FINANCE AND COMMERCE

DOLAN MEDIA COMPANY www.finance-commerce.com Wednesday, September 19, 2007 Periodicals Postage
Vol.120, No. 186 ■ $1.50

Medisyn Tech joins hunt for Alzheimer's drug

Minneapolis company uses computer models to speed the search for a promising new drug

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Minneapolis research company Medisyn Technologies is collaborating with the Mount Sinai School of Medicine to search for the first drug to prevent Alzheimer's disease.

The goal is to develop a drug that will lower "beta-amyloids" in the brain, a natural protein that is broken down in a healthy body but forms into hardened plaques in the brain of a person with Alzheimer's.

Studies have suggested that by helping to break down these proteins, drugs might postpone brain degeneration, if not prevent it.

To create such a drug, the company must find a compound or compounds that can achieve the desired effect, and then ensure that it's safe for patient consumption.

Dr. Giulio Pasinetti, professor of psychiatry, neuroscience and geriatrics at Mount Sinai in New York, has supplied a series of promising compounds that Medisyn will use to refine its search for a viable drug.

If successful, it would be the first drug to actually treat (though not reverse) the cause of Alzheimer's, rather than just reduce its symptoms. But don't be fooled. The process is not nearly as simple as it sounds.

"The most difficult piece is to discover the compound in the first place," said David Land, president of Medisyn Technologies.

That's where Medi-syn's use of advanced "molecular topology" offers a big advantage: a series of two-dimensional computer models that identify hidden chemical structures in drugs and unlock the key to their success.

About $30 billion is spent every year on the discovery and development of new drugs. The result is only 12 to 18 new chemical entities hitting the market annually, and most of those have simply evolved from existing drugs.

The search for the perfect compound involves plenty of trial and error, as there are millions of known compounds that can be tested.

"A typical pharmaceutical approach takes between 100,000 and 1 million compounds, and tests each of them," Land said. "Typically, by the time you're done, you only get one-tenth of 1 percent to react anyway."

Molecular topology takes a lot of the guesswork out of the process by identifying which chemical features to look for through elaborate computer models, narrowing the list of candidate drugs significantly before testing begins.

As a result of the modeling, researchers can in many cases test fewer than 100 compounds once they begin pre-clinical trials.

Streamlining research

Founded in 1999, Medisyn is one of the few companies using molecular topology to streamline the search for new pharmaceutical drugs, and Land believes it is the only one that uses the process as the main focus of its research.

David Land

"We keep everything in a purely abstract mathematical basis," Land said of the company's five full-time employees.

In many fields, such a claim would signal that the company was out of touch with reality. But in the search for revolutionary advances in medicine, mathematical models protect researchers from biasing the results of their findings and lead them down paths they would never have otherwise taken.

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Molecular topology is nothing new. It has been used for years for things such as circuit board design. But in the 1990s, researchers at the University of Valencia in Spain found that the process was superior to three-dimensional modeling and other pharmaceutical research methods when looking for chemical similarities in drugs.

The process can streamline the process of identification, which makes up a significant portion of the 12 to 15 years that it takes an average drug to get to market.

Even after a promising compound is discovered and testing begins, it's common in pharmaceutical research to hit a dead end. A promising group of compounds may be able to treat a disease, but they turn out to be toxic to patients in other ways. Then it's back to the drawing board.

With molecular topology, researchers can find compounds from several different chemical classes and improve their chance of success before testing begins. The compounds may seem completely different to researchers, but the computer uses 1,400 different "topological indices" to isolate structural similarities that would otherwise go unnoticed.

"The software is able to see correlations that the human eye, even the trained medical eye, cannot see," Land said.

The industry's dirty secret

It's the novelty of this approach that led Land to share the pharmaceutical industry's dirty secret.

"There are some drugs that make it to market that we're not entirely sure why they work," he said.

In fact, some well-known drugs were the result of "happy accidents."

A famous recent example was Viagra, which Pfizer researchers were testing as a drug to reduce hypertension and cardiovascular disease.

In clinical trials, subjects were surprised to find that it helped with erectile dysfunction — and had little effect on hypertension — so the drug was marketed for its now-famous benefits.

While stumbling onto positive side effects isn't a bad thing, most surprises aren't so positive. If applied more broadly, molecular topology could help researchers better understand why some drugs do what they do.

It could also cut testing time considerably, whether it's early trials on cells in a petri dish ("in vitro") or pre-clinical trials on mice and other small animals ("in vivo").

Medisyn and Mount Sinai have been unofficially collaborating for more than a year, but the announcement last week came because preliminary results have been "very promising" and researchers hope to begin some pre-clinical trials with test compounds by the beginning of 2008.

"We are making progress such that one day very soon we will be able to find something completely new with the potential to lower beta-amyloids in the body safely," Pasinetti said, adding that he is "cautiously optimistic" about making major progress in the next few months.

From there, it's still a long road to market, as both groups are seeking additional third-party funding to continue their research. Beyond that, the path from clinical trials to the pharmacy will take many years.

But it's worth noting that a little-known Minnesota startup is taking the first steps toward bringing hope to millions of patients and families dealing with Alzheimer's disease.