



Master project 2024-2025

Personal Information

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Group	Structural Bioinformatics and Network Biology

Project

Pharmacoinformatics & systems pharmacology

Project Title:

Blanding biology, chemistry and AI to enable systems pharmacology

Keywords:

Bioinformatics, Bioactivity Signatures, Drug Design, AI Generative Models, Systems Pharmacology, Biological Big Data

Summary:

Large-scale small molecule bioactivity data are not routinely integrated in daily biological research to the extent of other 'omics' information. Compound data are scattered and diverse, making them inaccessible to most researchers and not suited to standard statistical analyses. We recently developed the Chemical Checker (CC), a resource that provides processed, harmonized and integrated bioactivity data on small molecules (1-3). The CC divides data into five levels of increasing complexity, ranging from the chemical properties of compounds to their clinical outcomes. In between, it considers targets, off-targets, perturbed biological networks and several cell-based assays such as gene expression, growth inhibition and morphological profiles. In the CC, bioactivity data are expressed in a vector format, which naturally extends the notion of chemical similarity between compounds to similarities between bioactivity signatures of different kinds. We showed how CC signatures can boost the performance of drug discovery tasks that typically capitalize on chemical descriptors, and we demonstrated and experimentally validated that CC signatures can be used to reverse and mimic biological signatures of disease models and genetic perturbations, options that are otherwise impossible using chemical information alone (4). We are now developing a generalized connectivity mapping, as a form of virtual phenotypic screening, to discover novel chemical or genetic modulators able to revert the specific signatures of disease and 'cancel out' the phenotypic traits of complex disorders.

References:

1. Duran-Frigola M, et al. Extending the small-molecule similarity principle to all levels of biology with the Chemical Checker, *Nature Biotechnology*, 2020, 38(9):1087-1096. 2. Bertoni M, et al. Bioactivity descriptors for uncharacterized compounds, *Nature Communications*, 2021, 12:1-13. 3. Fernández-Torras A, et al. Connecting chemistry and biology through molecular descriptors, *Current Opinion in Chemical Biology*, 2022, 66:10290. 4. Pauls E, et al. Identification and drug-induced reversion of molecular signatures of Alzheimers disease onset and progression in AppNL-GF, AppNL-F and 3xTg-AD mouse models, *Genome Medicine*, 2021, 13:168.

Expected skills:

Excellent Python programming skills. Knowledge of machine learning packages (e.g. Scikit, Keras, Pytorch) is an asset. Excellent interpersonal and communication skills. Highly motivated. Fluency in English.

Possibility of funding:

Yes

Possible continuity with PhD:

Yes

Comments:

We offer a salary of 600€/month, and we encourage the students to join the lab as summer visiting students (also remunerated), which provides a nice ramp phase to start the MSc project.