New computational method to create drugs more efficiently

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Researchers of the University of Barcelona have developed a more efficient computational method to identify new drugs. The study, published in the scientific journal *Nature Chemistry*, proposes a new way of facing the discovery of molecules with biological activity.

Since it is based on a different principle, this method complements conventional tools and allows going forward in the path of rational drug design. ICREA researcher Xavier Barril, from the Faculty of Pharmacy and Food Sciences and The Institute of Biomedicine of the University of Barcelona (IBUB), has led this project, which has the participation of professor Francesc Xavier Luque and PhD student Sergio Ruiz Carmona, members of the same Faculty.

The improvement on efficiency and effectiveness in the discovery of drugs is a key target in pharmaceutical research. In this process, the target are molecules that can be added to a target protein and modify its behavior according to clinical needs. "All current methods to predict if a molecule will join the wished protein are based on affinity, that is, in the complex's thermodynamic stability. What we are proving is that molecules have to create complexes that are structurally stable, and that it is possible to distinguish between active and inactive by looking at what specific interactions are hard to break", says Professor Xavier Barril.

This approach has been applied in software that identifies molecules with more possibilities to join the targeted protein. "The method allows

selecting molecules that can be starting points to create new drugs", says Barril. "Moreover, -he continues- the process is complementary with existing methods and allows multiplying five times the efficiency of the current processes with lower computational prices. We are actually using it successfully in several projects in the field of cancer and infectious diseases, among others".

A new vision for the protein-ligand drugs

This work introduces a new way of thinking regarding the ligand-protein interaction. "We don't look at the balancing situation, where two molecules make the best possible interactions, but we also think how the complex will break, which the breaking points are and how we can improve the drug to make it more resistant to separation. Now we have to focus on this phenomenon to understand it better and see if by creating more complex models we can still improve our predictions", says the researcher. The team of the University of Barcelona is already using this method, which is open to all the scientific community.

More information: Sergio Ruiz-Carmona et al. Dynamic undocking and the quasi-bound state as tools for drug discovery, *Nature Chemistry* (2016). DOI: 10.1038/nchem.2660

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