Expanding the druggable genome with new computational tools

Xavier BARRIL

ICREA & Dept. Fisicoquímica, Facultat de Farmàcia, UB

The discovery of small molecules that bind to specific sites on a protein's surface is essential to interrogate biological systems, to validate potential mechanisms of action and, eventually, to develop new drug therapies. A wide-range of methods exist to identify initial 'hit' compounds, but the increasing availability of protein structures and recent progress in molecular simulations are revolutionizing computational structure-based methods and making them much more predictable. In this talk I will present some of the methods that the group has developed to identify new druggable sites, to better understand the process of molecular recognition, and to increase the success rate of virtual screening.[1-6] The potential of the methods will be exemplified on several projects carried out in house or in collaboration with companies, where non-standard binding sites have been proposed and active drug-like ligands discovered. Continuous evolution of computational methods, closer integration with experiments and a growing appreciation of non-standard molecular mechanisms of action will transform chemical biology and drug discovery.

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