Pharmacophores vs Emerging fragments. Analysis of polypharmacological and toxicological properties related to chemical derivatives

Pharmacophores correspond to common chemical features associated to an affinity for a specific receptor. They explain how structurally diverse ligands can bind to a common receptor site. Emerging fragments correspond to a conjunction of chemical features associated to a class of chemicals. These two notions are very close but one (pharmacophore) is based on the definition of common characteristic associated to a class of derivatives and the second (emerging fragment) is based on the comparison of chemical datasets (normally two datasets). This presentation will discuss their applications in polypharmacology and toxicology. Polypharmacological properties are associated to all molecules interacting with biological processes. The issue is to control these properties by a specific orientation towards therapeutic targets. Starting from our internal chemolibrary, the discovery of potential ligands for different receptors by structure and pharmacophore based virtual screening will be discussed. The comparison of the different pharmacophores was a guide to understand the polypharmacological properties of 5-HT4 ligands with an orientation, for therapy, towards neurological disorders. In toxicology, a recent method called the Frequent Emerging Molecular Pattern (FEMP) will be presented. Given a chemical dataset partitioned into two classes (toxic vs non toxic molecules), a FEMP is a conjunction of molecular fragments such that: (i) its frequencies between the classes are sufficiently different and (ii) its frequency in the target class is high enough to be significant to support an interpretation.

Biography

Pr. Ronan Bureau, actual President of the French Society of Chemoinformatics, is Professor of molecular modeling and computer sciences at the School of Pharmacy, University of Caen, France. After a Ph.D (1990) in chemistry (University of Rennes, France) and post doctoral studies in chemistry (Nagoya, Japan) and molecular modeling (Caen, France), he has been in charge, in 1992, of the development of molecular modeling studies related to drug design (CERMN, University of Caen, France). His research interests concern the notion of polypharmacology / toxicology related to systems biology and in parallel the development of new chemoinformatic approaches in environmental toxicology.