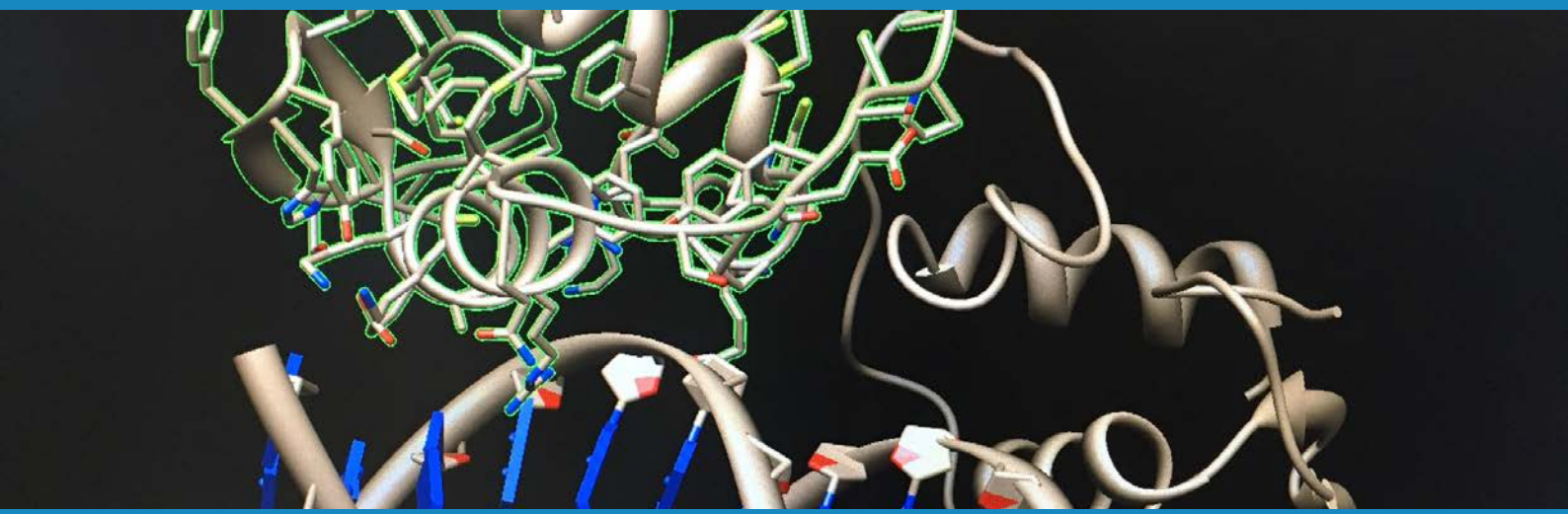
Programme

Biomedical Informatics



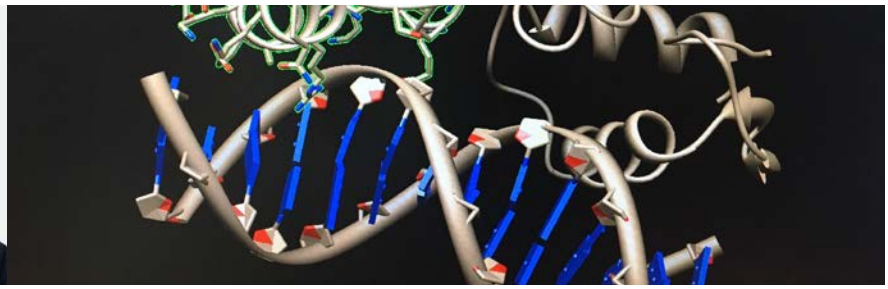
Biomedical Informatics

6 Research groups

25 Professionals

11 Research projects

28 Publications



Programme Director
Ferran Sanz

RESEARCH GROUPS

Evolutionary Genomics
Maria del Mar Albà

GPCR Drug Discovery
Jana Selent

Integrative Biomedical Informatics
Laura Inés Furlong and Ferran Sanz

Systems Pharmacology
Jordi Mestres

ASSOCIATED GROUPS

Computational Biology of RNA Processing
Roderic Guigó

Pharmacoinformatics
Manuel Pastor

The Research Programme on Biomedical Informatics (GRIB) is a joint research unit of the Hospital del Mar Medical Research Institute (IMIM) and the Department of Experimental and Health Sciences of the Pompeu Fabra University (UPF).

The mission of GRIB is to develop and apply computational methods and information technologies for a better understanding and prediction of biological phenomena, placing special emphasis on those related to human diseases, their diagnosis and pharmacological treatment.

GRIB is recognized and funded by the Catalan government. It is the node for Biomedical Informatics of the Spanish Institute of Bioinformatics (INB) and, jointly with Farmaindustria, GRIB coordinates the Spanish Technological Platform for Innovative Medicines (PTEMI). GRIB also participates in the Bioinformatics Barcelona Association (BIB), which aims to promote training, research, and technology transfer in bioinformatics. Ferran Sanz, the director of GRIB, is the co-coordinator of PTEMI and vice-president of BIB.

GRIB staff is involved in pre- and postgraduate teaching at UPF, where they coordinate the Master's Program in Bioinformatics for Health Sciences. This master degree aims to provide professionals and researchers with expertise and skills geared towards developing new computational strategies and IT systems that are useful in biomedical research.

People and research areas

GRIB is currently composed of more than 60 members, with a highly multidisciplinary background, including biologists, chemists, computer scientists, physicists, mathematicians, medical doctors, etc. More than 30% of the members are senior scientists or postdocs. The programme includes six IMIM research groups:

- The **Evolutionary Genomics group** led by M. Mar Albà (ICREA) uses comparative genomics and transcriptomics methods to discover new genes and characterize their functions.
- The **PharmacoInformatics group** led by Manuel Pastor (UPF) is devoted to the development and application of computational methods and tools in pharmaceutical research, with a particular focus on computational toxicology.
- The **Systems Pharmacology group** led by Jordi Mestres performs research at the interface between chemistry, biology, and informatics to develop novel computational approaches to designing safer, more efficacious, personalized drugs. Some of the results of the group have been commercialized via the spin-off biotech company Chemotargets.
- The **GPCR Drug Discovery group** led by Jana Selent (Miguel Servet) focuses on the functionality of G-protein-coupled receptors (GPCRs) within the context of CNS-related disorders, taking into account receptor plasticity, activation mechanism, signalling bias, ligand binding and the effect of the membrane and other interaction partners.

- The **Integrative Biomedical Informatics group** led by Laura I. Furlong (Miguel Servet) and Ferran Sanz, works on new methods and tools for knowledge extraction and linkage from biomedical literature and other publicly available sources, and develops strategies for the research reuse of clinical data.
- The **Computational Biology of RNA Processing group** is devoted to the development and application of methods to identify functional domains in genomic sequences. The main researcher in this group is Roderic Guigó (CRG).

Most relevant issues in 2018

The GRIB has wide experience in participating and coordinating research projects funded by the European Commission and other research funding agencies. It also has a long tradition of collaboration with the pharmaceutical and biotechnological industry within the framework of R&D projects and providing services, especially in the development of computational methods for drug discovery and toxicity assessment.

During the year 2018, the Programme coordinated two large scale scientific initiatives:

- The Innovative Medicines Initiative (IMI) project eTRANSAFE (Enhancing Translational Safety Assessment through Integrative Knowledge Management), which aims to develop an advanced data integration infrastructure together with innovative computational methods to improve safety in drug development processes. (2017-2022)
- The H2020 project MedBioinformatics, focused on the translational and clinical application of bioinformatics. (2015-2018)

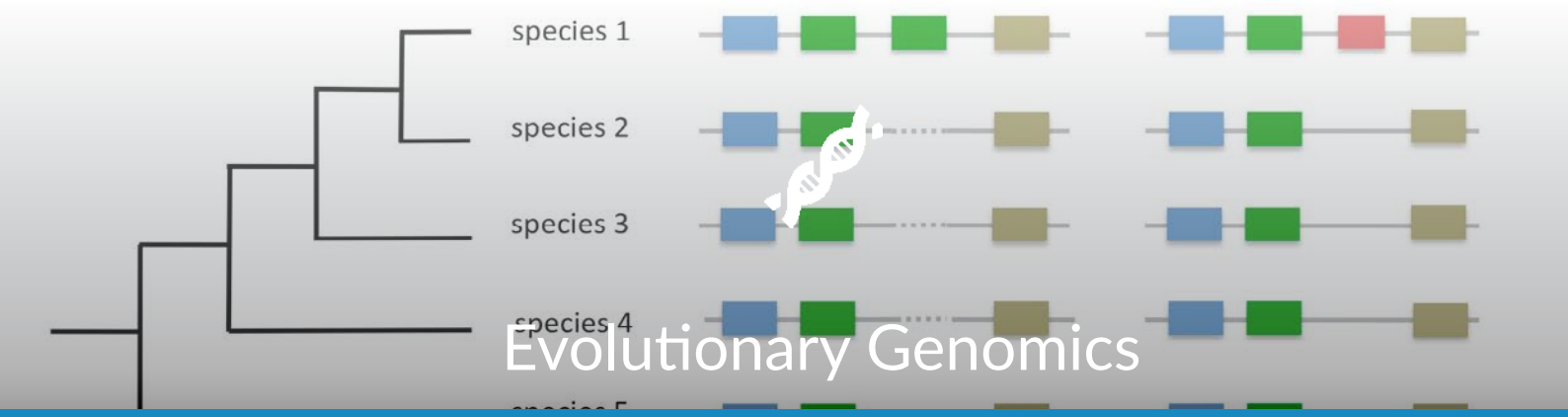
The GRIB was also a partner in other EU-funded projects, such as the following IMI projects:

- TransQST (Translational Quantitative Systems Toxicology), which aims to develop novel computational approaches using the best available data from the public and private domains to address the problems of drug safety.
- EMIF (European Medical Information Network), which aims to develop a common information framework of patient-level data that will link up and facilitate access to diverse medical and research data sources, opening up new avenues of research for scientists.
- iPiE (Intelligence Led Assessment of Pharmaceuticals in the Environment), which aims to develop a predictive framework for the environmental impact of drugs.

The GRIB was also partner of the following H2020 projects:

- EU-ToxRisk, which aims to achieve a paradigm shift in toxicology towards a more efficient and animal-free chemical safety assessment.
- ESCAPE-NET (European Sudden Cardiac Arrest Network), focused on the prevention, education and new treatment of this disease.
- ELIXIR-EXCELERATE, which aims to accelerate the implementation of Europe's life-science data infrastructure.

The research activities of GRIB have led to the creation of several spin-off companies such as BioCloud (2015), Acellera (2007), Chemotargets (2006) and Pharmatools (2002), and the development of commercial and open-source scientific software, such as the DisGeNET resource on gene-disease associations. For further details, see http://grib.imim.es/software-services/software/



Evolutionary Genomics

Biomedical Informatics RESEARCH GROUP

Group Leader
Maria del Mar Albà Soler
(ICREA Professor)

malba@imim.es

Members

Jorge Ruiz Orera (Researcher)
William Robert Blevins (PhD Student)
Simone Moro (Technician)

The Evolutionary Genomics group, led by Mar Albà, uses comparative genomics and large-scale data analysis to understand the complexity of gene regulation and evolutionary innovation. The group develops bioinformatics pipelines to analyze large amounts of genomics data. We use novel approaches to reconstruct and quantify the transcriptome using high-throughput RNA sequencing data, including long-read technologies such as Nanopore. We are also using techniques for sequencing ribosome-protected RNA fragments, also known as ribosome profiling. Using these techniques we have been able to discover many novel translated small ORFs (sORFs). Some of these sORFs correspond to highly conserved small proteins, or micropeptides, that can have important cellular functions. Others are intermediates in the process of generation of de novo genes, new types of gene that arise from previously non-coding parts of the genome. We are also interested in using transcriptomics data to study adaptation to extreme conditions, such as hibernation in mammals. In this regard, we have recently characterized the molecular mechanisms associated with the induction of torpor in hibernating species of lemurs, which may lead to future applications in human medicine.

Main Publications

- Faherty SL, Villanueva-Cañas JL, Blanco MB, Albà MM, Yoder AD. Transcriptomics in the wild: hibernation physiology in free-ranging dwarf lemurs. Mol Ecol 2018; 27(3): 709-722. IF 6.131. D1.

Ongoing Research Projects

- Mecanismos de formación de genes nuevos
  - Financing institution: Ministerio de Economía y Competitividad (BFU2015-65235-P)
  - Period: from 2016 to 2019
  - Principal investigator: Albà Soler, Maria del Mar

GPCR Drug Discovery

Biomedical Informatics RESEARCH GROUP

Group Leader
Jana Selent

jana.selent@upf.edu

Members

Tomasz Stepniewski Maciej (PhD Student)

The group is focused on the functionality of G-protein-coupled receptors (GPCRs) within the context of CNS-related disorders, taking into account: receptor plasticity, activation mechanism, signalling bias, ligand binding, the effect of the membrane and other interaction partners. The ultimate goal is to translate the molecular insights obtained into the design of drug candidates with improved therapeutic profiles.

The main research lines are:

- In-silico Multi-Receptor Profiling of Antipsychotic Drugs, focusing on deciphering the molecular mechanisms of this complex interplay of current antipsychotic drugs that are responsible for their clinical efficacies.
- GPCR Dimers as a Drug Target for the Treatment of Schizophrenia. Our group provides support for the design of bivalent ligands that selectively target a specific GPCR dimer. Once a target is validated, we apply diverse computational tools to obtain first small drug-like molecules towards this target.
- Membrane Lipid-Mediated Effects on GPCR signalling by studying direct and indirect membrane effects on receptor monomers and dimers using all-atom as well as coarse-grained simulation setups.
- Database for GPCR dynamics. The main mission of this project is to provide dynamic insights into crystallized receptors at a publicly accessible platform.

Main Publications

- Stepniewski T, Torrens M, Rodríguez-Espigares I, Giorgino T, Primdahl KG, Vik A, Stenstrøm Y, Selent J, Hansen TV. Synthesis, molecular modelling studies and biological evaluation of new oxoeicosanoid receptor 1 agonists. Bioorgan Med Chem 2018; 26(12): 3580-3587. IF 2.881. Q2.

Ongoing Research Projects

- La modulación alostérica del receptor D2 de la dopamina forma parte del mecanismo de acción del litio: de la evidencia molecular a la neuroimagen funcional
  - Financing institution: Fondo de Investigación Sanitaria. ISCIII (PI15/00460)
  - Period: from 2016 to 2019
  - Principal investigator: Selent, Jana

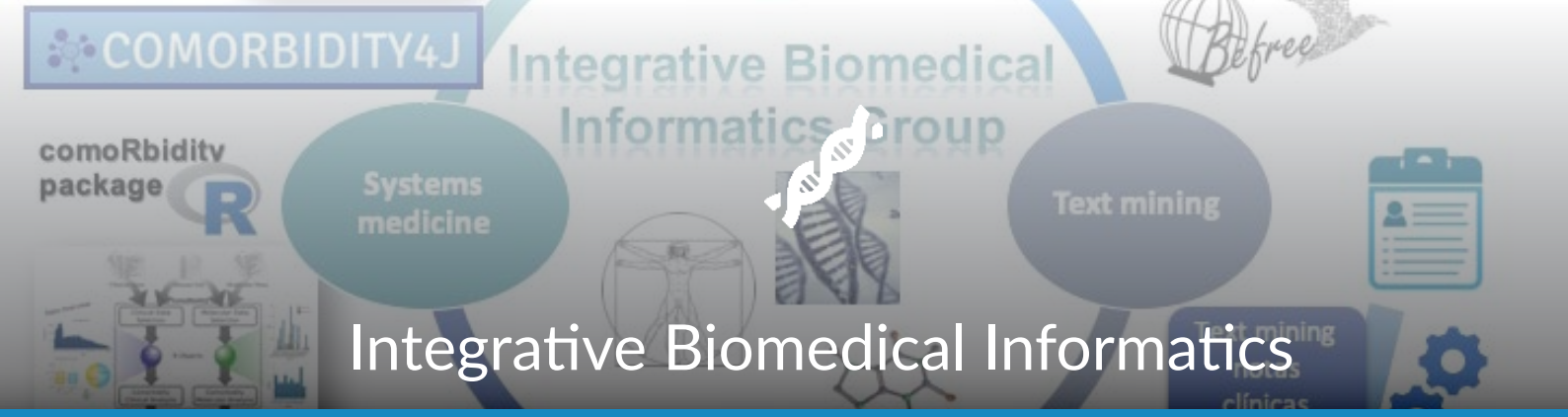
Theses

- Rodríguez-Espigares I. GPCRmd - A web platform for collection, visualization and analysis of molecular dynamics data for G protein-coupled receptors: Bridging the gap between receptor dynamics and receptor functionality. Universitat Pompeu Fabra.
  - Directors: Selent, Jana; Sanz Carreras, Ferran
  - Date of defense: 04/04/2018

Other

Book Chapter

- Kaczor AA, Bartuzi D, Stepniewski TM, Matosiuk D, Selent J. Protein-Protein Docking in Drug Design and Discovery. Methods Mol Biol, 2018; 1762: 285-305.



Integrative Biomedical Informatics

Biomedical Informatics RESEARCH GROUP

Group Leader
Laura Inés Furlong Nespolo

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Group Leader
Ferran Sanz Carreras

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Members

Alexia Giannoula (Researcher)
Miquel Àngel Mayer Pujadas (Researcher)
Janet Piñero González (Researcher)
Alejandro Speck (Researcher)
Emilio Centeno Ortiz (Technician)
Emre Güney (Technician)
Francesco Ronzano (Technician)
Josep Saüch Pitarch (Technician)
María Jesús Donlo Fernández (Research Assistant)
Alfons González Pauner (Research Assistant)
Carina Oliver Dutrem (Research Assistant)

The huge wealth of biomedical information that is currently available is underused because of the difficulties in seeking, integrating and analyzing the relevant information. There is also considerable great difficulty involved in identifying and using clinically actionable information. The goal of the Integrative Biomedical Informatics (IBI) group is to develop computational methods and tools to address these challenges, with the aim of better understanding human health and disease and contributing to the design of more effective and safer therapeutic interventions.

The ongoing research areas of the IBI group are the following:

- Text mining
- Knowledge management and linked data
- Real World Data (RWD) analytics in health
- Systems biology and network medicine for the study of human diseases and drug toxicity
- Integrative knowledge management and exploitation in drug discovery and development

Main Publications

- Piñero J, Furlong LI, Sanz F. In silico models in drug development: where we are. Curr Opin Pharmacol, 2018; 42: 111-121. IF 6.313. D1.
- Gutiérrez-Sacristán A, Bravo A, Giannoula A, Mayer MA, Sanz F, Furlong LI. comoRbidity: An R package for the systematic analysis of disease comorbidities. Bioinformatics, 2018; 34 (18): 3228-30. IF 5.481. D1.
- Piñero J, González-Pérez A, Guney E, Aguirre-Plans J, Sanz F, Oliva B, Furlong LI. Network, Transcriptomic and Genomic Features Differentiate Genes Relevant for Drug Response. Front Genet, 2018; 9: 412. IF 4.151. Q1.
- Souza T, Trairatphisan P, Piñero J, Furlong LI, Sáez-Rodríguez J, Kleinjans J, Jennen D. Embracing the Dark Side: Computational Approaches to Unveil the Functionality of Genes Lacking Biological Annotation in Drug-Induced Liver Injury. Front Genet, 2018; 9: 527. IF 4.151. Q1.
- Giannoula A, Gutiérrez Sacristán A, Bravo A, Sanz F, Furlong LI. Identifying temporal patterns in patient disease trajectories using dynamic time warping: A population-based study. Sci Rep, 2018; 8(1): 4216. IF 4.122. Q1.
- López-Massaguer O, Pinto-Gil K, Sanz F, Amberg A, Anger LT, Stolte M, Ravagli C, Marc P, Pastor M. Generating modelling data from repeat-dose toxicity reports. Toxicol Sci, 2018; 162(1): 287-300. IF 4.081. Q1.
- Pastor M, Quintana J, Sanz F. Development of an Infrastructure for the Prediction of Biological Endpoints in Industrial Environments. Lessons Learned at the eTOX Project. Front Pharmacol, 2018; 9: 1147. IF 3.831. Q1.

- Aguirre-Plans J, Piñero J, Menche J, Sanz F, Furlong LI, Schmidt HHHW, Oliva B, Guney E. Proximal Pathway Enrichment Analysis for Targeting Comorbid Diseases via Network Endopharmacology. Pharmaceuticals 2018; 11(3): E61. SJR:1,293. Q1.

Ongoing Research Projects

- eTRANSAFE: Enhancing TRANslational SAFEty Assessment through Integrative Knowledge Management
  - Financing institution: Innovative Medicines Initiative-IMI (777365)
  - Period: from 2017 to 2022
  - Principal investigator: Sanz Carreras, Ferran
- TransQST: Translational quantitative systems toxicology to improve the understanding of the safety of medicines
  - Financing institution: Innovative Medicines Initiative-IMI (116030)
  - Period: from 2017 to 2021
  - Principal investigator: Sanz Carreras, Ferran
- CliKA-MinE: Clinical Knowledge Aggregation by Mining medical rEports
  - Financing institution: Fondo de Investigación Sanitaria. ISCIII (PI17/00230)
  - Period: from 2018 to 2020
  - Principal investigator: Furlong Nespolo, Laura Inés
- EXCELLERATE: Fast-track ELIXIR implementation and drive early user exploitation across the life-sciences
  - Financing institution: European Comission H2020 (676559)
  - Period: from 2015 to 2019
  - Principal investigator: Sanz Carreras, Ferran
- iPiE: Intelligence Led Assessment of Pharmaceuticals in the Environment
  - Financing institution: Innovative Medicines Initiative-IMI (115735)
  - Period: from 2015 to 2019
  - Principal investigator: Sanz Carreras, Ferran
- MedBioinformatics: Creating medically-driven integrative bioinformatics applications focused on oncology, CNS disorders and their comorbidities
  - Financing institution: European Commission H2020 (634143)
  - Period: from 2015 to 2018
  - Principal investigator and coordinator of the consortium: Sanz Carreras, Ferran
- MedSisCom: Medicina de sistemas para el estudio de las comorbilidades
  - Financing institution: Fondo de Investigación Sanitaria. ISCIII (PI13/00082)
  - Period: from 2014 to 2018
  - Principal investigator: Furlong Nespolo, Laura Inés

Participation in Research Networks

- Ferran Sanz is the co-president of the Plataforma Tecnológica Española de Medicamentos Innovadores (PTEMI), vicepresident of Bioinformatics Barcelona Association (BIB) and PI of the node for Biomedical Informatics of the Spanish Institute of Bioinformatics (INB).

Group's Recognitions

- Officially recognised as a consolidated research group by the Generalitat de Catalunya: Grup de Recerca en Biomedicina Computacional (2017-2020)
  - Agència de Gestió d'Ajuts Universitaris i de Recerca (SGR 519)
  - Principal investigator: Sanz Carreras, Ferran

Theses

- Rodríguez-Espigares I. GPCRmd - A web platform for collection, visualization and analysis of molecular dynamics data for G protein-coupled receptors: Bridging the gap between receptor dynamics and receptor functionality. Universitat Pompeu Fabra.
  - Directors: Selent, Jana; Sanz Carreras, Ferran
  - Date of defense: 04/04/2018

Systems Pharmacology

Biomedical Informatics RESEARCH GROUP

Group Leader
Jordi Mestres López

jmestres@imim.es

Members

Xavier Jalencas Giménez (Researcher)
Andreu Bofill Pumarola (PhD Student)
María José Falaguera Mata (Technician)

The Research Group on Systems Pharmacology, led by Dr. Jordi Mestres, conducts research at the interface between chemistry, biology and informatics to develop novel computational methods that contribute to designing safer, more efficacious, drugs. In this respect, the group is actively involved in several initiatives to explore the mechanisms of action leading to severe adverse drug reactions, with special emphasis on cardiotoxicity and hepatotoxicity, and to investigate the impact of the human endogenous metabolome on the efficacy and safety of drugs. Current efforts are focused on ultimately gaining a better understanding of drug polypharmacology within the context of biological systems as a means of advancing towards precision medicine.

The group is also the seed of the biotech company Chemotargets SL, founded in 2006 and currently employing ten people, seven of whom are former PhD students or post-doctoral researchers of the group. The company develops and markets the CLARITY® intelligence and discovery platform for large-scale prediction of the pharmacology, safety, and diseases of small-molecule pharmaceuticals and cosmeceuticals, currently in use worldwide by sixteen big pharma, small and medium biotech companies, academic centers, and not-for-profit organizations, such as the FDA.

Main Publications

- Antolín AA, Mestres J. Dual Inhibitors of PARPs and ROCKs. ACS Omega 2018; 3: 12707-12712. SJR: 0,749. Q1.
- Reyes-Resina I, Samadi A, Navarro G, Saadeh HA, Khasawneh MA, Mestres J, Marco-Contelles J, Franco R. Identification of a Tool Compound to Study the Mechanisms of Functional Selectivity between D-2 and D-3 Dopamine Receptors. ACS Omega 2018; 3(12): 17368-17375. SJR: 0,749. Q1.

Ongoing Research Projects

- El impacto del metaboloma endógeno sobre la farmacología y seguridad de pequeñas moléculas exógenas
  - Financing institution: Ministerio de Economía y Competitividad. SAF2017-83614-R
  - Period: from 2018 to 2020
  - Principal investigator: Mestres López, Jordi
- European Sudden Cardiac Arrest network: towards Prevention, Education and NEw Treatment
  - Coordinator: Academic Medical Center of the University of Amsterdam (NL)
  - Financing institution: European Union (733381)
  - Period: from 2017 to 2021
  - Principal investigator from IMIM: Mestres López, Jordi
- EU-OPENSCREEN DRIVE: Ensuring Long-Term Sustainability of Excellence in Chemical Biology within Europe and Beyond
  - Coordinator: Forschungsverbund Berlin e. V. (Germany)
  - Financing institution: European Union (INFRADEV-03-2018-2019)
  - Period: from 2019 to 2022
  - Principal investigator from IMIM: Mestres López, Jordi
- EOSC-Life: Providing an Open Collaborative Space for Digital Biology in Europe
  - Coordinator: ELIXIR @ European Molecular Biology Laboratory (UK)
  - Financing Institution: European Union (INFRAEOSC-04-2018)
  - Period: from 2019 to 2022
  - Principal investigator from IMIM: Mestres López, Jordi

Participation in Research Networks

- EU-OPENSCREEN: European Infrastructure of Open Screening Platforms for Chemical Biology (261861)

Group's Recognitions

- Our research group is part of the Grup de Recerca en Biomedicina Computacional, officially recognised as a consolidated research group by the Generalitat de Catalunya (2017-2020)
  - Agència de Gestió d'Ajuts Universitaris i de Recerca (SGR 0519)
  - Principal investigator: Sanz Carreras, Ferran

Theses

- Carrascosa MC. Next generation of informatics tools for big data analytics in drug discovery. Universitat Pompeu Fabra
  - Director: Mestres López, Jordi
  - Date of defense: 20/03/2018

Other

- Jordi Mestres obtained the Advanced Research Acreditation by the Agència per a la Qualitat del Sistema Universitari de Catalunya (AQU). December 11th, 2018.
- Jordi Mestres was appointed by the QSAR & Modeling Society to be the Organizer of the European QSAR Symposium that will take place in Barcelona on September 2020. October 2nd, 2018.
- Jordi Mestres was admitted as a Fellow of the Royal Society of Chemistry. June 12th, 2018.

Masters

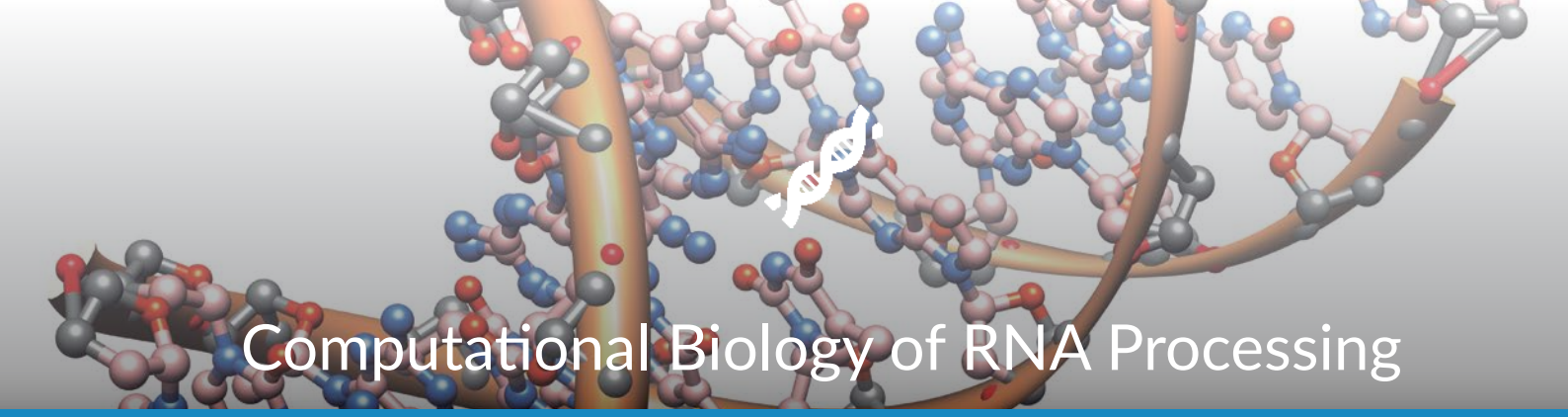
- Falaguera MJ. Identification of the core chemical structure in SureChEMBL patents. Pompeu Fabra University.
  - Director: Mestres López, Jordi
  - Date of defense: 02/07/2018.

Invited Presentations at International Conferences

- Annual Meeting of the Chem-Bio Informatics Society. Tokyo, Japan. Invited conference: Identification of safety events linked to drug classes. Mestres J. October 9-12, 2018.

Attendance to Courses

- Summer Course on Quantitative Pharmacology. Pamplona, Spain. Falaguera MJ. July 2-5, 2018.
- PRBB Intervals Course: Scientific Writing. Falaguera MJ. November 9, 16, 23, 30, 2018.



Computational Biology of RNA Processing

Biomedical Informatics ASSOCIATED GROUP

Group Leader
Roderic Guigó

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The overarching theme of the research in our group is the understanding of the information encoding in genomic sequences, and how this information is processed in the pathway leading from DNA to protein sequences. More specifically, we are interested in the regulation of the primary production (transcription) and post-processing (splicing) of RNA, and how this regulated production relates to cell, tissue and organism phenotypes. Our research is increasingly incorporating high throughput and experimental approaches. In addition, but related to this basic component of our research, our group is also involved in the development of software for functional annotation in genomic sequences. Our group has actively participated in the analysis of many eukaryotic genomes and is involved in a number of international projects: ENCODE, GTEx, BluePrint and the International Cancer Genome Consortium, among others.

We are the Genomics node of the Spanish Instituto Nacional de Bioinformática.

Main Publications with IMIM

- Ferreira PG, Reverter F, Sá Godinho CP, Sousa A, Amadoz A, Sodaei R, Hidalgo MR, Pervouchine D, Carbonell-Caballero J, Nurtdinov R, Breschi A, Amador R, Oliveira P, Çubuk C, Curado J, Aguet F, Oliveira C, Dopazo J, Sammeth M, Ardlie KG, Guigó R. The effects of death and post-mortem cold ischemia on human tissue transcriptomes. Nat Commun 2018; 9(1): 490. IF 12.353. D1.
- Garrido-Martín D, Palumbo E, Guigó R, Breschi A. ggsashimi: Sashimi plot revised for browser- and annotation-independent splicing visualization. PLoS Comput Biol 2018; 14(8): e1006360. IF 3.955. D1.

MORE INFO

PharmacoInformatics

Biomedical Informatics ASSOCIATED GROUP

Group Leader
Manuel Pastor Maeso

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Members

Núria Boada Centeno (Researcher)

The PharmacoInformatics research group is devoted to the development and application of computational methodologies in the area of drug design and development.

Nowadays, computational methodologies are widely applied in many steps of the drug discovery and development; from the structural modeling of a pharmacological target to the prediction of the ligand binding affinity. However, in the vast majority of cases the limitations of current technology allow us only to obtain approximate representations of the complex biological phenomena that are the focus of interest in the development of new drugs.

The PharmacoInformatics group aims to improve the current state-of-the-art with a pragmatic approach. We want to develop useful tools that increase the efficiency of the pharmaceutical R&D process. At the same time, the need to produce robust models led us to go beyond reductionist approaches and to develop multi-scale methods, depicting richer and more realistic representations of the phenomena under study than those produced by classical computational methods.

Main Publications with IMIM

- López-Massaguer O, Sanz F, Pastor M. An automated tool for obtaining QSAR-ready series of compounds using semantic web technologies. Bioinformatics 2018; 34(1): 131-133. IF 5.481. D1.
- López-Massaguer O, Pinto-Gil K, Sanz F, Amberg A, Anger LT, Stolte M, Ravagli C, Marc P, Pastor M. Generating modelling data from repeat-dose toxicity reports. Toxicol Sci 2018; 162(1): 287-300. IF 4.181. Q1.
- Pastor M, Quintana J, Sanz F. Development of an Infrastructure for the Prediction of Biological Endpoints in Industrial Environments. Lessons Learned at the eTOX Project. Front Pharmacol 2018; 9: 1147. IF 3.831. Q1.
- Romero L, Cano J, Gomis-Tena J, Trenor B, Sanz F, Pastor M, Saiz J. In Silico QT and APD Prolongation Assay for Early Screening of Drug-Induced Proarrhythmic Risk. J Chem Inf Model 2018; 58(4): 867-878. IF 3.804. Q1.

MORE INFO