[L14] Challenges and Successes in Using In Silico Tools in Kinase Research

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Protein kinases are therapeutic targets involved in many diseases particularly in cancer and inflammation. Since the first small molecule kinase inhibitor (SMKI) drug approved by the FDA in 2001, a large number of diverse SMKIs with various pharmacological profiles have been developed and over 25 small molecules are currently approved by the FDA. The identification of novel kinase inhibitors is still an active research field in drug discovery and the success of kinase research is due, but not limited, to strong collaborations between different scientific disciplines. Together, medicinal chemistry, biology, screening technologies, "omics" analysis, structural biology, bioinformatics and chemoinformatics are today fully involved in almost all kinase inhibitor design projects. The large number of available data in the public domain such as biological activities, crystallographic information and chemical structures offers great opportunities for ligand-based and structure-based drug design. *In silico* tools are regularly applied in early drug discovery to identify IP free scaffolds, to predict mode of binding of a series, to optimize biological activity of ligands, to improve selectivity of a lead or to circumvent ADME-tox issues. Amongst all the developed *in silico* tools, virtual screening, QSAR modelling, molecular dynamics simulations and data mining are usually applied in kinase research. In this presentation, we will highlight some difficult challenges that are often faced by modelers in the kinase research field and will present some examples where molecular informatics has successfully contributed to the identification of potent and selective kinase inhibitors.