Idle computers get busy screening drug targets for cancer

Sure, your computer can send e-mails, create spreadsheets and assemble PowerPoint presentations. But can it save lives? Any computer with access to the Internet can now help discover cancer drugs by running a special screensaver.

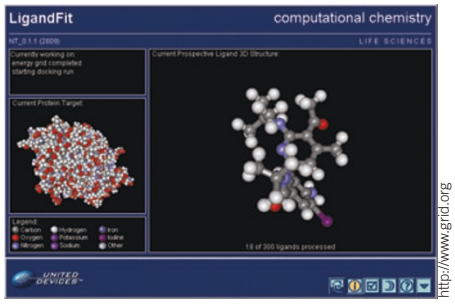
Launched in 2001, the Screensaver-Lifesaver program uses parallel computing power and virtual screening to assess the interactions between small drug-like molecules and predetermined cancer-causing targets.

More than 3 million personal computers worldwide are screening a library of 3.5 billion molecules against these targets to identify potential candidate drugs. This may shave up to 3 years off the drug discovery process, researchers say.

"What the screensaver adds to the discovery process is an enormous amount of computer power, dwarfing what even the biggest pharmaceutical company can do," says Graham Richards, chairman of chemistry at the University of Oxford. "In our hands it provides sheer power to do things that would be beyond the capabilities of even the biggest and most costly machines."

The latest scheme, launched in April, is testing several new protein targets—primarily kinases and phosphatases—for pancreatic cancer.

Each computer receives the screensaver program, which includes drug-design software, an initial packet of 100 molecules and a model of a target protein. The program calculates the binding energy between the small molecules and the targets. Molecules with the tightest binding have the best chance of becoming drug formulations because tighter bonding translates into fewer adverse effects and lower doses. Once processing is complete—typically in a day—the program sends the results back to a data center and requests more molecules.



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OK computer: The screensaver project cuts years from the drug discovery process.

"Using our best models and guesses, it would take hundreds of years of trial and error in the lab to test these protein targets," says lead investigator Daniel Von Hoff, director of the National Foundation for Cancer Research's Center for Targeted Cancer Therapies in Arizona. "The screensaver project can us save huge amounts of time and find the most optimal chemical structures—those that bind the tightest."

In addition to searching for cancer therapies, researchers are using the program to find drug targets for smallpox and anthrax. In less than four weeks, the Anthrax Research Project found 376,064 potential candidates for new antianthrax drugs; 12,000 of those are being investigated.

Another screensaver project aims to predict the structure of proteins found in the human genome. The structures of only an estimated 30% of proteins encoded by the human genome are known. The Human Proteome Folding Project is deciphering the three-dimensional structure of human proteins with no known structural homologs, proteins made by pathogens and those encoded by genomes of environmental microbes. The project is slated for completion by the end of 2005.

"This is an example of a project so big that no one thought it was solvable," says Ed Hubbard, President of United Devices, the company that powers the program's computing platform. "But it is possible and it's changing the way researchers think about problems."

Amy K Erickson, Phoenix

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Unchecked by government, genetic tests sell hope and hype

Have a few hundred bucks to spare? You could order a genetics test and check whether your kids are really yours, whether your diet matches your DNA and whether you or your future children are at risk for breast cancer.

But there is no guarantee that you'll actually understand the results. Experts say few genetic tests on the market explain the huge chasm between the genotype they can confirm and the physical manifestation of the genes. The tests are also largely unregulated and can vary wildly in quality.

The latest to join the market is a controversial set of tests manufactured by San Francisco–based DNA Direct to check potential reasons for infertility and multiple pregnancy loss. The company's website directs customers to a local blood collection center. A contracted laboratory then tests for disease genes—such as those associated with cystic fibrosis or fragile X syndrome—based on the customers' self-reported risk factors, and sends the results to DNA Direct. The company then attaches a packet of supporting materials and posts it online for the customers.

Genetic counselors are available by phone, but Jennifer Graham, director of product development for DNA Direct and one of two genetic counselors on staff, says the number of people who call is "remarkably low."

Companies have been expanding their range from paternity tests to genetic diseases in the past three years but, apart from requirements for lab standards, the tests are unregulated. The US Food and Drug Administration (FDA) may have jurisdiction over the tests in some circumstances—if the tests are sold as kits or use certain reagents, for instance. But most DNA testing is done with 'homebrew' tests that the FDA has not attempted to regulate.

The Secretary's Advisory Committee on Genetics, Health, and Society, under the US Department of Health and Human Services, has taken on the matter, albeit at a glacial pace. Established in 2003, the committee began examining the topic a year ago; it is set to meet with FDA officials in June to discuss assigning responsibility for regulating the field.

In the meantime, the US Centers for Disease Control and Prevention has also convened a panel to examine the tests. "The FDA hasn't done much," says Muin Khoury, director of the agency's Office of Genomics and Disease Prevention, whose panel is set to meet in May. "There are no other evidence-based reviews. We hope to fill that gap."

The problem with most of these tests, critics say, is that even those that are widely used give results that are hard to interpret.

For instance, many outfits sell tests for the breast cancer susceptibility genes *BRCA1* and *BRCA2*, but the significance of the results is far from simple, notes Kelly Ormond, president of the National Society of Genetic Counselors. Even if a disease-linked gene is present, she says, it would be important to know whether the gene carries mutations that confer risk.

Gail Javitt, a policy analyst at Johns Hopkins University's Genetics and Public Policy Center, says regulators at the various agencies need to put their heads together and make genetic testing a priority. "A clearer direction of oversight needs to be given either by [the Department of Health and Human Services] or Congress," she says. "Whether it will happen remains to be seen."

Emma Marris, Washington DC