Chemists develop Distributed Drug Discovery

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Researchers from Indiana University-Purdue University Indianapolis (IUPUI) have developed Distributed Drug Discovery (D3), a new low-cost strategy to accelerate the discovery of drugs to treat neglected diseases such as tuberculosis, leprosy, leshmaniasis, dengue fever, and Chagas disease.

Even in times of economic prosperity, the pharmaceutical industry has often been reluctant to get involved in developing treatments for diseases that occur primarily in low income countries. The low cost D3 approach, involving distributed global educational resources at the early stage of discovery, is even more attractive in this time of global economic downturn.

A distributed problem solving process breaks large problems into small pieces which are "distributed" to multiple, small, low-cost sites to obtain a solution. For decades astronomers have enlisted the help of the public, asking individuals around the world to leave their home computers on overnight. While normally idle, each one of these computers looks for patterns in a small subset of the incredibly large amount of space noise signals received by arrays of radio telescopes scanning the skies.

Two studies, published this year in the *Journal of Combinatorial Chemistry*, detail the first two steps in D3, developed by William Scott, Ph.D., research professor, and Martin J. O'Donnell, Ph.D., IUPUI Chancellor's Professor, both of the Department of Chemistry and Chemical Biology at IUPUI.

D3 uses a distributed problem approach at all three key stages of drug discovery. Step one is identifying candidate drug molecules. To do this, IUPUI researchers are soliciting the global advice of computational experts in neglected disease areas and utilizing the computational power of multiple personal computers around the world to scan the almost infinite number of molecules which the D3 synthesis process could make to identify the smaller number of drug candidate molecules they should make. Dr. Scott and Dr. O'Donnell believe this will lead to the selection, synthesis and development of innovative and inexpensive drugs to treat these neglected diseases.

In the second step, D3 uses an innovative, distributed educational approach to synthesize the candidate molecules. Undergraduate and graduate chemistry students from around the world synthesize subsets of these candidate molecules as part of their normal training in synthetic chemistry. Currently students at IUPUI, the University of Indianapolis, and universities in Poland, Russia and Spain have demonstrated their ability to make the molecules (or portions of the molecules) that can be identified by the personal computers as potential candidates for drug discovery.

Initial results are very promising, according to Dr. Scott. "While learning chemistry synthesis skills students across the globe synthesize new molecules to be tested as drug leads. The molecules meet the same quality standards as those required in industry. At the same time the students enthusiastically participate in the synthesis laboratories. They enjoy seeing how their work will advance science that is going to make a difference to individuals suffering from diseases which have been ignored," he said.

The third step in D3 is biological testing of the molecules synthesized by the students. Dr. Scott and Dr. O'Donnell hope the success of distributed problem solving at the computational and synthetic stages of drug

discovery will encourage their biological colleagues to develop simple, inexpensive tests to enable students worldwide to participate in this final stage of drug-lead discovery. Currently some of the molecules made are being evaluated through the resources of the National Institutes of Health. In the future, promising drugs will then go on to pre-clinical trials.

"The coordinated and recombined results of these distributed D3 resources can economically accelerate the identification of leads in the early stages of the drug discovery process. Simultaneously, this effort provides educational and job opportunities in both the developed and developing worlds, while building cultural and economic bridges for the common good," Dr. Scott and Dr. O'Donnell wrote in an accompanying perspective article.

Source: Indiana University (news : web)