

3rd Drug Discovery for Neurodegeneration Conference

Washington, DC - February 2-3, 2009

Park Hyatt Washington DC

Presented by the Alzheimer's Drug Discovery Foundation

Co-sponsored by the NIA, NINDS and ORD

PROCEEDINGS

The purpose of the conference was to advance drug discovery for neurodegenerative diseases by educating scientists on the process of translating basic research into novel therapies.

Speakers and chairs presented lectures and case studies on: Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis (ALS), Multiple Sclerosis (MS), and other orphan neurological diseases. The conference was organized around the following six sub-topics:

- I. **Basics of Medicinal Chemistry**
- II. **Hits & Leads: Early Phases of Drug Discovery**
- III. **Pre-Clinical Proof-of-Concept & Development**
- IV. **Issues in Technology Transfer: Interactions and Intellectual Property**
- V. **Ask the Experts: Drug Discovery for Neurodegenerative Disease**
- VI. **Resources and Services For Advancing Drug Discovery**

Date:	February 2-3, 2009
Location:	Washington, DC - USA
Organizer:	Alzheimer's Drug Discovery Foundation - www.alzdiscovery.org
Chair:	Howard Fillit, MD - Executive Director, Alzheimer's Drug Discovery Foundation
Venue:	Park Hyatt Washington DC
Objectives:	<p>The objectives of this Alzheimer's Drug Discovery Foundation (ADDF) conference are to:</p> <ol style="list-style-type: none">1. Train a cadre of interdisciplinary scientists in the principles of drug discovery for neurodegenerative disease.2. Provide a platform for scientists to exchange ideas, knowledge and resources about drug discovery for neurodegenerative disease.3. Stimulate pre-clinical research in the discovery and testing of novel compounds aimed at the prevention and treatment of neurodegenerative disease.4. Build public-private partnerships that will accelerate drug discovery for neurodegenerative disease.5. Publish the conference proceedings in a scientific journal available on PubMed.6. Provide Continuing Medical Education (CME) credits.
Specific Program:	<p>The purpose of the conference is to advance drug discovery for neurodegenerative diseases by educating academic scientists on the process of translating basic research into novel therapies.</p> <p>The conference will give participants knowledge and relevant resources about this field of scientific investigation and it will address the associated barriers and challenges.</p> <p>Speakers and chairs will present lectures and case studies on: Alzheimer's disease, Parkinson's disease, Huntington's disease, Amyotrophic Lateral Sclerosis (ALS) and other orphan neurological</p>

[top](#)

diseases. Ample time for questions and networking is also integrated into the program.

Topics and Format:

The conference is organized around the following six sub-topics:

- I. **Basics of Medicinal Chemistry**
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- III. **Pre-Clinical Proof-of-Concept & Development**
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Each session will be chaired by a leading expert and will consist of three to five 25-minute presentations, followed by a short Q&A session.

[top](#)

Session Synopses

An Overview of Drug Discovery for Neurodegenerative Disease

Plenary Speaker — Howard Fillit, MD, ADDF

The scope of discovery, development and delivery of a drug for neurodegenerative disease is often under-appreciated by those who have not been directly involved in pre-clinical research or clinical development. Success in this field requires an extremely broad and coordinated multidisciplinary effort. Impediments to success can arise from a large number of sources. A discussion of these challenges within a context of current targets for treating neurodegenerative diseases will be presented.

Session I. Basics of Medicinal Chemistry

Chair — D. Martin Watterson, PhD, Northwestern University

This session will focus on the fundamentals of drug discovery chemistry and how this is driven by later-stage considerations of pharmacokinetics, pathophysiology and production. Introductory lectures will address what physical and biological features make a chemical scaffold or small molecule "drug-like", and the potential impact of considering such properties on selection of compound libraries for screening and the follow-up medicinal chemistry refinement. The lectures will also introduce key concepts of medicinal chemistry refinement, with emphasis on CNS drug discovery, used in taking a screening hit into a lead compound and, eventually, into selection of a candidate for drug development. These introductory lectures will be followed by three case studies representing different classes of single molecular CNS targets that will demonstrate the application of these principles to project design and management. At the end of this session, participants should have familiarity with key concepts that are used in small molecule compound selection, and understand the general processes involved in medicinal chemistry refinement in early stage CNS drug discovery.

Session II. Hits & Leads: Early Phases of Drug Discovery

Chair — Marcie Glicksman, PhD, Harvard Medical School

A key component of the development of new therapeutic agents is the identification of molecules that can serve as initial lead structures on which drug discovery programs can be built. High-throughput screening of large collections of drug-like molecules for modulatory activity in disease-relevant assays is an important means to discovering these lead molecules. This session will first address strategies for the development of assays that are suitable for high-throughput screening and then strategies for secondary assays to validate the primary screening results. Most drug development efforts fail due to toxicity and ADME (**absorption, distribution, metabolism and excretion**) properties. This session will end with a presentation on technology used for *in vitro* toxicity and ADME testing.

Session III. **Pre-Clinical Proof-of-Concept & Development**

Chair — Edward Spack, PhD, SRI International

The focus of this session is the transition from lead compound to clinical testing, the scenic stretch of drug development often referred to as the "Valley of Death". Several factors converge to kill promising compounds at this translational stage, including lack of funding/resources/expertise, the delivery challenge of the blood brain barrier and common problems of toxicity, manufacturing and formulation. Drawing on examples of past successes and failures, this series of presentations will chart the course from lead optimization to initiation of clinical testing, highlighting emerging models for internal development, outsourcing and funding. Few investigators or new companies who survive this pre-clinical phase travel the clinical path alone. Therefore the pre-clinical decisions that support or hinder partnering will also be presented.

Session IV. **Issues in Technology Transfer: Interactions and Intellectual Property**

Chair — Kathleen Denis, PhD, Rockefeller University

This session will focus on the interactions among academic researchers, their technology transfer office and industry partners. An introduction will discuss the various roles and responsibilities of all of the parties involved and hope to begin to demystify academic – industry relations. The basics of patents will be presented with an emphasis on what they can and cannot successfully cover, as well as what a researcher needs to do to maximize the chances of a positive outcome. A variety of agreements used in academic – industry relationships will be discussed in the next talk, with an emphasis on the importance of creating a good relationship amongst all parties. Finally, the session will close with an honest appraisal of the good, the bad and the ugly of new company formation in the biotech industry.

Session V. **Ask the Experts: Drug Discovery for Neurodegenerative Disease**

Chair — Todd Sherer, PhD, Michael J. Fox Foundation

This breakout session will focus on disease-specific issues in drug discovery and development. The session will include 10 minute concurrent presentations from experts in Alzheimer's disease, Parkinson's disease, Huntington's disease, ALS, as well as 'orphan' neurodegenerative diseases. A 50-minute concurrent Q&A follows the presentations, allowing participants to ask specific questions pertaining to drug discovery. The ultimate aim of this session is to inform participants of specific issues related to the drug discovery process in certain disease areas (such as

selection of animal models, target validation and pre-clinical development), to devise potential solutions to these problems and to inform the funding agencies of where cross-cutting issues should be addressed by specific funding or legislative initiatives.

Session VI. **Resources and Services for Advancing Drug Discovery**

Chair — Lorenzo Refolo, PhD, National Institutes of Health/National Institute of Neurological Disorders and Stroke

This session will focus on descriptions of the resources available through a variety of mechanisms within academia, the National Institutes of Health (NIH), foundations and commercial vendors. Speakers will focus on resources for assay development, target identification, drug discovery, drug development, pre-clinical toxicology evaluation and other components needed for the translation of pre-clinical drug candidates into potential therapies tested in clinical trials. In particular, it will include specific descriptions of programs available to academic investigators through individual NIH Institutes, including the National Institute on Aging (NIA) and the National Institute of Neurological Disorders and Stroke (NINDS), as well as trans-NIH programs including the NIH *Roadmap for Medical Research* and the NIH *Blueprint for Neuroscience Research*.