Seminar

06-April-2018

Speaker:

Alessandro Di Domizio, PhD

Dept. of Pharmacological and Biomolecular Sciences, Università degli Studi di Milano, Milano, Italia.
SPILLOproject, Cinisello Balsamo (Mi), Italia

Email: alessandro.didomizio@spilloproject.com

Website: http://www.spilloproject.com/

Title:

A step forward in drug development and personalized medicine: identification of secondary targets responsible for drug side effects by SPILLO-PBSS

Abstract:

The property of a drug to act with multiple molecular targets usually represents a major drawback both in the drug development process, where toxicity is responsible for the high failure rate ('attrition rate problem') of drug candidates, and in medicine, where therapeutic agents often lead to side effects that can cause dose limitation or even discontinuation of treatment.

The innovative software *SPILLO Potential Binding Sites Searcher* (SPILLO-PBSS[1]) will be presented. It is designed to identify the biomolecular origin of adverse or therapeutic effects of small molecules by a fast identification of their target proteins on a proteome-wide scale (e.g., the whole available human structural proteome).

The uniqueness of SPILLO-PBSS lies in its ability to find the potential binding sites on protein 3D-structures even if they are highly distorted and/or apparently inaccessible (e.g., closed, buried, occupied) to the small molecule with respect to an ideal conformation suitable for the binding. In comparison to the other traditional *in silico* approaches, SPILLO-PBSS is more likely to find proteins responsible for side-effects and/or for additional positive effects of the small molecule (Polypharmacology - Drug repositioning).

The possibility to generate a clearer map of the drug-target interactions has remarkable implications both in the drug development process and in personalized medicine, where treatments with the lowest toxic impact may be selected taking into account individual protein level differences.

[1] Di Domizio A. et al. 'SPILLO-PBSS: Detecting hidden binding sites within protein 3D-structures through a flexible structure-based approach', *Journal of Computational Chemistry*, 35(27): 2005-2017, 2014.

Short presentation/CV:

Alessandro Di Domizio is an algorithm and scientific software developer devoted to the development of new technologies for Drug Discovery and Development.

He graduated in Chemical Sciences (specialization: 'Computational physical chemistry') in **2006** from the University of Milan, with a thesis on: "*Initial Events in Protein Folding*".

During the academic years, he built up a multidisciplinary curriculum covering various subjects, from bioinformatics to statistical thermodynamics and physics of proteins, with the aim of getting a wider view of the problems concerning proteins and molecular recognition phenomena.

In **2009** obtained a PhD in Chemical Sciences (specialization: 'Computational physical chemistry') from the University of Milano-Bicocca, with a thesis on "*New Methodologies for Molecular Docking and their Applications*".

He subsequently collaborated with the University of Milano-Bicocca and the University of Milan working at projects concerning molecular recognition phenomena.

From **2011** to **2013** he worked at the 'National Research Council' (CNR), Italy, on the optimization of antitumorigenic molecules and other projects of interest to both basic research and industry.

In **2013** he started the project called: 'SPILLOproject', with the aim of supporting public and private research centres for the optimization and acceleration of the Drug R&D process by using *in silico* technologies.

Amongst others, the innovative software SPILLO-PBSS, conceived and implemented by him (published in '*Journal of Computational Chemistry*', 2014) plays a central role in drug repositioning, in polypharmacology as well as in the prediction and/or clarification of side effects.

As from **2016** Alessandro Di Domizio is an adjunct professor of:

- "Statistics applied to epidemiology" and

- "'Methods of analysis applied to water, air, biological fluids, tissues, food and *In Silico* Methods in Toxicology"

Master Degree "Safety Assessment of Xenobiotics and Biotechnological products (SAXBi)" at the University of Milan.