Instituts thématiques

Inserm

Institut national
de la santé et de la recherche médicale

Past Inserm Workshops

from 2006 to 2011

Classification by topics

Note: For direct access to the area of interest, click on the topic.

GENOME - GENOMICS - MOLECULAR BIOLOGY

Inserm Workshops 2011

N° 211 - High throuput approaches in epigenomics

Organizers: Emmanuel Barillot (Institut Curie/INSERM/Mines ParisTech, Paris), Christophe Lavelle (CNRS, Muséum National d'Histoire Naturelle, Paris)
Aims: Through its polymorphism, as evidenced by the heterogeneity of its physicochemical properties, the chromatin is the support of an information -so-called "epigenetic"- which is superimposed to the genetic information -carried by DNA- to determine cell fate. While genetic sequencing, more and more efficient, provides data at a dizzying pace, the "epigenetic sequencing" is in turn becoming a priority in an attempt to gather all information necessary for the deciphering of cellular function. The challenge of this new quest is obvious when we know that, contrary to genetic information, epigenetic information varies from one cell to another (within the same organism) and in regard with the cell cycle, making the epigenome particularly difficult to establish. However, the first high-resolution epigenetical maps begin to emerge, including information as diverse (and complementary) as the position of nucleosomes, the presence of histone variants and their modifications, the distribution of transcription factors and remodeling factors, and location of DNA methylation. While these profiles accumulate, the need is urgent to develop analytical tools that allow efficient analysis of these data, in hopes of eventually cracking the epigenetic code.
The objective of this workshop is to present the most recent techniques (mainly ChIP-seq) in this area, focusing on possible problems commonly encountered in their implementation. Beyond the "wet" technical aspects, a presentation of the most common bioinformatics tools for analysis (peak finding, differential analysis, integrative analysis of profiles, databases ...) will also be provided.

N° 212 - Bioinformatics approaches to decipher genome regulation from high-throughput data

Organizers: Jacques van Helden (ULB, Belgium), Philipp Bucher (SIB/ISREC, Switzerland)
Aims: Genome regulation plays a crucial role in embryonic development, adaptation of cells, tissues and organisms to their environment, and evolution. This regulation occurs at multiple levels: transcription, RNA maturation (splicing, degradation), micro-RNA, nucleosome occupancy, chromosome conformation. New high-throughput methods offer unprecedented ways to characterize regulatory elements at a genome scale : expression microarrays, ChIP-on-chip, ChIP-seq, RNA-seq, protein binding arrays, etc. Sequencing platforms become available in many institutes, but researchers generally feel some perplexity when they are first confronted to the terabases of novel data. New software tools re being developed to answer those new needs, but their utilization requires to understand the underlying principles, master the parameters, and interpret the significance of the result.
The goal of this workshop is to provide researchers with a theoretical and practical training enabling them to apprehend the whole flow of data analysis, from data acquisition to biological interpretation of the results.

Inserm Workshops 2010

N° 207 - Targeted genome modification using custom-made endonucleases

Importantly, nucleases used in genome modification need to be highly specific in order to avoid unwanted off-target cleavage and unwanted genotoxicity. Consequently each precise genome sequence modification envisage requires designing a novel nuclease.

Inserm Workshops 2009

N° 200 - Functional organization of genomes in the nucleus: from molecular to *in vivo* approaches

Organizers: Frédéric Bantignies (IGH, Montpellier), Angela Taddei (Institut Curie, Paris).
Aims: Chromosomes are organized in the 3D nuclear space of eukaryotic cells and this organization plays a role in the regulation of genome function. This specific organization involves multiple interactions between genomic sequences, nuclear sub-structures and regulatory proteins. It also involves long-range contacts between genomic elements. Recent studies have revealed that these interactions are important for the coordination of gene expression. These interactions can also influence other fundamental nuclear processes such as replication, DNA damage repair and recombination, and have consequences for chromosomal rearrangements, which are observed in many cancers. It is therefore important to characterize this nuclear architecture to study its functional consequence.
The aim of the workshop is to cover the main advances in techniques that allow the study of genome organization. Three complementary aspects will be explored: 1) a molecular aspect with the "3 C" method ("Capturing Chromosome Conformation") and its extension to 4C and other high-throughput methods which allow screening of the entire genome for DNA sequences that interact with each other in the nuclear space; 2) a cytological aspect with the latest advances in DNA and RNA FISH, to visualize these interactions in fixed tissues; 3) an *in vivo* aspect on living cells with the "gene tagging" and "mRNA tagging" technologies, which allow the study of the dynamics of these interactions.

N° 193 - Polymorphism and genomic rearrangements: analysis of CGH and SNP array data, and deep sequencing data

Organizers: Emmanuel Barillot (Institut Curie, Paris), Yves Moreau (Université de Louvain, Belgique)
Aims: CGH and SNP microarrays are being used more and more frequently for the study of cancers and constitutional disorders. The emerging deep sequencing technology should succeed microarrays, and complement them. From a bioinformatics point of view, these technologies raise specific problems, at the level of primary data analysis (design of experiment, normalization, identification of chromosomal breakpoints and of recurrent aberrant regions) as well as for the biological interpretation of the results (classification, correlation with expression data, data integration, functional annotation, and so on). The use of bioinformatics tools must rely on a comprehensive understanding of data acquisition and of experimental biases, as well as of the assumption that underlie the modeling of this data. During this Inserm workshop, we will aim at providing to the participants the concepts and practical tools necessary for the analysis of this kind of data. The goal is both to master these approaches for fundamental research in molecular biology and for applications in clinical research or practice (diagnosis and prognosis).

Inserm Workshops 2008

N° 187 - Analysis of DNA replication and genome instability using DNA combing and other singlemolecule assays

Organizers: Jean-Sébastien Hoffmann (IPBS, Toulouse), Philippe Pasero (IGH, Montpellier), Étienne Schwob (IGMM, Montpellier)
Aims: Single-molecule techniques have proven to be powerful approaches to monitor DNA replication in a variety of organisms, including human cells. Unlike other replication assays, these techniques allow the direct visualization of individual replication forks progressing along single chromosomes. Recent evidence indicates that spontaneous replication defects represent a major source of genomic instability in precancerous lesions and play a central role in the cancer process. The recent development of single-molecule approaches opens new avenues to understand the nature of replication stress in tumor cells and for the design of original anticancer strategies targeting the replication forks. The most advanced version of these techniques, called DNA combing, has been developed in France, and is still used by a limited number of laboratories. There is now a strong demand in France and abroad for a wider use of this technique. The aim of the workshop is to provide to the participants the latest methodological aspects of DNA combing and similar approaches and to discuss their respective benefits and shortcomings in light of the recent conceptual progress on genome replication and stability. The goal is to master these techniques for fundamental research on DNA replication and for applications in cancer research.

Inserm Workshops 2007

N° 181 - Genomic screening with RNA interference in cells in culture

Organizers : François Dautry (CNRS, FRE2937, Villejuif), Jean Imbert (Inserm U599, Marseille), Jean-Jacques Lawrence, Représentant de l'Inserm aux Etats-Unis (Ambassade de France, Washington, DC)
Aims: The concept of genetic regulation by RNA interference is now well established. There are several pathways for the silencing of specific genes by various forms of interfering RNA and the molecular bases of their mechanisms have been partly deciphered. The importance of such regulations comes from their implication in fundamental biological processes as well as their usefulness for probing gene function and their potential therapeutic development. Two Inserm workshops have already being held on this theme, Interfering RNA and genomics, (2004), and Micro RNA and genetic expression regulation (2006). The need for the organization of a third workshop at an apparently short period after those two is motivated by the following points: 1) the rapid development of the field, due to, in particular, to the impact of the genomics: the deciphering of genomes allows investigators not only to study the regulation of specific genes but also to investigate the function of the full complement of genes; 2) the opportunity to organize the practical course of this workshop in close collaboration with the RNAi High Throughput Screening (HTS) platform run under the direction of Dr N. Perrimon at Havard Medical School (Drosophila RNAi Screening Center: http://flyrnai.org/).

N° 179 - Polymorphism and genome rearrangements: analysis of CGH and SNP array data

Organizers : Emmanuel Barillot (Institut Curie, Paris), Yves Moreau (Katholieke Universiteit Leuven, Leuven)
Aims: CGH and SNP microarrays are being used more and more frequently for the study of cancers and constitutional disorders. With a regard to bioinformatics, genomic DNA microarrays set specific problems, at the level of primary data analysis (design of experiment, normalization, identification of chromosomal breakpoints and of recurrent aberrant regions) as well as for the biological interpretation of the results (classification, correlation with expression data, data integration, functional annotation…). The use of bioinformatic tools must rely on a comprehensive understanding of data acquisition and of experimental biases, as well as of the assumption that underlie the modelling of this data.
The aim of the workshop is to provide to the participants the concepts and practical tools necessary for the analysis of this kind of data. The goal is both to master these approaches for fundamental research in molecular biology and for applications in clinical research or practice (diagnosis and prognosis).

N° 177 - Statistical methods and novel strategies to search for genes involved in common diseases

Organizers : Alexandre Alcais (Inserm U550, Paris), Philippe Broët (Inserm U780, Faculté de médecine, Paris), Emmanuelle Genin (Inserm U535, Paris), David Trégouët (Inserm U525, Paris)
Aims: The recent achievement of the human genome sequencing and the growing development in molecular techniques enable researchers to gather information on thousands of single-nucleotide polymorphisms (SNPs) (e.g. HapMap project). While the scientific community agrees that this information should offer new opportunities for a better understanding of the biological mechanisms underlying human diseases, there is still no consensus on how to analyze these data and, in particular, how to link the variability of the human genome to complex traits such as cardiovascular diseases, cancer, diabetes. The challenge is to define some new strategies and new statistical methods that will take into account, as best as possible, this breadth of genetic information. The aim of the workshop is to review and discuss the merits and pitfalls of the possible strategies including whole-genome association, candidate gene or system-biology driven approaches.

Inserm Workshops 2006

N° 169 - miRNAs and genome regulation in eucaryotes: expression patterns, genetic targets and mechanisms of action

Organizers : Daniel Aberdam (Inserm U634, Nice), Christophe Antoniewski (Institut Pasteur, Paris), Annick Harel-Bellan (CNRS UPR 9079, Institut Andre Lwoff, Villejuif)
Aims: MicroRNAs (miRNAs) are expressed by eukaryotes genomes as short, double-stranded hairpins. They represent about 1-2% of genes in vertebrates as invertebrates and repress gene expression through sequence-specific base pairing with target miRNAs. Biogenesis and mechanisms of action of miRNAs involve pathways that are overlapping with RNAi pathways. miRNA are involved in the control of cell proliferation, differentiation and apoptosis and growing body of evidence indicate that they play a key role in the regulation of many eukaryotes genetic programmes. What are the miRNAs involved in a given biological process? Essential questions are still open. How, where, and when are they expressed? What are their genetic targets? Novel and specific approaches have to be undertaken to address these questions. The

workshop will review the state of the art of our knowledge of the mode of action of miRNA and the conferences will illustrate the methods and experimental strategies implemented to study their functions.

N° 166 - Identification of non-coding functional regions in genomes

Organizers :

Inserm Workshops 2010

N° 203 - Interactomics: at the crossroads of biology and bioinformatics

Organizers: Christine Brun (TAGC U628, Marseille), Jérôme Reboul (Inserm U891, Marseille), Nicolas Thierry-Mieg (TIMC-IMAG, La Tronche).
Aims: Proteins rarely act alone: they often interact with other macromolecules in order to accomplish their functions. Protein-protein interactions are therefore critical to most

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functions but also for the understanding of the pathologies that are associated with these proteins and the establishment of new therapeutic strategies.

N° 175 - Automatisation of protein production for structural and functional proteomics

Organizers : Nathalie Declerck (Centre de Biochimie Structurale, Montpellier), Herman van Tilbeurg (IBBMC, Université de Paris Sud, Orsay)
Aims: The systematic genome sequencing programmes have uncovered the diversity of all proteins potentially synthesized by living organisms. But they have faced us also with the existence of a total lack of knowledge on the structure and function for a considerable part of these proteins. One of the major challenges in Biology over the coming decade will consist in the functional annotation and the determination of all interactions and structures of the ensemble of proteins constituting the proteome. With the aim of accelerating the access to protein samples for experimental approaches, technological structural and functional genomics programmes have been launched all over the world. By making use of advanced automatization and miniaturization, these novel methodologies are changing our methods for obtaining protein samples. It is now of urgent need that the community active in the field of structural and functional proteomics becomes aware of these technological advances in the field of high throughput protein production, purification and analysis.

N° 173 - Characterization and developments of biomarkers in fluids and tissue extracts: from basic research to clinical perspectives

Organizers : Jean-Paul Briand (CNRS UPR9021, Strasbourg), Marie-Hélène Metz-Boutigue (Inserm U575, Strasbourg)
Aims: The characterization of pathological biomarkers present in tissue extracts, fluids and cells represent a major challenge for the development of new tools in diagnosis, prognosis and the monitoring of undergoing treatment. These researches are based on the analysis of the complex proteome resulting of the high number of rare proteins, or temporarily present and also the multiplicity of the post-translational modifications. The aim of this workshop is to link the clinician expectations and the technological developments of classical proteomic analysis (2D electrophoresis-mass spectrometry), multiplex technics, immunochemical methods, microarrays and innovative biophysical methods. The use of these innovative methods is crucial to find biomarkers for numerous diseases such as cancers, diabetes, neurodegenerative, autoimmune, inflammatory and septic shock diseases. The ways for rigorous evaluations of biomarkers resulting of standardized and validated processes will be also presented.

Inserm Workshops 2006

N° 165 - Protein-glycan interaction: Biological roles and methodological approaches

Organizers : Anne Imberty (CNRS, Grenoble), Hugues Lortat-Jacob (CNRS-CEA-UJF, Grenoble).
Aims: Post-traductional modifications of proteins are known to be of high importance for their functions. In particular, a variety of glycoconjugates, including glycolipids, glycoproteins and glycosaminoglycans are expressed at the cell surface where they contribute to the regulation of numerous biological activities. The aim of the workshop will be to assess the current knowledge on biosynthesis and functions of glycoconjugates. The high structural diversity that characterizes carbohydrates enables them to specifically recognize a large array of proteins: antibody, lectins, adhesion molecules, viral envelopes, toxins, cytokines, growth factors… This workshop will review a panel of different methods at the interface of chemistry and biology that are needed for the characterization of specificity and affinity of such interactions.

BIOINFORMATICS - MODELING - BIOLOGICAL NETWORKS

Inserm Workshops 2011

N° 212 - Bioinformatics approaches to decipher genome regulation from high-throughput data

Organizers: Jacques van Helden (ULB, Belgium), Philipp Bucher (SIB/ISREC, Switzerland)
Aims: Genome regulation plays a crucial role in embryonic development, adaptation of cells, tissues and organisms to their environment, and evolution. This regulation occurs at multiple levels: transcription, RNA maturation (splicing, degradation), micro-RNA, nucleosome occupancy, chromosome conformation. New high-throughput methods offer unprecedented ways to characterize regulatory elements at a genome scale : expression microarrays, ChIP-on-chip, ChIP-seq, RNA-seq, protein binding arrays, etc. Sequencing platforms become available in many institutes, but researchers generally feel some perplexity when they are first confronted to the terabases of novel data. New software tools re being developed to answer those new needs, but their utilization requires to understand the underlying principles, master the parameters, and interpret the significance of the result.
The goal of this workshop is to provide researchers with a theoretical and practical training enabling them to apprehend the whole flow of data analysis, from data acquisition to biological interpretation of the results.

Inserm Workshops 2010

N° 203 - Interactomique : à la croisée des chemins entre biologie et bioinformatique

Organizers: Christine Brun (TAGC U628, Marseille), Jérôme Reboul (Inserm U891, Marseille), Nicolas Thierry-Mieg (TIMC-IMAG, La Tronche).
Aims: Proteins rarely act alone: they often interact with other macromolecules in order to accomplish their functions. Protein-protein interactions are therefore critical to most biological processes. Systematic approaches for identifying them have been developed over the years, such as yeast two-hybrid (Y2H) or affinity purification-mass spectrometry (AP-MS). These methods have enabled the mapping of complex interaction networks in various model organisms, which are profoundly modifying our understanding of cellular mechanisms by providing us with an integrated view of biological processes. However, due to their complexity, such networks can be intimidating and difficult to take advantage of by hypothesis-driven experimental biologists. The main difficulties are typically methodological and technical (for example knowledge and application of bioinformatics tools), but also and more fundamentally they stem from the changes in reasoning required by the systems biology approach. Protein-protein interaction networks being a very rich but neglected source of information, the workshop will present the main strengths and challenges in producing and using this data. Indeed, a better understanding of the processes, questions and solutions proposed by labs that produce and analyze interactomics data should facilitate its general use.

N° 202 - *In silico* discovery of molecular probes and drug-like compounds: success & challenges

Organizers: Maria Miteva (Inserm U973, Paris), Véronique Stoven (Inserm U900, Paris), Bruno Villoutreix (Inserm U973, Paris).
Aims: *In silico* methods play an important role in modern biomedical research. While *in silico* approaches have been used for many years to facilitate the development of bioactive molecules, recent reports demonstrate their successful application for discovery of new drugs. Numerous examples of hit molecules inhibiting enzymes or blocking macromolecular interactions identified by virtual screening have been reported. The objective of the workshop is to get a clear understanding of commonly used *in silico* ligand-based and structure-based virtual screening methods and to master these techniques as well as to present applications ot these methodology for discovery of innovative molecule hits. Hence, the workshop will present at the same time the theoretical methods, existing or under development, as well as recent success stories including hit discovery and lead optimization on important therapeutic targets. It will be demonstrated how *in silico* approaches can assist the classical experimental methods for discovery of novel compound hits more rapidly with reduced costs. This workshop will permit to adopt a common language (biology-chemoinformatics) and to facilitate creating new collaborations between biologists and chemoinformatics scientists.

Inserm Workshops 2008

N° 184 - Statistical Modeling and Analysis of Biological Networks

Organizers: Emmanuel Barillot (Institut Curie, Paris), Stéphane Robin (AgroParisTech/INRA UMR0518, Paris), Jean-Philippe Vert (Ecole des Mines, Paris)
Aims: The accumulation of high-throughput genomics and post-genomics data increases our understanding of molecular mecanisms that govern life at the cellular level. These data allow to study the behaviour of cells by providing an almost exhaustive description of some of its mecanisms, including structural properties of the genome, transcriptome or proteome. Nowadays it is known that different levels are organized into complex interconnected networks, and in order to decipher the logic of life we need to study these networks. These networks can be identified from direct observations or through correlation or back-engineering studies. Specific methodological tools are needed to attack problems such as network inference from experimental data, quantitative and qualitative dynamical study of large-scale networks, structure analysis of networks, predictions at different levels including for phenotypes, of joint analysis of graphs and other genomic data.
This workshop will present the new methodological questions raised by the analysis of biological networks, and review recent advances in modeling, statistics and bioinformatics for network analysis. It will also show how these new approaches can be useful for biologists and how they can contribute to a better understanding of the fundamental mecanisms of life.

N° 182 - Biophysical modeling and mathematical analysis in cellular biology

Organizers: Thierry Galli (Inserm/Institut Jacques Monod, Paris), David Holcman (Ecole Normale Supérieure, Paris)
Aims: The goal of this workshop is to introduce various concepts of biophysical modelling to analyze cellular biology processes. In the past 10 years, new technologies revealed events occurring in cell at the scale of few micrometers and few milliseconds and was applied to correlate in space and time, various parameters at the cellular level or inside the living tissue. It became possible to observe and to quantify processes such as diffusion of molecules and vesicles, transport, interaction and resident time in macromolecular assemblies. Modeling is a fundamental tool to describe and quantify these processes. We will explain and detail how modeling is used in cellular biology. In particular, we will discuss the connection between biophysical models its mathematical analysis. We will underlie how a modeling approach is relevant to study event at a molecular level and focus on particular questions such as: What is the meaning of a chemical reaction at a molecular level? How chemical reactions can be extracted when few molecules are involved. Other examples will be given such as: How to extract the activation time constant and the time a receptor spends inside microdomain, using FRAP or FCS experiments or how to model cellular and viral intracellular trafficking?

Inserm Workshops 2010

STEM CELLS

Inserm Workshops 2010

N° 204 - Human induced pluripotent stem cells, reprogramming and differentiation

Organizers: Annelise Bennaceur-Griscelli (Inserm U935, Paris), Ludovic Vallier (University of Cambridge, UK).
Aims: The recent possibility to reprogram somatic cells into pluripotent stem cells by simple overexpression of few pluripotency factors offers new opportunities and a large number of applications in science and medicine. Indeed, induced pluripotent stem cells (iPSCs) proliferate indefinitely *in vitro* while maintaining the capacity to differentiate into a broad number of functional cells type. Most importantly, iPSCs can be used to generate immuno-compatible cell type for cell base therapy thereby avoiding the use of immune suppressive treatment. iPSCs have also more immediate applications which consist in modelling *in vitro* genetic complex disease for basic studies and drug screening. However, iPSCs present new challenges which limit their wider utilisation. Indeed, iPSCs derivation requires specific skills in genetic modification and in pluripotent stem cells manipulations which can be difficult to acquire. Furthermore, generating mature and functional cell type form iPSCs remain a major issue. Finally, iPSCs technology is evolving extremely fast which renders difficult the identification of robust and efficient methods. During this Inserm workshop, we will aim at providing the expertise necessary to develop project with iPSCs. We will present and discuss the latest technical progress in iPSCs derivation and differentiation. In addition, basic notions concerning epigenetic reprogramming will also be included to determine the drawback and advantages of iPSCs. Finally, ethical issues and intellectual property questions will be examined and existing core facilities for iPSCs derivation will be presented. Overall, the objective of this workshop is to provide the basic knowledge necessary to generate, to use and to validate iPSCs in pre-clinical *in vivo* models and *in vitro* disease modelling.

Inserm Workshops 2009

N° 192 - Human pluripotential stem cells

Organizers: Claire Rougeulle (UMR Epigénétique et Destin Cellulaire, Institut Pasteur, Paris), Marc Lalande (University of Connecticut Stem Cell Institute, Farmington, USA).
Aims: Human embryonic stem cells (hESCs) are derived from embryos produced by in vitro fertilization and are pluripotent in that they can be induced to differentiate into different cell types. There is an enormous potential for hESCs in regenerative medicine and, in particular, for the development of cellreplacement therapies. Human embryonic stem cells are also an essential and powerful research tool for understanding early human development, both at the genetic and epigenetic levels. The 2004 law in Bioethics authorizes, under certain conditions, the use of hESC derived from supernumerary embryos, opening the door for hESC research in France. The main goal of this workshop is to provide to participants an overview of the current state of hESC research as well as the most promising areas for future study. Technical aspects of hESC manipulation and differentiation will be discussed as will their genetic and epigenetics properties, with a specific emphasis on the latter topic. The core facilities available in France and other countries will be described and legal and ethical aspects discussed.

Inserm Workshops 2006

N° 171 - Stem cells: from the concept to clinical trials

Organizers : Louis Casteilla (UMR 5018 CNRS UPS, Toulouse), Anne Dubart-Kupperschmitt (Institut Cochin, Inserm U567, Paris), Hélène Gilgenkrantz (Institut Cochin, Inserm U567, Paris)
Aims: Recent publications about stem cells raised therapeutic hopes needing confirmation by solid experimental data. The main goal of this workshop is to give to participants the state-of-the-art of the stemness concept and to address the practical and ethical questions raised by the development of clinical trials using progenitors or stem cells. Some major characteristics of stem cells such as self-renewal, plasticity and microenvironment will be developed. Two specific examples, the embryonic stem cell and the adult mesenchymal stem cell will then be presented. Discussions will also address our present knowledge about the immunogenicity of these cells. Finally, their use in cell therapy will be followed through examples of clinical trials currently performed.

MICROSCOPY - CELLULAR IMAGING

Inserm Workshops 2011

N°210 - Emerging Tools in Quantitative Fluorescence Microscopy for Systems Biology

Organizers: Carmo Fonseca (Instituto de Medicina Molecular, Portugal), Enrico Gratton (Laboratory for fluorescence dynamics, University of California, USA), Antonio Jacinto (Instituto de Medicina Molecular, Portugal)
Aims: Systems Biology relies on the development of new technologies for doing precise quantification of biological processes. Cells continuously process stimuli that they receive from their inside and outside, using interconnected signaling pathways that rely on the dynamical behavior of the macromolecular complexes and the transient interactions of macromolecules. A major challenge to systems biology is to infer the rate constants, binding affinities, and other parameters of theoretical models from experimental measurement data. Thanks to the engineering of fluorescent probes and the development of novel fluorescence microscopy and spectroscopy methods, quantitative parameters such as molecular concentrations, diffusion coefficients, stoichiometry and residence time of molecules within complexes can be obtained in different locations within the cell at different times with high temporal and spatial resolution. As a result, microscopic images are becoming increasingly sophisticated and can be acquired very fast, thus creating a growing need for novel image analysis, databases and visualization techniques to extract, compare, search and manage the biological information in large image datasets. The purpose of this Workshop is to bring together an international group of scientists and promote ample discussion around the research focus of quantitative fluorescence microscopy, covering recent advances in fluorescence microscopy enabling measurement and computational analysis of a wide range of cellular activities.

Inserm Workshops 2010

N° 208 - Advanced quantitative fluorescence imaging of host cell infection by pathogens

Organizers : Jean-christophe OLIVO-MARIN (CNRS URA 2582, Paris), Guy TRAN VAN NHIEU (Inserm U971, Paris).
Aims: Fluorescence imaging techniques to follow host pathogen interactions at tissular, cellular and molecular levels have met increased popularity in the past decade. This is success is due to important technical developments permitting dynamic, and highly resolutive analysis of pathogenic processes, combined with the establishment of pathogens as bona fide tools to unveil original aspects of fundamental host cell processes. However, the profusion of information derived from the increasing propularity of these integrated approaches introduces new constraints in terms of analysis. In these regards, it is expected that this trend will amplify in coming years due to the rapid evolution of fluorescent microscopy imaging techniques, allowing faster acquisition or single-molecule resolution. The proposed workshop aims at stimulating exchanges between scientists working on host-pathogen interaction models and advanced quantitative fluorescence microscopy techniques to set the emergence of concepts and methods that are likely to become standards in coming years.

Inserm Workshops 2009

N° 195 - Novel imaging techniques for biology: super-resolution and super-localization

Organizers : Benoît Dubertret (ESPCI, Paris), Olivier Haeberle (Université de Haute Alsace, Mulhouse), Vincent Loriette (ESPCI, Paris)
Aims: Few laboratories presently develop or master super-resolution or super-localization techniques in optical microscopy. The scientific interest of these new techniques is tremendous, opening the way to the investigation of biological phenomena which were totally inaccessible ten years ago. Some of these new tools are already available for biologists, while others are still under development in optical laboratories, but should be commercially available within the next five years. Implementing such imaging systems is however not easy, and imposes peculiar or new constraints for the preparation and handling of the samples. Understanding the operation of these new instruments is a crucial step in view of mastering the use and getting the best of their imaging capabilities (super-resolution, 3-D localization, tight full-field optical sectioning…).

Inserm Workshops 2008

N° 186 - Functional *in vivo* imaging methods: from molecules to cells

Organizers : Angela Giangrande, Michel Labouesse (IGBMC, Strasbourg)
Aims: Microscopy, which is an essential tool in developmental biology and neurobiology, has witnessed some major changes over the past ten years. Technological changes, with the development of ever more powerful microscopes, cameras and acquisition systems. Changes also in approaches, with the development of numerous fluorescent proteins, and their use in a wide array of methods relying on fluorescence, such FRAP, FRET, FLIM, FCS, FSM, etc… Physicists and cell biologists using tissue culture cells have undoubtedly been at the forefront in bringing up these changes. Their implementation, however, remains a challenge in live organisms, due to specific growth conditions to maintain them alive, due to problems arising from accessibility, phototoxicity, auto-fluorescence, or endogenous movements. The prime objective of the workshop will be to illustrate the most powerful strategies and approaches used to visualize biological processes in their dynamic aspects within live animals or tissues, regarding gene expression, transport of molecules/particles/vesicles, cell migration, junction rearrangements, cell division, calcium waves. Another objective will be to stress which techniques are available in live microscopy, what are their limitations, the predictable evolutions, and to review methods that allow to best overcome technical constraints attached to each experimental system.

SMALL ANIMAL IMAGING

Inserm Workshops 2008

N° 191 - Small animal imaging: medical techniques for *in vivo* anatomical, functional and molecular imaging

Organizers : Sylvie Chalon (Inserm U619, Tours), Marc Janier (Animage, Bron), Chantal Rémy (Grenoble Institut des Neurosciences, Grenoble)

Aims: Small animal imaging is becoming an important tool in several research fields such as genetically modified mice, metabolism studies, preclinical assessment of efficacy and toxicity of new therapies, studies of physiological and pathological mechanisms, and development of new imaging techniques. Rodents (mice and rats) are the most commonly used animal models, but small primates such as marmosets can also be studied. Small animal imaging can be performed using complementary and sophisticated techniques, which required methodological and experimental skills. Several imaging methods can be applied in vivo to small animal: optical imaging, X ray Computed Tomography (CT), Magnetic Resonance Imaging and Spectroscopy (MRI and MRS), Ultrasound Imaging (US), Positron Emission Tomography (TEP), Single Photon Emission Computed Tomography (SPECT). A wide variety of anatomical and functional parameters can be analysed using these methods. The aim of this educational workshop is to present to biologists and clinicians the different techniques currently available for small animal imaging, with their advantages and limits, as well as the obtained parameters, This will allow defining the most appropriate technique for a given application.

Inserm Workshops 2009

N° 194 - Tissue engineering: study of the interfaces materials/cells/tissues

Organizers : Joëlle Amédée (Inserm U577, Bordeaux), Jérôme Guicheux (Inserm U791, Nantes), Didier Letourneur (Inserm U698, Paris)

Aims: Regenerative medicine aims to restore the functional activities of tissues and organs by using the concept of cellular and tissue engineering. This concept includes all the technologies that use living cells and / or materials (synthetic or natural) in order to improve, regenerate or replace the impaired function of tissues or organs. This concept largely exceeds the traditional concepts of biocompatibility and requires a strong interdisciplinary work between physic, chemistry, cell biology, material science, and clinic. The aim of this workshop is to provide a broad public basis of cell and tissue engineering reporting on the latest scientific and technological advances in the fields of materials and their interfaces with the cells and tissues. The audience consists of basic researchers, clinicians and engineers that will exchange their views on the advanced techniques of molecular and physicochemical characterization of the interfaces cells / tissues / materials in an attempt to identify the advantages and the limits of the current therapeutic solutions based on tissue engineering concepts.

Inserm Workshops 2008

N° 190 - TLR receptors: from research to medical applications

Organizers : Charles Hétru (IBMC, Strasbourg), Valérie Quesniaux (Institut de Transgénose, Orléans)
Aims: Although most attention was long devoted to adaptive immunity, numerous animal species cope with pathogen aggressions in the absence of acquired immune system. Recent discoveries in invertebrate species boosted a renewal of interest for innate immunity in mammals. One of the key elements of innate immunity is the discovery in 1997 of transmembrane "Toll Like Receptors" (TLR), crucial for many responses to pathogens. Many scientists nowadays discover that TLRs are involved in the systems they study. The field of TLRs evolves rapidly. The twofold aim of this workshop is to deal with the multiple facets of TLR structure and biology, but also specific technical aspects and pitfalls. Discussions will also extend to most relevant experimental models and interactions between TLR and signalling pathways.

Inserm Workshops 2006

N° 167 - Physics of Molecular Motors - Measurements at the single molecule scale

Organizers : Patricia Bassereau (UMR 168, Institut Curie, Paris), Ulrich Bockelmann (Ecole Supérieure de Physique et Chimie Industrielle, Paris).
Aims: Recently a new class of experimental techniques has been developed in biology: micromechanical measurements at the scale of a single molecule. The study of molecular motors is a blooming field. It uses and contributes to the development of techniques at the interface between bio- and nanotechnologies. It attracts physicists and biologists, experimentalists and theoreticians. The goal of this workshop is to present the main techniques used to study biological molecules at the single molecule level and, at the same time, our current knowledge of molecular motors. In vitro biophysical studies on single molecules will be the main focus, but additional collective aspects and the functioning of these motors in integrated cellular systems will also be presented. Recent theoretical models describing the properties of the motors will be explained in an educational manner.

Inserm Workshops 2008

N° 183 - Molecular interactions: theory and biophysical tools for quantitative measurements

Organizers : Danièle Altschuh (UMR CNRS/ULP 7175, Illkirch), Pierre Bongrand (UMR Inserm 600/CNRS 6212, Marseille)
Aims: The quantitative analysis of molecular binding is essential in both fundamental and applied biomedical research. This approach is necessary for studying the molecular mechanisms involved in biological function. The process is also essential for studying the dysfunctions leading to pathological states and for developing new drugs. The aim of the workshop is to provide a critical assessment of molecular recognition techniques. The biophysical methods that allow a quantitative analysis of binding will be presented. The relationship between experimentally measured quantities and the structure of interacting surfaces will be discussed. Specific examples will be given to illustrate the applications of these biophysical methods in biology.

Inserm Workshops 2010

N° 206 - Microtubule dynamics in cell migration: molecular interactions, functional consequences and therapeutic perspectives in oncology

Organizers : Stéphane Honoré (Inserm U911, Marseille), Diane Braguer (Inserm U911, Marseille).
Aims: The objective of the workshop is to present methodology and recent knowledge about the molecular and cellular mechanism involving microtubules in cell migration and to specify the role of the protein complexes associated at the end + of microtubules (+TIPs) in this process. We will address structural and cellular biology of +TIPs: molecular interactions +TIPs/microtubules and +TIPs/+TIPs, tubulin and +TIPs post-translational modifications and their functional effects on microtubule dynamics and the coordination of the cytoskeletons. The workshop will also give an overview on the pharmalogical approaches targeting the protein complexes at microtubule + end and will present the strategies under development for the screening of specific inhibitors of +TIPs for applications in oncology.

Inserm Workshops 2009

N° 199 - Human memory and its impairment: multidisciplinary approach

Organizers : Béatrice Desgranges (Inserm U923, Caen), Francis Eustache (Inserm U923, Caen), Bernard Laurent (Hôpital de Bellevue, Saint-Etienne).
Aims: The purpose of this workshop is to provide an overview on the recent in the field of human memory in healthy subjects and patients suffering from degenerative cortical diseases (Alzheimer's disease, frontotemporal dementia, semantic dementia), permanent or transient amnesic syndromes and other organic and/or functional forms of amnesia. This workshop will address models of memory, links between memory and identity, between memory and emotion, the role of sleep in the consolidation, the cerebral bases of human memory and its disorders, the revalidation of memory deficits, and memory in animals.

Inserm Workshops 2008

N° 188 - Axonal transport defects and neurodegenerative diseases: strategies to understand and treat these pathologies

Organizers : Thierry Galli (Inserm/Institut Jacques Monod, Paris), Frédéric Saudou (Institut Curie, Orsay)
Aims: The aim of this course is to bring together biologists, physicists and clinicians working on various neurodegenerative disorders and/or on axonal transport to discuss the possible strategies to study and understand the role of disease proteins in the control of intracellular trafficking and their alteration in pathological situations. Through the examples of Huntington's and Alzheimer's diseases, spastic paraplegias, Charcot-Marie tooth disease and amyotrophic lateral sclerosis, we will ask the following questions: How can we study axonal transport, and how is axonal transport regulated? What are the imaging techniques available and for what applications? What are the limits? What are the strategies to model axonal pathologies *in vitro* and *in vivo*? How can we quantify these alterations?

Inserm Workshops 2007

N° 173 - Characterization and developments of biomarkers in fluids and tissue extracts: from basic research to clinical perspectives

Organizers : Jean-Paul Briand (CNRS UPR9021, Strasbourg), Marie-Hélène Metz-Boutigue (Inserm U575, Strasbourg)
Aims: The characterization of pathological biomarkers present in tissue extracts, fluids and cells represent a major challenge for the development of new tools in diagnosis, prognosis and the monitoring of undergoing treatment. These researches are based on the analysis of the complex proteome resulting of the high number of rare proteins, or temporarily present and also the multiplicity of the post-translational modifications. The aim of this workshop is to link the clinician expectations and the technological developments of classical proteomic analysis (2D electrophoresis-mass spectrometry), multiplex technics, immunochemical methods, microarrays and innovative biophysical methods. The use of these innovative

methods is crucial to find biomarkers for numerous diseases such as cancers, diabetes, neurodegenerative, autoimmune, inflammatory and septic shock diseases. The ways for rigorous evaluations of biomarkers resulting of standardized and validated processes will be also presented.

Inserm Workshops 2006

N° 172 - New approaches in pharmacoepidemiology

Organizers : Bernard Bégaud (Inserm U657, Bordeaux), Pascale Tubert-Bitter (Inserm U780, Villejuif)
Aims: New drugs are assessed before marketing, with necessarily restrictive conditions. At that point, efficacy and safety are only potential. After the marketing, the size of the exposed population as well as the prescription conditions change radically and the impact of the new drug on the public health, principally its risk, are to be evaluated. The stakes of this evaluation, of great importance considering the potential hazards, lead most countries to develop more or less efficient pharmacovigilance systems, observational studies and database studies with updated methodological approaches and contraints. The aims of the workshop is to present the context and the stakes of the drug evaluation in real use conditions. Recent methodological developments for surveillance and risk quantitative analysis will be described and discussed, with applications to real cases. The use of medical prescription databases for scientific purposes will be addressed.

EPIDEMIOLOGY - STATISTICS

Inserm Workshops 2011

N° 209 - Recent advances in statistics for causal analysis

Organizers: Antoine Chambaz (Université Paris Descartes, France), Michel Chavance (Inserm U1018, France)
Aims: The objective of this workshop is to disseminate the most recent methods for tackling the statistical analysis of causal problems, both from a methodological and applied point of view. The variety of methods illustrates how difficult these problems usually are, and reflects the diversity of approaches, which may sometimes seem or be contradictory. Confronting the methods, notably in an epistemological perspective, will foster the making of one's own understanding and practice of the statistical analysis of causal problems. Finally, it is worth emphasizing that the relevance of some of the methods presented goes beyond the framework of causal analysis.

Inserm Workshops 2010

N° 205 - Mixture modelling for longitudinal data

Organizers : Bruno Falissard (Inserm U669, Paris), Christophe Genolini (Université Paris X, Paris), Helene Jacqmin-Gadda (Inserm U897, Bordeaux), Cécile Proust-Lima (Inserm U897, Bordeaux).
Aims: Present, discuss and contrast several approaches to analyse heterogeneous longitudinal data and highlight profiles of change with time. Both cluster analysis methods and mixture models for longitudinal data will be presented with applications to medical and psychological data. Particular emphasis will be put on parameter interpretation, post-fit evaluation of model assumptions and conditions of use of the various approaches. The workshop will also include a presentation of joint models with latent classes for time-to-event and longitudinal outcome and an introduction to some other latent variable models.

Inserm Workshops 2009

N° 198 - Recent study designs in epidemiology

Organizers: Nadine Andrieu (Inserm U900, Paris), Michel Chavance (Inserm U780, Villejuif), Pascal Wild (INRS, Nancy).
Aims: Introduce and discuss recent epidemiological designs with observation limited to cases or with optimized complex sampling, present the statistical models used for their analysis.

Inserm Workshops 2007

N° 176 - Modelling incomplete observations: Sensitivity analyses

Organizers : Michel Chavance (Inserm U780, Villejuif), Hélène Jacqmin-Gadda (Inserm E338, Bordeaux), Geert Molenberghs (Center for Statistics, Hasselt University, Diepenbeek)
Aims: The observation of incomplete samples is the rule rather than the exception. It raises problems of bias and precision for which solutions are available when the observation process only depends on known quantities. The limitation of these approaches comes from the fact that it is not possible to determine whether their conditions of applications are met without obtaining the missing values for a representative subsample of the incomplete subjects. Sensitivity analyses complete these methods by assessing to what extent the study conclusions can or cannot be modified according to the assumptions which are formulated about the observation process. After the workshop, the participants should be able to better understand the problems raised by incomplete observations; Jointly model the effect of explanatory variables on an outcome variable and on the observation process; Be able to interprete the results of a sensitivity analysis.