New computational tool for cancer treatment

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Many human tumors express indoleamine 2,3-dioxygenase (IDO), an enzyme which mediates an immune-escape in several cancer types. Researchers in the Molecular Modeling group at the SIB Swiss Institute of Bioinformatics and Dr. Benoît J. Van den Eynde's group at the Ludwig Institute for Cancer Research Ltd (LICR) Brussels Branch developed an approach for creating new IDO inhibitors by computer-assisted structure-based drug design. The study was presented in the January 2010 online issue of the *Journal of Medicinal Chemistry*.

The docking algorithm EADock, used for this project, was developed by the Molecular Modeling Group over the last eight years. It provides solutions for the "lock-and-key" problem, wherein the protein active site is regarded as a "lock", which can be fitted with a "key" (usually a small organic molecule) able to regulate its activity. Once an interesting molecule has been obtained, synthesis and laboratory experiments are necessary to confirm or reject the prediction. This algorithm will soon be made available to the scientific community worldwide.

The scientists obtained a high success rate. Fifty percent of the molecules designed in silico were active IDO inhibitors in vitro. Compounds that displayed activities in the low micromolar to nanomolar range, made them suitable for further testing in tumor cell experiments and for in vivo evaluation in mice. If these studies are successful, scientists can begin evaluating these new compounds in patients undergoing cancer-immunotherapy.

According to Olivier Michielin, Assistant Member at the Lausanne

Branch of LICR and leader of the SIB Swiss Institute of Bioinformatics Molecular Modeling group, "This is a satisfactory proof of principle showing that computational techniques can produce very effective inhibitors for specific cancer targets with high yield. This is very encouraging for future drug developments in the academic environment."

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