



DISCOVERY RESEARCH NEWS

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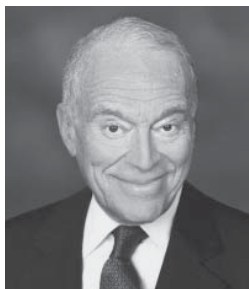
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CO-CHAIRPERSON'S MESSAGE

Leonard A. Lauder

In 1998, my brother Ronald and I had a vision that with Dr. Howard Fillit's expert assistance we could make a difference to

Alzheimer's research and the millions of people touched by this devastating disease. After reviewing scientists' needs and available funding, we learned that most non-profits generally fund basic research while pharmaceutical companies tend to fund later-stage drug development.

Realizing there was a major funding gap for innovative, early-stage drug discovery research for Alzheimer's disease, we established the Institute for the Study of Aging (ISOA). We wanted the ISOA to be a different kind of foundation with the sole mission of supporting scientists pursuing drug discovery for Alzheimer's disease and related dementias.

ISOA invited the world's leading experts to participate on our Scientific Review Board and utilized their networks to introduce the Institute to researchers in academia and the biotechnology industry. By 2004, we had received almost 500 proposals. Through ISOA funding, scientists screened millions of compounds, found new drug candidates, successfully tested them in animal models and in humans, and even started biotechnology companies.

Unfortunately, due to financial limitations, many worthy programs went unfunded. We realized we needed help to increase our chances of finding a cure. In late 2004, we founded the Alzheimer's Drug Discovery Foundation (ADDF), a public charity, to enable others to join us.

With the help of many people, ISOA/ADDF are expecting to give out \$3.9 million in grants by year's end, a 12% increase over last year. I encourage you to join us in accomplishing our mission to end the nightmare of AD.

RED WINE: A POTENTIAL SOURCE OF TREATMENT FOR ALZHEIMER'S?

Red wine is not just good for your heart, it may also preserve your memory. A recent study conducted by Mount Sinai School of Medicine found that moderate consumption of red wine, in the form of Cabernet Sauvignon, may reduce the risk of developing Alzheimer's Disease (AD).

Studies show that drinking moderate amounts of red wine, especially Cabernet Sauvignon, can reduce the risk of developing dementia.

The study led by Dr. Giulio Maria Pasinetti tested Cabernet in a mouse animal model of AD. Two groups received either Cabernet or pure alcohol in their drinking water, while another group drank only water. In a series of maze tests, the wine-drinking mice escaped faster than the other groups, showing that this wine has an effect on the disease process. These results support the possibility that one glass of red wine per day for women and two for men may reduce the risk of AD.

But what in wine causes this? A specific chemical found in the skin of red grapes, resveratrol, is known to have potent antioxidant properties. Resveratrol was first discovered in the roots of white hellebore, a plant used in traditional herbal remedies. Most recently, in a study led by Drs. David Sinclair at the Harvard Medical School and by Rafael de Cabo at the National Institute on Aging, resveratrol was reported to offset the bad effects of a high-calorie diet in mice and significantly extended their lifespan.

In order to further understand the benefits of red wine on brain function, ISOA is funding two studies that are investigating



EXECUTIVE DIRECTOR'S REPORT

Howard Fillit, MD

Recently there has been a lot of coverage on television and in newspapers about new remedies in the fight against Alzheimer's disease. But what do these findings really mean?

While some studies show promise, they are often far from proving that a specific chemical can actually treat the disease. The scientific process involved in developing new drugs is expensive, time-consuming and rigorous.

One way scientists get new ideas is from studying people living in their community over a long period of time, called epidemiologic studies. For example, studying thousands of people for several years, statistical analyses showed that drinking moderate amounts of red wine daily was associated with a lower risk of Alzheimer's disease. But what if the people who drank red wine also exercised more or ate a lower-calorie diet? Could the link between red wine and Alzheimer's be just a coincidence? And what, exactly, is the chemical in red wine that might prevent the disease?

Another way scientists get new ideas for drugs is from basic research on how the disease happens. For example, after scientists discovered that amyloid is deposited in the brains of people with Alzheimer's disease, they used brain cells grown in test tubes to study whether various synthetic chemicals or extracts from natural products such as green tea could reduce amyloid production. They then chemically optimize these molecules to make them more "drug-like." Finally, the improved chemicals are tested in animal models of Alzheimer's disease. After these pre-clinical studies, promising new chemicals may proceed into human clinical trials to prove their effectiveness as drugs.

The beginning stage of drug discovery is the riskiest, not that expensive, but the most critical in the path to new therapies. Much more funding is greatly needed to advance drug discovery research in Alzheimer's disease. ADDF supports scientists in their efforts to find innovative chemicals that can lead to new drugs. Our goal is to develop Alzheimer's drugs that treat and prevent the disease within the next five to seven years.

So the next time you read about a promising new idea for an Alzheimer's drug, find out if the research was done in test tubes, animals or in people. This will predict how close the scientists are to developing the drug.

What's Happening?

RECENTLY...

New Discoveries in Alzheimer's Disease: Dinner & Conversation

The ADDF held its first Dine & Learn Salon on August 8th at the Maroon Creek Club in Aspen, CO. The event was graciously hosted by Alison and Buzz Zaino and was attended by approximately 55 guests from all over the country.

A brief overview of Alzheimer's disease was presented by Dr. Howard Fillit. Dr. Jordan Tang, a medicinal chemist and founder of Zapaq Inc. discussed his work, which focuses on developing therapies that inhibit the production of β -secretase, a key enzyme that starts the chain of events leading to production of the toxic $A\beta$ peptide. A lively discussion followed the presentations.

Dine & Learn: The Latest Alzheimer's Research

On October 11th, the ADDF offered its fifth New York City Dine & Learn Salon at the Lotos Club that attracted 25 guests. Dr. Martin Watterson was the featured speaker and presented updates on his anti-inflammatory Alzheimer's research. The audience participated in a stimulating Q&A proceeding his talk.

COMING UP...

November 27, 2006 ADDF Informational Breakfast Meeting, San Francisco, CA

January 25, 2007 ADDF/Élan Awards Luncheon, San Francisco, CA

February 5-6, 2007 *Drug Discovery, Development and Delivery for Neurodegenerative Disease: A Course for Academic and Industry Scientists*
The Westin Hotel @ Times Square, New York City

May 2, 2007 *To Live is To Think: An Evening of Art, Wine and Discoveries*
Sotheby's, New York City
By Invitation Only



(Left) Ann Nitze, Leonard Lauder and Emily Frick



(Left) Evelyn Lauder and Candy Hamm



(Left) Paul Shor, Bill Solomon, Dr. Jordan Tang and Gay Solomon



(Left) Tina Beriro and Nancy Crown

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resveratrol can prevent the progression of AD. Dr. Gary Gibson at Weill Medical College of Cornell University will test whether resveratrol can reverse or delay inflammation and oxidative stress. He will also examine whether it can minimize the memory deficits and amyloid plaque formation that occur in animal models of AD.

In the second ISOA study, Dr. Phillippe Marambaud of the North Shore-Long Island Jewish Research Institute is building upon his earlier research, which found that resveratrol lowers the levels

of amyloid produced by nerve cells in culture. Now, Dr. Marambaud proposes to use resveratrol as the chemical backbone for developing new drugs with improved potency; and test the effects of these improved resveratrol-like drugs on levels of amyloid in animal models.

Although years away from becoming a proven drug for AD, resveratrol presents an exciting direction in drug discovery. Until then, toast to good health with Cabernet Sauvignon.

NEUROINFLAMMATION: A NEW TARGET FOR ALZHEIMER'S DRUG DEVELOPMENT

In Alzheimer's disease (AD), inflammation in the brain leads to nerve cell death and dysfunction, which in-turn causes dementia. The inflammation process is triggered by the overproduction of certain signaling molecules in brain cells known as glia.

As a way of fully understanding this process, D. Martin Watterson, PhD, Co-Director of the Center for Drug Discovery and Chemical Biology, John G. Searle Chair in Molecular Biology and Biochemistry, Professor of Molecular Pharmacology and Biological Chemistry at Northwestern University, is focusing his efforts on finding drugs that prevent the overproduction of these 'pro-inflammatory' signaling molecules by the glial cells. In addition, he is investigating drugs that attenuate synaptic dysfunction or neuronal death by targeting protein kinases in the neuron. Dr. Watterson and his team discovered a new class of anti-inflammatory compounds that reduce the nerve cell damage and cell death in a relevant AD animal model.

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Most recently, Dr. Watterson's team has improved the drug-like properties of the anti-inflammatory compounds and developed a method for large scale production of the drug candidate. Clinical development is being conducted by NeuroMedix, Inc., a biotechnology company that has licensed the commercialization of Dr. Watterson's novel class of compounds and specializes in developing therapeutic agents that treat degenerative and inflammatory diseases, such as Alzheimer's disease, traumatic brain injury and multiple sclerosis.

The lead anti-neuroinflammatory compound in development is called "Minozac" and is currently undergoing pre-clinical toxicology testing. Minozac is scheduled to start Phase I clinical trials in early 2007. The early stage high-risk drug discovery stage of this work was funded by ISOA/ADDF.

BUILDING AN AD BIOTECHNOLOGY COMPANY

Neuropeptides, a small group of amino acids, are believed to prevent neural damage associated with memory loss. Illana Gozes, PhD, Professor of Clinical Biochemistry at Tel Aviv University (TAU) and Chief Executive Scientist of Allon Therapeutics, Inc. has a passion for developing neuropeptides as drugs for neurodegenerative disorders.

Her work in this area began in 1999 at TAU with an initial grant from ISOA. During her initial studies, she showed that a neuropeptide derived compound protects neurons from toxins and cellular stresses.

Dr. Gozes realized that to move her research forward into clinical trials, she needed to form her own company, which she established in 2002 with the help of ISOA. Through its Biotechnology Founders Program, ISOA made a \$253,000 program-related investment in Allon and assisted Dr. Gozes with the development of its first business plan, as well as interviewing potential CEO's.

In 2004, the company merged with Neuro Discovery Inc. and went public. It now trades on the Toronto Stock Exchange (TSX: NPC). After the IPO, ISOA received a return on its investment by getting its loan back.

Through its Biotechnology Founders Program, ISOA helped create a company focused on developing neuropeptides as drugs for AD.

In early 2005, the company filed two Investigational New Drug applications (IND) with the FDA to begin clinical trials for the compound AL-108 as a treatment for AD and AL-208 as a treatment for mild cognitive impairment after cardiac artery bypass surgery. If successful, Allon could be among the first to develop a disease modifying therapy for AD.

PARTNER WITH US TO ACCELERATE A CURE

The ADDF seeks partners to accelerate drug discovery for Alzheimer's disease and cognitive aging through venture philanthropy. To discuss your partnership interests or other opportunities, contact Howard Fillit, MD, Executive Director, at 212-935-2402 or hfillit@alzdiscovery.org.

7th INTERNATIONAL CONFERENCE ON ALZHEIMER'S DISEASE DRUG DISCOVERY

October 12-13, 2006 ↻ New York City

The 7th International Conference on Alzheimer's Disease Drug Discovery attracted approximately 150 representatives from Pharmaceutical and Biotechnology companies and academia. This ADDF sponsored meeting is the only conference that focuses solely on the development of innovative drugs targeting AD and related dementias.



Scientific presentors included plenary speaker Dr. Robert Mahley who discussed the effects of targeting the structural and functional characteristics of Apolipoprotein E4 (ApoE4), a protein implicated in increased risk of familial Alzheimer's disease. Dr. Ottavio Arancio's presentation focused on efforts to block the harmful effects of Amyloid- β at the synapse. Dr. Arancio discussed his recent research using drugs targeting the consolidation of long-term memory as an alternative means to prevent AD.

Dr. Moussa Youdim discussed multi-functional drugs that are already in use targeting other diseases. This strategy pursues a number of promising candidates that are based on anti-depressant drugs called mono-amine oxidase inhibitors. Several talks presented methods to both prevent the formation of plaques and tangles and increase the clearance of amyloid deposits in the brain.

In contrast to more traditional views, Dr. Berslav Zlokovic spoke about recent findings that vascular changes contribute to cognitive decline. He is currently conducting research to develop therapeutics that both promote removal and prevent the re-entry of Amyloid- β from the blood vessels into the brain. Therapeutics tested to date showed improved learning and memory and increased flow of blood to the brain, believed to be beneficial in the treatment of the disease.

Next year's conference is scheduled for October 23-24, 2007. It will offer updates on research presented by this year's scientists, as well as highlight new studies and innovative research concepts.

Thank you to our meeting co-sponsors:
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HOW TO KEEP YOUR BRAIN HEALTHY WHILE AGING

With people now living longer, a priority health concern is preserving one's mind. Fortunately, maintaining cognitive vitality is possible through lifestyle interventions. Implementing the strategies below within your daily routine will help promote a healthy brain.

USE YOUR BRAIN

Take courses or engage in activities that require repeated training to stimulate the brain and improve cognitive function. Your brain is a muscle, so use it or lose it.

MANAGE CHRONIC ILLNESS

Manage medical conditions associated with cognitive decline such as hypertension, diabetes, obesity and high cholesterol. See your doctor(s) and take medication(s) on a regular basis.

DIET & NUTRITION

Eat a balanced, low-fat, low-calorie diet that includes antioxidant rich fruits and vegetables. Don't overeat. Maintain a healthy weight for your height and body type.

REDUCE STRESS

Find ways to cope with stress, which causes fatigue, disturbed sleep, poor concentration and memory lapses. Treat depression. Don't drink excess alcohol or take drugs.

EXERCISE

Regular physical activity has been shown to reduce your risk of AD, stroke, heart attacks, and some cancers. In fact, studies have shown that older adults who exercised at least three times a week for 30 minutes were less likely to develop Alzheimer's than those who were less active.

REMAIN ENGAGED

Participate in group activities that provide opportunities for social interaction, such as volunteering and group sports. Find activities that fulfill the desire to feel needed and connected to society and family.