Virtual BSC RS/ Life Session: Formatting Biological Big Data to Enable (Personalized) Systems Pharmacology

Objectives

Abstract: Big Data analytical techniques and AI have the potential to transform drug discovery, as they are reshaping other areas of science and technology, but we need to blend biology and chemistry in a format that is amenable for modern machine learning. In this talk, I will present the Chemical Checker (CC), a resource that provides processed, harmonized and integrated bioactivity data on small molecules. 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 show how CC signatures can boost the performance of drug discovery tasks that typically capitalize on chemical descriptors, including compound library optimization, target identification and anticipation of failures in clinical trials. Moreover, we demonstrate and experimentally validate 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. Indeed, using bioactivity signatures we have identified small molecules able to revert transcriptional signatures related to Alzheimer´s disease *in vitro* and *in vivo*, as well as compounds against Snail1, a transcription factor with an essential role in the epithelial-to-mesenchymal transition, showing that our approach might offer a new perspective to find small molecules able to modulate the activity of undruggable proteins.

References

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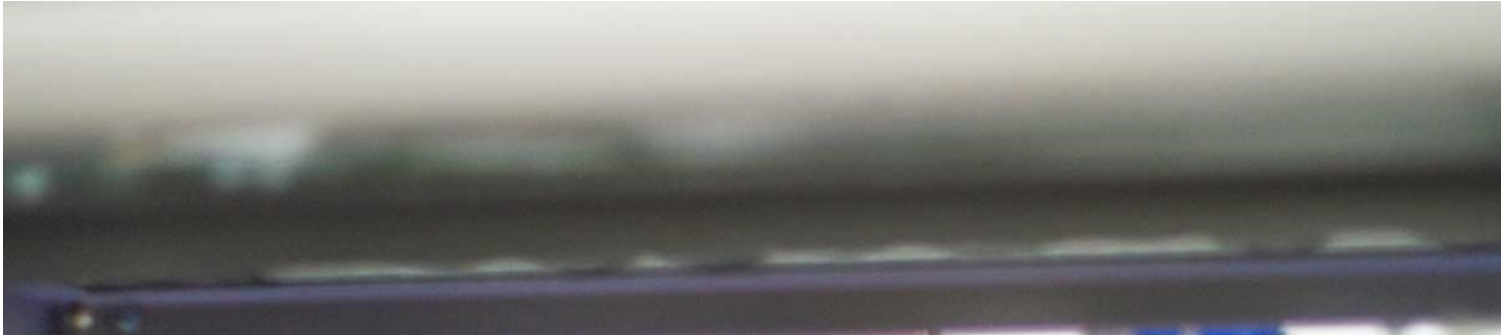
Bertoni *et al*. Bioactivity descriptors for uncharacterized chemical compounds. 2021. Nat Commun. 12:1-13.

Duran-Frigola *et al*. Extending the small molecule similarity principle to all levels of biology with the Chemical Checker. 2020. Nat Biotechnol. 38: 1087-1096.



Dr Patrick Aloy is an ICREA Research Professor and Principal Investigator of the Structural Systems Biology lab at the IRB. He has a BSc in Biochemistry and a MSc in Biotechnology from the Universitat Autònoma de Barcelona, Spain, and spent six years as postdoctoral researcher and staff scientist at the European Molecular Biology Laboratory, Heidelberg, Germany. For twenty years, Dr Aloy has been developing and implementing new technologies and algorithms, applying state-of-the-art methods to specific problems and bridging the gap between theoretical models and experiments in different disciplines. The main goal of his lab is to combine molecular, cell and computational biology to unveil the basic wiring architecture and dynamics of physio-pathological pathways to increase our understanding of how biological systems change from the healthy state to disease. In the last years he has been developing resources to process, harmonize and integrate bioactivity data on small molecules, providing compound bioactivity descriptors that push the similarity principle beyond chemical properties. Currently, the main research line in the lab is to collect heterogeneous datasets and develop novel methodologies to integrate different layers of regulation to unveil disease signatures. Moreover, they are convinced that artificial intelligence (AI) will transform drug discovery, as it is reshaping other areas of science and technology, and biological signatures are the key to guide the (semi) automated design of chemical compounds to globally revert disease states, beyond individual targets.

Speakers

Speaker: Patrick Aloy, ICREA Research Professor and Principal Investigator of the Structural Systems Biology lab at the IRB.

Host: Alfonso Valencia, BSC Life Sciences department director

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