



# LABORATORIES

LABORATORIES



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### INSERM

- The Généthron Research Division
- Institute for Stem Cell Therapy and Exploration of Monogenic Diseases - I-Stem
- Molecular Immunology and Innovative Biotherapies
- Stem Cells and Cardiogenesis
- Structure and Activity of Normal and Pathological Biomolecules
- Unit for Integrated Biology in Adaptations to Exercise (UBIAE)

### CNRS

- The Généthron Research Division
- Institute for Systems and Synthetic Biology (iSSB)
- Laboratory for Analysis and Modeling in Biology and the Environment (LAMBE)
- Metabolic genomics
- Statistics and the Genome

### INRA

- Plant Genomics Research Unit (URGV)
- Statistics and the Genome

### CEA

- Genoscope
- Laboratory for Analysis and Modeling in Biology and the Environment (LAMBE)
- Laboratory for the Genomics and Radiobiology of Keratinopoiesis
- Metabolic genomics
- The National Genotyping Center (CNG)
- Tumor Functional Genomics and Epigenetics

### UNIVERSITY OF ÉVRY

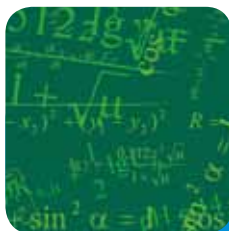
- The Généthron Research Division
- GenHotel
- Institute for Stem Cell Therapy and Exploration of Monogenic Diseases - I-Stem
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- Laboratory for Analysis and Modeling in Biology and the Environment (LAMBE)
- Metabolic genomics
- Molecular Immunology and Innovative Biotherapies
- Plant Genomics Research Unit (URGV)
- Statistics and the Genome
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## BioIntelligence Program



### MAIN TOPIC

An integrated software environment for the life science industry

### FIELD OF ACTIVITY

- Drug discovery.
- Systems biology.
- Product lifecycle management.
- Applications in oncology & toxicology.

### KEYWORDS

Drug discovery - Oncology - Toxicology -  
Systems biology - Product lifecycle  
management.

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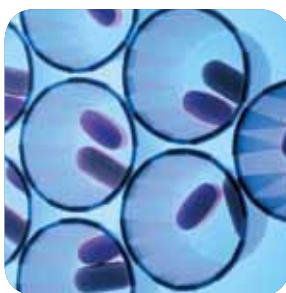
### RESEARCH THEMES

The Institute of Systems and Synthetic Biology is developing the Bio Intelligence Program (*cf page 30*).

The goal of the BioIntelligence Project is to elaborate an integrated software environment for product and compound R&D in the life science industry, with emphasis on the pharmaceutical and crop protection industries.

This innovative digital environment will:

- /// deliver a unified platform for collaborative biological synthesis and analysis;
- /// generate mathematical models for use in *in silico* digital simulation and comparison with experimental data;
- /// optimize life science R&D processes.





# Center for Mechanical Engineering and Automation Studies and Research [CERMA]



## MAIN TOPIC

Engineering sciences.

## FIELD OF ACTIVITY

- Development of new production methods, feasibility studies and specifications for products and machines requiring a multi-disciplinary approach.
- Applications in manufacturing, research and biology.

The ARIPA has been awarded "Technical Resource Center" status by the French Ministry of Research.

## KEYWORDS

Mechanical engineering - Robotics - Automation - Instrumentation - Process : development and feasibility - Prototyping.

**Supervisory bodies** ARIPA

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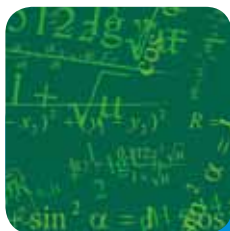
## RESEARCH THEMES

The CERMA stands out by its ability to provide total management of complex projects (from initial specification to commissioning) in fields including mechanical engineering, electronics, special sensors and industrial IT. As a Technology Transfer Center of the University of Évry, it designs, builds and implements innovative machines, products and automated processes for a range of industrial sectors (notably in the field of biology). The CERMA has particularly focused its work on the high-throughput automation of electrophoretic analysis and related techniques: sample preparation, dilution, PCR, UV luminescence imaging, etc.

The CERMA collaborates with other public- and private-sector establishments: CNS (*cf page 28*), Généthon (*cf page 89*), University of Évry (the IBISC lab *cf page 37*), University of Paris 7, University of Paris 11, the Gustave Roussy Institute, INRETS (LIVIC), Danone Research, etc. Since its creation, the CERMA has handled more than 250 projects in a variety of sectors: automated workstations in genetics, crash test beds in the automotive industry, industrial inkjet printers, medical electronics, etc.

## INDUSTRIAL COLLABORATIONS

- /// Several private-sector users: Oligo Express (oligonucleotide synthesis) in Montreuil, France; Metabolic Explorer (a green chemistry company developing and patenting industrial processes based on fermentation) in Saint-Beauzire, France.
- /// Equipment manufacturers and reagent producers: Genome Express (oligonucleotide synthesis) ; DNAgency.
- /// Other industrial collaborations: Danone Research, EDF, SKF, Schlumberger, Cerisiers, ID Fruits, Traiteurs de Paris, Calwatt, Otico, Ces, Azimut, Green Factory, Biobank, Alam Medical, CEA, Primadiag, Qualicyt, Herdegen, Silec Cable, Irsn, Corning, Risoud Precision, Ehbio, France Ponte, Aegilops, Cornilleau, Fanuc, Genewave, Adres, Comelli, Thema Concept.



## Epigenomics Program



### MAIN TOPIC

A multidisciplinary modeling approach for systems biology and synthetic biology.

### FIELD OF ACTIVITY

- Modeling and simulation of biological processes in a (post)genomics context.
- Epi-organization of genomes.

### KEYWORDS

Modeling - Simulation - Engineering - Macromolecular networks - Epigenesis.

**Supervisory bodies** Genopole®

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### RESEARCH THEMES

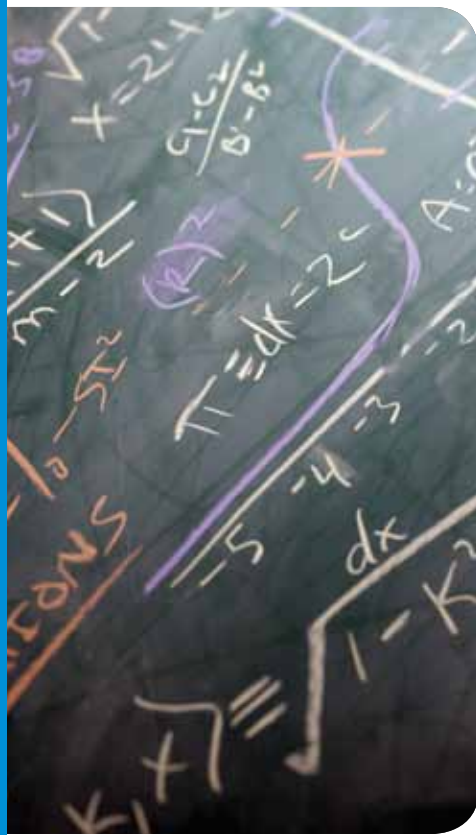
The Institute of Systems and Synthetic Biology is developing the Epigenomics Program (*cf page 30*).

The Genopole Epigenomics Project (founded in 2002 and whose slogan is "modeling for understanding") aims first and foremost to be a forum for dialogue in order to catalyze research on complex biological problems *via* contributions from a range of disciplines: biology, computing, mathematics, theoretical physics, artificial chemistry and so on.

The Program simultaneously serves as :

- a vector for training researchers in disciplines other than their own,
- a visiting researcher program,
- a hotbed of pioneering science (stimulating the invention of new research subjects and supporting them through targeted, thematic activities),
- a collaborative program that federates Évry-based research efforts on modeling in biology.

All the activities funded by the Epigenomics Program are highly thematically targeted and are based around a small number of leading researchers.





### MAIN TOPIC

Genomics and postgenomics of spondylarthropathies.

### FIELD OF ACTIVITY

- Constitution of DNA banks and clinical/ immunological databases.
- Physiopathology of spondylarthropathies.
- Characterization of genetic factors other than HLA B27.
- Function of HLA B27.
- Clinical epidemiology.

### KEYWORDS

Genetics - Immunology - Ankylosing spondylitis - Spondylarthropathies.

### RESEARCH THEMES

Ankylosing spondylitis (AS) is the archetypal (and most frequent) spondylarthropathy. The Euroas association (which consists of 10 rheumatology research labs and clinical centers from 9 European countries) has achieved one of its main objectives: building an European genomic bank (EGB) for cataloguing the genetic and clinical characteristics of patients suffering from SA or other spondylarthropathies and those of their families. The bank's current collection of 7 000 samples (collected by the consortium members from 1 230 families) includes a large cohort of B27-negative subjects and some B27-positive subjects.

The EGB has enabled selection of a large research cohort and the launch of a high-resolution MHC and genome study. The goal is to screen for potential susceptibility and/or severity genes involved in the genesis of spondylarthropathies in general and SA in particular, thus elucidate the fundamental molecular mechanisms of these diseases and open up new opportunities for developing novel diagnostic techniques and treatments (including cell and gene therapies).

### Supervisory body

Euroas Association - University Paris V

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## The Genethon Research Division



### MAIN TOPIC

Gene therapy for rare genetic diseases.

### FIELD OF ACTIVITY

Design development and production of innovative therapies for rare genetic diseases in general and neuromuscular diseases in particular.

### KEYWORDS

Rare diseases - Biotherapies - Neuromuscular diseases - Gene therapy, cell therapy - Therapeutics based on genetic knowledge - Vector and targeting technology - Biomanufacturing - Gene transfer, stem cells, pharmaceutical development, regulatory affairs, preclinical and clinical development (bioassays, imaging, functional investigation, drug testing) - GMP facility for the production of gene transfer vectors (the ETGC).

### RESEARCH THEMES

The Genethon Research Division has 5 main research themes:

Identification of new therapeutic approaches for progressive limb girdle dystrophies: Investigation of physiopathological mechanisms and identification of *in vivo* gene therapy strategies based on the use of adeno-associated vectors.

This work is carried out by the limb girdle dystrophy research group of Genethon headed by Isabelle Richard, PhD, DR1 CNRS. The group's main administrative authority is Genethon. The group is part of the joint unit UMR 8587.

Development of new approaches for *ex vivo* gene therapy and study of the issues related to the use of viral vectors for gene transfer. Use of stem cells in cell and gene therapy and analysis of stem cell differentiation, the stability of gene correction and the epigenetic modifications induced.

This work is performed by the joint INSERM/Genethon/University of Évry-Val-d'Essonne/École Pratique des Hautes Etudes research unit, UMR 951 ("Molecular Immunology & Innovative Therapies", cf page 35), led by Anne Galy, PhD.

**Supervisory bodies** Genethon - INSERM -

University Évry-Val-d'Essonne - CNRS

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Gene therapy of X-linked myotubular myopathy and Charcot-Marie-Tooth type myotubular neuropathies.

This work is carried out by the ATIGE research group "Myotubularin-related Myopathies", led by Anna Buj-Bello, PhD, CR2 INSERM.

Development of innovative approaches for viral targeting and innovation in the field of bioprocesses.

This work is performed by Genethon researchers and supervised by Philippe Moullier, MD, PhD.

Characterization and control of the patient's immune response to gene transfer.

This work is carried out by Genethon researchers and supervised by Philippe Moullier, MD, PhD.



## GenHotel European Research Laboratory for Rheumatoid Arthritis - EA 3886



### MAIN TOPIC

Genomics - Postgenomics.

### FIELD OF ACTIVITY

Research on the genetic susceptibility to rheumatoid arthritis and on the pharmacogenetics of the disease.

### KEYWORDS

Rheumatoid Arthritis - Family studies - Autoimmune and multifactorial diseases - Pharmacogenetics

### Supervisory body

University Évry-Val-d' Essonne - EA 3886

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### RESEARCH THEMES

Rheumatoid Arthritis, the most common autoimmune disease, is a painful chronic disease which leads to progressive joint destruction. This multifactorial disease probably involves a large number of genetic factors. New biotherapies have recently improved the treatment outcomes for RA.

GenHotel's goal is to determine the multifactorial determinism of rheumatoid arthritis (RA) by studying genetic and environmental factors in sufferers and their families. This work should lead to new drug targets, with a view to preventing and curing this disease. The research methodology will be extended to other diseases with a major impact on public health. Familial studies performed at GenHotel contribute significantly to the confirmation of new genetic factors.

GenHotel has confirmed the importance of five suspected factors and is now studying 25 newly proposed factors. Additional analyses of genomic variations are being performed. In parallel, familial studies are being extended by a GenHotel group based in the Auvergne region of central France. The objective is to specify the risks due to the association of genetic and environmental factors in RA families.

### ACHIEVEMENTS/ COLLABORATIONS/ HIGHLIGHTS

- GenHotel is involved in several collaborations on the Genopole® campus, notably with the Statistics and Genome Laboratory (Professors C. Ambroise and B. Prum; *cf page 38*), Genoscope (Professor J. Weissenbach; *cf page 28*) and the French National Genotyping Centre (Professor M. Lathrop; *cf page 36*).
- GenHotel has set up programs at the South Ile-de-France Medical Center in Évry-Corbeil (Professor Hilliquin) and at Lariboisière University Medical Center in Paris (Professor Bardin), in order to develop transcriptome analysis and study the pharmacogenetics of RA biotherapies.
- One of GenHotel's particular characteristics is its commitment to sharing, thanks to funding from the French Rheumatoid Arthritis Society (Association française des polyarthritiques): sharing funds by hosting guest researchers in its labs, sharing results on the [www.genhotel.com](http://www.genhotel.com) website and sharing skills in additional projects.



## Genoscope - CNS CEA/Genomics Institute



### MAIN TOPIC

Genomics and post-genomics of various species, including microorganisms sourced from the environment.

### FIELD OF ACTIVITY

- High-throughput production of DNA sequences.
- Genome analysis.
- Functional genomics.
- Applications (research on biological solutions for the replacement of chemical synthesis).

### KEYWORDS

Sequencing - Genomics - Biochemistry - Metabolism - Bioconversion - Comparative genomics - Metabolic engineering.

### RESEARCH THEMES

Since 1998, Genoscope has been responding to the high-throughput sequencing needs of the French scientific community (380 Mbases per day).

Genoscope has also participated in international collaborative sequencing efforts such as the Human Genome Project (chromosome 14), plant genome projects (algae, the banana plant, *Arabidopsis*, grapevine, rice, cocoa tree etc.) and animal genome projects (*Tetraodon*, *Anopheles*, etc.), fungi (truffles, a fungal pathogen, *Leptosphaeria maculans*) and has sequenced more than fifty prokaryotic genomes.

The Genoscope lab keeps up with the state of the art in sequencing and sequence analysis; 97.3% of our DNA sequence output is generated using the latest Flex and Illumina technologies. The sequencing facility is constituted by 3 Roche 454 GS FLEX Titanium, 2 Illumina GALIX and 1 Solid machines and 17 ABI 3730 capillary sequencers, which will be progressively replaced by new-generation sequencers. The current average daily throughput is around 10 billion bases.

Genoscope is currently focusing its research activity on the genomics of environmental micro-organisms in particular marine protists (the "TARA Oceans" project), the bacterial flora of the human digestive tract and those involved in effluent treatment.

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The exploitation of sequence data (now extended to the identification of biological functions, notably in the biocatalysis field) is opening up new perspectives for developments in industrial biotechnology. In the field of sustainable development, Genoscope is searching for biological solutions in synthetic chemistry, in order to reduce pollution and energy & fossil fuel consumption.

To this end, the centre has developed an enzyme activity screening platform and a metabolic engineering laboratory. This research is performed in close collaboration with the UMR 8030 Metabolic Genomics research unit (*cf page 34*).

### INDUSTRIAL COLLABORATIONS:

- /// Global Bioenergies (*cf page 95*)
- /// Isthmus
- /// Suez Environnement.





## MAIN TOPIC

Postgenomics and cell therapy of monogenic diseases.

## FIELD OF ACTIVITY

Evaluation of the full therapeutic potential of all types of human pluripotent stem cells (stem cells from all sources) in the treatment of monogenic diseases. Set against this background, the group is particularly exploring substitutive cell therapies for degenerative diseases on one hand and the use of stem cell lines carrying pathological mutations as drug screening targets on the other.

## KEYWORDS

Cell therapy - Disease modelling -  
Stem cells - Monogenic diseases.

I-STEM is composed by two research entities : INSERM/ UEVE and CECS. I-STEM is developing 12 research themes:

- // Neurodegenerative diseases (cell therapy, modeling of Huntington's disease).
- // Neuromuscular diseases (disease modeling of myotonic dystrophy).
- // Motor neuron diseases (molecular and cell mechanisms involved in the development of motor neuron diseases such as myotonic dystrophy).
- // Muscle diseases (disease modeling, repair).
- // Neuroplasticity and therapeutics (study of molecular mechanisms involved in neural development).
- // Neurovascular damage (disease modeling and cell therapy).
- // Retinopathies and neural development diseases (cell therapy, disease modeling).
- // Genodermatoses (disease, cell therapy).
- // Biotechnology of human stem cells (mass production of cells, genetic engineering).
- // High-throughput screening.
- // Use of induced pluripotent stem cells as disease models in drug screening.
- // Functional genomics (development of dedicated technological tools for the study of monogenic diseases).

## Supervisory bodies INSERM

University Évre-Val-d'Essonne - AFM - CECS

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Participation in French National Research Agency programs, a Medicen Paris Region cluster program and several European Union projects.

## ASSOCIATED RESEARCH GROUPS

"Differentiation of human melanocytic lineage and pathological modelling of waarenburg Syndrome using mutant human Embryonic Stem Cells".  
Leader: Christine Baldeschi.

## INDUSTRIAL COLLABORATIONS

- // GenoSafe (cf page 93)
- // LTKFarma (cf page 104)
- // Roche
- // Collectis.



## MAIN TOPIC

Systems and synthetic biology.

## FIELD OF ACTIVITY

- Modeling, simulation and engineering of biological processes.
- Metabolic engineering.
- Molecular Biology.
- Bioinformatics.
- Microfluidics.

## KEYWORDS

Synthesis - Engineering - Modeling -  
Simulation - Macromolecular networks.

## RESEARCH THEMES

The Institute of Systems & Synthetic Biology (iSSB) is structured into 5 research teams. Systems Biology integrates experimental, theoretical, and computational studies to model living systems. In this research area, the MEGA and Metamorphosis teams study the structure, architecture, expression, and evolution of genomes. Synthetic biology uses systems biology models to design, build, and test new biological circuits and devices (Xenome, Synth-Bio and Bio-RetroSynth teams).

/// The **MEGA** research group analyses the topology of transcriptional networks in time and space. Its recent work has dealt with the functional organization of the nucleus, genome evolution & organization and links between carbon metabolism and DNA replication. The group's theoretical work is prompting bench experiments that examine the cell's regulatory networks on the genome-wide scale.

/// The **Metamorphosis** group studies three aspects of the genome of the African clawed frog *Xenopus tropicalis*: genome structure (DNA transposons and their use in genome engineering experiments), expression of the genome during ontogenesis, and genome evolution.

/// The **Synth-Bio** research group is developing computational methods for designing biological and metabolic circuits within bacteria. These biological circuits are then characterized *in vivo*. Lastly, the bench data feed into established models and thus close the loop.

## Supervisory bodies

Genopole® - University Évry-Val-d'Essonne - CNRS

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/// The **Bio-RetroSynth** group's research interests cover the use of retrosynthetic methods for designing and building new metabolic networks. Retrosynthesis consists in choosing a set of exogenous enzymes which, when introduced in a host organism, produce the desired target compound. The method is being applied to the production of drug compounds in bacteria.

/// The ultimate aim of the **Xenome** team is to design and engineer novel cellular components ("xeno"-nucleic acids, XNA) to elaborate safe GMOs whose *in vivo* generation and functionality can be strictly controlled, and which therefore allow the development of new and advanced applications in biotechnology.

## ASSOCIATED "ATIGE" RESEARCH GROUPS

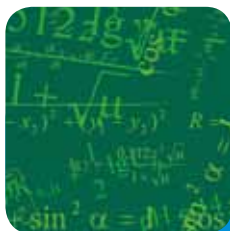
/// "Towards Reliable Synthetic Biology".  
Leader : Alfonso Jaramillo.

/// "Metabolic production of therapeutic compounds by bioretrosynthesis".  
Leader : Jean-Loup Faulon.

/// "Xenome".  
Leader : Piet Herdewijn.

## INDUSTRIAL COLLABORATIONS

/// WatchFrog (*cf page 130*).



## IT for Integrated Biology and Complex Systems - IBISC



### MAIN TOPIC

Computer science, bioinformatics, ICT and engineering science applied to biological systems.

### FIELD OF ACTIVITY

- Bioinformatics, analysis, modeling.
- Identification and simulation of biological processes.
- Learning.
- Formal methods.
- Operational research.
- Communication & transport networks.
- Agent-based & communicative systems.
- Biomedicine & healthcare (signals, machine-assisted medical procedures, Assistive technology in handicap).
- Biometrics.
- Multimodal man-machine inter-facing.
- Road safety.
- Biology of the cellular micro-environment/ Modeling in physiology.

### KEYWORDS

Bioinformatics - Postgenomics - Data integration and advanced databases - Formal methods - Algorithmics - Optimization - Learning - Complexity sciences - Data - Signal and image processing - Virtual reality - Augmented reality - Haptics - Intelligent vehicles - Cell migration - The physiome.

### RESEARCH THEMES

The group's scientific activity is organized into three themes: biological systems, assistance robotics and airborne vehicles.

Within Genopole®, IBISC's specificity involves studying potential applications of computing science and automation to genomics and systems biology. Research in this area covers three main themes:

- /// The representation, analysis and comparison of DNA, RNA and protein sequences; the determination of functional motifs, annotation, etc.
- /// The organization and analysis of transcriptomic, proteomic and metabolomic data, together with statistical learning based on these data with a view to the development of systems biology tools.

**Supervisory bodies** University Évry-Val-d'Essonne

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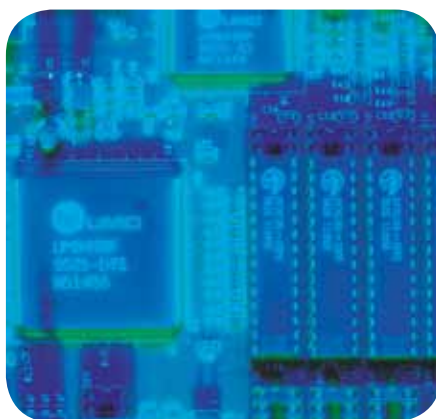
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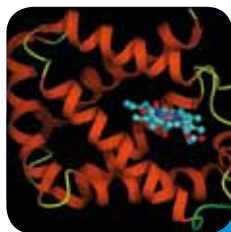
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/// The representation, modeling, simulation and identification of biological processes, with a focus on the simulation of cellular and tissue processes (renal physiology, development); regulatory networks and cell / micro-environment interactions during metastatic spreading.

### INDUSTRIAL COLLABORATIONS

In addition to its participation in around ten European Union projects and twenty or so French National Research Agency projects, IBISC collaborates directly with a number of industrial partners, including: Arent - Cliris - Continental - Oktal.



## MAIN TOPIC

Chemistry, biology and physics applied to the analysis and modeling of biomolecules and materials.

## FIELD OF ACTIVITY

- Mass spectrometry structural analysis of macromolecular systems of biological interest.
- Classical and *ab initio* modeling of the structure, dynamics and reactivity of biomolecules.
- Electrochemistry and activity of materials at interfaces in confined media (toxic radioactive elements).
- Biophysics and macromolecular synthesis.

## KEYWORDS

Mass spectrometry - Proteomics - Glycomics - Synthetic polymers - Gas-phase reactivity - Classical and *ab initio* modeling - Molecular dynamics - Reactivity and thermochemistry of radionuclides - Redox reactions of the actinides - Chemistry of solutions - Electrochemistry - Supramolecular assemblies - Nanopores - Bionanotechnology.

## RESEARCH THEMES

- // Proteomic studies (analysis of post-translational modifications, immunopurified protein complexes, etc.) by using MALDI/TOF, electrospray/Q/TOF, capillary electrophoresis/ion trap and LTQ orbitrap mass spectrometers.
- // Development of new MS-coupled techniques.
- // Study of the role of metal cations in the catalysis and activation of model biological compounds (amino acids, nucleotides, saccharides, etc.) in the gaseous phase.
- // Multiscale modeling of the structure and function of biological assemblies.
- // Development of coarse-grained force fields *via* protein-protein binding.
- // Prediction and modeling of the long-term behavior of final electronuclear waste.
- // Study of the transport (translocation) of single macromolecules through nanometer-scale protein-based pores and artificial biomimetic pores (nanolithography).

## Supervisory bodies

CNRS - CEA - University Evry-Val-d'Essonne

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// Synthesis of polymer gene therapy vectors and analysis of their *in vitro* and *in vivo* structure and function.

// Synthesis of biosourced polymers.

## ASSOCIATED "ATIGE" RESEARCH GROUPS

"Protein translocation and folding at the nanopore outlet: a comparison between natural and biomimetic systems; applications".  
Leader: Juan Pelta.

## INDUSTRIAL COLLABORATIONS

- // EDF
- // AREVA
- // ANDRA (French National Agency for the Management of Radioactive Waste)
- // ARCELOR
- // Synchrotron Soleil
- // CEVA (Centre for the Study and Exploitation of Algae)
- // Global Bioenergies (*cf page 95*)
- // Horiba Jobin Yvon
- // Onidol
- // SNPE.



## Laboratory for the Genomics and Radiobiology of Keratinopoiesis



### MAIN TOPIC

Stem cells of the human epidermis.

### FIELD OF ACTIVITY

- Stem cell biology.
- Radiobiology.
- Cancer.

### KEYWORDS

Somatic stem cells - Human skin - Genomics - Transcription factors - Skin organogenesis - Regenerative medicine - Radiobiology - Hypersensitive patients - Ionizing and UV radiation - DNA damage and repair

### RESEARCH THEMES

Homeostasis, regenerative potential and radiosensitivity of human epidermal stem cells.

Human interfollicular epidermis is the multilayered epithelium that covers the human skin. This tissue is in perpetual renewal, a process named keratinopoiesis which is maintained through stem cells and their ability to self-renew.

Although potentialities of human epidermal stem cells have been exploited for clinical purposes for more than 20 years, they are still poorly known. Keratinocyte stem cells are located in the basal layer of epidermis.

They are defined as undifferentiated and quiescent cells, capable of a large proliferative potential when stimulated. Their direct progeny, called keratinocyte progenitors, are responsible for the short-term maintenance of epidermis. These keratinocyte progenitors divide in the basal compartment and then migrate to upper layers of epidermis to give rise to the differentiated cells. Our laboratory aims at better characterizing these two basal cell populations, both in normal skin homeostasis and after genotoxic stress.

Our group dissects the determinants of stemness and self-renewal in keratinocyte stem cells, notably those related to the TGF- $\beta$ 1 network. We also aim at understanding the mechanisms that maintain genomic stability in the basal keratinocytes, which are the major target of skin carcinogenesis after ionizing or UV radiation. DNA damage and repair are characterized in normal and hypersensitive skin, derived from patients with rare genetic dermatologic diseases.

**Supervisory body** CEA (IRCM)

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## Metabolic Genomics CEA/Genomics Institute - UMR 8030



### MAIN TOPIC

Genomics - The biochemical diversity of living systems.

### FIELD OF ACTIVITY

- Analysis of eukaryotic and prokaryotic genomes.
- Metagenome analysis.
- Metabolic biochemistry, biocatalysis, metabolic networks, anaerobiosis.
- Bioremediation.
- Organic chemistry, analytical chemistry.

### KEYWORDS

Sequencing - Biochemistry - Metabolism - Metabolomics - Comparative genomics - Functional genomics - Enzyme - Biocatalysis - Transcriptomics - Mass Spectrometry.

### RESEARCH THEMES

The unit's themes are as follows:

- // Sequence analysis of eukaryotic and prokaryotic genomes.
- // Metabolic and microbial biodiversity of wastewater treatment plants.
- // Metabolic networks.
- // Reconstruction of metabolic pathways and systematic, functional gene analysis in *Acinetobacter baylyi*.
- // New enzymatic functions.
- // Research of new biocatalysts.

The Metabolic Genomics Group (UMR 8030) is the basic research structure of the Genoscope-National Sequencing Center (*cf page 28*). Historically, the principal theme of the unit was tightly linked to Genoscope's sequencing and sequence analysis activities (eukaryotic and prokaryotic genomes). The sequence analysis activities are still ongoing but have been extended by the functional identification of as yet unknown metabolic enzymes.

### Supervisory bodies

CNRS - CEA - University Évry-Val-d'Essonne

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The search for new enzyme activities fits into a larger framework with two central objectives:

- // Obtaining an integrated vision of the metabolism of a bacterium.
- // Completing the construction of bacterial metabolic pathways which are as yet unknown (or about which very little is known) and the anaerobic pathways in particular.

These two objectives require very diverse skills in scientific fields ranging from bioinformatics to chemistry. They are based on knowledge of full sequence data and sequence analyses generated using metagenomics approaches.

To address these questions, we have progressively established two specific genomic resources over the last few years:

- // A pangenomic collection of *Acinetobacter baylyi* mutants.
- // A large collection of metagenomic sequences of prokaryotic flora from wastewater treatment plants.

Critical examination of these resources constitutes the starting point for a whole series of questions which will then be addressed by either experimental or bioinformatic approaches or a combination of the two.



## Molecular Immunology and Innovative Biotherapies

INSERM Unit 951



### MAIN TOPIC

Biotherapies of immune deficiencies and muscular dystrophies.

### FIELD OF ACTIVITY

Applied research in the field of gene therapy of genetic diseases of the blood and immune system.

### KEYWORDS

Gene therapy - Clinical trials - Immune deficiencies - Muscular dystrophies - Wiskott Aldrich syndrome - Lentiviral vectors - Adeno-associated vectors - Group II introns - Stem cells.

**Supervisory bodies** Genethon - INSERM

University Évry-Val-d'Essonne

École Pratique des Hautes Études

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### RESEARCH THEMES

This Research Group is affiliated with Genethon as well as with INSERM and University of Évry-Val-d'Essonne, École Pratique des Hautes Études and is established within Genethon's facilities (*cf page 89*) in Évry, thereby facilitating the development of biotherapies for the treatment of rare genetic diseases.

The research projects cover:

- // The development of novel approaches in gene and cell therapies for genetic diseases, notably for immune system diseases.
- // Clinical trials of gene therapy for Wiskott Aldrich Syndrome.
- // Applications of lentiviral vectors.
- // The use of stem cells in cell and gene therapies and the study of epigenetic modifications induced by gene therapy.
- // Analysis of the immune reactions that lead to the rejection of genetically modified cells and the use of viral vectors for gene transfer.





## The National Genotyping Center [CNG] CEA/Genomics Institute

**CNG** CENTRE NATIONAL DE GENOTYPAGE



### MAIN TOPIC

Genomics and postgenomics in human diseases.

### FIELD OF ACTIVITY

The CNG is primarily devoted to the discovery and characterization of genes involved in human disease.

### KEYWORDS

Genotyping and related genomics technologies.

**Supervisory bodies** CEA

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### RESEARCH THEMES

Since its creation, the CNG has maintained its international competitiveness by incorporating the many technological developments produced worldwide in the field of genotyping. It has set up a whole range of integrated platforms for studying the genes responsible for diseases or other traits (cardiovascular, auto-immune, neurological, psychiatric, dermatological and infectious diseases, diabetes, etc.):

- // A biological resource laboratory,
- // High-throughput SNP genotyping platforms for performing whole-genome association studies and linkage analyses (1534 multiplexed probes on a 96-sample chip and very-high-density Illumina and Affymetrix chips) and high-resolution genotyping and gene mapping (MALDI-TOF, KASPar, Taqman, Sequenom).
- // An SNP discovery and mutation detection platform.
- // A high-throughput re-sequencing platform on a Solexa Genome Analyzer.
- // A gene expression laboratory.
- // A proteomics laboratory.
- // An epigenetics laboratory.
- // A quality control laboratory.
- // A bioinformatics and computational biology laboratory.

The CNG participates in major European programs on both technological development and disease research. It is involved in a major "Genomics and Cancer" national program in collaboration with other programs funded by the French National Cancer Institute. The CNG's production infrastructure is widely used by the French and European scientific communities. Following scientific review, CNG groups have performed over 200 research projects submitted by scientists from across France and Europe.

Between 1999 and 2006, the CNG's integrated infrastructure for genetic studies has enabled implementation of collaborative projects from around 300 French labs and 60 labs from outside France. The CNG's activity as a whole has helped generate more than 250 publications. The Center also hosts training fellowships (with over 110 researchers since 1999) and student projects (with over 100 interns and 70 students since 1999). It provides mid-term hosting for INRA and INSERM research groups involved in collaborative projects and runs international exchange programs with Japan, Russia and Thailand.

### COLLABORATIONS

- // Suez Environnement
- // Le Pecq.



#### MAIN TOPIC

Genomics, transcriptomics and proteomics of model plants and crop plants.

#### FIELD OF ACTIVITY

Genomics and computing resources in plant biology.

#### KEYWORDS

Plant genomics - Plant models - Crop plants.

#### Supervisory bodies

University Évry-Val-d'Essonne - INRA

#### Director Heribert Hirt

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#### RESEARCH THEMES

The URGV's goals are to develop plant genome analysis tools and use them to identify genes which impact on agriculture (crop growth and seed production), the environment (disease resistance genes) and/or the agrifood industry (genes influencing the quality of crop-derived products).

The unit's research themes fall into three main categories:

##### // Functional analysis of the *Arabidopsis* model genome

- Development of transcriptome analysis tools and of RNAseq.
- Development of pan-genome microarray chips.
- Post-transcriptional studies/protein modifications.
- Analysis of the PPR (pentatricopeptide repeat) family involved in organelle function.
- Analysis of MAP kinases and their role in adaptation to biotic and abiotic stress.

##### // Analysis of crop genomes

- Comparative analysis of plant genome structure (wheat, canola, grapevine and forest trees).
- Positional cloning of agriculturally important genes.
- Development of reverse genetic tools (gene tilling).
- Studies of polyploidy, gender determinism and viral resistance.
- Grapevine genome transcript analysis.

##### // Bioinformatics

- Development of a database (FLAGdb) on the *Arabidopsis* model genome and bioinformatics tools for managing and analyzing the data outputs.
- Creation of new analysis tools for facilitating genome synteny conservation studies and work on plant improvement. Development of analytical tools for gene regulation sequences.
- Collaboration with the Genoscope and URGI on the annotation of the grapevine and canola genome.

#### INDUSTRIAL COLLABORATIONS:

- // Biogemma
- // Genewave (cf page 91)
- // Serial Genetics
- // Partnership (cf page 115)
- // BASF
- // Bayer
- // Semillas Fyto
- // Medicago.

# Statistics and the Genome

CNRS UMR 8071



## MAIN TOPIC

Mathematics and bioinformatics applied to the analysis of genomic and post-genomic data.

## FIELD OF ACTIVITY

- Development of mathematical models and tools for the analysis of biological sequences and networks (Gene expression, SNP).

## KEYWORDS

Bayesian - Modeling - Statistical analyses - Sequence evolution - Large-scale comparisons - Biomolecular genetics.

## RESEARCH THEMES

Design of statistical methods for the analysis of DNA/protein sequence & expression data.

Making these methods available to the biology community of biologists via the internet.

Our research axes notably include:

- /// Sequence analysis using Markov chains or hidden Markov chains.
- /// Statistical inference of biological networks (interaction, regulation, metabolic pathways) from statistical or dynamical data.
- /// Analysis of genomic data for the identification of genes involved in the etiology of diseases (SNP analysis); time-domain analysis of gene expression mechanisms (Markovian modeling or otherwise).
- /// Study of inter-gene relationships, support for automatic annotation *via* large-scale sequence comparisons. Transposable elements.
- /// Study of protein sequence evolution.
- /// Analysis of transcriptome/proteome data.





## Stem cells and cardiogenesis

INSERM UMR 633-FRM\* Label team



### MAIN TOPIC

The genetic and epigenetic mechanisms underlying the cardiac specification of embryonic stem cells (ESCs): early cardiogenesis.

### FIELD OF ACTIVITY

- Genetic and epigenetic regulation of cardiogenesis, using embryonic cells and early mouse embryos.
- Modeling of genetic heart diseases using reprogrammed somatic cells from patients (laminopathies and cardiomyopathies, filamin A mutations and valve diseases).
- Preclinical studies of cell therapies for ischemic and congenital heart diseases.

### KEYWORDS

Early cardiac development -  
Cell therapy - disease modeling -  
Stem cells - Reprogrammed cells.

### RESEARCH THEMES

The group is working on 5 topics:

- // Understanding the dual role of the transcription factor Oct-4 in the pluripotency and mesendodermal & cardiac specification of human ESCs and mouse embryos.
- // Understanding the impact of the epigenetic variability of human ESC lines on the latter's cardiac specification.
- // Establishing heart valve progenitors for use in research on the embryonic development of heart valves; modeling genetic diseases (filamin A mutations) that affect the valves; cell therapy for valve degeneration.
- // Modeling of laminopathies by using a mutated ESC model and reprogrammed somatic cells from patients: the study of structural and transcriptional hypotheses (including chromatin modifications) in this disease context.
- // The use of cardiomyocyte progenitors for regenerative medicine in patients suffering from ischemic or congenital cardiomyopathies: preclinical and clinical studies.

**Supervisory bodies** INSERM

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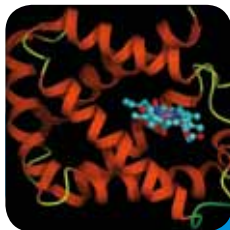
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### COLLABORATIONS

- // Professor Philippe Ménasché: HEGP, INSERM U633 (Paris, France): cell therapy of ischemic cardiomyopathies (a clinical project).
- // Dr Mark Mercola, Burnham Institute, La Jolla, CA, USA: high-throughput screening of molecules, inducing early and late cardiac specification in ESCs and cardiac progenitor cells.
- // Dr Stéphane Zaffran, INSERM UMR 910 (Marseille, France): valve progenitors in the embryo.
- // Dr Virginie Lambert and the group led by J.-F. Renaud, (Marie Lannelongue Hospital and the CNRS unit at Le Plessis Robinson): cell therapy of congenital cardiomyopathies in a porcine model.
- // Dr C. Cowan, Department of Stem Cell and Regenerative Biology, Harvard University, Cambridge, MA, USA: embryonic stem cells and human iPS.
- // Professor Joseph Itskovitz-Eldor, Technion Institute (Haifa, Israel): culture of ESCs and a clinical project.
- // Dr S Evans, UCSD, La Jolla, CA, USA: lineage tracing of cardiac progenitors *in vivo*.
- // Dr Daniel Aberdam, INSERM Nice and Technion Institute, Haifa: molecular signatures of ESCs and the role of a non-cardiac factor in cardiogenesis.

\* Fondation pour la recherche médicale (Foundation for the medical research).



# Structure and Activity of Normal and Pathological Biomolecules

INSERM - UEVE U829



Institute  
thématiques

**Inserm**

Institut national  
de la santé et de la recherche médicale

## MAIN TOPIC

Tubulin dynamics.

## FIELD OF ACTIVITY

- Cell biology.
- Cancer.
- Neuroscience.
- Medicine.
- Drug design.

## KEYWORDS

Structure - Proteins - NMR - AFM - Tubulin -  
Cancers - Nervous system - Mutations - AIDS.

## RESEARCH THEMES

- // Physiopathology of the microtubule cytoskeleton and impact on the cell cycle and neuronal function.
- // Functional genomics of the centriole.
- // Structure, folding, stability & dynamics of proteins in solution.
- // Protein/protein, ligand/protein and protein/nucleic acid interactions.
- // Development of a multifunctional biomolecule fluorescent marker based on nanodiamonds.

## ASSOCIATED "ATIGE RESEARCH GROUP"

"Centrioles and Associated Pathologies".  
Leader : Pascale Dupuis-Williams.

## INDUSTRIAL COLLABORATIONS

- // Bioquanta (a biotech R&D service company), Genopole®, Evry.
- // Protera (innovative biotech company, spin-off of the Scientific Campus of the University of Florence with a core business in the R&D of new drug candidates), Florence (Italy).

## Supervisory bodies

University Évry-Val-d'Essonne - INSERM

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## Tumor Functional Genomics and Epigenetics - An ATIGE Research Group



### MAIN TOPIC

Tumor genomics, postgenomics  
and biotherapies.

### FIELD OF ACTIVITY

- Functional genomics for translational research.
- Regulatory networks.
- Epigenetics.

### KEYWORDS

RNA interference - Synthetic lethality -  
Gene regulation - Epistasis - Cancer in  
humans - Cell models - Drug targets -  
prognostic markers.

### RESEARCH THEMES

// Genome-wide identification of gene interactions  
synthetic lethal with recurrent oncogenic mutations  
(TP53, KRAS, NRAS, BRCA1...).

// Identification of genes involved in therapeutic  
resistance.

By using isogenic human cell pairs to model critical steps of cancer progression and by exploiting genome-wide short hairpin RNA libraries, we assess the vulnerabilities induced by defined oncogenic alterations. We are especially seeking to identify interfering RNAs that are synthetic lethal with oncogenic mutations in our model system and then evaluate their significance in relevant clinical situations. This should shed light on the genetic and epigenetic reprogramming of human cells by oncogenic events and provide new therapeutic leads for translational research.

**Supervisory bodies** CEA (IRCM)

**Responsible** Claude Gazin

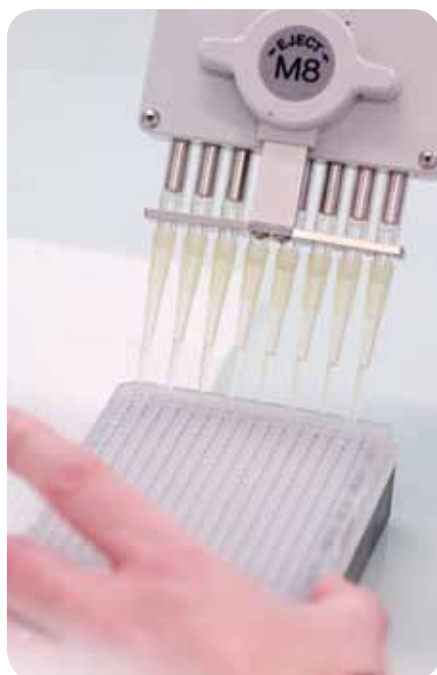
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## Unit for Integrated Biology in Adaptations to Exercise (UBIAE) INSERM U902



Institut national  
de la santé et de la recherche médicale

### MAIN TOPIC

Physiology, genomics and post-genomics for the implementation of physical exercise protocols.

### FIELD OF ACTIVITY

- Genomics and bioenergetics of muscle activity in healthy subjects and patients
- Analysis of the physiological responses to acute and chronic exercise (training) in the mammal (the human, the mouse and the horse in particular).
- E-learning for health by exercise by electronic and GPRS data transmission.
- Analysis of physiological and perceptive response to exercise.

### KEYWORDS

Cardiovascular and muscular capacity -  
Exercise - Heart - Mitochondrion -  
Muscle - Oxygen uptake - Hypoxia.

### RESEARCH THEMES

The laboratory's work is set against a public health context, with the objective of optimizing motor performance. Our group analyzes the bioenergetic responses to muscle exercise (from physiology to molecular biology) in humans and animals (with murine and equine models). Our expertise in the field of effort training and re-training enables improvements in motor performance in both patients and experienced athletes. In fact, we develop physical training methods, which are specifically adapted to an individual's physiological profile, in order to reconcile performance and health.

### Supervisory bodies Genopole®

University Évry-Val-d'Essonne - INSERM

### Director Véronique Billat

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Unit 902 performs research in physiology and integrative biology. One particular novel feature relates to the Unit's integrative approach on four different levels:

/// In terms of experimental models, we study the mouse and the horse, as well as humans.

/// In terms of methodological approaches, we study the biological reactions to physical exercise on the physiological, cellular and molecular (genetic) levels.

/// Our approach is based on human exercise performed in the laboratory but also in the field, so as not to interfere with spontaneous regulation of the speed of movement (notably during competitive sport).

/// Our goal is to contribute to health by prevention thanks to the education for health by exercise with the e-learning and telemedicine and physiological measurement.

In summary, our laboratory is at the cutting edge of efforts to develop new methods for analyzing bioenergetic responses to exercise (from physiology through to molecular biology) in healthy or diseased humans and animals. This involves a wide range of techniques, from the validation of DNA chips to the use of telemedicine.