Innovative Projects for International Business Opportunities and R&D Collaborations



FRENCH ACADEMIC STRENGTHS IN EPIGENETICS AND CANCER



alliance nationale pour les sciences de la vie et de la santé

THERAPEUTIC INNOVATION IN ONCOLOGY Projects Book October 2016

Strategic Tech Transfer Field: Therapeutic Innovation in Oncology

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The Urgi Bioinformatic Platform





ATGC bioinformatics



Eric RIVALS

Dr Workforce: 2

Keywords:

- High Throughput Sequencing (NGS, TGS)
- Phylogenetic inference
- Long read error correction
- RNA-seq analysis
- Ribosome profiling analysis
- Transcriptomics

Research Center, Town:

Laboratoire d'Informatique, de Robotique et de Microélectronique de Montpellier (LIRMM) – Computer Science Lab of University of Montpellier

Administrative affiliations: CNRS & University of Montpellier

Tech Transfer Office: CNRS

Services & collaborations:

Available for academic teams (intern or extern) and private companies



Platform address:

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Platform Website : http://www.atgc-montpellier.fr/

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Description:

Since 2001, ATGC is a bioinformatic platform that provides services, programs, and solutions for computational biology. ATGC is hosted by the computer science lab of Montpellier University, but is an endeavor of several institutes involved in bioinformatics and computational biology (LIRMM, CIRAD, IRD, etc.). The user can either run analyses and simulations through services on our web server or download our programs and run the analysis on its own platform. All distributed software and services are free of charge for non commercial uses. ATGC is well known for its expertise in phylogeny (PHYML software and phylogeny.fr web services), in comparative genomics, in Next Generation Sequencing analysis (CRAC and LORDEC software for instance). Its original goal was to distribute all bioinformatics solutions issued from the research of bioinformatics teams in Montpellier area. Soon, the demand has fostered the development of user friendly interfaces to simplify the utilization of popular bioinformatic tools. For instance, the phylogeny.fr web server offers various modes from One-click until Expert to fit the needs of our users. Since 2009, ATGC is offering NGS analyses tools and services, and is, since their creation, part of the two major French Platform Networks: namely, the Institut Français de Bioinformatique (IFB) and France Génomique. ATGC is active in education and proposes three training programs targeted to academic and industrial researchers, engineers and technicians (see CNRS Formation Entreprises).



Certifications:

- 1. Institut Français de Bioinformatique (IFB)
- 2. IBISA,
- 3. ReNaBi
- 4. France Génomique
- 5. Cancéropole Grand Sud-Ouest

Recent/key publications:

• Colib'read on Galaxy: A tools suite dedicated to biological information extraction from raw NGS reads. Y. Le Bras, O. Collin, C. Monjeaud, V. Lacroix, E. Rivals, C. Lemaitre, V. Miele, G. Sacomoto, C. Marchet, B. Cazaux, A. Zine El Aabidine, L. Salmela, S. Alves-Carvalho, A. Andrieux, R. Uricaru, P. Peterlongo. GigaScience, Feb 11;5:9. doi: 10.1186/s13742-015-0105-2. eCollection 2016.

• Computational Pan-Genomics: Status, Promises and Challenges. T. Marschall et al. Briefings in Bioinformatics, doi:10.1093/bib/bbw089, 2016. (http://biorxiv.org/content/early/2016/03/29/043430).

• Read mapping on de Bruijn graphs. A. Limasset, B. Cazaux, E. Rivals, P. Peterlongo. BMC Bioinformatics doi:10.1186/s12859-016-1103-9, 17:237, 2016.

• TRM6/61 connects PKCĐ with translational control through tRNAi(Met) stabilization: impact on tumorigenesis. Macari F, El-Houfi Y, Boldina G, Xu H, Khoury-Hanna S, Ollier J, Yazdani L, Zheng G, Bièche I, Legrand N, Paulet D, Durrieu S, Byström A, Delbecq S, Lapeyre B, Bauchet L, Pannequin J, Hollande F, Pan T, Teichmann M, Vagner S, David A, Choquet A, Joubert D.

Oncogene. 2016 Apr 7;35(14):1785-96. doi: 10.1038/ onc.2015.244. Epub 2015 Aug 3.

• LoRDEC: accurate and efficient long read error correction. L. Salmela, E. Rivals. Bioinformatics, doi:10.1093/ bioinformatics/btu538, 30 (24): 3506-3514, 2014.

• An improved genome of the model marine alga Ostreococcus tauri unfolds by assessing Illumina de novo assemblies. Romain Blanc-Mathieu, Bram Verhelst, Evelyne Derelle, Stephane Rombauts, Francois-Yves Bouget, Isabelle Carré, Annie Chateau, Adam C Eyre-Walker, Nigel Grimsley, Herve Moreau, Benoit Piegu, Eric Rivals, Yves van de Peer, Wendy Schackwitz and Gwenael Piganeau. BMC Genomics, 15:1103 doi:10.1186/1471-2164-15-1103 2014.

Grants:

• 3GENSEQ from Institut Français de Bioinformatique (IFB) (2016-2018): argetedhttps://www.france-bioinformatique.fr/fr/projets2015/3genseq

• France Génomique, co-head Workpackage 2.5 «Transcriptome» (2013-2016) with D. Gautheret d'Orsay.

• Evolutionary Bioinformatics from Institut Français de

Bioinformatique (IFB) (2015-2018).

• NGPhylogeny.fr from Institut Français de Bioinformatique (IFB) (2016-2018)

Our expertise in the bioinformatic analyses of deep sequencing data obtained from the second and third generation of sequencing technologies. This comprises transcriptomics (RNA-seq and ncRNA identification), as well as Ribo-seq analysis, and analysis of DNA sequencing.

We have collaborated to the European COST Action 2011-2015 Next Generation Sequencing Data Analysis Network or SeqAhead. We propose three training programs targeted to non specialists, life scientists and technicians, coming from the academic and industrial communities. One training focuses on NGS data analysis.

Our experience includes the prediction of smalll non coding RNA, and of Ribo-seq data.

As mentioned above, ATGC is member of two major French Platform Networks: namely, the Institut Français de Bioinformatique (IFB) and France Génomique.

Techniques/services available to analyze chromatin and epigenetic modifications:

- · Bioinformatic analyses of deep sequencing data
- \cdot Read mapping
- \cdot Read error correction
- RNA-seq and Ribo-seq analyses
- TF binding site (motif) searching in whole genomes

Unique selling points in epigenetics:

- Open to academic and industrial partnerships
- ATGC part of Institut Français de Bioinformatique (IFB) and of France Génomique networks.
- Collaborations with MGX and GeneOuest



On-the-fly analysis of local coverage during mapping with CRAC

(Philippe et al. Genome Biol. 2013)



Computational Pan Genomics (review) Marschall et al. BioRxiv http://dx.doi.org/10.1101/043430





Signature classification for ncRNA identification (Philippe et al. NAR 2014)







Institut Curie Bioinformatics platform



Director: Emmanuel Barillot ; Deputy Director : Philippe Hupé PhD

Workforce: 28 engineers

Keywords:

- NGS data analysis
- High Performance Computing
- Proteomics analysis
- Statistical analysis

Research Center, Town: Institut Curie, Paris

Administrative affiliations: U900 INSERM, Institut Curie

Tech Transfer Office: Institut Carnot Curie-Cancer

Services & collaborations:

Available for academic teams and/or private companies



Together, let's beat cancer.

Platform address:

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Platform Website : https://science.curie.fr/ plateformes/bioinformatique/

Email Contact : Emmanuel.Barillot@curie.fr Philippe.hupe@curie.fr

Description:

The Bioinformatics platform fulfills several missions related to the integration and analysis of high-throughput data produced in the frame of institut Curie and INSERM clinical or research projects. This data can be of many types : NGS sequences, microarrays, RPPA, mass spectrometry, clinical records, phenotypic information (images)... The bioinformatics platform provides collaborative support to clinicians, researchers, and to the engineers and technicians in charge of the other high-throughput biotechnological platforms. More than thirty analysis projects are supported yearly. Additionnally the platform provides advices and trainings in biostatistics, bioinformatics and computational systems biology, and coordinates the institutional activities in these fields.

In the recent past, the platform has setup an integrative environment in the frame of the SIRIC and ICgex projects for personnalized medicine, was involved in the first institutional personnalized medicine clinical trial SHIVA for data management and genomic information analysis, has substantially extended its capabilities in NGS data analysis (where new technologies appeared, and new application types arose), and has anabled large-scale storage and high-performance computing with the Computer Department.

Certifications:

• The platform is part fo APLIBIO, the alliance of bioinformatics platforms from Ile-de-France, which has obtained the IBISA label.

Recent/key publications:

• Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. Le Tourneau C, Delord JP, Gonçalves A, Gavoille C, Dubot C, Isambert N, Campone M, Trédan O, Massiani MA, Mauborgne C, Armanet S, Servant N, Bièche I, Bernard V, Gentien D, Jezequel P, Attignon V, Boyault S, Vincent-Salomon A, Servois V, Sablin MP, Kamal M, Paoletti X; SHIVA investigators. Lancet Oncol. 2015 Oct;16(13):1324-34.

 Mechanical induction of the tumorigenic D-catenin pathway by tumour growth pressure. Fernández-Sánchez ME, Barbier S, Whitehead J, Béalle G, Michel A, Latorre-Ossa H, Rey C, Fouassier L, Claperon A, Brullé L, Girard E, Servant N, Rio-Frio T, Marie H, Lesieur S, Housset C, Gennisson JL, Tanter M, Ménager C, Fre S, Robine S, Farge E. Nature. 2015 Jul 2;523(7558):92-5.
 Combinatorial code governing cellular responses to complex stimuli. Cappuccio A, Zollinger R, Schenk M, Walczak A, Servant N, Barillot E, Hupé P, Modlin RL, Soumelis V. Nat Commun. 2015 Apr 21;6:6847

• Using Transcriptional Signatures to Assess Immune Cell Function: From Basic Mechanisms to Immune-Related Disease. Touzot M, Dahirel A, Cappuccio A, Segura E, Hupé P, Soumelis V. J Mol Biol. 2015 May 15. pii: S0022-2836(15)00290-9.

• HiC-Pro: an optimized and flexible pipeline for Hi-C data processing. Servant N, Varoquaux N, Lajoie BR, Viara E, Chen CJ, Vert JP, Heard E, Dekker J, Barillot E. Genome Biol. 2015 Dec 1;16:259. doi: 10.1186/s13059-015-0831-x

Grants:

• Cancéropôle Ile-de-France, INCa 2016: diagnostic par NGS en clinique (coord E. Barillot)

• Cancéropôle Ile-de-France, INCa 2016: Exomes RNAseq project (coord S. Roman-Roman)

• FRM 2015: régulation de la polyadénylation alternative (coord M. Dutertre)

• INSERM Plan Cancer 2014-2019: Transcriptome noncodant et tumorigénèse de la vessie (coord C. Rougeulle)

• France Génomique 2014-2019 : Infrastructure Nationale de Biologie et Santé (coord E. Barillot)

• FRM 2014-2017: déterminants des fonctions de longs ARN non codants (coord A. Shkumatava)

• European Commission 2012-2017: Rational molecular Assessments and Innovative Drug Selection in cervix cancer (coord S. Scholl)

• ANR Investissement d'Avenir 2012-2017: Solutions Algorithmiques, Bioinformatiques et Logicielles pour le Séquençage Haut Débit (coord E. Barillot)

The bioinformatics platform has extensive expertise in the analysis of NGS data. In particular, the group has developed several bioinformatics approaches for epigenetic analysis. In this context, we developed bioinformatics pipelines for the analysis of chromatin modifications (ChIP-seq) or chromatin accessibility data (ATAC-seq). We also recently developed new methods for the analysis of chromatin conformation data such as Hi-C or 5C data. More recently, we also started a transversal project which aims at analyzing all these data in an allele specific manner. We therefore explored different bioinformatics strategies and proposed a new pipeline to answer this question. The pipelines and methods that we developed are available and used by the national and international community in the field.

Finally, the bioinformatics platform of the Institut Curie is also involved in the organization of national working group related to epigenetics analysis, such as the workpage 2.6 of the "France Genomique" project.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Bioinformatics pipeline for small non coding RNA analysis (Chen, Servant et al, 2012)
- Bioinformatics tool for Hi-C data analysis (Servant et al. 2012, Servant et al, 2015)
- Bioinformatics pipelines for allele specific analysis (RNA-seq, ChIP-seq, ATAC-seq)
- Computational cluster with 2,000 cores and 2 Pb storage

Techniques/services available to analyze chromatin and epigenetic modifications:

• Expertise for NGS bioinformatics analysis for miRNA, Hi-C and most C techniques, DNA methylation (bisulfite sequencing), histone modifications (ChIPseq), ATAC-seq, etc.

Unique selling points in epigenetics:

- Scientific expertise in small non-coding RNA, chromosome conformation, DNA methylation, chromatin accessibility, histone modification analysis based on NGS
- Know-how in the development of algorithms and pipelines for high-throughput data analysis
- · Integration of molecular data for functional interpretation
- · Participation to co-development projects



Hi-C and chromatin organization

Expression, chromatin accessibility and chromatin conformation along the Xi chromosome. (Giorgetti et al. 2016)





NGS & Epigenomics



RNA-seq allele specific analysis







Bordeaux Bioinformatics Center (CBiB)



Macha Nikolski

Dr., DR CNRS

Workforce: Permanent staff : 2 research scientists, 2 University professors, 4 engineers Temporary staff : 1 postdoctoral scientist, 3 engineers, 3 PhD students

Keywords:

• "omics" data analysis (DNA, RNA, metabolomics and proteomics analysis services)

 Standard and custom biological data analyses

• Deployment of «Big data» approaches for data analysis

• Development and maintenance of biological databases

Research Center, Town:

CGFB (Functional Genomic Center of Bordeaux), Bordeaux

Administrative affiliations: University of Bordeaux

Tech Transfer Office: SATT Aquitaine Sciences Transfert

Services & collaborations: Services and collaborations are available for academic teams and private partners



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Platform Website : http://www.cbib.u-bordeaux.fr

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Description:

The Bordeaux Bioinformatics Center (CBiB) is a bioinformatics research and core facility that provides access to high-performance computing resources, data analysis and programming expertise. The resources serve scientists and private labs to master the bioinformatics needs of their research in an efficient and cost-effective manner.

We offer state-of-the-art technologies for working with clinical, translational, and basic science data – from acquisition and storage to analysis and sharing. Our resources are secure and standards-compliant. From a few samples to several tens of thousands, our Innovation Centre provides complete DNA, RNA, metabolomics and proteomics analysis services.

Certifications:

• We are an IBISA facility and a founding member of IFB (Institut Francais de Bioinformatique). We are affiliated with the SIRIC BRIO as a technological "bench to bedside and back" facility. Moreover, CBiB has been approved by Lloyd's Register Quality Assurance to the following Quality Management System Standards: ISO 9001:2008

Recent/key publications:

• Y. Le Bras, O. Collin, C. Monjeaud, V. Lacroix, Eric Rivals et al. Colib'read on galaxy: a tools suite dedicated to biological information extraction from raw NGS reads, GigaScience, BioMed Central, 2016, 5 (1), doi: 10.1186/s13742-015-0105-2

• P. Rocca-Serra, R. M. Salek, M. Arita, E. Correa, S. Dayalan, M. Nikolski et al. Data standards can boost metabolomics research, and if there is a will, there is a way, Metabolomics, 2015, doi: 10.1007/s11306-015-0879-3

• N. Quenel-Tueux, M. Debled, J. Rudewicz, G. McGrogan, M. Pulido et al. Clinical and genomic analysis of a randomised phase II study evaluating anastrozole and fulvestrant in postmenopausal patients treated for large operable or locally advanced hormone-receptorpositive breast cancer, British Journal of Cancer, Cancer Research UK, 2015, pp.bjc.2015.247, doi: 10.1038/ bjc.2015.247

• M. El-Kebir, H. Soueidan, T. Hume, D. Beisser, M. Dit-

trich, M. Nikolski et al. xHeinz: an algorithm for mining cross-species network modules under a flexible conservation model, Bioinformatics, 2015, 31 (19), doi: 10.1093/bioinformatics/btv316

• M. Thomas-Chollier, E. Darbo, C. Herrmann, M. Defrance, D. Thieffry, J. Van Helden, A complete workflow for the analysis of full-size ChIP-seq (and similar) data sets using peak-motifs, Nature Protocols 7, 1551–1568 (2012) doi:10.1038/nprot.2012.088

Grants:

Ongoing:

• EU ELIXIR "Management of Human Research Data" Implementation Study

• COBRA Plant-KBBE ÁNR-13-KBBE-0006, 2013-2016

• PIA BioDataCloud, 2013-2016, Investissements d'Avenir, Developpement de l'Economie Numerique «Cloud computing» Call, n.3 - Big data

The CBiB offers bioinformatic analysis services to study epigenetic modifications across the entire genome, including DNA methylation, histone modification and DNA-protein interactions. Our experience includes analyzing the methylome data for both human and plant applications by offering the analysis of bisulfite sequencing data. In this context we have put in place a collaboration with Cellomet (www.cellomet.com). Moreover, we develop methods for bioinformatic analysis of Hi-C data to identify long-range genomic interactions.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- In-house computing cluster:
- storage GPFS (350 TO)

- 512 computing cores (512 cœurs, 7To RAM) + 1 BigMem node (32 cœurs 2.1 GHz, 1 To RAM)

Standard analysis workflows

Techniques/services available to analyze chromatin and epigenetic modifications:

- DNA Methylation : WGBSseq, MeDIPseq, oxBSseq
- Histones modifications : ChIPseq
- Chromatin conformation : HiC

- "omics" data analysis facility open for external collaboration
- Part of Institut Francais de Bioinformatique and France Genomique national networks
- Established collaboration with national and European partners (both academic and private)



CBiB computing cluster



Hi-C data analysis methods



Standard methyl-seq data Analysis pipelines





Functional Epigenomics Facility



Scientific Leader : Pierre-Antoine Defossez, PhD Technical Leader : Laure Ferry

Workforce: Technical staff: 2

Keywords:

• DNA methylation

• Pyrosequencing

Research Center, Town: Epigenetics and Cell Fate, Université Paris 7, Paris

Administrative affiliations: UMR 7216 (CNRS & Paris 7)

Tech Transfer Office: SATT Idfinnov

Services & collaborations: Available for academic teams (internal or external)



Platform address: 5^{ème} étage Bât. Lamarck B, room 529 35, rue Hélene Brion 75205 Paris Cedex 13

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Platform Website : http://parisepigenetics.com/ecf/

Email Contact : pierre-antoine.defossez@univ-parisdiderot.fr laure.ferry@univ-paris-diderot.fr

Description:

Our platform has been established with the support of University Paris Diderot and CNRS and is attached to a scientific department that specializes in the study of epigenetics. We aim to provide services to internal and external academic users in the fields of biology and medicine.

Recent/key publications:

- Kebir et al, Mol Psychiatry, 2016
- Velasco et al, in prep
- Fournier et al, in prep

Grants:

Actions structurantes Paris 7
DIM Biotechnologies

We are expert at designing, realizing, and interpreting a number of experiments related to epigenetics and chromatin. Our specialty is the study of DNA methylation, for which we use LUMA, CoBRA, MeDIP, and pyrosequencing. Our services can be very valuable to validate data obtained using high-throughput approaches such as RRBS, WGBS, or commercial methylation arrays.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Pyromark Q24, Qiagen
- IP-Star Automated System, Diagenode
- qPCR: Viia7, 7500Fast (x2), 7900, Applied Biosystems
- Bioruptor Pico, Diagenode
- Pipetting robot, Tecan
- Bioanalyzer 2100, Agilent

Techniques/services available to analyze chromatin and epigenetic modifications:

- LUMA (Luminometric Methylation Assay)
- MeDIP (Methylated DNA ImmunoPrecipitation)
- Bisulfite Pyrosequencing
- CoBRA (Combined Bisulfite Restriction Analysis)

Unique selling points in epigenetics:

- · Advice on experimental design and interpretation
- · High expertise in DNA methylation analysis
- · Custom validation of high-throughput data



Lamarck Building



IP-Star Automated System, Diagenode



PyroMark Q24, Qiagen



Pyrogram generated by pyrosequencing of bisulfite-treated DNA to accurately quantify site-specific DNA-methylation.







Denis Milan

Scientific Manager

Workforce: Our team is composed of 30 people, experts in genomics, bioinformatics and biostatistics.

Keywords:

- Genomic
- Transcriptomic
- DNA methylation: WGBSseq, MeDIPseq, RRBS
- ChIPseq
- smallRNAseq
- miRNome

Research Center, Town: Institut National de la Recherche Agronomique - Toulouse

Administrative affiliations: INRA – INSA - INSERM

Tech Transfer Office: INRA Transfert

Services & collaborations:

Access for all academic and private labs: i) projects in collaboration, partnership, ii) service provision adapted to the user's need. GeT offers (i) management of projects, (ii) development of new protocols, (iii) training on the core facility site (National and Transnational access), (iv) workshops.



Platform address:

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Description:

Genomic and Transcriptomic Platform of Toulouse (GeT) has been established in 2001. It is a core facility providing to the community equipment and expertise in the fields of Next Generation Sequencing, micro-array and medium scale genotyping, high throughput real time PCR and single cell.

The main scientific questions addressed by teams working on the core-facility are: (i) identification of genes influencing traits of interests (traits of agronomical interest for plants and animals, disease genes in human ...), (ii) study of genetic diversity in all reigns, (iii) study of gene expression regulation (iv) sequencing and genomic comparison.

We are collaborating with 140 research teams per year. Our participation on project usually leads to co-authorship in reviewed publications (50 publications from 2012 to 2015).

Several Next Generation Sequencing technologies are available in this core facility, such as the Illumina HiSeq3000, 3 MiSeq sequencers, PGM and S5 from Life

Technologies, Pacific Biosciences third generation sequencing technology (PACBIORSII). We also have Fluidigm BioMark and C1, Agilent and Affymetrix Microarrays. New capability coming soon: Pacific BioSciences Sequel system, Oxford Nanopore or other 4th generation sequencing technology.



Certifications:

• Two sites of GeT were certified ISO9001 in 2008. We were labeled as IBiSA (Infrastructures for Biology Health and Agronomy) in 2008 and as "Infrastructure for the future" in the "France Genomic" project. We actively participate to «France Genomic» infrastructure in management and animation of «Wet-Lab" workshops. GeT is an «INRA strategic core facility» (CNOC).

Recent/key publications:

• Insulators recruit histone methyltransferase dMes4 to regulate chromatin of flanking genes. EMBO J. 2014 Jul 17;33(14):1599-613.

• Transient hypermutagenesis accelerates the evolution of legume endosymbionts following horizontal gene transfer. PLoS Biol. 2014 Sep 2;12(9).

• Phylogenomic analysis of Oenococcus oeni reveals specific domestication of strains to cider and wines. Genome Biol Evol. 2015 May 14;7(6):1506-18.

• Reinforcement of STAT3 activity reprogrammes human embryonic stem cells to naive-like pluripotency, Nat Commun. 2015 May 13;6:7095. doi: 10.1038/ ncomms8095.

• Specific macrophage subtypes influence the progression of rhabdomyolysis-induced kidney injury. J Am Soc Nephrol. 2015 Jun;26(6):1363-77

Grants:

• GeT is involved in 17 collaborative projects in 2015 (ANR, Europeens, ...). For example, Get-PlaGe is involved in collaborative projects to study structural and functional descriptions of bacterial communities from coastal sediments contaminated with hydrocarbons (FUNHYMAT), to perform large-scale identification of the causative genetic variants influencing milk production in French dairy breed (CARTOSEQ), diversity study for Honeybee, or to improve yield stability in a changing environment for Sunflower (SUNRISE international project)

- The MIRDIET project (JPI HDHL BioNH, N°ANR-14-HDHL-0001) aims at identifying circulating miRNAs as quantitative biomarkers for dietary intake to supersede dietary surveys used in nutritional studies. MIRDIET exploits adipose tissue and plasma miRNome studies to discover molecular species with relationship to dietary intake. Several dietary interventions with careful assessment of dietary intake and, adipose tissue and blood samples are available for this purpose. The main MIRDIET goal is to identify new sensitive, specific, cost-effective and noninvasive biomarkers.

- GeT has developped an expertise in WGBS and RRBS especially concerning the Chickstress ANR program and is involved in HiC experiments in collaboration with GenPhySE lab in the FAANG project (Functional Annotation of Animal Genomics Project).

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Illumina sequencers (2HiSeq 3000, 3MiSeq)
- PacBio RSII sequencer
- Ion S5 sequencer
- Microarray platforms (Agilent, Affymetrix)
- Biomark HD system

Techniques/services available to analyze chromatin and epigenetic modifications:

- · DNA methylation: WGBSseq, MeDIPseq, RRBS
- ChIPseq
- smallRNAseq
- miRNome

Unique selling points in epigenetics:

- Expertise in NGS library preparation and sequencing
- Bioinformatic QC of NGS data, data repository platform (NG6)
- Expertise in biostatistical analysis of microarray data (miRNome, GE)
- Part of France Genomique national network



GeT-Team



HISEQ3000



PACBIO RSII



Bioinfo/ Biostat analysis





Genome Transcriptome facility of Bordeaux



Pascal Sirand-Pugnet

Ph.D

Workforce: Technical staff : 5 Bioinformatics : 1

Keywords:

Next generation sequencing

- Massarray genotyping (Sequenom)
- Genotyping by sequencing
- Transcriptomics

Research Center, Town: INRA, Univ. Bordeaux, Cestas Pierroton

Administrative affiliations: UMR 1202 BIOGECO, INRA, Univ. Bordeaux

Tech Transfer Office: INRA Transfert

Services & collaborations: Available for academic teams and private companies



Platform address:

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Phone: 05-57-12-27-77 (Franck Salin, responsable technique)

Platform Website : http://www.pgtb.u-bordeaux2.fr/

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Description:

The Genome Transcriptome Facility of Bordeaux (PGTB) is an academic structure specialized in sequencing and genotyping. PGTB is a part of the Functional Genomic Center of Bordeaux (CGFB), a federation of seven technology platforms, offering access to equipment, cutting-edge technologies and expertise for a wide scientific community. PGTB helps academic and industrial research teams through their project in genotyping and sequencing by providing technical expertise in various fields: agronomy and forest research, human health, microbiology, environment. PGTB offers tailor-made services of sequencing on Illumina (MiSeq) and Ion Torrent (PGM, Proton) sequencers and of genotyping using microsatellites, genotyping by sequencing and massarray-based detection of SNP and indels on Sequenom. Services also include research & development, technical equipment, expertise & consulting. PGTB is part of France Genomique national network.

Certifications:

• PGTB is quality labelled ISO 9001:2008 and NFX 50-900. It guarantees a realiable traceability, high quality results and analyses.

Recent/key publications:

Le Morvan, V., Litière, S., Laroche-Clary, A., Ait-oufe-roukh, S., Bellott, R., Messina, C., Cameron, D., Bonnefoi, H., and Robert, J. (2015). Identification of SNPs associated with response of breast cancer patients to neoadjuvant chemotherapy in the EORTC-10994 randomized phase III trial. Pharmacogenomics J 15, 63–68.
Mandrou, E., Denis, M., Plomion, C., Salin, F., Mortier, F., and Gion, J.-M. (2014). Nucleotide diversity in lignification genes and QTNs for lignin quality in a multi-parental population of Eucalyptus urophylla. Tree Genetics & Genomes 10, 1281–1290.

• Freyburger, G., Labrouche, S., Hubert, C., and Bauduer, F. (2015). Haemostaseome-associated SNPs: has the thrombotic phenotype a greater influence than ethnicity? GMT study from Aquitaine including Basque individuals. Thromb. Haemost. 113, 66–76.

• Albertin, W., Chasseriaud, L., Comte, G., Panfili, A., Delcamp, A., Salin, F., Marullo, P., and Bely, M. (2014b). Winemaking and bioprocesses strongly shaped the genetic diversity of the ubiquitous yeast Torulaspora delbrueckii. PLoS ONE 9, e94246.

• Naudion, S., Moutton, S., Coupry, I., Sole, G., Deforges, J., Guerineau, E., Hubert, C., Deves, S., Pilliod, J., Rooryck, C., et al. (2015). Fetal phenotypes in otopalatodigital spectrum disorders. Clin. Genet.

Grants:

- EquipEx Xyloforest
- Trees4future (7 PCRD)
- CPERIBISA

Nouvelle Aquitaine Grant

PGTB regularly collaborates with a growing number of scientific teams interested in epigenetics on eukaryots and prokaryots. Projects on epigenetics include next-generation sequencing of ncRNAs, bisulfite-sequencing and integrated comparison of transcriptome and methylome. One specific service proposed by PGTB is a MassArray-based targeted study of methylation. This approach enables to validate candidates on a large number of samples by simultaneous study of several dozens of CpG on amplicons up to 600 bp.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Illumina sequencer (MiSeq)
- · Ion Torrent sequencers (PGM, Proton)
- MassARRAY System Agena Bioscience (Sequenom)

Techniques/services available to analyze chromatin and epigenetic modifications:

- NGS sequencing of ncRNAs
- Bisulfite sequencing
- · MassARRAY-based detection of methylation

Unique selling points in epigenetics:

by NGS

- MassARRAY-based detection of methylation
- Platform opened for collaborations and R&D
- Part of France Genomique national network
- On-site training and coaching for do-it-yourself projects

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Detection of aneuploïdies in foetal DNA



MassARRAY System - Agena Bioscience™



PGTB laboratory



PGTB building





GenomEast Platform



Christelle Thibault-Carpentier

Ph.D Workforce: Wetlab 7 / Bioinformatics 6

Keywords:

- Next Generation sequencing
- Transcriptomics
- Genomics
- Epigenetics
- Bioinformatics

Research Center, Town: GIE CERBM/IGBMC, Illkirch

Administrative affiliations: CNRS UMR 7104 - Inserm U 964 -Université de Strasbourg

Tech Transfer Office: CNRS Délégation Régionale Alsace, Service «Partenariat et Valorisation »

Services & collaborations: Available for academic teams (intern or extern) and private companies



Platform address: 1 rue Laurent Fries, 67404 Illkirch Cedex

Phone: 33 (0) 3 65 88 34 26

Platform Website: http://genomeast.igbmc.fr/

Email Contact : christelle.thibault@igbmc.fr

Description:

Under the scientific supervision of Irwin Davidson, the GenomEast platform is dedicated to provide technological resources and expertise in functional genomics to the research community. A large panel of services is offered for transcriptomic-, genomic- and epigenetic-profiling using three complementary technologies: Illumina deep sequencing, Fluidigm nanofluidics and Affymetrix microarrays. We proposed full services, from support for experimental design and quality check of starting samples up to final data analysis.

Created in 2000, our platform has acquired its first Illumina sequencer in 2008 and has been selected as a partner of France Génomique consortium in 2011. Our technical team uses standardized protocols and regularly implements new ones for small RNA-, total RNA- or mRNA-seq, ChIP-seq and DNA-seq. Our bioinformaticians, on the other side, offer personalized support for basic or indepth data analysis through scientific collaborations as well as training for students and users. They have established RNA-seq, ChIP-seq and targeted DNAreseq pipelines using publically available tools or in house software. In addition, together with the IGBMC IT department, they have set up GalaxEast (http:// www.galaxeast.fr/), a local instance of the Galaxy platform that provides over 180 tools for Omics data analysis.

Certifications:

- Platform RIO/IBISA since 2003
- Certified IS09001 since 2007
- Certified NFX50-900 since 2015

Recent/key publications:

Langer D, Martianov I, Alpern D, Rhinn M, Keime C, Dollé P, Mengus G, Davidson I. Essential role of the TFIID subunit TAF4 in murine embryogenesis and embryonic stem cell differentiation. Nat Commun (2016)
Achour M, Le Gras S, Keime C, Parmentier F, Lejeune FX, Boutillier AL, Néri C, Davidson I, Merienne K. Neuronal identity genes regulated by super-enhancers are preferentially down-regulated in the striatum of Huntington's disease mice. Hum Mol Genet (2015)

• Õbri A, Ouararhni K, Papin C, Diebold ML, Padmanabhan K, Marek M, Stoll I, Roy L, Reilly PT, Mak TW, Dimitrov S, Romier C, Hamiche A. ANP32E is a histone chaperone that removes H2A.Z from chromatin. Nature (2014)

• Ye T, Ravens S, Krebs AR, Tora L. Interpreting and visualizing ChIP-seq data with the seqMINER software. Methods Mol Biol (2014).

• Neyret-Kahn H, Benhamed M, Ye T, Le Gras S, Cossec JC, Lapaquette P, Bischof O, Ouspenskaia M, Dasso M, Seeler J, Davidson I, Dejean A. Sumoylation at chromatin governs coordinated repression of a transcriptional program essential for cell growth and proliferation. Genome Res. (2013)

Grants:

- ANR-10-INBS-09-08 : France Génomique consortium
 Appel d'offre IdEX 2015, équipement mi-lourd : IdEX
 INISTRA
- Appel d'offre Plateformes IBiSA 2015 : GIS IBiSA

Our platform benefits from a privileged context with the proximity of numerous internationally recognized IGBMC research teams in the fields of epigenomics (Torres-Padilla, Tora, Davidson, Schneider, Gronemeyer, Hamiche, Kastner, Chan, and Sexton). We also share expertise in the France Génomique consortium through the bioinformatics working group on ChIP, methylation and smallRNA. Over the past 8 years, we have acquired experience on library preparation and data analysis for ChIP-seq, CaptureBS-seq, MNAse-seq and smallRNA-seq. We have further QC and sequence numerous ready-made libraries and perform data analysis for ATAC-seq, FAIRE-seq and MeDIP-seq. Expert in ChIP-seq data analysis, we have developed the seq-MINER programme to establish qualitative and quantitative correlations between multiple ChIP-seq data set.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Illumina HiSeq 4000
- Ultrasonicator Covaris E220 AFA system
- · Computing power : 224 cores (16 blades : 96-128 Gb RAM)
- Storage (RAID) : 260 TB

Techniques/services available to analyze chromatin and epigenetic modifications:

- Histone modification and protein binding sites analysis: ChIP-seq
- DNA methylation : Capture BS-seq, MeDIP-seq
- Open chromatin identification: ATAC-seq, FAIRE-seq
- Nucleosomes mapping : MNAse-seq
- Prediction and counting of small non coding RNAs : Small RNA-seq

- High expertise in NGS technology : >6000 samples sequenced since 2011
- Personalized support for experimental design and data analysis
- Over 30 publications co-authored in epigenetics since 2011
- Partner of "France Génomique" consortium





GenomEast sequencing activity







Peak clustering using seqMINER

Low input ChIP-seq analysis





Genomics Platform



David Gentien

Research Engineer, PhD student.

Workforce: Technical staff: 4 Engineers (Audrey Rapinat, Benoit Albaud, Emilie Henry, Cécile Reyes) and 1 Assistant Engineer (Aude Vieillefon)

Keywords:

- Core facility
- Genomics
- Transcriptomics
- Epigenomics
- Clinical trials

Research Center, Town: Institut Curie Research Center, Paris

Administrative affiliations: Translational research department, headed by Dr Sergio Roman Roman, Pharm-D

Tech Transfer Office: Institut Curie « Valorisation et

Partenariats Industriels » department

Services & collaborations:

Available for academic teams (intern or extern) and private companies



Platform address:

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Phone: +33(0)156246297

Platform Website : https://science. curie.fr/plateformes/genomique/

Email Contact : dgentien@curie.fr

Description:

The Genomics platform provides services in molecular biology for teams who need helps in the field of genomics. Actually composed of 6 people, the Genomic team setup and apply technics to prepare samples, to extract and control nucleic acids, to analyze genome and its expression using high throughput methods. Our services are highly used by the Institut Curie fellowship, French cancer center, public and private organizations. The platform helps to design studies, facilitates setup of projects and clinical trials, and can work for results submission.

Recent/key publications:

• Gurard-Levin ZA, Wilson LO, Pancaldi V, Postel-Vinay S, Sousa FG, Reyes C, Marangoni E, Gentien D, Valencia A, Pommier Y, Cottu P, Almouzni G.

Chromatin Regulators as a Guide for Cancer Treatment Choice.

Mol Cancer Ther. 2016, 15(7):1768-77

• Urrutia A, Duffy D, Rouilly V, Posseme C, Djebali R, Illanes G, Libri V, Albaud B, Gentien D, Piasecka B, Hasan M, Fontes M, Quintana-Murci L, Albert ML; Milieu Intérieur Consortium.

Standardized Whole-Blood Transcriptional Profiling Enables the Deconvolution of Complex Induced Immune Responses.

Cell Rep. 2016 Sep 6;16(10):2777-91

• Chicard M, Boyault S, Colmet Daage L, Richer W, Gentien D, Pierron G, Lapouble E, Bellini A, Clement N, Iacono I, Bréjon S, Carrere M, Reyes C, Hocking T, Bernard V, Peuchmaur M, Corradini N, Faure-Conter C, Coze C, Plantaz D, Defachelles AS, Thebaud E, Gambart M, Millot F, Valteau-Couanet D, Michon J, Puisieux A, Delattre O, Combaret V, Schleiermacher G. Genomic copy number profiling using circulating free tumor DNA highlights heterogeneity in neuroblastoma. Clin Cancer Res, 2016 Jul 20, [Epub ahead of print]

• Alsafadi S, Houy A, Battistella A, Popova T, Wassef M, Henry E, Tirode F, Constantinou A, Piperno-Neumann S, Roman-Roman S, Dutertre M, Stern MH. Cancer-associated SF3B1 mutations affect alternative splicing by promoting alternative branchpoint usage. Nat Commun. 2016 Feb 4;7:10615

• Gentien D, Kosmider O, Nguyen-Khac F, Albaud B, Rapinat A, Dumont AG, Damm F, Popova T, Marais R, Fontenay M, Roman-Roman S, Bernard OA, Stern MH. A common alternative splicing signature is associated with SF3B1 mutations in malignancies from different cell lineages. Leukemia. 2014 Jun;28(6):1355-7 • Piqueret-Stephan L, Marcaillou C, Reyes C, Honoré A, Letexier M, Gentien D, Droin N, Lacroix L, Scoazec IY, Vielh P.

Massively parallel DNA sequencing from routinely processed cytological smears.

Cancer Cytopathol. 2016 Apr;124(4) :241-53

• Le Tourneau C, Delord JP, Gonçalves A, Gavoille C, Dubot C, Isambert N, Campone M, Trédan O, Massiani MA, Mauborgne C, Armanet S, Servant N, Bièche I, Bernard V, Gentien D, Jezequel P, Attignon V, Boyault S, Vincent-Salomon A, Servois V, Sablin MP, Kamal M, Paoletti X; SHIVA investigators.

Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. Lancet Oncol. 2015 Oct;16(13):1324-34.

• Chaligné R, Popova T, Mendoza-Parra MA, Saleem MA, Gentien D, Ban K, Piolot T, Leroy O, Mariani O, Gronemeyer H, Vincent-Salomon A, Stern MH, Heard E. The inactive X chromosome is epigenetically unstable and transcriptionally labile in breast cancer. Genome Res. 2015 Apr;25(4):488-503

• Boeva V, Popova T, Lienard M, Toffoli S, Kamal M, Le Tourneau C, Gentien D, Servant N, Gestraud P, Rio Frio T, Hupé P, Barillot E, Laes JF.

Multi-factor data normalization enables the detection of copy number aberrations in amplicon sequencing data.

Bioinformatics. 2014 Dec 15;30(24):3443-50

The research centre is composed of several international expert teams in the field of Epigenetics: Pr E. Heard (Mammalian Developmental Epigenetics), Dr D. Bourc'his (Epigenetic Decisions and Reproduction in Mammals), Dr A. Morillon (Non-coding RNA) and Dr G. Almouzni (Chromatin Dynamics). The Genomic platform helps those teams in the measurement of genome and transcriptome alterations for basic research and translational studies (Chaligne R et al, Gurard-Levin ZA, et al).

Thanks to a translational research program on Uveal Melanomas, genome organization is being studied by D Gentien,

PhD student, codirected by Pr Edith Heard and S Roman Roman to characterize epigenetics properties linked to gene expression, in collaboration with D. Bourc'his, R. Margueron, MH Stern, E. Barillot. This EpiUm project is supported by the Institut Curie, PACRI and H2020 grants.

Recently, collaboration with Cambridge Epigenetix and the NGS facitlity has been signed in order to extend our expertise and services in epigenetics specially to identify mC, hmC, etc.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Nanostring nCounter systems (2 Flex systems + 2 Prep stations)
- Affymetrix GCS3000 (2 ovens, 4 fluidic stations, 1 7G Scanner)
- Affymetrix Genetitan 4C

Techniques/services available to analyze chromatin and epigenetic modifications:

- Histones modifications : ChIp-String, ChIp-on-Chip from extracted nucleic acids.
- Coding and Non coding genes quantificaiton: miR, ncRNA, cRNA, quantified by arrays (cartridges or 96 array plates) or by direct multiplexing methods (Nanostring, up to 800 different molecules) from tissue, cells, etc.
- Chromatin conformation : HiC libraries preparations for Next generation sequencing from tissue, cells, etc.
- DNA Methylation : WGBS libraires preparation from tissue, cells, etc.

Unique selling points in epigenetics:

- High scientific background in Epigenetics from the Institut Curie
- High throughput in RNA, and DNA analysis
- Expertise in gene expression signature evaluation
- Open to collaborations with researcher and companies to test and use new methods to enlarge our portfolio of activities (Collaboration with Cambridge Epigenetix company for oxBS)



Interaction map



When an experiment starts



Nanostring Cartridge

MIRs and ncRNA detection



Detection of mir using the Nanostring technic or Affymetrix tools





Human and Environmental Genomics platform (HEG)



Jean Mosser PU-PH Philippe Vanderkoornhuyse PR-UR1

Workforce: Sophie Michon-Coudouel AI CNRS Marc Aubry IR UR1 Marine Biget IE UR1 July Hémon IE UR1 Régis Bouvet TCN CHU Amandine Etcheverry IR CHU

Keywords:

Next Generation Sequencing

- Health & Environnemental research
- Genomics, Epigenomics, Transcriptomics

Research Center, Town: Rennes, Campus de Beaulieu & Campus de Villejean

Administrative affiliations: OSUR, BIOSIT, CHU, Université Rennes1, CNRS

Tech Transfer Office: SATT Ouest Valorisation

Services & collaborations:

Academic teams and private companies

Platform address:

Campus de Beaulieu Sophie MICHON-COUDOUEL or Marine BIGET Université de Rennes 1 -Campus de Beaulieu CNRS – OSUR Bat. 14A - Bureau 037 263 avenue du Général Leclerc 35042 RENNES Cedex - France

Campus de Villejean Marc AUBRY or July HEMON Laboratoire de Génomique Médicale BMT-HC Jean Dausset (Etage 1) 2, avenue Henri Le Guilloux 35033 Rennes Cedex 9 - France

Platform Website : https://geh.univ-rennes1.fr

Email Contact : genomics@univ-rennes1.fr

Description:

The HEG platform results from the fusion of two previous platforms of Université Rennes1: "Environmental and Functional genomics" and "Health Genomics".

The purpose of the HEG platform is to carry out and assist your NGS projects, from library preparation to primary bioinformatics analyses. For that purpose the platform has two Illumina sequencers (MiSeq, HiSeq 1500) and an IT solution for data analysis and storage. The HEG platform also provides a self-service access to advanced equipment needed for NGS library preparation and sequencing.

The platform benefits from a scientific working environment combining both ecological and medical fields of research. This strength enables thee platform to offer original sequencing strategies and make possible transfers of knowledge and skills gained in both domains. Moreover, with this original scientific positioning, we aim to develop innovative strategies in order to achieve most of your sequencing projects using up-to-date genomics technologies.



Certifications:

• The HEG platform (part of the "Biogenouest genomics" network) obtained the IBISA label in April 2012 (i.e. technological platform of strategic importance at the national scale) and belong to the France Genomics network.

• The HEG platform is certified ISO9001 (v2008) since December 31, 2012. An audit is planned in November 2016.

• The HEG platform is inserted within the national infrastructure 'AnaEE-France' for mass sequencing data production and high throughput genes quantification services.

Recent/key publications:

• Dynamics of Viral Abundance and Diversity in a Sphagnum-Dominated Peatland: Temporal Fluctuations Prevail Over Habitat. Ballaud F, Dufresne A, Francez A-J, Colombet J, Sime-Ngando T and Quaiser A. Front. Microbiol. 2016 jan.

• Routine molecular profiling of patients with advanced non-small-cell lung cancer: results of a 1-year nationwide programme of the French Cooperative Thoracic Intergroup (IFCT). Barlesi F1, Mazieres J2, Merlio JP3, Debieuvre D4, Mosser J5, Lena H6, Ouafik L7, Besse B8, Rouquette I9, Westeel V10, Escande F11, Monnet I12, Lemoine A13, Veillon R14, Blons H15, Audigier-Valette C16, Bringuier PP17, Lamy R18, Beau-Faller M19, Pujol JL20, Sabourin JC21, Penault-Llorca F22, Denis MG23, Lantuejoul S24, Morin F25, Tran Q25, Missy P25, Langlais A26, Milleron B27, Cadranel J27, Soria JC8, Zalcman G28; Biomarkers France contributors. Lancet. 2016 Apr

• The epigenetic processes of meiosis in male mice are broadly affected by the widely used herbicide atrazine. Gely-Pernot A., Hao C., Becker E., Stuparevic I., Kervarrec C., Chalmel F., Primig M., Jégou B. and Smagulova F. BMC Genomics. 2015 oct.

• Cell-Cycle-Dependent Reconfiguration of the DNA Methylome during Terminal Differentiation of Human B Cells into Plasma Cells. Caron G, Hussein M, Kulis M, Delaloy C, Chatonnet F, Pignarre A, Avner S, Lemarié M, Mahé EA, Verdaguer-Dot N, Queirós AC, Tarte K, Martín-Subero JI, Salbert G, Fest T. Cell Rep. 2015 oct.

• DGKI Methylation Status Modulates the Prognostic Value of MGMT in Glioblastoma Patients Treated with Combined Radio-Chemotherapy with Temozolomide. Etcheverry A*, Aubry M*, Idbaih A, Vauleon E, Marie Y, Menei P, Boniface R, Figarella-Branger D, Karayan-Tapon L, Quillien V, Sanson M, de Tayrac M, Delattre JY, Mosser J. PloS One. 2014 Sep.

Grants: • CPER 2017

Since 2008, the HEG platform has developed a technical & scientific expertise in the study of DNA methylation by microarray. The HEG platform conducted the screening of national multicentric cohorts in order to improve solid tumors personalized medicine by identifying new relevant prognostic and predictive epigenetic and genetic biomarkers. Now, the HEG platform is diversifying its offer by implementing NGS approaches to study histone modifications (ChIP sequencing) and DNA methylation (ChIP sequencing, whole-genome bisulfite sequencing, captured bisulfite sequencing).

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Hiseq 1500 and Miseq (Illumina)
- iScan (Illumina)
- M220 (Covaris)
- Bravo (Agilent)
- Bioanalyzer (Agilent)

Techniques/services available to analyze chromatin and epigenetic modifications:

- DNA methylation (microarray*, bisulfite and ChiP-seq**)
- Histone modifications (ChiP-seq^{**})

Unique selling points in epigenetics:

- Less than 1 month from library validation to library sequencing
- Scientific expertise in DNA methylation data analysis and interpretation
- Open to scientific collaboration to develop new innovative applications
- Scientific working environment combining both ecological and medical fields of research
- ISO9001 (v2008) certification

* self-service access. ** from library preparation to primary data analysis.



Hiseq 1500 (Illumina)



Miseq (Illumina)



NAS 21 Tb (RAID 5)

4 nœuds – 48 cœurs 192 Gb RAM



HEG staff

IT solution





IBENS genomic platform



Stéphane LE CROM (scientific head)

Ph D, University professor

Workforce: 6 engineers: 4 permanent positions, 1 non permanent and 1 apprentice.

Keywords:

• Functional genomics

- RNA-Seq
- ChIP-Seq
- Bioinformatics analysis
- High throughput sequencing

Research Center, Town: Institut de Biologie de l'École normale supérieure (IBENS), Paris

Administrative affiliations: ENS, CNRS UMR 8197, Inserm U 1024

Tech Transfer Office: École normale supérieure partnership office

Services & collaborations: Available for academic teams and private companies



Platform address:

Plateforme Génomique Institut de Biologie de l'École normale supérieure - IBENS 46, rue d'Ulm 75230 Paris Cedex 05 - France

Phone: +33 1 44 32 23 81

Platform Website: https://genomique.biologie.ens.fr

Email Contact: genomique@biologie.ens.fr

Description:

The IBENS genomic platform has been created in 1999 for providing access to functional genomic expertises to any public or private laboratory. The continued national recognition set up with microarray technology and continued with High Throughput Sequencing (HTS) through RIO, RNG, IBiSA and "Investissement d'Avenir", associated with local and regional financial supports allowed the platform to fulfil its main objectives: (i) make functional genomic technologies available for all laboratories; (ii) help researchers managing their high throughput genomic projects and (iii) disseminate high scale genomic approaches among the scientific community.

From all the applications offered by HTS, the IBENS genomic platform choose to focus on functional genomic ones through transcriptome analyses by RNA-Seq and ChIP-Seq to study gene regulation and epigenetic mechanisms.

In addition to this experimental expertise, the IBENS genomic platform set up several bioinformatics tools, to automate primary data treatment and to accompany the user as far as possible in more elaborate data analysis. For example, we were the first in France to develop data distributed analysis on cloud computing infrastructures for genomic applications.

Certifications:

• ISO 9001:2015, NF X50-900, IBISA

Recent/key publications:

• Diodato A, Ruinart de Brimont M, Yim YS, Derian N, Perrin S, Pouch J, Klatzmann D, Garel S, Choi GB, Fleischmann A. Molecular signatures of neural connectivity in the olfactory cortex. Nat Commun. 2016 Jul 18;7:12238.

• Carradec Q, Götz U, Arnaiz O, Pouch J, Simon M, Meyer E, Marker S. Primary and secondary siRNA synthesis triggered by RNAs from food bacteria in the ciliate Paramecium tetraurelia. Nucleic Acids Res. 2015 Feb 18;43(3):1818-33.

• Singh DP, Saudemont B, Guglielmi G, Arnaiz O, Goût JF, Prajer M, Potekhin A, Przybòs E, Aubusson-Fleury A, Bhullar S, Bouhouche K, Lhuillier-Akakpo M, Tanty V, Blugeon C, Alberti A, Labadie K, Aury JM, Sperling L, Duharcourt S, Meyer E. Genome-defence small RNAs exapted for epigenetic mating-type inheritance. Nature. 2014 May 22;509(7501):447-52.

• Veluchamy A, Lin X, Maumus F, Rivarola M, Bhavsar J, Creasy T, O'Brien K, Sengamalay NA, Tallon LJ, Smith AD, Rayko E, Ahmed I, Le Crom S, Farrant GK, Sgro JY, Olson SA, Bondurant SS, Allen AE, Rabinowicz PD, Sussman MR, Bowler C, Tirichine L. Insights into the role of DNA methylation in diatoms by genome-wide profiling in Phaeodactylum tricornutum. Nat Commun. 2013;4:2091.

• Jourdren L, Bernard M, Dillies MA, Le Crom S. Eoulsan: a cloud computing-based framework facilitating high throughput sequencing analyses. Bioinformatics. 2012 Jun 1;28(11):1542-3.

Grants:

- $\boldsymbol{\cdot}$ National Infrastructure in Biology and Health, Future Investment
- IBiSA
- SESAME Île de France
- ANR
- Fondation Pierre Gilles de Gennes
- PSL et École normale supérieure

Our expertise in epigenetics focus on ChIP-Seq experiments. During the 2012-2016 period we took in charge 38 projects using this technology and we processed more than 350 samples on 10 different species (Arabidopsis, Drosophila, Human, Mouse, Xenopus and Yeasts). We set up strong interactions with Morgane Thomas-Chollier in Denis Thieffry's lab in order to add to our Eoulsan analysis software the ability to work with ChIP-Seq data.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- NextSeq 500 (Illumina) High throughput sequencer;
- Biomark HD (Fluigdim) belonging to the ENS qPCR-HD platform.

Techniques/services available to analyze chromatin and epigenetic modifications:

• ChIP-Seq.

- ISO 9001:2015 and NF X50-900 quality standard;
- Open at 70% to projects outside IBENS;
- 38 ChIP-Seq projects (350 samples) analyzed since 2013;
- Functional genomics expert since 1999;
- 4 public permanent engineers;
- A balance team between experimental biology and bioinformatics;
- Part of France Genomique and IBiSA consortia;
- Open to research and development collaborations.



Functional genomics experts



High throughput sequencers



Bioinformatics team



Sample handling automation





ICGex NGS Platform



Sylvain Baulande

Ph.D

Workforce: Technical staff : 5 / Bioinformatics : 1

Keywords:

Next generation sequencing

- Cancer research
- Genomics
- Epigenetics
- Transcriptomics

Research Center, Town:

Paris Research Center / Institut Curie, Paris

Administrative affiliations: Scientific supervision from Olivier Delattre (U830)

Tech Transfer Office: Institut Curie « Valorisation et Partenariats Industriels » department

Services & collaborations: Available for academic teams (intern or extern) and private companies



Platform address:

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Email Contact : sylvain.baulande@curie.fr

Description:

Under the supervision of Olivier Delattre and Alain Nicolas and thanks to the Equipex grants obtained in 2012, The ICGex platform of the Institute provides state of the art services in next-generation sequencing. This includes the organization of pre-run meetings where the choice of the most appropriate technical strategy is defined in order to best address the biological question of collaborators. Multiple sequencing protocols have been developed and routinely used in the platform to cover most commonly used applications in genetics and epigenetics (Genome, Exome and targeted resequencing, RNA sequencing, DNA methylation sequencing, ChIP-seq ...). Furthermore, we are also willing to co-develop more specific protocols according to the need of research teams of the Institute.

Once the technical aspects are defined, samples are provided by collaborators and libraries compatible to the dedicated sequencing devices (Illumina or PacBio) are then prepared by the NGS team. After sequencing, raw data are transferred to the bioinformatics team (U900) for quality controls and basic analysis. At the end, sequence data are provided to research teams under a Galaxy user-friendly interface and a bioinformatics support is available to help in data analysis.

The platform is not restricted to basic research, we are also involved in multiple translational research projects in collaboration with U830, the translational research department and the Hôpital Curie (SHIVA, SAFIR02 ...). The molecular characterization of clinical samples within few days is used by clinicians to evaluate the best therapeutic options for patient care during MTB (Molecular Tumor Board).

Recent/key publications:

• Lebofsky, R., Decraene, C., Bernard, V., Kamal, M., Blin, A., Leroy, Q., Rio Frio, T., Pierron, G., Callens, C., Bieche, I., Saliou, A., Madic, J., Rouleau, E., Bidard, F.-C., Lantz, O., Stern, M.-H., Le Tourneau, C., and Pierga, J.-Y. Circulating tumor DNA as a non-invasive substitute to metastasis biopsy for tumor genotyping and personalized medicine in a prospective trial across all tumor types. Molecular Oncology. (2015).

• Tourneau, C.L., Delord, J.-P., Gonçalves, A., Gavoille, C., Dubot, C., Isambert, N., Campone, M., Trédan, O., Massiani, M.-A., Mauborgne, C., Armanet, S., Servant, N., Bièche, I., Bernard, V., Gentien, D., Jezequel, P., Attignon, V., Boyault, S., Vincent-Salomon, A., Servois, V., Sablin, M.-P., Kamal, M., Paoletti, X., and SHIVA investigators Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. Lancet Oncol. (2015).

• Le Loarer, F., Watson, S., Pierron, G., de Montpreville, V.T., Ballet, S., Firmin, N., Auguste, A., Pissaloux, D., Boyault, S., Paindavoine, S., Dechelotte, P.J., Besse, B., Vignaud, J.M., Brevet, M., Fadel, E., Richer, W., Treilleux,

I., Masliah-Planchon, J., Devouassoux-Shisheboran, M., Zalcman, G., Allory, Y., Bourdeaut, F., Thivolet-Bejui, F., Ranchere-Vince, D., Girard, N., Lantuejoul, S., Galateau-Sallé, F., Coindre, J.M., Leary, A., Delattre, O., Blay, J.Y., and Tirode, F. SMARCA4 inactivation defines a group of undifferentiated thoracic malignancies transcriptionally related to BAF-deficient sarcomas. Nat Genet. (2015). • Grünewald, T.G.P., Bernard, V., Gilardi-Hebenstreit, P., Raynal, V., Surdez, D., Aynaud, M.-M., Mirabeau, O., Cidre-Aranaz, F., Tirode, F., Zaidi, S., Perot, G., Jonker, A.H., Lucchesi, C., Le Deley, M.-C., Oberlin, O., Marec-Bérard, P., Véron, A.S., Reynaud, S., Lapouble, E., Boeva, V., Frio, T.R., Alonso, J., Bhatia, S., Pierron, G., Cancel-Tassin, G., Cussenot, O., Cox, D.G., Morton, L.M., Machiela, M.J., Chanock, S.J., Charnay, P., and Delattre, O. Chimeric EWSR1-FL11 regulates the Ewing sarcoma susceptibility gene EGR2 via a GGAA microsatellite. Nature Genetics. (2015).

• Eleveld, T.F., Oldridgé, D.A., Bernard, V., Koster, J., Dage, L.C., Diskin, S.J., Schild, L., Bentahar, N.B., Bellini, A., Chicard, M., Lapouble, E., Combaret, V., Legoix-Né, P., Michon, J., Pugh, T.J., Hart, L.S., Rader, J., Attiyeh, E.F., Wei, J.S., Zhang, S., Naranjo, A., Gastier-Foster, J.M., Hogarty, M.D., Asgharzadeh, S., Smith, M.A., Auvil, J.M.G., Watkins, T.B.K., Zwijnenburg, D.A., Ebus, M.E., van Sluis, P., Hakkert, A., van Wezel, E., van der Schoot, C.E., Westerhout, E.M., Schulte, J.H., Tytgat, G.A., Dolman, M.E.M., Janoueix-Lerosey, I., Gerhard, D.S., Caron, H.N., Delattre, O., Khan, J., Versteeg, R., Schleiermacher, G., Molenaar, J.J., and Maris, J.M. Relapsed neuroblastomas show frequent RAS-MAPK pathway mutations. Nat. Genet. (2015).

Grants:

- ANR-10-EQPX-03 (Equipex)
- ANR-10-INBS-09-08 (France Génomique Consortium)
- INCa-DGOS- 4654 (SiRIC-Curie program)

The Research Center of the Institut Curie hosts several international expert teams in the field of Epigenetics like Edith Heard (Mammalian Developmental Epigenetics), Déborah Bourc'his (Epigenetic Decisions and Reproduction in Mammals), Antonin Morillon (Non-coding RNA, Epigenetics, and Genome Fluidity) and Geneviève Almouzni (Chromatin Dynamics). The ICGex NGS platform has a close collaboration with these teams and performs epigenetics analyses in DNA methylation (WGBSseq, oxBSseq, MeDIPseq), histone modifications (ChIPseq), open chromatin region identification (ATACseq, FAIREseq) and chromatin conformation (Capture-C, 5C and HiC). In addition to routine NGS applications, the facility is involved in implementing new approaches to study epigenetics based on next-generation sequencing supported by the bioinformatics platform (U900) of the Institut. Recently, a collaboration with a company called Cambridge Epigenetix has been signed in order to extend our expertise and services in epigenetics.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- · Illumina sequencers (2 MiSeq, 2 HiSeq)
- PacBio long read sequencer (Sequel)

Techniques/services available to analyze chromatin and epigenetic modifications:

- · DNA Methylation : WGBSseq, MeDIPseq, oxBSseq
- Histones modifications : ChIPseq
- Open chromatin identification : ATACseq, FAIREseq
- Chromatin conformation : 5C, HiC, Capt-C

- High scientific background in Epigenetics from the Institut Curie
- Expertise in NGS various library preparation and sequencing
- NGS Platform open for external collaboration
- Collaboration with Cambridge Epigenetix company
- Part of France Genomique national network













LIGAN-PM Genomic Platform



Director: Philippe Froguel Scientific leader: Amélie BONNEFOND Technical leader: Emmanuelle DURAND Services contact : Véronique DHENNIN

Title Director: (MD, PhD)

Workforce: Technical Staff: 5 / Bioinformatics : 3 / BioStatistic : 3

Keywords:

- Next Generation Sequencing
- Personalized and precision medicine
- Genomics
- System biology
- Transcriptomics
- Epigenetics

Research Center, Town:

Institut de Biologie de Lille, EGID (European Genomic Institute for Diabetes)

Administrative affiliations: CNRS UMR8199

Tech Transfer Office: SATT Nord

Services & collaborations: With academic teams and private

companies

Platform address:

Institut de Biologie de Lille, 1 rue du professeur Calmette 59000 Lille
EGID (European Genomic Institute for Diabetes), Pôle Recherche,
1 place de Verdun 59045 LILLE CEDEX

Phone: 03.20.87.10.44

Platform Website : http://ligan.good.cnrs.fr/

Email Contact : contact-good@listes.egid.fr

Description:

Located at the Pasteur Institute of Lille, and at the Lille University Hospital, the LIGAN-PM platform is dedicated to the next-generation sequencing (NGS) in humans and animal models. Our latest high throughput next-generation sequencing systems (HiSeq 4000) are oriented to achieve high quality, cost-effective, customized DNA and RNA sequencing for patients with common diseases such as diabetes, obesity, Alzheimer's disease and cancers (in particular breast and ovarian cancers). Funded by an Equipex grant obtained in 2011 the LIGAN-PM platform has established high throughput capacities to sequence at low cost genomes and has diversified our portfolio. This project should eventually identify new genes and variants that play a key role in the development of common diseases towards precision medicine. A variety of state of art sequencing protocols have been developed (whole-genome sequencing, whole-exome sequencing, targeted DNA-seq, RNA-seq, ChIP-seq, Methyl-seq, Hi-C, Capture-C, 4C-seq...). This platform enables collaboration with researchers to provide most effective cutting edge tools for their genomic projects.



Certifications: • IBISA

Recent/key publications:

• What Is the Best NGS Enrichment Method for the Molecular Diagnosis of Monogenic Diabetes and Obesity? Philippe J, Derhourhi M, Durand E, Vaillant E, Dechaume A, Rabearivelo I, Dhennin V, Vaxillaire M, De Graeve F, Sand O, Froguel P, Bonnefond A. PLoS One. 2015

• Genetic variants in LEP, LEPR, and MC4R explain 30% of severe obesity in children from a consanguineous population. Saeed S, Bonnefond A, Manzoor J, Shabir F, Ayesha H, Philippe J, Durand E, Crouch H, Sand O, Ali M, Butt T, Rathore AW, Falchi M, Arslan M, Froguel P.Obesity (Silver Spring). 2015

• Contribution of the low-frequency, loss-of-function p.R270H mutation in FFAR4 (GPR120) to increased fasting plasma glucose levels. Bonnefond A, Lamri A, Leloire A, Vaillant E, Roussel R, Lévy-Marchal C, Weill J, Galan P, Hercberg S, Ragot S, Hadjadj S, Charpentier G, Balkau B, Marre M, Fumeron F, Froguel P. J Med Genet. 2015

• Low copy number of the salivary amylase gene predisposes to obesity. Falchi M, El-Sayed Moustafa JS, Takousis P, Pesce F, Bonnefond A, Andersson-Assarsson JC, Sudmant PH, Dorajoo R, Al-Shafai MN, Bottolo L, Ozdemir E, So HC, Davies RW, Patrice A, Dent R, Mangino M, Hysi PG, Dechaume A, Huyvaert M, Skinner J, Pigeyre M, Caiazzo R, Raverdy V, Vaillant E, Field S, Balkau B, Marre M, Visvikis-Siest S, Weill J, Poulain-Godefroy O, Jacobson P, Sjostrom L, Hammond CJ, Deloukas P, Sham PC, McPherson R, Lee J, Tai ES, Sladek R, Carlsson LM, Walley A, Eichler EE, Pattou F, Spector TD, Froquel P. Nat Genet. 2014

• Association between large detectable clonal mosaicism and type 2 diabetes with vascular complications. Bonnefond A, Skrobek B, Lobbens S, Eury E, Thuillier D, Cauchi S, Lantieri O, Balkau B, Riboli E, Marre M, Charpentier G, Yengo L, Froguel P.Nat Genet. 2013

Grants:

- Equipex LIGAN PM. ANR-10-EQX-07-01
- Labex EGID; ANR-10-LABX-46
- ERC Advanced Grant GEPIDIAB
- ERC Starting Grant (Reg-Seq)
- ANR project EPI-GDM
- IMI projects IMIDIA, DIRECT and RHAPSODY

Philippe Froguel has obtained in 2012 an ERC advanced grant "GEPIDIAB" whose the main goal was to identify DNA methylation variation associated with the risk of type 2 diabetes. Since then, the lab has optimized several protocols for analyzing differentiated methylation regions (DMRs) when compared cases and controls in several metabolic tissues: Illumina Infinium HumanMethylation450/850K BeadChip, Illumina Infinium MethylationEPIC BeadChip, QIAGEN-based pyrosequencing, low-pass whole-genome bisulfite sequencing, whole-exome Methyl-seq (using NimbleGen capture in combination with Illumina HiSeq4000), targeted Methyl-seq (using NimbleGen capture in combination with Illumina HiSeq4000), targeted Methyl-seq (using NimbleGen capture in combination with Illumina HiSeq4000). Our dedicated team of three bioinformaticians and three biostatisticians has developed all programs so as to optimally analyzed DMRs and to correlate this DMRs with expression changes (when transcriptomic analyses are performed in parallel with methylation analyses). This expertise will be used for the new 2016 ANR project EPI-GDM on the methylome of women with gestational diabetes and their children. The lab has also developed other technologies related to epigenetics including ChIP-seq, HiC (in progress), Capture-C, 4C-seq and in-depth RNA-seq so as to analyse lncRNA/miRNA/piRNA.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Illumina sequencers (2 MiSeq, 1 NextSeq 500, 2 HiSeq 2500 and 1 HiSeq 4000)
- Qiagen pyrosequencer Q48
- Illumina IScan
- Bioinformatics analysis of high-throughput sequencing data

Techniques/Services available to analyze chromatin and epigenetic modifications:

- DNA Methylation, with NimbleGen captures
- · ChIP-seq, MeDIP-seq, 4C-seq, Capture-C
- Epic Array

- Expertise in NGS various library preparation and sequencing
- NGS Platform open for external collaboration
- Collaboration with Imperial College London, Weill Cornell
 Qatar



Illumina array



Illumina HiSeq 2500 & 4000



EGID



Overview of a sequencing run on NextSeq500





Micro and Nano EPigenetic Profiling (MaNEP)



Fabien Guidez

Ph.D, HDR

Workforce: 2 engineers and 1 researcher (and IRs from the associated IUH plateforms)

Keywords:

- Cell epigenetic mark detection by immunofluorescence (flow cytometry, HIC, confocal microscopy)
- Isoform detection of epigenetic proteins at the nanometric level : Nanofluidic protein detection
- Epigenetic enzymatic activity
- Small samples analysis

Research Center, Town:

Institut Universitaire d'Hématologie (IUH), Paris

Administrative affiliations: Université Paris Diderot-INSERM

Tech Transfer Office: INSERM transfert

Services & collaborations:

Available for academic teams and private companies (collaboration with Diagenode and ProteinSimple)



Platform address:

Centre Hayem, 2eme étage, IUH, Hopital St Louis, Paris 10

Platform Website : IUH platform (Imaging and Genomic) website http://www.univ-parisdiderot.fr/IUH/pq.php?np=32

Email Contact : fabien.guidez@inserm.fr

Description:

As abnormal epigenetic landscapes and mutations in the epigenetic machinery are increasingly associated in diseases and cancer, we have recently developed at the IUH new technologies to assess their impact on pathogenic mechanisms. These technologies are developed to address issues of scarce samples at diagnosis and during disease progression and treatment (biomarker/surrogate marker monitoring) as also preclinical studies (in vitro and in vivo). Our MANEP service, located at the IUH, provides state of the art detection techniques and purification methods based on already existing epigenetic tools used in NGS-based whole genome studies (e.g epigenetic marker antibodies). In collaboration with the IUH imaging facility (N. Setterblad), several technics (including Immunofluorescence, Flow cytometry, Nanofluidic protein detection) are routinely used to assess epigenetic defects (both in epigenetic marks and modifiers) in patient and also in animal samples (e.g. In-house disease and epigenetic animal models).

Recent/key publications:

• Caye A, Strullu M, Guidez F, Cassinat B, Gazal S, Fenneteau O, Lainey E, Nouri K, Nakhaei-Rad S, Dvorsky R, Lachenaud J, Pereira S, Vivent J, Verger E, Vidaud D, Galambrun C, Picard C, Petit A, Contet A, Poirée M, Sirvent N, Méchinaud F, Adjaoud D, Paillard C, Nelken B, Reguerre Y, Bertrand Y, Häussinger D, Dalle JH, Ahmadian MR, Baruchel A, Chomienne C, Cavé H. Juvenile myelomonocytic leukemia displays mutations in components ot the RAS pathway and the PRC2 network (2015). Nat Genet. 47 (11):1334-40.

• McConnell MJ, Durand L, Langley E, Coste-Sarguet L, Zelent A, Chomienne C, Kouzarides T, Licht JD, Guidez F. Post Transcriptional control of the epigenetic stem cell regulator PLZF by Sirtuin and HDAC deacetylases (2015). Epigenetics Chromatin 24;8:38.

• Duval R, Fritsch L, Bui LC, Berthelet J, Guidez F, Mathieu C, Dupret JM, Chomienne C, Ait-Si-Ali S and Rodrigues-Lima F. An acetyltransferase assay for CRE-BP-binding protein based on reverse phase-ultra-fast chromatography of fluorescent histone H3 peptides (2015). Anal Biochem. 1;486:35-7.

• Puszyk W, Down T, Grimwade D, Chomienne C, Oakey RJ, Solomon E & Guidez F. The epigenetic regulator PLZF represses L1 retrotransposition in germ and progenitor cells (2013). EMBO J., 32: 1941-52

Grants:

ITMO cancer 2013-2016
ANSES 2016-2019

Over the years, MaNEP has gained expertise in both chromatin and DNA/RNA immunoprecipitation procedures and is actively involved in implementing new epigenetic approaches based on small cell number using next-generation sequencing (MeDIP, ChIP and ATACseq) with the support of the genomic platform of the IUH and Diagenode Inc. We aimed in a near future to open a fully operational Epigenetic platform. Finally, in collaboration with F. Rodrigues-Lima (BFA, CNRS UMR 8251, UP7), we have developed a sensitive fluorescent method (RP-UFLC) to measure immuno-purified epigenetic modifier activity (e.g. CBP), an approach particularly useful to assess enzymatic activity from cell extract and easily adaptable for other epigenetic modifiers.

Our team offers its services and expertise to researchers (inside or outside the IUH) and are dedicated to both translational and basic research projects. Collaborations include meetings, where the best technical approach(es) are defined to address the scientific question, samples treatment and (co-)development of compatible specific protocols. Overall, we provide a full range of epigenetic tests using a wide range of Imagery, biochemistry and whole genome approaches in order to characterize and evaluate the epigenetic status of rare clinical samples.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- LSM 510 and 880 Zeiss Confocal (IUH Imagery platform)
- NanoPro fluidic protein detection (NanoPro 1000 (UMR1131))
- Illumina sequencers (1 Miseq, 1 Hiseq, 1 Nextseq500 (IUH genomic platform))
- FPLC (BFA, CNRS UMR 8251, UP7)

Techniques/services available to analyze chromatin and epigenetic modifications:

- Histone/non-histone proteins modifications: Single Cell Immunofluorescence, NanoProteic detection, ChIP-seq (under development)
- · DNA methylation: MeDIPseq
- Histones modification: IF, FACs, Nanoproteic detection, ChIPseq
- Open chromatin identification: ATACseq
- Enzymatic activity detection: Reverse-phase ultra-fast liquid chromatography (RP-UFLC)

Unique selling points in epigenetics:

- High scientific background in Epigenetics from the MaNEP and the IUH
- Development of Epigenetic tools for rare disease biological samples (Micro and nano technologies)
- \cdot MaNEP and NGS platforms open for external collaboration
- Expertise in NGS library sequencing
- Collaborations with Diagenode (Innovating Epigenetic Solutions) and ProteinSimple (Powering Protein Research)

Detection by Flow Cytometry of methylated DNA (anti-5-MeC) and Panacetyl histone H3 (anti-acH3) in leukemic cells before and after treatment by an hypomethylating agent (5-aza) or an inhibitor of acetylase (HATi)





Acetylation profile obtained with the nanofluidic detection of the PLZF epigenetic protein in untreated (PLZFwt) or treated by a CBP inhibitor (CBPi) cells



Immunoflorescence detection of H3K27me3 in normal or mutated cells for the EZH2 protein associated to the Polycomb Repressive Complex 2



Detection of CBP acetyltransferase activity using a fluorescent H3K18 peptide by RP-UFLC (determination of CBP kinetic)





Plateforme Post-génomique de la Pitié Salpétrière (P3S)



Olivier SILVIE

M.D. Ph.D.

Workforce: 7 engineers: 6 permanent positions and 1 apprentice.

Keywords:

- Genomics
- Proteomics
- Microarrays
- Medical Research

Research Center, Town:

Université Pierre et Marie Curie (UPMC), Site Pitié Salpétrière, Paris

Administrative affiliations: UPMC, UMS Omique, Inserm US 29

Tech Transfer Office: UPMC, Direction générale de la recherche & du transfert de technologie (DGRTT)

Services & collaborations: Available for academic teams and private companies



Platform address: Plateforme P3S Faculté de Médecine Pierre et Marie Curie Site Pitié-Salpêtrière, Etage 4, porte 411 91, boulevard de l'hôpital 75634 Paris cedex 13

Phone: +33.1.40.77.81.32

Platform Website : http://www.p3s.chups.jussieu.fr/

Email Contact : p3s@upmc.fr

Description:

The P3S facility was created in 2001 and offers to academic and private laboratories its expertise and equipment across three different fields of activities.

1. A high-throughput microarray facility (Illumina). This platform offers a range of applications including genotyping, expression and methylation microarrays.

2. A proteomic facility, equipped with two mass spectrometers, which, together with bidimensional electrophoresis, offers various applications to users including relative quantitation of proteins by 2D-DIGE approaches, quality controls of peptide or recombinant proteins, protein identification in purified or complex samples, analysis of post-translational modifications, whole protein profiling or MALDI imaging.

3. A direct access to shared equipments to allow for the best usage of academic funding for the purchase and sharing of expensive devices.

The P3S facility benefits from its unique position at the interface between Inserm and UPMC research units, two University Hospital Institutes (ICM and ICAN), and the hospital departments from Assistance Publique-Hôpitaux de Paris (AP-HP). The platform engineers have established close collaborative links with these teams and have developed a specific expertise in handling samples from medical research projects.

Certifications:

• ISO 9001:2015, NF X50-900, IBiSA

Recent/key publications:

 Merino-Jiménez C, Aragón J, Ceja V, Rodríguez-Martínez G, Cázares-Raga FE, Chardonnet S, Pionneau C, Rendon A, Montañez C.. Dp71Δ78-79 dystrophin mutant stimulates neurite outgrowth in PC12 cells via upregulation and phosphorylation of HspB1. Proteomics. 2016 May;16(9):1331-40.

• Arnold L, Perrin H, de Chanville CB, Saclier M, Hermand P, Poupel L, Guyon E, Licata F, Carpentier W, Vilar J, Mounier R, Chazaud B, Benhabiles N, Boissonnas A, Combadiere B, Combadiere C. CX3CR1 deficiency promotes muscle repair and regeneration by enhancing macrophage ApoE production. Nat Commun. 2015 Dec 3;6:8972.

• Charbonnier-Beaupel F, Malerbi M, Alcacer C, Tahiri K, Carpentier W, Wang C, During M, Xu D, Worley PF, Girault JA, Hervé D, Corvol JC. Gene expression analyses identify Narp contribution in the development of L-DOPA-induced dyskinesia. J Neurosci. 2015 Jan 7;35(1):96-111.

• Canault M, Ghalloussi D, Grosdidier C, Guinier M, Perret C, Chelghoum N, Germain M, Raslova H, Peiretti F, Morange PE, Saut N, Pillois X, Nurden AT, Cambien F, Pierres A, van den Berg TK, Kuijpers TW, Alessi MC, Tregouet DA. Human CalDAG-GEFI gene (RASGRP2) mutation affects platelet function and causes severe bleeding. J Exp Med. 2014 Jun 30;211(7):1349-62. • Eyries M, Montani D, Girerd B, Perret C, Leroy A, Lonjou C, Chelghoum N, Coulet F, Bonnet D, Dorfmüller P, Fadel E, Sitbon O, Simonneau G, Tregouët DA, Humbert M, Soubrier F. EIF2AK4 mutations cause pulmonary veno-occlusive disease, a recessive form of pulmonary hypertension. Nat Genet. 2014 Jan;46(1):65-9.

Grants:

DIM Île de France
IBiSA

The Illumina microarray platform is currently operating the Infinium MethylationEPIC BeadChip technology. With the Infinium MethylationEPIC BeadChips, researchers can interrogate over 850,000 methylation sites quantitatively across the genome at single-nucleotide resolution. Multiple samples, including FFPE, can be analyzed in parallel to deliver high-throughput power while minimizing the cost per sample. The technology provides a pan-enhancer and coding region view of the methylome that can be used for epigenome-wide association studies on a variety of human tissues. The platform has a high demand from our medical team partners for this new support, and we have several ongoing projects involving large-scale cohorts (DECIPHER-HD and Methyl-HT).

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Illumina Platform (BeadStation 500)
- MALDI-TOF/TOF Autoflex speed (Bruker)
- Ion Trap HCT ultra (Bruker) coupled to a nanoLC U3000 liquid chromatography system (Thermo Scientific)

Techniques/services available to analyze chromatin and epigenetic modifications:

Infinium MethylationEPIC BeadChip

- Expertises in genomics and proteomics gathered on one site;
- Specific expertise in handling samples from medical research projects;
- Efficient and dynamic organization to quickly answer our user needs and make the most of our current devices;
- Illumina Bead Station operating >4,000 samples each year.



Illumina BeadStation platform



Automated sample management



Data analysis



Proteomic LC-MS/MS platform





ProfileXpert



Joel LACHUER

PhD and Professor

Workforce: 2 Bioinformaticians, 5 engineers (Molecular Biology), 5 referent scientists (Neurosciences, Cancerology, Infectiology, Pharmacology/Toxicology)

Keywords:

- Single cell genomics
- New generation sequencing
- Transcriptomics
- Epigenomics
- Genomics

Research Center, Town:

SFR Santé Lyon Ést, UCBL UMS 3453 CNRS-US7 INSERM

Administrative affiliations: University Claude Bernard, Lyon 1

Tech Transfer Office:

Lyon Ingénierie Projet (LIP) and Ezus Lyon

Services & collaborations:

Available for public and private laboratories or companies



Platform address:

Faculty of Medicine and Pharmacy Rockefeller, 8 avenue Rockefeller, 69008 Lyon

Phone: + (33) 4 78 77 28 89

Platform Website : www.profilexpert.fr

Email Contact : contact@profilexpert.fr

Description:

ProfileXpert is a technological platform of the university Lyon1 co-founded in 2003 by Pr Joel Lachuer and Dr Catherine Legras-Lachuer. The platform merged in 2009 with the laboratory for Molecular Characterisation of Tumours (LCMT) directed by Pr Charles Dumontet (hemato oncologist in Hospices civils de Lyon and currently assistant director of the platform). The platform was labelised Ibisa in 2009 and entered the France Genomque network in 2015. ProfileXpert is specialised in genomics, transcriptomics, epigenomics and regulomics analyses using microarrays and new generation sequencing. The platform has implemented for several years competencies and technologies to perform genomics analysis 1) from small quantities of DNA/RNA (including single cell genomics analysis) 2) from degraded samples (as FFPE tissues) and 3) heterogeneous samples (as cells infected by virus). Different projects using the implemented technologies are ongoing including 1) the study of intratumor heterogeneity in collaboration with the Cancer Research Centre of Lyon 2) Characterisation of molecular markers associated to melanoma using laser capture microdissection applied to FFPE tissues. A bioinformatic platform has been also implemented with a HP calculator with 50To memory and 9 cores (1,5 To RAM/ 32 threads) allowing single cell genomics analysis. The platform is involved in more than 130 publications since 2003 (including Cancer Cell, EMBO, PLos Genetics, Gastroenterology..).

Certifications:

• The platform is labelised Ibisa and belongs to the France Genomique network.

• The platform is certified Iso9001 and NFX 50-900 version 2016

• The plateform is certified MOT by ANSM (Authorization to work on Micro-Organisms and Toxines)

Recent/key publications:

• Hepatitis E virus mutations associated with ribavirin treatment failure result in altered viral fitness and ribavirin sensitivity. Debing Y, Ramière C, Dallmeier K, Piorkowski G, Trabaud MA, Lebossé F, Scholtès C, Roche M, Legras-Lachuer C, de Lamballerie X, André P,Neyts J. J Hepatol. 2016 May 9. pii: S0168-8278(16)30187-8.

• Foy JP, Tortereau A, Caulin C, Le Texier V, Lavergne E, Thomas E, Chabaud S, Perol D, Lachuer J, Lang W, Hong WK, Goudot P, Lippman SM, Bertolus C, Saintigny P. The dynamics of gene expression changes in a mouse model of oral tumorigenesis may help refine prevention and treatment strategies in patients with oral cancer. Oncotarget. 2016 Mar 24.

• Roche M, Wierinckx A, Croze S, Rey C, Legras-Lachuer C, Morel AP, Fusco A, Raverot G, Trouillas J, Lachuer J. Deregulation of miR-183 and KIAA0101 in Aggressive and Malignant Pituitary Tumors. Front Med (Lausanne). 2015 Aug 10;2:54.

• The complex pattern of epigenomic variation between natural yeast strains at single-nucleosome resolution Filleton F, Chuffart F, Nagarajan M, Bottin-Duplus H, Yvert G. Epigenetics Chromatin. 2015 Jul 31;8:26. Vernin C, Thenoz M, Pinatel C, Gessain A, Gout O, Delfau-Larue MH, Nazaret N, Legras-Lachuer C, Wattel E, Mortreux F HTLV-1 bZIP Factor HBZ Promotes Cell Proliferation and Genetic Instability by Activating OncomiRs. Cancer Res. 2014 Nov 1;74(21):6082-93.
Caramel J, Papadogeorgakis E, Hill L, Browne GJ, Richard G, Wierinckx A, Saldanha G, Osborne J, Hutchinson P, Tse G, Lachuer J, Puisieux A, Pringle JH, Ansieau S, Tulchinsky E. A Switch in the Expression of Embryonic EMT-Inducers Drives the Development of Malignant Melanoma. Cancer Cell. 2013 Oct 14;24(4):466-80.

Grants:

• ANR Clarence (as Partner) Effect of bisphenol A on transcriptome and methylome of breast cancer cell lineages.

• SIGEXPOSOME project (as partner) (Cancéropôle Lyon Auvergne Rhône Alpes): Impact of pesticides on winemakers population.

• (International) Head and Neck Prevention ACT (as partner) (Cancéropôle Lyon Auvergne Rhône Alpes): Characterization of molecular biomarkers in oral cancers by transcriptomics analysis on laser capture micro-dissection.

• Gis-Ibisa platform subvention (own project) : Subvention for acquisition of the DEParray technology (100 k \in) for single cell genomics.

• Pair melanoma (INCA) (as partner): Second primary melanomas and mechanisms of resistance to targeted therapies in metastatic melanoma.

ProfileXpert is involved, as R&D partner or as a service core facility, in different projects (ANR, INCA, CLARA, International Agency for Research on Cancer) needing epigenomics analysis. By the expertise of the staff and the technologies implemented for several years (iScan station, Nextseq 500, Hiseq2500, Affymetrix station and a 7900 HT fast real time PCR) we propose different approaches to address epigenomics problematics (including DNA methylation, Histone modification, miRNA and Long non coding RNA expression) in different areas including Cancerology, Pharmaco/ Toxicology and Infectiology. We are currently developing approaches to investigate epigenetics events at single cell resolution level (as single cell methylation EPIC beadchips (Illumina), Whole genome methylation analysis by NGS and also the RRBS technology (Reduced Representation Bisulfite Sequencing). For miRNome 3 technologies are available: the Affymetrix miRNA arrays, Taqman low density array card miRNA and Small RNA-seq. We have also developed bioinformatics pipeline for data analysis and focus currently on the integration of epigenomics data with transcriptomic data.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- iScan (Illumina)
- · 3 NGS equipments (Hiseq2500, Nextseq 500, MiSeq from Illumina)
- 7900 HT fast real time PCR (Applied Biosystem)
- Affymetrix station
- C1 Single cell Autoprep system (Fluidigm)/laser capture microdissection (Arcturus) and DEParray (Silicon Biosystem) for single cell epigenomics analysis

Techniques/services available to analyze chromatin and epigenetic modifications:

- DNA methylation : Infinium MethylationEPIC beadchips (Illumina), WGBS, Reduction Representation of bisulfite sequencing (RRBS), MeDIP-seq.
- Histone analysis : ChIP-seq
- miRNome : Affymetrix miRNA arrays, Small RNA-seq and Taqman low density array card miRNA

- Availability of different technologies (Beadchips, NGS, Taqman Low density arrays) in the same platform to address different problematic (in particularly when small quantities of miRNA are available)
- High Expertise on technology for methylation analysis (including Infinium MethylationEPIC beadchips processing and data analysis)
- $\boldsymbol{\cdot}$ Expertise for libraries preparation from small DNA or RNA quantities
- Collaborative projects to implement epigenetics analysis at single cell
 resolution level





Location of profileXpert: Faculty of Medicine and Pharmacy Rockefeller, Lyon



iScan and Hiseq equipment (Illumina)



Violin map representation of single cell transcriptome analysis







Anne-Françoise Adam-Blondon

PhD, INRA Research Director Workforce: 18 personnes (7 ETP)

Keywords:

- Computing resources
- Transposable elements
- Data integration

Research Center, Town: INRA center of Versailles

Administrative affiliations: Research Unit in Genomics Info (URGI), INRA, Versailles

Tech Transfer Office: Génoplant-Valor

Services & collaborations: Available for academic teams and private companies



Platform address: Unité de Recherche en Génomique-Info (URGI) INRA Centre de Versailles-Grignon R10 Route de Saint-Cyr 78026 Versailles Cedex

Phone: +33 1 (0)1 30 83 31 00

Platform Website : urgi.versailles.inra.fr

Email Contact : joelle.amselem@versailles.inra.fr

Description:

The URGI platform is hosted by the URGI INRA research unit. The platform belongs to the « Institut Français de Bioinformatique « (IFB) the french node of Elixir , the european network of bioinformatics platforms. Platform services cover database design, software engineering, software hosting, data integration and training. The platform activity is closely related to URGI research activity (data integration, repeat annotation, genome structure and dynamics). The platform develops and maintains a modular and interoperable information system (GnpIS) for plant and pest genomics to enable scientists to mine genomic and genetic data. The platform has a strong expertise in developing pipelines dedicated to genome analyses and particularly to annotate and study the role of transposable elements in genome dynamics and evolution.

The areas of competence and expertise of the platform members are mainly focused on:

- Development of analysis pipelines (Python)
- Interface development (Java J2EE)
- Databases (PostgreSQL, MySQL) and NoSQL technologies (ElasticSearch, SolR)
- Genome analysis (structure and dynamics) : Repeat annotation (specifically transposable elements), Gene Annotation (structural and functional), RNA-Seq

Certifications:

- IBISA
- ISO9001

Recent/key publications:

Jouffroy O, Saha S, Mueller L, Quesneville H, Maumus F: Comprehensive repeatome annotation reveals strong potential impact of repetitive elements on tomato ripening. BMC Genomics, 2016, 17 (1): 1-15.
Hoede C, Arnoux S, Moisset M, Chaumier T, Inizan O, Jamilloux V, Quesneville H: PASTEC: An Automatic Transposable Element Classification Tool. PloS one 2014, 9(5):e91929.

• Steinbach D, Alaux M, Amselem J, Choisne N, Durand S, Flores R, Keliet AO, Kimmel E, Lapalu N, Luyten I, Michotey C, Mohellibi N, Pommier C, Reboux S, Valdenaire D, Verdelet D and Quesneville H: GnpIS: an information system to integrate genetic and genomic data from plants and fungi. Database : the journal of biological databases and curation 2013, 2013:bat058.

• Maumus F, Quesneville H: Ancestral repeats have shaped epigenome and genome composition for millions of years in Arabidopsis thaliana. Nature communications 2014, 5:4104.

• Mayer KFX, Rogers J, Dolezel J, Pozniak C, Eversole K, Feuillet C, Gill B, Friebe B, Lukaszewski AJ, Sourdille P et al: A chromosome-based draft sequence of the hexaploid bread wheat (Triticum aestivum) genome. Science 2014, 345(6194).

Grants:

• "Investissement d'Avenir" projects: RENABI-IFB, Phenome, Breedwheat, Amaizing, Rapsodyn, Peamust, France-Génomique, Biomasse for the Future

We are internationally recognized experts in transposable element annotation and their analysis. We have been involved in more than 40 genome annotations in the frame of international sequencing consortia. We studied transposable element epigenetic regulation and epigenetic impact on genes for years, through small RNAs and related epigenetic marks. We developed methods and pipelines for these analysis that leads to number of scientific publications in high impact journals.

Tools/Instruments/Equipments to analyze chromatin and epigenetic modifications:

- Repeats and transposable element annotation and analysis pipelines (the REPET package)
- Galaxy server with standard NGS tools (bwa, bowtie, tophat, samtools, bedtools, s-mart, MACS, ...)
- Large computing resources for data analysis on HPC cluster
- GnpIS information system for genetic and genomic data. Includes in-house development and links with intermines, genome browsers, search tools, ...

Techniques/services available to analyze chromatin and epigenetic modifications:

- Repeat and transposable element genome annotation
- Computing resources for big data analysis and management (training, consulting, monitoring, access, ...)
- · Databasing and data integration

Unique selling points in epigenetics:

- Internationally recognized expertise in transposable element annotation and analysis. Involved in more than 40 genome annotations in the frame of international sequencing consortia.
- Study of transposable element epigenetic regulation, related epigenetic marks, and epigenetic impact on genes.



Transposable element annotation pipelines



HPC cluster







GnpIS: Information system for genomic and genetic data

If you want more information or to be included in this book, please contact **alice.bousselet@aviesan.fr**

