# [P27] Broad profiling prediction of protein kinase inhibitors via Kinochemometrics approach

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Human species count 518 proteins in the kinase family[1]. They are all involved in the mechanism of target protein phosphorylation, responsible for a large contribution of the biological processes. A variation of the protein kinase expression may occur when their regulation pathway is modified, or when their nucleic acid sequence is mutated. Such modification of protein expression could lead to cancer, diabetes or inflammatory diseases. Hence, significant resources are given to find potent and selective protein kinase inhibitors.

Because the protein kinase ATP binding site is highly conserved in the protein family, the design of high selective inhibitors is a big challenge, and the degree of selectivity contributes to the failure of pharmaceutical drug pipeline. Here, we will use the protein kinase structure similarity to develop multiple proteochemometrics models[2] able to predict selective kinase inhibitors. Our models use an original protein kinase descriptor based on protein structures. It describes accurately the active sites by taking into account highly conserved residues and their pairwise distances (figure1). We have already demonstrated that this descriptor successfully classify protein kinases based on their family. We are now applying this approach, combined with a molecular descriptor, and biological data from academic and corporate sources, to develop statistical models to predict activities on a large panel of protein kinases. This kinochemometrics approach will help researchers to understand and to describe protein-ligand interactions and to design better guided polypharmacological compounds.

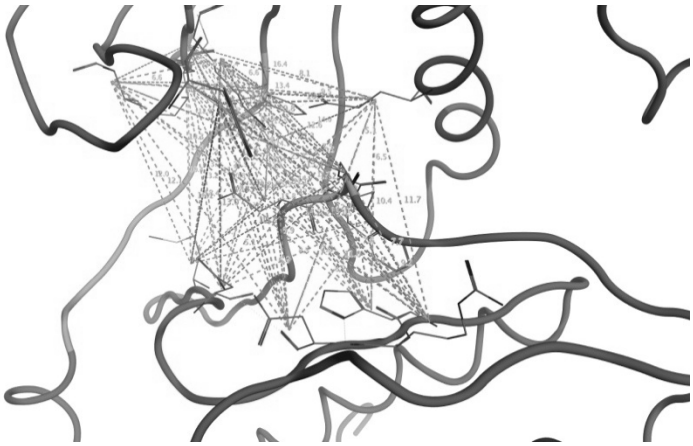

Figure 1: Representation of the protein kinase description. Distances are represented by dash-line and their extremities are the selected residues.

[1] Manning, G., Whyte, D. B., Martinez, R., Hunter, T. & Sudarsanam, S. T. Science 298 (2002), 1912–1934.
[2] Van Westen, G. J. P., Wegner, J. K., IJzerman, A. P., van Vlijmen, H. W. T. & Bender, A. Med Chem Comm 2 (2011), 16.