelium, cell membrane) and several components (mechanical and physico-chemical barriers and enzymatic barriers). The development of these therapeutic innovations also involves the use of biomimetic systems to promote the understanding of the role of different molecules or recognition sites to remove some of these barriers. The detailed knowledge of these barriers at the molecular and cellular level and their interaction with the micro and nanotechnologies encapsulating the drug also represents a major challenge.

université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 4: Stem cells, cell therapies and gene therapies

Coordinators :

- Anne GALY (Inserm, Université Evry Val d'Essonne, Evry) : galy@genethon.fr
- Annelise BENNACEUR-GRISCELLI (Université Paris-Saclay, Villejuif) : annelise.bennaceur@aphp.fr

Biotherapies resulting from genome sequencing and life sciences have opened up major perspectives in the treatment of many pathologies with unmet therapeutic needs. These biotherapies constitute a new class of drugs resulting from biotechnology and engineering based on adult or pluripotent stem cells, tissue compositions, genetic vectors / editing to modify / repair cellular functions or reprogram living cells ex vivo / in vivo, or a combination of these approaches. They are produced either for an individual patient or where possible as ready-to-use products for a target population. Their production and use in humans requires a high degree of complexity requiring excellent translational research activity uniting fundamental research with therapeutic research in connection with the pharmaceutical and industrial world.

All the teams and structures of the Université Paris-Saclay (UPSaclayy) within the Biotherapies pole aim to accelerate this translational research which is initiated by concepts from fundamental science and move forward to early clinical studies. Several teams have already contributed to real successes in cell and gene therapies providing high visibility and unique skills in the field. These include the ex vivo lentiviral gene therapy approaches used for instance for CAR-T cells or in various rare diseases, as well as the remarkable advances obtained with adeno-associated vectors to treat neuromuscular diseases in a systemic manner. New technological breakthroughs in cell reprogramming, engineering of pluripotent stem cells (iPSC and ESC) or specific tissues, cell engineering and organ construction in 3D and genome engineering by genome editing open up considerable perspectives in the area of regenerative medicine, cell and gene therapies, personalized medicine with targeted therapies and the search for new targets. These therapies are generating growing interest from the pharmaceutical industry in search of new commercial products. In this context, the UPSaclay teams have a leading position at the national and international level. In cell therapy, CITHERA of the Université Paris-Saclay / INSERM (Center for iPSC Therapy) coordinates the INGESTEM national infrastructure (https://ingestem.com) and has set up at Génopôle d'Evry the clinical grade platform for the design and production of cell therapies based on cGMP engineering of IPSC stem cells and derivative products for therapeutic purposes in oncology and frequent diseases, in partnership with biotechs within the framework of the European consortium (https://www.restore-horizon.eu) and international (GAIT www.gait.global). In gene therapy, several teams are contributing to pioneering trials, European consortia are underway and a platform for accelerating technological research in genomic therapy has been installed by Inserm at the Génopôle d'Evry (ART-TG, www.art -tg.com). Private partnerships are in place in several teams (industry and patient associations).

CITHERA and ART-TG have been awarded the label of « Industrial Integrator » (MAGENTA), from the government PIA4 plan to support the challenge of biomedicines (https://www.gouvernement.fr/labellisation-des-integrateurs-industriels-par-le-grand-defi - biomedicines).
The areas of medical interest of the cluster's teams include immunotherapy and immuno-oncology, cell and gene therapies for hematological diseases and cancers, regenerative medicine for frequent diseases, therapies for genetic diseases, and rare diseases.
The cluster's research and innovation actions will aim to support and strengthen collaborations between teams to meet major challenges in science and technology:

- The design of new therapeutic strategies, proofs of concept and preclinical studies,
- The development of advanced and relevant preclinical models,
- Developments in technological platforms for the manufacture of innovative products including their characterization for medical or industrial applications,
- Identification of biomarkers and molecular analyzes for in-depth analysis of patient responses to innovative therapies (immune responses, pharmacological studies, genotoxicity, etc.),
- Clinical research and implementation of early-phase clinical trials.

A network of cooperation and synergy between different fields such as genetics, molecular and cell biology, virology, immunology, pharmaceutical and medical sciences, industrialization and regulatory agencies will be needed to develop cell and gene therapies and immunotherapies. The cluster will also develop collaborative projects with other IRMIT clusters, in medical fields and complementary expertise. An educational path will be strengthened for the training of new professions, with the DU "stem cells and regenerative medicine" extended to all biotherapies, IFSBM, and a Cofund project with the Evry Genopole for the recruitment and training of talented post-docs.

université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 5: Cardiovascular, lung & hemostasis

Coordinators :

- Ana Maria GOMEZ (Inserm, Université Paris-Saclay, Châtenay-Malabry) : ana-maria.gomez@inserm.fr
- Marc HUMBERT (Inserm, Université Paris-Saclay, Le Plessis-Robinson) : marc.humbert@universite-paris-saclay.fr

Cardiovascular, pulmonary and hemostasis diseases are major causes of morbidity and mortality worldwide, through heart failure, arrhythmias, sudden death, pulmonary hypertension, thromboembolic diseases and hemorrhagic syndromes. The scientific objectives of the cardiovascular, pulmonary and hemostasis axes are to better understand cardiovascular, pulmonary and hemostasis physiology and pathophysiology in order to support therapeutic innovation.

Cardiovascular teams want to better understand the main functions of cardiomyocyte (electrical activity, excitation-contraction coupling, contractility, metabolism). This functional approach is enriched by the exploration of vascular tissue and techniques of biochemistry, pharmacology and molecular biology, as well as in vivo experiments in animals. A better understanding of the cellular and molecular bases of the normal and pathological heart will help to better describe dysfunctional pathways especially in heart failure and arrhythmias. The primary objective of the lung teams is to better understand the pathophysiology and therapeutic management of idiopathic, hereditary or venous thromboembolic pulmonary disease, left heart failure and chronic respiratory disease. Understanding the mechanisms of pulmonary vascular remodeling and better assessing the consequences on the right ventricle will identify new therapeutic strategies in different forms of pulmonary hypertension. A special feature of the lung teams in this axis is the complete integration of preclinical, medical and surgical teams. Experimental surgery, therapeutic innovation and new technologies for the management of pulmonary hypertension are particularly innovative and structuring elements of these teams. Hemostasis diseases are particularly important with a desire to better understand the fundamental foundations governing the dynamic exchanges between vascular cells and hemostasis actors. Experimental models and clinical interfaces support the exploration of new therapeutic pathways in hemostasis diseases.

By promoting synergies and multidisciplinarity within the different laboratories of this axis, it will be possible to set up a consortium combining biologists, physiologists, pharmacologists, doctors, surgeons and health professionals, in order to collectively improve the research and care of cardiopulmonary diseases and hemostasis.

université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 6: Immunity, inflammation, infection

Coordinators :

- Françoise BACHELERIE (Inserm, Université Paris-Saclay, Clamart) : francoise.bachelerie@universite-paris-saclay.fr
- Xavier MARIETTE (Université Paris-Saclay, Assistance Publique-Hôpitaux de Paris, Inserm, Le Kremlin-Bicêtre) : xavier.mariette@aphp.fr

Immune and infectious diseases are major causes of morbidity and mortality worldwide. Infectious diseases remain the leading cause of death in developing countries and continue to be a burden in developed countries, as dramatically evidenced by emerging infectious diseases such as the COVID-19 pandemic that constitute a new public health issue, HIV infection for which there is still no curative treatment, and the increased prevalence of multi-resistant antibiotic infections.

In addition to infectious diseases that are often associated with immune deficiency, immunopathological diseases include primary immune deficiencies, allergic and autoimmune diseases and immune tissue cancers. The last 20 years have been marked by a burst of immunotherapies based on biodrugs such as rituximab in the treatment of lymphoma or anti-TNF therapy in several inflammatory and autoimmune diseases, or based on the use of small molecules such as inhibitors of JAK, involved in the pathogenesis of chronic inflammation, in the treatment of rheumatoid arthritis. These immunotherapies have gone beyond the scope of immunopathological diseases and represent a revolution in the treatment of cancer such as "immune checkpoint" inhibitors.

For all these reasons, it is fundamental that all teams interested in immunology, inflammation and infectiology coordinate their efforts to better understand the pathophysiology of these immune and infectious diseases in order to identify new biomarkers and develop new therapeutic strategies.

In this context, the teams of pole 6 investigating infectious diseases are focusing on potential therapeutic targets at the level of the infectious agents, the host or the environment, whether it be the mechanisms of bacterial multi-resistance, the persistence of HIV infection, the physiopathology of endogenous viruses (i.e. retrovirus or Papillomavirus-virome), or zoonosis due to Leishmania infection. In these frameworks as in the search of new vaccine approaches an important link is established between immunity and infection control.

Pole 6 organization specifically aims to strengthen collaborations between these teams with those interested in fundamental immune mechanisms such as the microbiota, immunochemistry of the immune response, calcium signaling or cell death, and with those developing researches in immunopathology related to the pathogenesis and treatment of inflammatory, autoimmune or allergic diseases, adverse drug reactions, organ transplant rejection, as well as ways to improve the immune responses to cancer. Beyond, the objective is to foster the synergies between the different teams of biologists and the chemists, pharmacists, physicians, surgeons and healthcare professionals involved in immunopathological and infectious diseases, in order to improve the knowledge, but also the care of patients through the improvement of the safety of existing immunotherapies and the identification of new biomarkers and innovative treatments.

université PARIS-SACLAY

Programme Interdisciplinaire – ISIT / HEALTHI

Institut de recherche en Santé et en Innovation Thérapeutique

Health and Therapeutic Innovation

Axis 7: Cancer

Coordinators :

- Mounira AMOR-GUERET (CNRS, Université Paris-Saclay, Curie, Orsay) : mounira.amor@curie.fr
- Christophe MASSARD (Université Paris-Saclay, Gustave-Roussy, Villejuif) : Christophe.massard@gustaveroussy.fr

The Cancer Center of the Paris-Saclay Health and Therapeutic Innovation Institute aims to bring together teams working on programs extending from basic to early clinical research and dedicated to the management of patients with cancer (solid and hematological tumors). These teams will share their reflections, results and experiences of work extending from the characterization of new mechanisms of oncogenesis to the identification of new therapeutic approaches: cytotoxic chemotherapies, radiotherapy, targeted therapies, immunotherapies and new classes of anticancer drugs. In addition, they will also consider the optimal combination of these different treatments.

The elucidation of new mechanisms of oncogenesis will make it possible to develop new diagnostic methods and to identify new diagnostic, prognostic or theranostic markers, together with potential treatment targets, paving the way for innovative treatments. This research aims to identify targets or methods that are “actionable”, making it possible to propose the development of treatments for a defined subtype of cancers.

The identification of mechanisms of susceptibility, but also of resistance to different treatments in tumor cells will make it possible to develop new strategies for increasing treatment efficacy or overcoming this resistance, and for identifying and validating markers predictive of the response, or lack of response, to treatment. These biomarkers may be identified in the tumor cells, the cells in the tumor microenvironment or in the host. The technologies developed may be diverse, without limitations.

The Cancer Center will also have the vocation of developing collaborative projects with the other ISIT centers, to develop new molecules, potentially specific for newly identified target cells, for example. The identification of new markers in groups of tumors may lead to the screening of a chemical library and the identification of new molecules, for which structural optimization may be possible and the target cells must be sought.

The identification of these new “actionable” targets or the deciphering of resistance mechanisms will also be validated through preclinical research, leading to collaborative projects in clinical research, with the establishment of early-phase clinical trials to identify the same mechanisms in patients with advanced cancers, for whom new therapeutic approaches could be proposed.

Axis 8: Hepato-biliary pathophysiology

Coordinators :

- Jean-Charles DUCLOS-VALLEE (Université Paris-Saclay, Inserm, Villejuif) : jean-charles.duclos-vallee@aphp.fr
- Thierry TORDJMANN (Inserm, Université Paris-Saclay, Orsay) : thierry.tordjmann@universite-paris-saclay.fr

Basic and clinician researchers within the "Hepatology Axis" share expertise covering a wide spectrum of liver diseases from bench to bedside. We explore on the one hand key signalling pathways involved in cellular stress, liver repair, biliary homeostasis, gut-liver axis (ie interactions between gut microbiome and the liver) and carcinogenesis; on the other hand, in continuity with those basic studies, we aim to build therapeutic strategies, including liver transplantation, against acute liver failure, inflammatory disorders in nutritional liver diseases (alcoholic liver disease, ALD, and non-alcoholic fatty liver disease, NAFLD), hepatocellular carcinoma and genetic cholestasis. The research programs of this axis include mainly mechanistic studies of hepatobiliary pathophysiology, liver organoid bioconstruction, innovation in diagnostic tools and liver surgery, and analysis of the role of the gut microbiome in disease pathogenesis including in cohorts of well characterized patients with ALD and NAFLD. All these programs integrate valorisation/development studies in the prospect of clinical applications, and are backed on reference clinical centres for liver transplantation and rare liver diseases.

Major achievements in the fields of pathophysiology, diagnosis and treatment of liver diseases have been obtained by the different research groups, in particular in the context of the DHU *Hepatinov*, the RHU *iLiTe*, and the LERMIT. Therapeutic innovation has been the hallmark of our teams in genetic cholestasis, in ALD and NAFLD, in liver repair, liver cancer and liver surgery. In these fields indeed, the lack of curative therapies calls for a crucial need in basic and translational research programs.
Main projects will be initiated within the Hepatology axis, obviously by interacting with the transversal axis *"Target and molecules"*, in particular with teams involved in medicinal chemistry. Several of our projects identified molecular or cellular targets for which we aim to design new therapeutic options in the context of liver repair, genetic cholestasis, nutritional liver diseases and liver cancer.

Axis 9: Innovative therapies: access, personalized medicine, evaluation and patient care

Coordinators :

- Philippe BROET (Université Paris-Saclay, Inserm, Villejuif) : philippe.broet@universite-paris-saclay.fr
- Eric FOUASSIER (Université Paris-Saclay, Châtenay-Malabry) : eric.fouassier@universite-paris-saclay.fr
- Raphaèle SEROR (Assistance Publique-Hôpitaux de Paris, Université Paris-Saclay, Inserm, Le Kremlin-Bicêtre) : raphaele.seror@aphp.fr

The two last decades have been marked by the emergence of numerous targeted therapies in various fields of medicine, such as biologics, small molecules and anti-cancer immunotherapies. The explosion of these innovative therapies, their variety of mechanisms of action and therapeutic targets, their various modalities of administration, their concomitant or sequential use in single individuals was a great opportunity for treating patients but put the scientific community in front of new challenges. Among them, the evaluation of their safety profile, the personalization of their use, patient acceptance of and education to these new drugs.

This axis is very multidisciplinary and involves complementary teams experienced in clinical epidemiology, pharmacoepidemiology, biostatistic, statistical genomics, public health, health economics juridical issues, but also patient care and education. This axis is one of the originality of ISIT, and will address these issues having in mind the pivotal concern of patient's benefit. Moreover, this axis will also focus on developing interdisciplinary research programs that will be transverse and will sweep away research silos by creating new networks in ISIT. These projects will consider the whole process, from basic biology information to the delivery of the drug involving the exploitation of various structured/unstructured data coming from laboratories and patient cohorts.

One of the tasks of this axis will be to evaluate benefit risk ratio of innovative treatments, this evaluation usually made specialty by specialty. However, same treatments are usually in different contexts and diseases, the transversal nature of this pole will encourage this interdisciplinary global evaluation across specialties. In addition, this evaluation implicates the use of big data, such as SNDS database and large scale population-based or clinical-based cohorts, and specific complex method of analysis, in which teams of the pole are used too.

Another important issue of ISIT focused on pathophysiology of disease and thus immunological or molecular mechanisms of disease emergence, from the basic science point of view. When exploring such hypothesis, confirming pathophysiological mechanisms by their clinical impact. Thanks to involvement of the E3N team and the clinical epidemiology team in ISIT, some of these

hypothesizes could be translated to clinical results.

Another task will be to develop innovative solutions in the field of evaluation of efficacy, safety and personalized medicine in the context of big data.
With the rise of high dimensional data availability at various levels (cellular, biological system, patient, population,..) that are obtained from multiple sources (laboratories, public repositories, public databases) there is an urgent need to develop innovative methodologies to evaluate the efficacy, safety and precision of the new therapies to help delivering the right drug for the right patient at the right time (personalized medicine).
This task will require developing new frameworks for integrating this huge quantity of heterogeneous information to target various disease outcomes. For personalized medicine, this axis will consider various strategies ranging from classical to new machine learning approaches but keeping in mind that they should achieve a good balance between predictive accuracy and diseases understanding that are mandatory in the medical field. Our task will also be to make these results available to the public health and clinical research communities through the development of computerized tools.

The axis 9 of ISIT will also address the issue of access to innovative care and treatment. This economic evaluation of the cost and benefits of treatments at the time of their marketing authorization, but also the evaluation of these therapies in real life conditions requires the use of medico-economic evaluations. These studies allow a comparative analysis of the respective costs and consequences of competing treatment strategies. In the future, the evaluation of the efficiency of these therapeutics in real life conditions will be based on the use of new models and the exploitation of big data from medico-administrative databases, matched with clinical databases.
Patient care also presupposes new modes of cooperation between healthcare professionals; the legal implications of which need to be examined, particularly in terms of the transfer and sharing of responsibility. In particular, the methods for deploying the new legal missions of pharmacists (therapeutic education, pharmaceutical interviews, shared medication reviews, etc.) must be studied to accelerate their implementation. These new missions may indeed raise legal difficulties (scope of activities, competition law...) but also raise the question of the evolution of the pharmacist's remuneration method.

Moreover, patients' early access to therapeutic innovation is accompanied by an increased need for legal certainty. Societal acceptance of therapeutic progress therefore requires promoting compensation for victims of possible damage related to care or the use of health products. However, this should not lead to a disproportionate risk for health professionals and industries, which would hinder innovation. The conditions for this difficult balance will have to be sought.