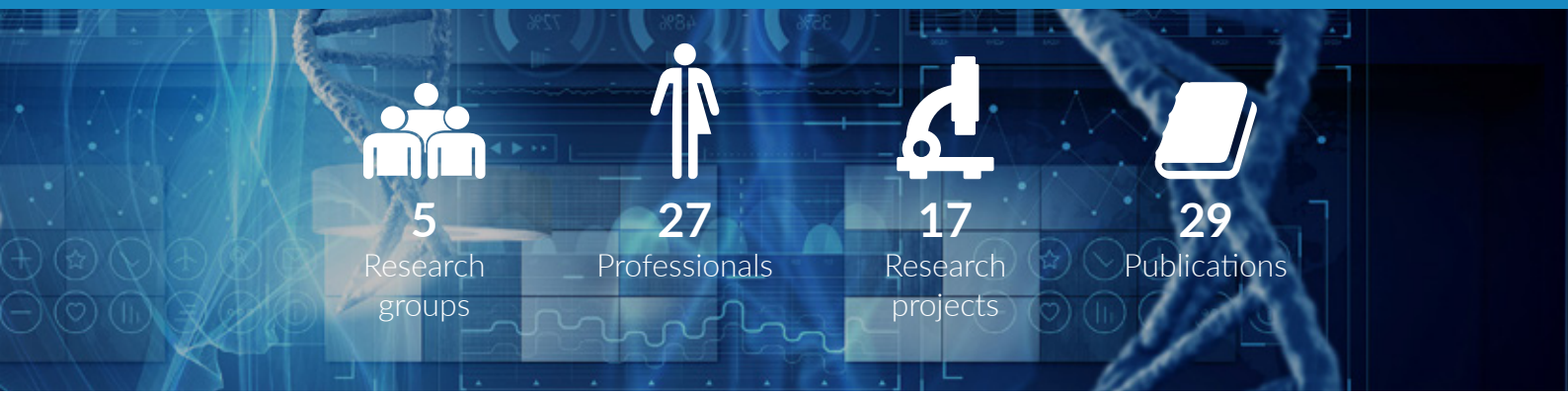
Programme

Biomedical Informatics

Biomedical Informatics



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

Pharmacoinformatics
Manuel Pastor

The mission of the joint Research Programme on Biomedical Informatics (GRIB) of IMIM and the Pompeu Fabra University (UPF) 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 has five research groups affiliated to IMIM: Evolutionary Genomics (M. Albà), GPCR Drug Discovery (J. Selent), Integrative Biomedical Informatics (L. Furlong and F. Sanz), PharmacoInformatics (M. Pastor) and Systems Pharmacology (J. Mestres).

Outstanding scientific achievements

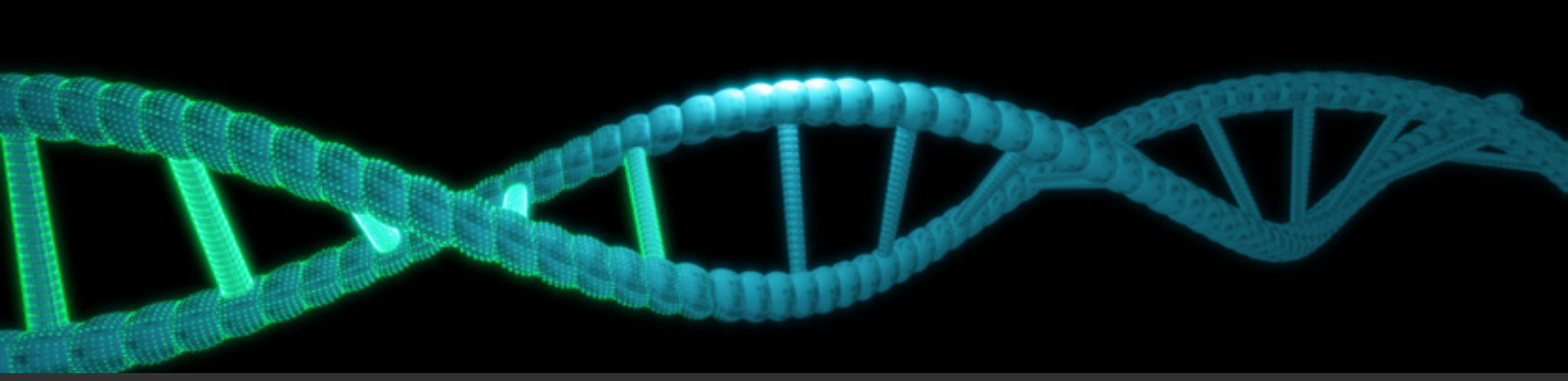
During 2019, GRIB coordinated two EU-funded projects, eTRANSAFE and NEURON PSYBIAS, and participated as a partner in seven more projects: FAIRplus, TransQST, EU-ToxRisk, Escape-net, EOSC-Life, EU-OPENSCREEN DRIVE and EXCELERATE, as well as other national projects and contracts with the industry.

GRIB's research activities led to the creation of the spin-off company MedBioinformatics Solutions, which develops products and services based on DisGeNET, an internationally recognised knowledge resource on disease genetics (50,000+ users per year).

Mar Albà's research on *de novo* genes was featured in *Nature* on Oct 16, 2019.

Some scientific publications

- IMEx Consortium Curators *at al*. (incl. Piñero J & Furlong LI). Capturing variation impact on molecular interactions in the IMEx Consortium mutations data set. Nat Commun 2019; 2; 10(1): 10.
- Ruiz-Orera J, Albà MM. Translation of Small Open Reading Frames: Roles in Regulation and Evolutionary Innovation. Trends Genet. 2019; 35(3): 186-98.
- Bofill A, Jalencas X, Oprea TI, Mestres J. The human endogenous metabolome as a pharmacology baseline for drug discovery. Drug Discov Today 2019; 24(9): 1806-20. (Drug Discovery Today included an Editorial on this paper and Nature Reviews Drug Discovery commented it).
- Leis A, Ronzano F, Mayer MA, Furlong LI, Sanz F. Detecting Signs of Depression in Tweets in Spanish: Behavioral and Linguistic Analysis. J Med Internet Res 2019; 21(6): e14199.



Evolutionary Genomics

> Biomedical Informatics

RESEARCH GROUP

Group Leader
Maria del Mar Albà Soler
(ICREA Professor)

malba@imim.es

Members

William Robert Blevins (Technician)
José Carlos Montañés Domínguez (Technician)
Simone Moro (Technician)

The Evolutionary Genomics group, led by Mar Albà, uses comparative genomics and large-scale transcriptomics data to understand the complexity of gene regulation and evolutionary innovation processes.

We are developing 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.

Finally, we are also using transcriptomics data to study the emergence of novel transcripts and neoantigens in cancer.

Main Publications

- Ruiz-Orera J, Albà MM. Translation of Small Open Reading Frames: Roles in Regulation and Evolutionary Innovation. Trends Genet 2019; 35(3): 186-198. IF 10.627. D1.
- Blevins WR, Tavella T, Moro SG, Blasco-Moreno B, Closa-Mosquera A, Díez J, Carey LB, Albà MM. Extensive post-transcriptional buffering of gene expression in the response to severe oxidative stress in baker's yeast. Sci Rep 2019; 9: 11005. IF 4.011. Q1.
- Blevins WR, Carey LB, Albà MM. Transcriptomics data of 11 species of yeast identically grown in rich media and oxidative stress conditions. BMC Res Notes 2019; 12: 250. SJR 0.661. Q2.
- Ruiz-Orera J, Albà MM. Conserved regions in long non-coding RNAs contain abundant translation and protein–RNA interaction signatures. NAR Genomics and Bioinformatics 2019; 1(1): e2.

See all Publications

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

See all Projects

Appointments

- Maria del Mar Albà Soler. Member of the jury of Premi Ciutat de Barcelona Ciències de la Vida. Barcelona, 10-20 January 2019.
- Maria del Mar Albà Soler. Member of the jury of Fitch Prize Annual Meeting Society for Molecular Biology and Evolution. SMBE'19. Manchester, UK, 23 July 2019.

Outreach

Dissemination to Society and Initiatives of Citizen Participation

- William Robert Blevins. Pint of Science: Dur la recerca científica als bars. 13 September 2019.
- William Robert Blevins; José Luis Villanueva-Cañas. Pint of Science: Beyond Jurassic Park. Frontiers of Science and Science Fiction. BlackLab (Barcelona), 22 May 2019.

GPCR Drug Discovery

> Biomedical Informatics

RESEARCH GROUP

Group Leader
Jana Selent

jana.selent@upf.edu

Members

Tomek Stepniewski (PhD Student)

The group is focused on the functionality of G-protein-coupled receptors (GPCRs) in 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. We study the molecular mechanisms 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

• Ghosh E, Dwivedi H, Baidya M, Srivastava A, Kumari P, Stepniewski T, Kim HR, Lee MH, van Gastel J, Chaturvedi M, Roy D, Pandey S, Maharana J, Guixà-González R, Luttrell LM, Chung KY, Dutta S, Selent J, Shukla AK. Conformational Sensors and Domain Swapping Reveal Structural and Functional Differences between β-Arrestin Isoforms. Cell Rep 2019; 28(13): 3287-3299.e6. IF 7.815. Q1.

• Sánchez-Melgar A, Albasanz JL, Guixà-González R, Saleh N, Selent J, Martín M. The antioxidant resveratrol acts as a non-selective adenosine receptor agonist. Free Radical Biol Med 2019; 135: 261-273. IF 5.657. Q1.

• Abraham MJ, Apostolov RP, Barnoud J, Bauer P, Blau C, Bonvin AMJJ, Chavent M, Chodera JD, Condic-Jurkic K, Delemotte L, Grubmüller H, Howard RJ, Jordan EJ, Lindal E, Ollila OHS, Selent J, Smith DGA, Stansfeld PJ, Tiemann JKS, Trellet M, Woods CJ, Zhmurov A. Sharing Data from Molecular Simulations. J Chem Inf Model. 2019; 59(10): 4093-4099. IF 3.966. Q1.

See all Publications

Ongoing Research Projects

• A novel paradigm for effective and safer treatment of schizophrenia: biased (ant) agonists with a characterized polypharmacological profile

- Financing institution: ERA-Net NEURON – European Commission / ISCIII
- Period: from 2018 to 2021
- Principal investigator: Selent, Jana

• Disección de los fundamentos de la eficacia superior de la clozapina para el tratamiento de la esquizofrenia: desde pruebas moleculares hasta evidencias cerebrales

- Financing institution: Fondo de Investigación Sanitaria. ISCIII (PI18/00094)
- Period: from 2018 to 2021
- Principal investigator: Selent, Jana

• 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 2020
- Principal investigator: Selent, Jana

See all Projects

Participation in Research Networks

- European Research Network on Signal Transduction (ERNEST)
  - Financing institution: European Commission
  - Period: from 2019 to 2023
  - Vice chair: Selent, Jana

Integrative Biomedical Informatics

Group Leader
Laura Inés Furlong Nespolo

laura.furlong@upf.edu

Group Leader
Ferran Sanz Carreras

ferran.sanz@upf.edu

Members

Eduardo Eyras Jiménez (Researcher)
Alexia Giannoula (Researcher)
Miguel Ángel Mayer Pujadas (Researcher)
Janet Piñero González (Researcher)
Juan Manuel Ramírez Anguita (Researcher)
Gabriel Santpere Baró (Researcher)
Judith Pérez Granado (PhD Student)
Emre Güney (Technician)
María de los Ángeles Leis Machín (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

- Leis A, Ronzano F, Mayer MA, Furlong LI, Sanz F. Detecting Signs of Depression in Tweets in Spanish: Behavioral and Linguistic Analysis. J Med Internet Res 2019; 21(6): e14199. IF 4.945. D1.
- Ronzano F, Gutiérrez-Sacristán A, Furlong LI. Comorbidity4j: a tool for interactive analysis of disease comorbidities over large patient datasets. Bioinformatics 2019; 35 (18): 3530-3532. IF 4.531. Q1.
- Pérez-Granado J, Piñero J, Furlong LI. ResMarkerDB: a database of biomarkers of response to antibody therapy in breast and colorectal cancer. Database (Oxford) 2019; 2019: baz060. IF 3.683. Q1.

See all Publications

Ongoing Research Projects

- FAIRplus
  - Financing institution: Innovative Medicines Initiative – IMI (802750)
  - Period: from 2019 to 2021
  - Principal investigator: Sanz Carreras, Ferran

- Enhancing TRANslational SAFEty Assessment through Integrative Knowledge Management (eTRANSAFE)
  - Financing institution: Innovative Medicines Initiative – IMI (777365)
  - Period: from 2017 to 2022
  - Principal investigator: Sanz Carreras, Ferran
- Translational quantitative systems toxicology to improve the understanding of the safety of medicines (TransQST)
  - Financing institution: Innovative Medicines Initiative – IMI (116030)
  - Period: from 2017 to 2021
  - Principal investigator: Sanz Carreras, Ferran
- Clinical Knowledge Aggregation by Mining medical rEports (CliKA-MinE)
  - 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 Commission H2020 (676559)
  - Period: from 2015 to 2019
  - Principal investigator: Sanz Carreras, Ferran

See all Projects

Participation in Research Networks

- Plataforma Tecnológica Española de Medicamentos Innovadores (PTEMI)
  - Period: from 2006
  - Principal investigator: Sanz Carreras, Ferran; co-president of the platform
- Bioinformatics Barcelona Association (BIB)
  - Period: from 2015
  - Principal investigator: Sanz Carreras, Ferran; vice-president
- Spanish Institute of Bioinformatics (INB)
  - Period: from 2005
  - Principal investigator: Sanz Carreras, Ferran; PI of the node for Biomedical Informatics

Systems Pharmacology

> Biomedical Informatics

RESEARCH GROUP

Group Leader
Jordi Mestres López

jmestres@imim.es

Members

Andreu Bofill Pumarola (PhD Student)
Emilio Centeno Ortiz (Technician)
María José Falguera Mata (Technician)

The Research Group on Systems Pharmacology 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 12 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 21 big pharma, small and medium biotech companies, academic centers, and not-for-profit organizations, such as the FDA.

Main Publications

- Bofill A, Jalencas X, Oprea TI, Mestres J. The human endogenous metabolome as a pharmacology baseline for drug discovery. Drug Discov Today 2019; 24(9): 1806-1820. (Highlighted in the Editorial of the same issue in Drug Discovery Today 2019 and in Nature Reviews Drug Discovery 2019). IF 6.88. D1.
- Olivés J, Mestres J. Closing the Gap between Therapeutic Use and Mode of Action in Remedial Herbs. Front Pharmacol 2019; 10: 1132. IF 3.845. Q1.
- Dyballa S, Miñana R, Rubio-Brotons M, Cornet C, Pederzani T, Escaramis G, Garcia-Serna R, Mestres J, Terriente J (2019). Comparison of Zebrafish Larvae and hiPSC Cardiomyocites for Predicting Drug-Induced Cardiotoxicity in Humans. Toxicol Sci 2019; 171(2): 283-295. IF 3.564. Q1.
- Vogt I, Mestres J. Information Loss in Network Pharmacology. Mol Inf 2019; 38(7):e1900032. (Journal cover of Volume 38, Issue 7, July 2019). IF 2.375. Q1.
- Brennecke P, Rasina D, Aubi O, Herzog K, Landskron J, Cautain B, Vicente F, Quintana J, Mestres J, Stechmann B, Ellinger B, Brea J, Kolanowski JL, Pilarski R, Orzaez M, Pineda-Lucena A, Laraia L, Nami F, Zielenkiewicz P, Paruch K, Hansen E, von Kries J, Neuenschwander M, Specker E, Bartunek P, Simova S, Lesnikowski Z, Krauss S, Lehtiö L, Bilitewski U, Brönstrup M, Taskén K, Jirgensons A, Lickert H, Clausen MH, Andersen JH, Vicent MJ, Genilloud O, Martínez A, Nazaré M, Fecke W, Gribbon P. EU-OPENSCREEN: A Novel Collaborative Approach to Facilitate Chemical Biology. SLAS Discov 2019; 24(3): 398-413. IF 2.192. Q3.

See all Publications

Ongoing Research Projects

- EOSC-Life: Providing an Open Collaborative Space for Digital Biology in Europe
  - Financing institution: European Commission (INFRAEOSC-04-2018)
  - Period: from 2019 to 2022
  - Principal investigator at IMIM: Mestres López, Jordi
- EU-OPENSCREEN DRIVE: Ensuring Long-Term Sustainability of Excellence in Chemical Biology within Europe and Beyond
  - Financing institution: European Commission (INFRADEV-03-2018-2019)
  - Period: from 2019 to 2022
  - Principal investigator at IMIM: Mestres López, Jordi
- The impact of the endogenous metabolome on the pharmacology and safety of exogenous small molecules
  - Financing institution: Ministerio de Economía y Competitividad
  - Period: from 2018 to 2020
  - Principal investigator: Mestres López, Jordi

- ESCAPE-NET: European sudden cardiac arrest network: towards prevention, education and new treatment
  - Financing institution: European Commission (H2020)
  - Period: from 2017 to 2021
  - Principal investigator at IMIM: Mestres López, Jordi

See all Projects

Theses

- Szabo V. Polypharmacy in the elderly: data, models and strategies. Universitat Pompeu Fabra
  - Director: Mestres López, Jordi
  - Date of defense: 13/03/2019

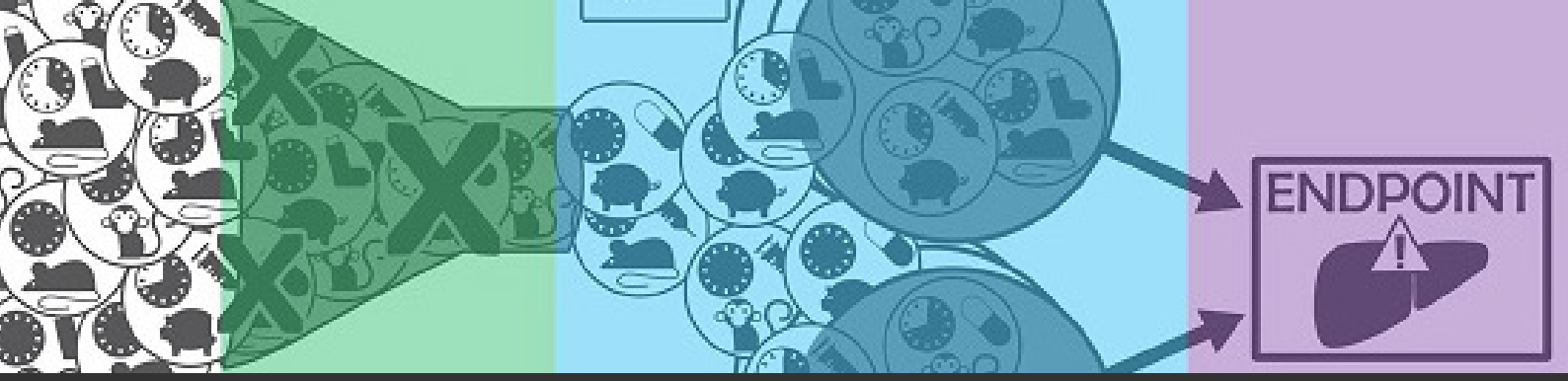
Appointments

- Jordi Mestres. Member of the Scientific Advisory Board, ChemBioFrance. October 2019.

Outreach

Conferences, Seminars and Courses

- Jordi Mestres. Invited Conference. A structure-based machine-learning approach to design ligands for new emerging and difficult targets. Chem-Bio Informatics Society Annual Meeting. Tokyo, Japan, 21-25 October 2019.
- Jordi Mestres. Invited Conference. Why do drugs have the affinities they have? Drug Discovery: Current Trends and Future Prospects. Tucson (AZ), USA, 21-24 February 2019.



PharmacoInformatics

> Biomedical Informatics

ASSOCIATED GROUP

Group Leader
Manuel Pastor Maeso

manuel.pastor@upf.edu

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 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. We develop tools aimed at improving the efficiency of the pharmaceutical R&D process and apply them to the building of predictive models. We try to avoid reductionist approaches and 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

- Escher SE, Kamp H, Bennekou SH, Bitsch A, Fisher C, Graepel R, Hengstler JG, Herzler M, Knight D, Leist M, Norinder U, Ouédraogo G, Pastor M, Stuard S, White A, Zdrazil B, van de Water B, Kroese D. Towards grouping concepts based on new approach methodologies in chemical hazard assessment: the read-across approach of the EU-ToxRisk project. Arch Toxicol, 2019; 93(12): 3643-3667. IF 5.741. Q1.

MORE INFO