

5th DRUG DISCOVERY FOR NEURODEGENERATION:

An Intensive Course on Translating Research into Drugs

February 6-8, 2011 • San Diego, CA

Presented by the Alzheimer's Drug Discovery Foundation

www.alzdiscovery.org

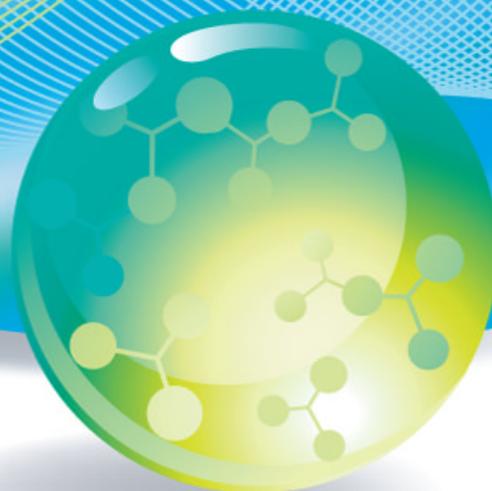


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ABOUT ADDF



Mission

The Alzheimer's Drug Discovery Foundation's (ADDF) sole mission is to rapidly accelerate the discovery and development of drugs to prevent, treat and cure Alzheimer's disease (AD), related dementias and cognitive aging.

The ADDF was established in 2004 to expand upon the programs initiated by the Institute for the Study of Aging (ISOA) Inc., a private foundation founded by the Estée Lauder family in 1998. We use a venture philanthropy investment model to bridge the global funding gap between basic research and later-stage development, recycling any return on investment to support new research.

The ADDF has an impressive track record of selecting and supporting excellent Alzheimer's disease drug discovery research. Our scientists have created entirely new classes of drugs in development for AD, screened millions of compounds, identified hundreds of leads, executed tens of patents and licenses, and have advanced compounds into clinical trials. To date, we have awarded over \$45M for more than 325 research programs and conferences in 17 countries.

Our Annual Conferences

ADDF organizes two international scientific conferences yearly as part of our ongoing efforts to increase researchers' knowledge about Alzheimer's disease (AD) and the drug discovery process. The conferences promote networking to catalyze the exchange of ideas and foster alliances that accelerate the development of new treatments for AD.

Our annual *International Conference for Alzheimer's Drug Discovery*, held in the fall, focuses on the discovery and development of drugs targeting Alzheimer's disease and related dementias. The *Drug Discovery for Neurodegeneration* conference, held in the winter, is designed to educate scientists on the process of translating basic neuroscience research into innovative therapies. The ADDF also plans smaller "catalyst conferences" that center around a relevant topic in the field of neurodegeneration.

WELCOME NOTES



On behalf of the **Alzheimer's Drug Discovery Foundation** (ADDF), I am pleased to welcome you to the *5th Drug Discovery for Neurodegeneration: An Intensive Course on Translating Research into Drugs*.

This course will advance the development of new drugs for neurodegenerative diseases by educating scientists on the principles of drug discovery. The course will also give participants knowledge and relevant resources about this field of scientific investigation and address the associated barriers and challenges, including issues such as target validation, lead discovery, pre-clinical proof-of-concept and HTS.

I would like to extend my personal thanks to the scientific advisory committee, program chairs and speakers for investing their time and energy into bringing today's event to fruition. Their dedication and commitment make this course intensive, focused and of practical value to participants.

We encourage you to visit the poster presentations by our talented young investigator award and scholarship winners. We are proud of their efforts and encourage them to continue pursuing their work in the neurodegeneration field.

This meeting is made possible by the generous support of our partners and sponsors: the National Institute on Aging and the National Institute of Neurological Disorders and Stroke; Merck Research Laboratories; The Michael J. Fox Foundation for Parkinson's Research; JSW Life Sciences, Beyond the Batten Disease Foundation, Novus Biologicals, ALS Therapy Development Institute and Fast Forward LLC. We would also like to thank our exhibitors and media partners for their commitment to making this meeting a great success.

Please fill out the enclosed evaluation form and provide us with your input on the conference's format, content and presentations. Your responses will help us determine whether the conference achieved its objectives and provide us with valuable feedback to develop meetings that better address the emerging needs of our drug discovery and neurodegenerative disease community.

Thank you for joining us and welcome once again to the ADDF's *5th Drug Discovery for Neurodegeneration: An Intensive Course on Translating Research into Drugs*.

Howard Fillit, MD
Executive Director
Alzheimer's Drug Discovery Foundation

PROGRAM

February 6, 2011

2:30 pm – 4:30	Registration
4:30 – 4:50	Welcome & Opening Remarks: Overview of Drug Discovery for Neurodegenerative Diseases Howard Fillit, MD, Alzheimer's Drug Discovery Foundation
4:50 – 5:20	Plenary Lecture: The Neurovascular Unit: Biology of Blood Brain Barrier in Neurodegenerative Diseases - Berislav V. Zlokovic, MD, PhD, University of Rochester
5:20 – 5:30	Q&A
5:30 – 5:35	Closing Remarks - Howard Fillit, MD, Alzheimer's Drug Discovery Foundation
5:35 – 7:00	Welcome Reception

February 7, 2011

8:00 am – 8:30	Continental Breakfast
8:30 – 8:35	Welcome & Opening Remarks - Howard Fillit, MD, Alzheimer's Drug Discovery Foundation

I. Basics of Medicinal Chemistry - Chair: D. Martin Watterson, PhD, Northwestern University

8:35 – 8:55	Session Overview - Medicinal Chemistry Rules of Thumb, Myths and Realities in CNS Drug Discovery - D. Martin Watterson, PhD, Northwestern University
8:55 – 9:05	Q&A
9:05 – 9:35	Designing Small Molecules with Increased Potential for CNS Penetration - Laura Chico, PhD, Northwestern University
9:35 – 9:45	Q&A
9:45 – 10:15	Synthetic Chemistry Essentials for Biologists - Heather Behanna, PhD, JMP Securities LLC
10:15 – 10:25	Q&A
10:25 – 10:55	Structure Assisted Ligand Design - Vicki Nienaber, PhD, Zenobia Therapeutics, Inc.
10:55 – 11:05	Q&A
11:05 – 11:35	BREAK / VIEW POSTERS

II. Early Phases of Drug Discovery - Chair: Kurt R. Brunden, PhD, University of Pennsylvania

11:35 – 11:40	Session Overview - Kurt R. Brunden, PhD, University of Pennsylvania
11:40 am – 12:00 pm	Basics of High Throughput Screening (HTS) - James Inglese, PhD, National Institute of Health Chemical Genomics Center
12:00 – 12:10	Q&A
12:10 – 12:30	After HTS: Solubility, Selectivity, Safety and Stability in Addition to Potency - Kurt R. Brunden, PhD, University of Pennsylvania
12:30 – 12:40	Q&A
12:40 – 1:00	Overview of Safety Evaluation of Novel Therapeutics to Enable First in Human Dosing - John E. Sagartz, DVM, PhD, DACVP, Seventh Wave Laboratories
1:00 – 1:10	Q&A
1:10 – 2:25	LUNCH / VIEW POSTERS

III. Pre-Clinical Proof-of-Concept and Development - Chair: Edward G. Spack, PhD, Fast Forward, LLC

2:25 – 2:30	Session Overview - Edward G. Spack, PhD, Fast Forward, LLC
2:30 – 2:50	What Makes a Clinical Candidate? - William Z. Potter, MD, PhD, Merck Research Laboratories (Retired)
2:50 – 3:05	Q&A
3:05 – 3:20	Requirements for an IND - Edward G. Spack, PhD, Fast Forward, LLC
3:20 – 3:30	Q&A
3:30 – 4:00	BREAK / VIEW POSTERS
4:00 – 4:20	The Limitations and Value of Animal Models for Neurodegenerative Disease - Steve Perrin, PhD, ALS Therapy Development Institute
4:20 – 4:30	Q&A
4:30 – 4:50	Regulatory Requirements in Preparing for Clinical Trials - Eric Bastings, MD, Food and Drug Administration
4:50 – 5:00	Q&A
5:00 – 5:05	Closing Remarks - Howard Fillit, MD, Alzheimer's Drug Discovery Foundation
5:05 – 7:00	Networking and Poster Session

PROGRAM

February 8, 2011

7:30 am – 8:00	Continental Breakfast
8:00 – 8:05	Welcome & Opening Remarks - Neil S. Buckholtz, PhD, National Institute on Aging
IV. Issues in Technology Transfer: Interactions and Intellectual Property - Chair: Kathleen A. Denis, PhD, The Rockefeller University	
8:05 – 8:10	Session Overview - Kathleen A. Denis, PhD, The Rockefeller University
8:10 – 8:40	Working Effectively with Your TTO: Technology Evaluation Process and IP Protection - Kathleen A. Denis, PhD, The Rockefeller University
8:40 – 8:50	Q&A
8:50 – 9:20	Creating Mutually Beneficial Relationships with Industry: Needs, Wants and Paperwork - Louis P. Berneman, EdD, CLP, Texelerate
9:20 – 9:30	Q&A
9:30 – 10:00	Should You Start a Biotechnology Company? - John S. Swartley, PhD, University of Pennsylvania
10:00 – 10:10	Q&A
10:10 – 10:40	BREAK / VIEW POSTERS
V. Beyond Small Molecules: Natural Products, Biologics and Repurposing - Chair: Diana Shineman, PhD, Alzheimer's Drug Discovery Foundation	
10:40 – 10:45	Session Overview - Diana Shineman, PhD, Alzheimer's Drug Discovery Foundation
10:45 – 11:05	Natural Products as Drug Starting Points - Frank E. Koehn, PhD, Pfizer Inc.
11:05 – 11:15	Q&A
11:15 – 11:35	Neurotrophic Factors for Alzheimer's Disease: Unique Challenges and Promise - Joao Siffert, PhD, Ceregene, Inc.
11:35 – 11:45	Q&A
11:45 am – 12:05 pm	The Road to Repurposing a Drug: Isradipine - D. James Surmeier, PhD, Northwestern University
12:05 – 12:15	Q&A
12:15 – 1:15	LUNCH / VIEW POSTERS
VI. Case Studies - Chair: Brian Fiske, PhD, The Michael J. Fox Foundation for Parkinson's Research	
1:15 – 1:20	Session Overview - Brian Fiske, PhD, The Michael J. Fox Foundation for Parkinson's Research
1:20 – 1:40	Neurotrophic Factor Mimetics: Target Validation to Lead Optimization - Frank M. Longo, MD, PhD, Stanford University
1:40 – 1:50	Q&A
1:50 – 2:10	Development of Tysabri for Multiple Sclerosis - Ted Yednock, PhD, Elan Pharmaceuticals, Inc.
2:10 – 2:20	Q&A
2:20 – 2:40	Novel Ways to Reduce Protein Aggregation - Alan D. Snow, PhD, ProteoTech, Inc.
2:40 – 3:00	Q&A
3:00 – 3:30	BREAK / VIEW POSTERS
VII. Resources and Services For Advancing Drug Discovery - Chair: Suzana Petanceska, PhD, National Institute on Aging	
3:30 – 3:35	Session Overview - Suzana Petanceska, PhD, National Institute on Aging
3:35 – 3:55	Academic Models of Drug Discovery Services and Utilizing CROs - Marcie Glicksman, PhD, Harvard NeuroDiscovery Center
3:55 – 4:05	Q&A
4:05 – 4:30	Resources at the National Institute of Health - Rebecca Farkas, PhD, National Institute on Neurological Disorders and Stroke; Neil S. Buckholtz, PhD, National Institute on Aging
4:30 – 4:50	Q&A
4:50 – 5:00	Closing Remarks - Howard Fillit, MD, Alzheimer's Drug Discovery Foundation

SCIENTIFIC ADVISORY COMMITTEE

Kurt R. Brunden, PhD, *University of Pennsylvania*
Neil S. Buckholtz, PhD, *National Institute on Aging*
Kathleen A. Denis, PhD, *The Rockefeller University*
Howard Fillit, MD, *Alzheimer's Drug Discovery Foundation*
Brian Fiske, PhD, *The Michael J. Fox Foundation for Parkinson's Research*
William Matthew, PhD, *National Institute on Neurological Disorders and Stroke*
Lorenzo Refolo, PhD, *National Institute on Aging*
Suzana Petanceska, PhD, *National Institute on Aging*
Todd Sherer, PhD, *The Michael J. Fox Foundation for Parkinson's Research*
Diana Shineman, PhD, *Alzheimer's Drug Discovery Foundation*
Edward G. Spack, PhD, *Fast Forward, LLC*
D. Martin Watterson, PhD, *Northwestern University*

CONTINUING MEDICAL EDUCATION

This activity has been planned and implemented in accordance with the Essential Areas and policies of the Accreditation Council for Continuing Medical Education (CME) through the joint sponsorship of PESI, LLC and the Alzheimer's Drug Discovery Foundation (ADDF). PESI, LLC is accredited by the ACCME to provide continuing medical education for physicians.

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The PESI, LLC designates this educational activity for a maximum of 14.25 *AMA PRA Category 1 Credit(s)*[™]. Physicians should only claim credit commensurate with the extent of their participation in the activity.

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International Physicians are formally eligible for *AMA PRA Category 1 Credit(s)*[™]. Physician Assistants AAPA accepts Category 1 credit from AOACCME, Prescribed credit from AAFP, and *AMA PRA Category 1 Credit*[™] for the PRA from organizations accredited by ACCME.

OTHER CONFERENCE DELIVERABLES

The conference presentations will be recorded and the resulting videocast will be made available on the ADDF's website (www.alzdiscovery.org). Recordings from the 2010 edition are available on the website. The ADDF will also produce a written summary of the course that will be made available to the research community.

SPONSORS and EXHIBITORS

Funding for this conference was made possible in part by Cooperative Agreement 2U13AG031125 from the National Institute on Aging and the National Institute of Neurological Disorders and Stroke.

The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Department of Health and Human Services; nor does mention by trade names, commercial practices, or organizations imply endorsement by the U.S. Government.

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OBJECTIVES:

- ☑ Highlight scientific progress on drug discovery programs aimed at treating Alzheimer's disease and related dementias.
- ☑ Increase networking opportunities for scientists to share information and resources.
- ☑ Foster interdisciplinary and public-private partnerships and alliances.

TARGET AUDIENCE

- ☑ Academic and industry scientists engaged in Alzheimer's drug discovery research
- ☑ Business development and licensing professionals
- ☑ Alliance management professionals
- ☑ Venture capitalists and other investors.

SCHOLARSHIPS

- ☑ The Alzheimer's Drug Discovery Foundation invites applications for the 2011 ADDF Young Investigator Scholarships. See details on website.

www.alzdiscovery.org

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2011 ADDF AWARDS and SCHOLARSHIPS

Congratulations to all the winners of the 2011 ADDF Outstanding Young Investigator Awards and Young Investigator Scholarships! These highly prestigious Awards and Scholarships recognize the early achievements of talented young investigators and seek to encourage the career development of the next generation of research scientists.

2011 ADDF OUTSTANDING YOUNG INVESTIGATOR AWARDS

Melissa Barker-Haliski, *University of Utah*

Sara Brownell, *Stanford University*

Bryan Chen, *Stanford University*

James Kraus, *Northwestern University*

Pascal Sanchez, *The J. David Gladstone Institutes/University of California*

2011 ADDF YOUNG INVESTIGATOR SCHOLARSHIPS

Brinda Bradaric, *Northwestern University*

Kieren Egan, *University of Edinburgh*

Kaushik Ghosal, *Cleveland Clinic, Lerner Research Institute*

Mahaveer Golechha, *University of Delhi*

Jia Guo, *Stanford University*

Veer Bala Gupta, *Edith Cowan University*

James Hogan, *American Life Science Pharmaceuticals, Inc.*

Ali Jawaid, *University Hospital Zurich*

Michael Jones, *Simon Fraser University*

Amanda Kauffman, *Princeton University*

Jongho Lee-Armandt, *Boston University School of Medicine*

Angela McKoy, *Princeton University*

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- Tau
- Ubiquitin

Parkinson's Disease

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- DJ1/PARK7
- GDNF
- HtrA2
- Huntingtin
- Huntingtin Interacting Protein (HIP1)
- LRRK2/PARK8
- Neurturin
- Parkin
- Tau
- phospho-Tau [Thr181]
- UCHL1/PGP9.5

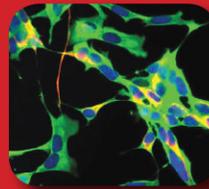
Amyotrophic Lateral Sclerosis

- BDNF
- FLAD1
- GDNF
- KIF1B
- Senataxin
- Superoxide Dismutase 1 (SOD1)
- TARDBP
- TRPM7
- VEGFA

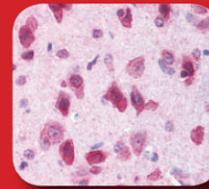
Multiple Sclerosis

- B Cells & T Cells
- Interferon beta
- Myelin Oligodendrocyte Glycoprotein (MOG)
- Myelin Basic Protein (MBP)
- Proteolipid Protein (PLP)
- Epstein-Barr Virus (EBV)

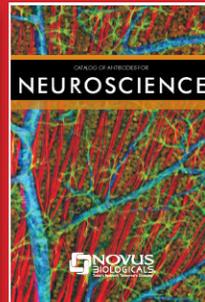
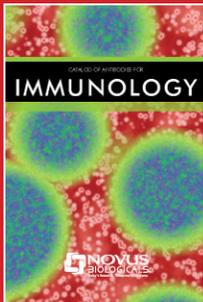
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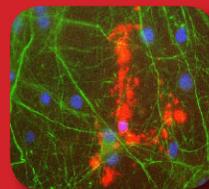
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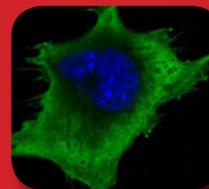
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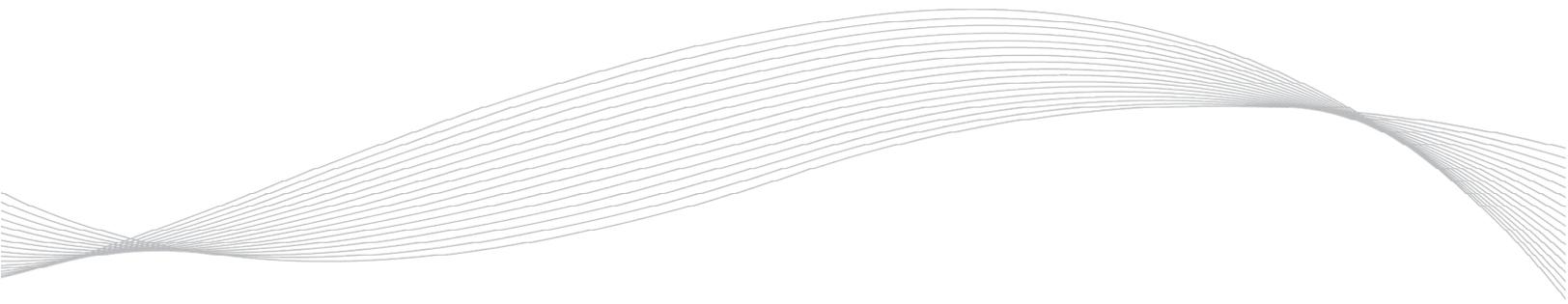


BEYOND BATTEN DISEASE
F O U N D A T I O N

**The Beyond Batten Disease Foundation
is pleased to partner with the
Alzheimer's Drug Discovery Foundation on the
*5th Drug Discovery for Neurodegeneration:
An Intensive Course on Translating Research into Drugs*
and the following
*Drug Discovery in JNCL Conference.***

To learn more about JNCL (also called Batten Disease) and the
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CHAIRS AND SPEAKERS



BIOS AND ABSTRACTS

Howard Fillit, MD, Alzheimer's Drug Discovery Foundation



Howard Fillit, MD, a geriatrician and neuroscientist, is the founding Executive Director of the Institute for the Study of Aging, Inc. as well as its affiliated public charity the Alzheimer's Drug Discovery Foundation, both of which are dedicated to funding drug discovery for Alzheimer's disease. Dr. Fillit was formally the Corporate Medical Director for Medicare at NYLCare Health Plans (now a division of Aetna, Inc.), where he was responsible for over 125,000 Medicare members in 8 regional markets. He has also had a distinguished academic career at The Rockefeller University and The Mount Sinai Medical Center (NY), where he is currently a clinical professor of geriatrics and medicine and a professor of neurobiology. Dr. Fillit has received many awards and honors, including the Rita Hayworth Award for Lifetime Achievement from the Alzheimer's Association. He is a fellow of the American Geriatrics Society, the American College of Physicians, the Gerontological Society of America, and the New York Academy of Medicine. Dr. Fillit is the author or co-author of more than 250 publications, including the leading international Textbook of Geriatric Medicine and Gerontology. He served as a consultant to a variety of individuals, managed care organizations, health care systems, and pharmaceutical and biotechnology companies.

An Overview of Drug Discovery for Neurodegenerative Disease

Howard Fillit, MD

Alzheimer's Drug Discovery Foundation, New York, NY

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.

Berislav V. Zlokovic, MD, PhD, University of Rochester



Berislav V. Zlokovic, PhD, MD, is Dean's Professor, Professor of Neurosurgery and Neurology, and Director, Center for Neuro-degenerative & Vascular Brain Disorders at the University of Rochester. He earned an MD (1975) and a PhD (1983) from the University of Belgrade. Zlokovic received postdoctoral training in Transport Biology at Queen Elizabeth College and Neurobiology/Blood-Brain Barrier Transport Physiology at King's College London with Hugh Davson. He has conducted research in the neuroscience field for more than 30 years. He provided original insights into Alzheimer's disease pathogenesis and treatments by discovering that brain vascular genes and receptors control reductions in brain microcirculation, cerebral blood flow and faulty amyloid beta-peptide clearance at the blood-brain barrier preceding neuronal injury and loss. He works on protein C pathway in brain that has therapeutic implications for several neurological disorders such as stroke, brain trauma, amyotrophic lateral sclerosis, and others. His accomplishments have earned him a MERIT Award from the National Institute on Aging (2004) "in recognition of his sustained contribution to aging and his leadership and commitment to the field"; the ISOA/Elan award (2006) "for novel approaches to drug discovery for Alzheimer's disease"; the MetLife Award (2006) which is given to "neuroscientists who made significant contributions to our understanding of Alzheimer's disease and who bring us closer to a cure"; the Javits Award from the National Institute of Neurological Disorders and Stroke (2007) for "his distinguished record of substantial contributions in a field of neurological science"; the Potamkin Prize from the American Academy of Neurology (2009) "in recognition of his outstanding achievements in research of Alzheimer's and related neurodegenerative diseases"; and the McCune 10th Annual Award (2009) "which is given to a researcher who has made a difference in Alzheimer's disease."

Plenary Lecture: The Neurovascular Unit: Biology of Blood Brain Barrier in Neurodegenerative Diseases

Berislav V. Zlokovic, MD, PhD

University of Rochester, Rochester, NY

The blood-brain barrier (BBB) is a highly specialized brain endothelial structure within the neurovascular unit. The neurovascular unit is comprised of vascular cells (i.e., endothelial cells pericytes, vascular smooth muscle cells), glial cells (i.e., astrocytes, microglia, oligodendroglia) and neurons. In concert with pericytes, astrocytes, and microglia, the BBB separates components of the circulating blood from neurons. Moreover, the BBB maintains the chemical composition of the neuronal "milieu" which is required for proper functioning of neuronal circuits, synaptic transmission, synaptic remodeling, angiogenesis and neurogenesis in the adult brain. Recent findings indicate that brain perfusion stress, from one hand, and the BBB breakdown, from the other, may initiate and/or contribute to a "vicious circle" of the disease process resulting in a loss of synapto-dendritic connections, neuronal dysfunction and neuronal loss in neurodegenerative diseases such as Alzheimer's disease and amyotrophic lateral sclerosis. I will also discuss our recent evidence showing that pericytes control key functions within the neurovascular unit that are necessary for maintaining proper neurovascular functions and neuronal structure and function in the adult brain and during aging process. I will next show data demonstrating that pericytes degeneration due to deficient PDGFRb signaling can initiate vascular-mediated secondary

neurodegenerative process. I will next talk about *the two hit vascular hypothesis* for Alzheimer's disease according to which an initial vascular damage precedes cerebrovascular and brain accumulation of Alzheimer's toxin amyloid b-peptide (A β) (*hit 1*) which in turn amplifies neurovascular dysfunction preceding neurodegenerative changes (*hit 2*). Examples of cerebral hypoperfusion-mediated vascular damage leading to a secondary Ab accumulation in brain, and Ab-mediated primary vascular damage will be provided. The role of brain vascular-specific genes relevant to AD discovered through genomic screening (e.g., *MEOX2*, *MYOCARDIN*) and receptors at the BBB (i.e., LRP1, RAGE) in controlling reductions in brain microcirculation, cerebral blood flow and faulty amyloid b-peptide clearance at the BBB preceding neuronal loss will be discussed. Finally, I will touch on potential therapeutic approaches that could be developed for chronic neurodegenerative disorders based on the vascular concept of neurodegeneration. Examples of some cellular and molecular targets within the neurovascular unit and at the BBB will be presented.

SESSION I

Basics of Medicinal Chemistry

Chair — D. Martin Watterson, PhD, Northwestern University

Session Overview: Medicinal Chemistry Rules of Thumb, Myths and Realities in CNS Drug Discovery

D. Martin Watterson, PhD, Northwestern University

Designing Small Molecules with Increased Potential for CNS Penetration

Laura Chico, PhD, Northwestern University

Synthetic Chemistry Essentials for Biologists

Heather Behanna, PhD, JMP Securities LLC

Structure Assisted Ligand Design

Vicki Nienaber, PhD, Zenobia Therapeutics, Inc.

D. Martin Watterson, PhD, Northwestern University



Dr. Watterson holds the John G. Searle Endowed Chair in Molecular Biology and Biochemistry at Northwestern University and is Professor of Molecular Pharmacology and Biological Chemistry at the Northwestern University Feinberg School of Medicine in Chicago. He has published extensively in the areas of drug discovery, signal transduction, structural biology, pharmacology and medicinal chemistry, and has developed immunodiagnostics and novel small molecule therapeutic candidates licensed to industry. Dr. Watterson has worked successfully with major pharmaceutical and biotech companies in diverse areas

of drug discovery, participated actively in bringing new drug candidates to clinical development, served on the Board of Directors for technology companies, and assisted colleagues and various government agencies with science and technology development. Related to the latter advisory and administrative experience, he founded one of the first academic-based drug discovery programs in the country in 1996, the Drug Discovery Program at Northwestern University's Feinberg School of Medicine, which later became the university-wide Center for Drug Discovery and Chemical Biology and is currently the Center for Molecular Innovation and Drug Discovery. This premier drug discovery program serves as a model for other academic institutions. He serves on diverse NIH, foundation and international advisory committees in the areas of drug discovery and signal transduction. Dr. Watterson's doctoral training in chemical sciences was at Emory University, followed by postdoctoral training in biochemistry/bioorganic chemistry at Duke University Medical Center where he was supported by a National Research Service Award from the National Institutes of Health. Dr. Watterson held faculty positions at The Rockefeller University, where he was an Andrew Mellon Fellow, and at Vanderbilt University Medical Center, where he was Professor of Pharmacology and Howard Hughes Investigator, before moving to Northwestern University. At Northwestern, he has served as a Department Chair, Drug Discovery Program Director, and Co-Director of a University Center.

Medicinal Chemistry Rules of Thumb, Myths and Realities in CNS Drug Discovery

D. Martin Watterson, PhD

Northwestern University, Chicago, IL

This presentation will provide an introduction to the drug discovery and drug development continuum from the perspective of medicinal chemistry goals, and scientific background to concepts that will be covered in more detail by the three main lectures in this session.

Laura Chico, PhD, Northwestern University



Dr. Chico is currently a healthcare research analyst at Robert W. Baird & Company and holds an adjunct faculty position at Northwestern University. Previously, Dr. Chico was the founder and president of privately-held LKC Pharma Services, a consulting firm focused on the development of proprietary computational algorithms for pharmacological and chemical sciences to facilitate client “Go/NoGo” decisions or project prioritizations in drug discovery and early-stage product development, rendering significant time and cost savings in the short term and major risk reduction at later stages. She received her PhD in pharmacology and MS in computational biology from Northwestern University. Dr. Chico’s past research contributions facilitated advancement of novel small molecule drugs into late stage drug development for CNS disorders and the discovery of new classes of small molecule drug candidates for cancer therapeutics.

Designing Small Molecules with Increased Potential for CNS Penetration

Laura Chico, PhD

Northwestern University, Chicago, IL

This talk will provide an overview of the role of molecular properties in designing compounds with a higher probability of penetrating the CNS. Key areas to be covered include the application of molecular properties considerations during early drug discovery, discussion of available commercial tools for property calculations, and small molecule case studies.

Learning objectives:

1. Learn what makes a molecule “drug-like” and how molecular properties criteria can be used as prioritization tools.
2. Discuss how molecular properties can influence pharmacokinetic outcomes, such as cytochrome P450 metabolism and what matters most to CNS drug discovery campaigns.
3. Become familiar with the unique properties requirements associated with the CNS and how these may change through the evolution of hits to clinical candidates.

Heather Behanna, PhD, JMP Securities LLC



Dr. Behanna is Biotechnology Research Associate at the JMP Securities LLC. Prior to that, Dr. Behanna was a Senior Scientist at the Astellas Research Institute of America (ARIA). She received her PhD in organic chemistry from the Department of Chemistry at Northwestern University, and did postdoctoral training at the Feinberg School of Medicine in pharmaceutical chemistry. Her past research has included novel compound discovery chemistry as well as developing a synthetic scheme for large scale production of clinical grade material under FDA regulated conditions.

Synthetic Chemistry Essentials for Biologists

Heather Behanna, PhD

JMP Securities LLC, Chicago, IL

This talk will provide an overview of the medicinal chemistry skill sets needed in the drug discovery process, including pattern recognition and synthetic chemistry planning. The use of these skill sets in the early drug discovery process, including choice of compounds for inclusion in a screening library and the recursive task of taking hits to lead compounds and then to clinical candidates, will be covered.

Learning objectives:

1. Develop an appreciation for the key roles of synthetic chemistry in the multidisciplinary team and when to engage qualified assistance and collaboration.
2. Learn what constitutes a "hit" versus a lead compound from a chemistry perspective.
3. Become familiar with the linked but different goals for hit-to-lead refinement, lead optimization, and clinical material production.

Vicki Nienaber, PhD, Zenobia Therapeutics, Inc.



Vicki Nienaber, PhD is President, CSO and founder of Zenobia Therapeutics. She is known for her pioneering work in the field of drug discovery using fragment-based screening and structure-based drug design. Vicki has managed both drug discovery and development programs giving her a unique perspective on the specifications of early lead compounds that will yield high-quality clinical candidates. Vicki was most recently the Chief Scientific Officer at ActiveSight, a division of Rigaku Americas Corporation, where she built a diverse team of protein biochemistry, X-ray crystallography and drug discovery experts. Before that, she was the Senior Director of Lead Discovery and Crystallography at SGX Pharmaceuticals, where she oversaw strategic drug discovery and structural biology alliances with Novartis and Eli Lilly and initiated their internal kinase lead discovery project. While at Abbott Laboratories, she was the lead inventor of crystallographic fragment-based screening, co-inventor of the ACTOR robotic system for automated crystal sample handling and a leader in structure-based drug design methods. Vicki has written numerous peer-reviewed scientific publications and patents and has been recognized with several awards including the Commitment to Excellence award while a post-doctoral fellow at DuPont-Merck and the Chairman's Award for significant contributions while at Abbott Laboratories.

Structure Assisted Ligand Design

Vicki Nienaber, PhD

Zenobia Therapeutics, Inc., San Diego, CA

Diseases of the central nervous system (CNS) are among the most devastating to patients and their families. Despite this, treatments have lagged behind other therapeutic areas in part because of the challenge for compounds that cross the blood brain barrier. Recent analyses of successful drugs have shown that their chemical properties have not changed substantially over the past 40 years while the properties of compounds entering the clinic have become inflated. This property inflation has only exacerbated the challenges of CNS drug discovery as the requirements for delivery to the brain are even more stringent than those for other tissues. In this presentation, we will discuss the merits of fragment based lead discovery and how it may be used to address the chemical property challenges of CNS drug discovery. Optimization of fragments and other lead compounds using structure-directed drug design will also be discussed in the context of CNS drug discovery. We include results from our internal programs targeting protein kinases and other enzyme classes in neurodegenerative diseases.

SESSION II

Early Phases of Drug Discovery

Chair — Kurt R. Brunden, PhD, University of Pennsylvania

Session Overview

Kurt R. Brunden, PhD, University of Pennsylvania

Basics of High Throughput Screening (HTS)

James Inglese, PhD, National Institute of Health Chemical Genomics Center

After HTS: Solubility, Selectivity, Safety and Stability in Addition to Potency

Kurt R. Brunden, PhD, University of Pennsylvania

Overview of Safety Evaluation of Novel Therapeutics to Enable First in Human Dosing

John E. Sagartz, DVM, PhD, DACVP, Seventh Wave Laboratories

James Inglese, PhD, National Institute of Health Chemical Genomics Center



Dr. Inglese is currently establishing the Laboratory of Assay and Screening Technology Development focused on rare and neglected diseases in the newly formed NIH Center for Translational Therapeutics (NCTT). He is also co-founder of the NIH Chemical Genomics Center (NCGC) and Associate Investigator of the National Human Genome Research Institute (NHGRI). Dr. Inglese received his PhD in Organic Chemistry from the Pennsylvania State University and completed post-doctoral training in the laboratory of Prof. Robert J. Lefkowitz at Duke University Medical Center. Dr. Inglese has led research teams at the Princeton-based biotech Pharmacoepia and Merck Research Laboratories before coming to the NIH. Over the past two decades Dr. Inglese has contributed to over 150 publications and patents and has made major contributions to the early drug discovery process through the development of novel assay formats and high throughput screening paradigms. Dr. Inglese is the Founding Editor (2002) and Editor-in-Chief of the journal, *ASSAY and Drug Development Technologies*.

Basics of High Throughput Screening (HTS)

James Inglese, PhD

National Institute of Health Chemical Genomics Center, Bethesda, MD

The rapid testing of chemical libraries for biological activity is the primary aim of high throughput screening (HTS). Advances in HTS have paralleled those in molecular biology, instrumentation and automation, and informatics, and the increased availability of arrayed compound libraries, sophisticated high sensitivity assays and the associated technologies required to implement these assays in HTS have been largely developed within the pharmaceutical industry for the identification of new chemical matter for drug development. However, HTS approaches are now widely available in academia to address broader questions within biological research and expand the disease portfolio for therapeutic development. In this presentation I will describe the components of HTS and provide examples of strategies used to identify novel chemotypes for specific biological targets or phenotypes using large and targeted chemical libraries. I will illustrate with specific case studies how this approach can be used in the identification of chemical modulators or probes for processes that form the basis of neurological disorders.

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Kurt R. Brunden, PhD, University of Pennsylvania



Dr. Kurt R. Brunden received his BS degree from Western Michigan University, with dual majors of Biology and Health Chemistry. He obtained his PhD in Biochemistry from Purdue University, and did a post-doctoral fellowship at the Mayo Clinic in Rochester, MN. Dr. Brunden subsequently joined the Biochemistry faculty at the University of Mississippi Medical Center, with a research focus on the regulation of myelination. He was later recruited to the biotechnology sector, where he advanced to VP of Research at Gliatech, Inc. and later served as Sr. VP of Drug Discovery at Athersys, Inc. In these positions, he oversaw projects in Alzheimer's disease (AD), cognition, schizophrenia, inflammation and metabolic disease. Several of these programs were partnered with or acquired by pharmaceutical and biotechnology companies. In addition to his oversight of drug discovery programs, Dr. Brunden was responsible for the preparation of patents, the management of patent portfolios, and the preparation of IND/CTA documents. In 2007, Dr. Brunden became Director of Drug Discovery in the Center for Neurodegenerative Disease Research (CNDR) at the University of Pennsylvania, where he presently oversees drug discovery programs in the areas of AD, frontotemporal lobar degeneration and Parkinson's disease. Dr. Brunden also serves as the chair of the NSD-C translational research study section for the National Institutes of Neurological Diseases and Stroke, is a reviewer for the Alzheimer's Drug Discovery Foundation and an ad hoc reviewer for several scientific journals. He has over 65 publications, a number of issued U.S. patents and several pending patent applications.

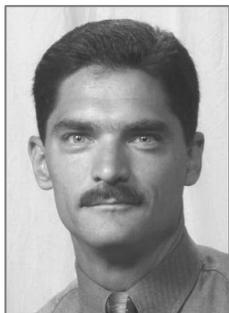
After HTS: Solubility, Selectivity, Safety and Stability in Addition to Potency

Kurt R. Brunden, PhD

University of Pennsylvania, Philadelphia, PA

The completion of high-throughput screening (HTS) of compound libraries often triggers a series of subsequent drug discovery activities that include secondary testing of initial HTS leads, selection of preferred chemotypes, and initiation of medicinal chemistry efforts. As chemical analogues are generated, they must be evaluated not only for their potency at the desired drug target but also for key attributes such as aqueous solubility, target selectivity, pharmacological safety, metabolic stability and, in the case of CNS drug targets, blood-brain barrier permeability. This session will provide examples of assays that can be established and utilized in academic centers to gain a better understanding of these key compound characteristics before progressing to more advanced toxicological and efficacy testing in animals.

John E. Sagartz, DVM, PhD, DACVP, Seventh Wave Laboratories



John E. Sagartz, DVM, PhD, Diplomate, ACVP is President of Seventh Wave Laboratories, LLC. He received his PhD from The Ohio State University, Department of Veterinary Biosciences, Columbus, OH, completed his Residency in Veterinary Pathology at Ohio State University, Department of Veterinary Pathobiology, Columbus, OH, Doctor of Veterinary Medicine from Kansas State University, College of Veterinary Medicine and his BS from Kansas State University, College of Agriculture in Manhattan, Kansas. From 1997 to 2003 he held positions as a Investigative Pathologist, Section Head, Assistant Director, Director and Site Head, Pharmacia Fellow Manager at Global Investigative Toxicology, St. Louis, MO. John has been the recipient of numerous honors and awards including recognition as a Pharmacia Fellow in 2003. The Pharmacia Fellow Program recognizes individuals who demonstrated outstanding proficiency and accomplishment in their field and a strong record of technical leadership. In addition, Dr. Sagartz received the W.E. Upjohn award in 2001 which is granted to individuals with sustained high impact contribution to the performance of Pharmacia Corporation. Further, Seventh Wave Laboratories was awarded the 2009 Outstanding Entrepreneur Award by the St. Louis County Economic Council. Past Professional Activities include Chair, American College of Veterinary Pathologists Endowment Committee, Endocrine Pathology Program Planning Committee, American College of Veterinary Pathologists annual meeting, 1999. Dr. Sagartz is a member of the Society of Toxicologic Pathologists, Society of Toxicology, American Society of Investigative Pathology, American College of Veterinary Pathologists, and American Veterinary Medical Association. He has authored and coauthored numerous publications related to experimental and spontaneous disease.

Overview of Safety Evaluation of Novel Therapeutics to Enable First in Human Dosing

John E. Sagartz, DVM, PhD, DACVP

Seventh Wave Laboratories, Chesterfield, MO

Upon selection of a molecule for formal development, a series of safety studies must be conducted to enable dosing of human subjects, either healthy volunteers or patients. Although there is variation by world region and by therapeutic indication in the expectations of the supporting safety package, at a minimum, an evaluation of the potential for genetic toxicology, adverse pharmacology (cardiovascular, respiratory, CNS), and general toxicity is expected prior to the initiation of clinical trials. This session will provide an overview of the regulatory guidelines and specific studies for the evaluation of new chemical entities prior to first in human dosing.

SESSION III

Pre-Clinical Proof-of-Concept and Development

Chair — Edward G. Spack, PhD, Fast Forward, LLC

Session Overview

Edward G. Spack, PhD, Fast Forward, LLC

What Makes a Clinical Candidate?

William Z. Potter, MD, PhD, Merck Research Laboratories (Retired)

Requirements for an IND

Edward G. Spack, PhD, Fast Forward, LLC

The Limitations and Value of Animal Models for Neurodegenerative Disease

Steve Perrin, PhD, ALS Therapy Development Institute

Regulatory Requirements in Preparing for Clinical Trials

Eric Bastings, MD, Food and Drug Administration

William Z. Potter, MD, PhD, Merck Research Laboratories (Retired)



William (Bill) Z. Potter earned his BA, MS, MD, and PhD at Indiana University, after which he functioned in positions of increasing responsibility and seniority over the next twenty-five years at the National Institutes of Health (NIH) focused on translational neuroscience. While at the NIH, Bill was widely published and appointed to many societies, committees, and boards; a role which enabled him to develop a wide reputation as an expert in psychopharmacological sciences and championing the development of novel treatments for CNS disorders. Bill left the NIH in 1996 to accept a position as Executive Director and Research Fellow at Lilly Research Labs, specializing in

the Neuroscience Therapeutic Area and in 2004 joined Merck Research Labs as VP of Clinical Neuroscience, then the newly created position of Translational Neuroscience in 2006, a position from which he retired in January of this year. His experience at Lilly and MRL in identifying, expanding and developing methods of evaluating CNS effects of compounds in human brain cover state of the art approaches across multiple modalities. These include brain imaging and cerebrospinal fluid proteomics (plus metabolomics) as well as development of more sensitive clinical, psychophysiological and performance measures allowing a range of novel targets to be tested in a manner which actually addresses the underlying hypotheses. Bill has become a widely recognized champion for the position that more disciplined hypothesis testing of targets in humans is the best near term approach to moving CNS drug development forward for important neurologic and psychiatric illnesses.

What Makes a Clinical Candidate?

William Z. Potter, MD, PhD

Merck Research Laboratories (Retired)

The complexities and demands of bringing a new chemical entity to the stage of readiness for studies in humans – clinical candidacy – have been underestimated even by senior management in pharmaceutical companies. Lessons learned over the last two decades may help a wider audience of stakeholders in new drug development for serious illnesses focus efforts to deal with a persisting gap in translating basic science to therapeutics.

The core issue is that drug development was optimized for “me too” and maybe slightly better compounds whereby the optimization for clinical studies of any new chemical entity could follow a known pathway. This now classic pathway involved a very sophisticated approach to synthesizing compounds which had a series of properties in terms of in vitro potency and metabolism, short term safety in two animal species, ease of manufacture and specificity of action in one or more in vivo animal models. Thus, once one had a series of in vitro assays for a cholinesterase inhibitor, one could screen literally 100’s of thousands of compounds in a “library” over days to weeks for a “hit”, advance these through various filters over the next few months, synthesize variations to increase specificity and potency and then see which of these would reach the brain in some animal (usually rats or mice). This iterative process would take a year or so on average to find two or three compounds that would go into more extensive animal studies to establish safety and by the end of two years (or even less) one might have a “new” cholinesterase inhibitor ready to go into humans.

But what about compounds that are not only new in the sense of having a different chemical structure but “novel” in the sense of having a primary biochemical action that remains to be

shown to be valid for treating a particular disorder? Here, much more experimentation and science have emerged as necessary to “validate” the compound as appropriate to test a particular hypothesis in humans. Such tools as studies in genetically engineered mice have played a much bigger role but may require months of studies when looking at processes such as beta amyloid deposition in brain. Since the same biochemical processes can play different roles in the function of different species there remains a substantial risk that the animals will not be predictive requiring a much more thorough investigation of safety concerns.

The stages of “me too” vs “novel” development to reach clinical candidacy will be summarized with a focus on implications for actions that stakeholders across advocacy groups, academia, NIH, FDA and industry can take to increase the flow of potential breakthrough clinical candidates.

Edward G. Spack, PhD, Fast Forward, LLC



Dr. Spack received his doctoral degree from The Johns Hopkins University and his postdoctoral fellowship in cellular immunology at Stanford University. He worked in Bay area biotech companies for 14 years developing therapies for autoimmunity, cancer, and infectious disease spanning discovery and preclinical development through Phase III trial support. At SRI International, Dr. Spack directed the PharmaSTART program, a consortium of SRI, Stanford, UC Berkeley, UCSD, and UCSF chartered to support translational development. His responsibilities included designing preclinical development plans for academic researchers, foundations, NIH programs, and start-up companies. He consulted with the NIH translational core services committee and several individual NIH institutes on preclinical development and served as an advisor on the NIH Regional Centers of Excellence for Biodefense and Emerging Infectious Diseases Produce Development Working Group. As Senior Director of Business Development for SRI's Bioscience Division, Dr. Spack was responsible for alliance management, in-licensing, and out-licensing of drug candidates. He has served on scientific advisory boards, grant review boards, or national board of directors for several foundations, and is currently a managing director at Fast Forward LLC, supporting a translational development program advancing therapeutics for the prevention/reversal of neurodegeneration in multiple sclerosis in partnership with EMD Serono.

Requirements for an IND

Edward G. Spack, PhD

Fast Forward, LLC, San Francisco, CA

Preclinical development encompasses the activities that link drug discovery in the lab to initiation of human clinical trials. The details of each preclinical development package can vary, but all have some common features. Rodent and nonrodent mammalian models are used to delineate the pharmacokinetic (PK) profile and general safety, as well as to identify toxicity patterns. One or more species may be used to determine the drug's mean residence time in the body, which depends on inherent absorption, distribution, metabolism, and excretion (ADME) properties. For drugs intended to treat Alzheimer's disease or other brain-targeted diseases, the ability of a drug to cross the blood brain barrier may be a key issue. Toxicology and safety studies identify potential target organs for adverse effects and define the Therapeutic Index (TI) to set the initial starting doses in clinical trials. Pivotal preclinical safety studies generally require regulatory oversight as defined by U.S. Food and Drug Administration Good Laboratory Practices (GLP) and international guidelines, including the International Conference on Harmonisation. Concurrent preclinical development activities include developing the Clinical Plan (Phase 1) and preparing the new drug product including the associated documentation to meet stringent FDA Good Manufacturing Practices regulatory guidelines. A wide range of commercial and government contract options are available for investigators seeking to advance their candidate(s). Government programs such as the Small Business Innovative Research and Small Business Technology Transfer grants and the National Institutes of Health Rapid Access to Interventional Development Pilot Program provide funding and services to assist applicants in preparing the preclinical programs and documentation for their drugs. Increasingly, private foundations are also funding preclinical work. Close interaction with the FDA, including a meeting to prepare for submission of an Investigational New Drug (IND) application, is critical to ensure that the preclinical development package properly supports the planned Phase I clinical trial.

Steven Perrin, PhD, ALS Therapy Development Institute



Dr. Steven Perrin is currently the Chief Executive Officer and Chief Scientific Officer at the ALS Therapy Development Institute (ALS TDI) in Cambridge, MA. He earned his PhD at Boston University Medical Center studying the transcriptional regulation of genes during adipocyte and myocyte differentiation. Dr. Perrin moved into the pharmaceutical industry in 1997 holding positions at the Hoechst-Ariad Genomics Center, Aventis Pharmaceuticals and more recently as Director of Molecular Profiling at Biogen Idec. Dr. Perrin joined ALS TDI in 2007 as part of historical collaboration between the Muscular Dystrophy Association, Augie's Quest and ALS TDI to develop effective therapeutics for

ALS patients. Since joining ALS TDI Steven has spearheaded the development of computational biology capabilities and information management systems to more clearly understand the molecular mechanisms associated with disease onset and progression in neurodegenerative diseases. He has expanded ALS TDI's drug screening program to include expertise in the generation and assessment of gene therapy vectors and protein biologics in preclinical models of neurodegeneration. He has developed a business plan to facilitate pharmaceutical partnerships for rapid clinical development and commercialization of promising targets for ALS patients. Dr. Perrin is a frequent participant in international conferences in computational biology, genomics, drug development, and neurodegeneration.

The Limitations and Value of Animal Models for Neurodegenerative Disease

Steven Perrin, PhD

ALS Therapy Development Institute, Cambridge, MA

Identification of *SOD1* as the mutated protein in a significant subset of familial amyotrophic lateral sclerosis (FALS) cases has led to the generation of transgenic rodent models of autosomal dominant *SOD1* FALS. Mice carrying 23 copies of the human *SOD1*^{G93A} transgene are considered the standard model for FALS and ALS therapeutic studies. To date, there have been at least 50 publications describing therapeutic agents that extend the lifespan of this mouse. However, no therapeutic agent besides riluzole has shown corresponding clinical efficacy. We used computer modeling and statistical analysis of 5,429 *SOD1*^{G93A} mice from our efficacy studies to quantify the impact of several critical confounding biological variables that must be appreciated and should be controlled for when designing and interpreting efficacy studies. Having identified the most critical of these biological variables, we subsequently instituted parameters for optimal study design in the *SOD1*^{G93A} mouse model. We retested several compounds reported in major animal studies (minocycline, creatine, ritonavir, celecoxib, sodium phenyl butyrate, ceftriaxone, WHI-P131, thalidomide, and riluzole) using this optimal study design and found no survival benefit in the *SOD1*^{G93A} mouse for any compounds (including riluzole) administered by their previously reported routes and doses. The presence of these uncontrolled confounding variables in the screening system, and the failure of these several drugs to demonstrate efficacy in adequately designed and powered repeat studies, leads us to conclude that the majority of published effects are most likely measurements of noise in the distribution of survival means as opposed to actual drug effect. We recommend a minimum study design for this mouse model to best address and manage this inherent noise and to facilitate more significant and reproducible results among all laboratories employing the *SOD1*^{G93A} mouse.

Eric Bastings, MD, Food and Drug Administration



Eric Bastings, MD, is Deputy Director of the Division of Neurology Drug Products, Center for Drug Evaluation and Research, Food and Drug Administration (FDA). Prior to joining the FDA in 2000, Dr. Bastings was on Faculty at Wake Forest University School of Medicine (Winston-Salem, North Carolina), where he was a member of the Neurorehabilitation section of the Department of Neurology, and he developed the transcranial magnetic stimulation (TMS) laboratory. Dr. Bastings received his medical degree from the University of Liege, Belgium in 1990. After completing his Neurology residency (University of Liege, Belgium) in 1995, he subspecialized in Neurological Rehabilitation during a 2-year fellowship at Wake Forest University. Before coming to the FDA, Dr. Bastings designed or participated in multiple clinical studies (industry or NIH-funded), mostly investigating new drugs for spasticity and multiple sclerosis, and studying recovery after stroke using TMS and functional MRI brain mapping.

Regulatory Requirements in Preparing for Clinical Trials

Eric Bastings, MD

Food and Drug Administration, Silver Spring, MD

This presentation will provide an overview of key regulatory requirements sponsors should take into consideration while preparing for clinical trials. The following elements will be discussed: IND preparation and review process, clinical holds, standards for approval, how to interact with the FDA, safety reporting, and pitfalls in drug development.

SESSION IV

Issues in Technology Transfer: Interactions and Intellectual Property

Chair — Kathleen A. Denis, PhD, The Rockefeller University

Session Overview

Kathleen A. Denis, PhD, The Rockefeller University

Working Effectively with Your TTO: Technology Evaluation Process and IP Protection

Kathleen A. Denis, PhD, The Rockefeller University

Creating Mutually Beneficial Relationships with Industry: Needs, Wants and Paperwork

Louis P. Berneman, EdD, CLP, Texelerate

Should You Start a Biotechnology Company?

John S. Swartley, PhD, University of Pennsylvania

Kathleen A. Denis, PhD, The Rockefeller University



Kathleen A. Denis, PhD, is the Associate Vice President of Technology Transfer at The Rockefeller University, a premier biomedical research institution located in New York City. She is a Past President of the Licensing Executives Society USA/Canada (LES), and has served on the Board of Directors of the Association of University Technology Managers (AUTM) and the Pennsylvania Biotechnology Association. She is a Certified Licensing Professional.

Specializing in the management of intellectual assets in the life sciences, she has worked with academic institutions and industry clients to manage intellectual property portfolios, evaluate new technologies, market and license technologies and start new technology-based businesses. Dr. Denis is active in numerous professional organizations and speaks frequently about early stage technology evaluation, formation of start-up companies, conflict of interest and other issues of academic technology transfer. Dr. Denis holds a PhD in immunology from the University of Pennsylvania, an MA in Human Genetics from University of Texas Medical Branch at Galveston, and an undergraduate degree in genetics from Cornell University.

Working Effectively with Your TTO: Technology Evaluation Process and IP Protection

Kathleen A. Denis, PhD

The Rockefeller University, New York, NY

Technology transfer refers to the numerous interactions between universities and industry. It can mean the publication of research, the delivery of seminars, consultancy, or the transfer of the skills and knowledge that a student brings to his or her future employers. Formally, however, the term denotes the management of intellectual property from research that is sponsored by a company but carried out at a university, and the licensing of university intellectual property to both established and start-up companies.

Technology Transfer Offices (TTO's) have been established at almost all research universities over the past 25 years. Their role is to promote and support the research enterprise at the university by creating relationships with the private sector to develop, protect, transfer and commercialize research results for the public benefit. This session will examine the legal and university policy underpinnings of technology transfer, the various tasks performed by the TTO, how to assess discoveries from your laboratory and how to truly protect them with intellectual property (or not!) and how researchers can productively interact with their TTO.

Louis P. Berneman, EdD, CLP, Texelerate



Louis P. Berneman is an experienced intellectual property licensing and business development executive. He has founded and financed intellectual property-based entrepreneurial ventures, built and managed university technology transfer programs, and has been involved in patenting and licensing since 1982 as both a licensee and licensor. Since September 2005, Dr. Berneman has been the Principal of Texelerate, a consultancy specializing in monetizing intellectual property. From 1995-2005, Dr. Berneman was Managing Director of the Center for Technology Transfer (CTT) at the University of Pennsylvania. From 1989-1995, Dr. Berneman was Director, Licensing and Business Development at Virginia's Center for Innovative Technology patenting and licensing on behalf of the eight public research universities in Virginia. Dr. Berneman is a Past President of the Association of University Technology Managers (AUTM) and a former Vice President and Trustee of the Licensing Executives Society (LES USA & Canada). He currently serves as an advisor and member of the Advisory Board of the Paul Capital Partners Royalty Healthcare Fund. Dr. Berneman holds a baccalaureate degree in history from the Pennsylvania State University, a teaching credential from University of California at Santa Barbara, and masters and doctoral degrees in education from Teachers College, Columbia University.

Creating Mutually Beneficial Relationships with Industry: Needs, Wants and Paperwork

Louis P. Berneman, EdD, CLP

Texelerate, Philadelphia, PA

Academic institutions' technology transfer offices (TTOs) have become increasingly efficient and effective at working with industry. Companies have likewise recognized the value of collaborating with academe. However, conflicting roles, values, drivers, and agendas create numerous challenges in establishing and maintaining positive and productive relationships between academic institutions and companies. Despite differences and challenges, institutions and companies can collaborate to achieve mutual and respective interests. This session will address key issues in forging academic – industry relations related to confidentiality disclosure (CDA), material transfer (MTA), consulting, sponsored and collaborative research (SRA), patent options and licenses, creating start ups, and inter-institutional agreements (IIA).

John S. Swartley, PhD, University of Pennsylvania



John S. Swartley, MBA, PhD, is Deputy Executive Director of the Center for Technology Transfer at the University of Pennsylvania, where he leads technology licensing efforts and the formation of new ventures from Penn discoveries and faculty expertise. Prior to joining Penn in 2007, Dr. Swartley served as Senior Vice President and Partner of BCM Technologies (BCMT), the venture capital investment subsidiary of Baylor College of Medicine. Dr. Swartley joined BCMT in 2003 from the Yale University Office of Cooperative Research where he served as Associate Director of the Medical Campus. Dr.

Swartley has participated in the formation and oversight of more than two dozen university spin-out companies that have collectively raised nearly one billion dollars of investment capital. He holds a BS in Biology from Bates College, an MBA from the Goizueta School of Business at Emory University, and a PhD in Microbial & Molecular Genetics from Emory University.

Should You Start a Biotechnology Company?

John S. Swartley, PhD

University of Pennsylvania, Philadelphia, PA

A recent issue of the Licensing and Activity Survey from the Association of University Technology Managers states that 596 new start-up companies were launched from academic institutions in FY2009. The same report states that over 6,000 new companies have been formed based on university technologies since 1980 (3,423 still in active operation). These start-ups range from companies that simply take a license to university technologies, new ventures that are founded and incubated within the academic institution itself, and everything in between. Companies spun out of academia exhibit an increasingly important economic impact, locally, nationally and globally, and are one of the main drivers of numerous high tech industries, including the biotechnology industry.

This session will examine the criteria and rationale for forming new companies based on discoveries made in academia, followed by an exploration of the process of new venture formation from the scientific founders' perspective. Issues relating to founder expectations, specific roles and responsibilities, potential outcomes, and likely challenges will be covered.

SESSION V

Beyond Small Molecules: Natural Products, Biologics and Repurposing

Chair — Diana Shineman, PhD, Alzheimer's Drug Discovery Foundation

Session Overview

Diana Shineman, PhD, Alzheimer's Drug Discovery Foundation

Natural Products as Drug Leads

Frank E. Koehn, PhD, Pfizer Inc.

Neurotrophic Factors for Alzheimer's Disease: Unique Challenges and Promise

Joao Siffert, PhD, Ceregene, Inc.

The Road to Repurposing a Drug: Isradipine

D. James Surmeier, PhD, Northwestern University

Diana Shineman, PhD, Alzheimer's Drug Discovery Foundation



Diana Shineman, PhD, is the Assistant Director for Scientific Affairs at the Alzheimer's Drug Discovery Foundation, where she is responsible for developing and managing all aspects of the Foundation's drug discovery research programs. Dr. Shineman earned her PhD in Cell and Molecular Biology from the University of Pennsylvania (Penn). At Penn's renowned Center for Neurodegenerative Disease Research led by Drs. Virginia Lee and John Trojanowski, she studied signal transduction pathways that alter amyloid generation in Alzheimer's disease. Dr. Shineman also worked with the Center's

Drug Discovery Group to perform high-throughput screening using cell-based assays. In addition to her dissertation research, Dr. Shineman was as an Editorial Intern for the Journal of Clinical Investigation and was an active member of the Penn Biotechnology Group. Dr. Shineman received a BA in Biology with a Nutrition concentration from Cornell University, where she was named a Howard Hughes Undergraduate Research Scholar. She is also a member of the Society for Neuroscience and an author on numerous peer-reviewed publications.

Frank E. Koehn, PhD, Pfizer Inc.



Frank E. Koehn is Research Fellow and Head of the Natural Products Laboratory at Pfizer Worldwide R&D. Dr. Koehn obtained his BS degree in Chemistry from Butler University, Indianapolis Indiana in 1977, and did his PhD research on marine red tide neurotoxins at the University of Wisconsin–Madison, USA. Following postdoctoral work in plant natural products at the University of Pennsylvania, he joined the Harbor Branch Oceanographic Institution in Fort Pierce, Florida, USA, where he spent the next decade identifying biologically active molecules from marine macro and micro-organisms. Intrigued by the therapeutic potential of natural product-based drug candidates, Dr. Koehn joined the Natural Products and Analytical Chemistry program at Lederle Laboratories in 1994, which subsequently became Wyeth Research. In 2010 he joined Pfizer as Natural Products Laboratory head. At Pfizer, Dr. Koehn’s research group is focussed on the discovery and application of microbial natural products to address unmet medical need.

Natural Products as Drug Leads

Frank E. Koehn, PhD

Pfizer Inc., Groton, CT

Natural products, compounds produced by plants, microbes and animals have historically served as an unsurpassed direct source of new medicines, and an equally vast source of chemical inspiration for synthetic drug leads. In addition, natural products have been a primary means of discovering new drug targets. Over the past decade, evolution of the drug discovery landscape has simultaneously brought a reduction in traditional natural products methods and an emergence of new approaches based on genomics, chemical biology and biosynthesis. This talk will introduce how these new approaches play a role in modern lead generation, and how they impact the search for new medicines for neurodegenerative diseases.

Joao Siffert, PhD, Ceregene, Inc.



Dr. Siffert has been Chief Medical Officer of Ceregene since 2007 and oversees the clinical development activities in Parkinson's and Alzheimer's disease. Previously, Dr. Siffert served as the Chief Medical Officer at Avera Pharmaceuticals, a CNS specialty pharma company. Prior to joining Avera, Dr. Siffert held positions with Pfizer as the Worldwide Medical Team Leader in areas of pain and epilepsy of various products including Relpax, Lyrica and Neurontin. He was also instrumental in the Phase 3b/4 program development and global launch of Lyrica. Prior to Pfizer, Dr. Siffert held academic positions at Beth Israel Medical Center, where he served as director of the Adult Neuro-Oncology program, and Albert Einstein College of Medicine, where he was assistant professor of neurology. During his tenure at Beth Israel, Dr. Siffert was actively involved in clinical research of novel therapies for patients with brain and spinal cord tumors. He completed residencies in pediatrics at New York University School of Medicine and in neurology at Harvard Medical School. Dr. Siffert was certified by the American Board of Neurology and Psychiatry. He holds an MD degree from the University of São Paulo School of Medicine as well as an MBA degree from Columbia University Business School.

Neurotrophic Factors for Alzheimer's Disease: Unique Challenges and Promise

Joao Siffert, PhD

Ceregene, Inc., San Diego, CA

Loss of neurons of the nucleus basalis of Meynert (NBM), a major source of cholinergic innervation to the cerebral cortex, has been linked to the cholinergic deficiency and associated cognitive loss in Alzheimer's disease (AD). Indeed, most available AD treatments work by inhibiting the breakdown of the neurotransmitter acetylcholine (ACh) in these neurons. However, because of dose-limiting toxicity (due to effects on other cholinergic neurons), none provide satisfactory or lasting symptomatic relief. Moreover, none prevent further neurodegeneration or cell death, and therefore do not improve disease progression. Thus, a significant medical need exists which might be significantly improved by treatments that more selectively target these neurons. Human β -nerve growth factor (NGF) has shown a robust ability to improve the function and protect degenerating neurons of the NBM in numerous animal models. Thus, administration of NGF to the NBM of AD patients may provide symptomatic benefit (by restoring function) as well as modify the disease course (by preventing further degeneration). However, neurotrophic factors do not readily cross the BBB and lead to serious adverse events following systemic injections. Poor protein diffusion in brain parenchyma limits the ability to reach targets when injected directly into brain. Convection-enhanced delivery (CED) significantly increases the volume of protein spread but increases the risk of off-target adverse effects. Gene transfer has been shown to circumvent delivery issues by directly transducing genes into degenerating neurons. Transduced cells express and secrete a constant supply of the neurotrophic factor at the site where it is needed. CERE-110 is an AAV2-based vector engineered to deliver NGF to the NBM. Nonclinical studies demonstrated that CERE-110 was effective in preventing the degeneration of cholinergic neurons in the rat fimbria-fornix lesion and the aged rat models. Together with extensive safety and feasibility testing in animals, these studies provided the basis for the initial study in humans. An initial feasibility and dose-escalation study in 10 subjects with AD showed that bilateral administration of CERE-110 to the NBM was safe. With a minimum follow-up of 2-5+ years, the safety profile of CERE-110 has remained favorable. A multicenter, randomized, double-blind Phase 2 study in 50 subjects with mild/moderate AD being conducted in collaboration with the Alzheimer's Disease Cooperative Study (ADCS) is underway.

D. James Surmeier, PhD, Northwestern University



Dr. James Surmeier is the Nathan Smith Davis Professor and Chair of the Department of Physiology at the Feinberg School of Medicine at Northwestern University and Director of the Morris K. Udall Parkinson's Disease Research Center of Excellence at Northwestern University. Dr. Surmeier received his PhD in Physiology and Biophysics from the University of Washington in 1983. He trained with leaders in the field of neurophysiology, including Dr. Arnold Towe, Dr. William Willis and Dr. Stephen Kitai. In 1998, he moved to the Department of Physiology at Northwestern University and assumed his current position in 2001. Dr. Surmeier's research program focuses on the mechanisms underlying neural activity in the basal ganglia and how it changes in disease

states, like Parkinson's disease. He has pioneered the application of modern patch clamp, single cell gene profiling and optical approaches to understanding basal ganglia physiology, authoring over 125 peer-reviewed publications in journals such as *Science*, *Nature*, *Neuron*, *Nature Neuroscience* and the *Journal of Neuroscience*. He has served in several advisory capacities to the National Institutes of Health, including chairing study sections for NINDS and acting as a Councilor for NIAAA. He also serves on the scientific advisory boards of the Hereditary Disease Foundation, the Dystonia Medical Research Foundation, the Hartman Foundation, and the Bachmann-Strauss Dystonia and Parkinson's Disease Foundation. He also serves on a number of editorial boards, including those of *Neuron* and *Current Opinion in Neurobiology*. He has received many scientific awards including the NARSAD Established Investigator award, the Riker Award and the Jacob Javits Neuroscience Investigator Award.

The Road to Repurposing a Drug: Isradipine

D. James Surmeier, PhD

Northwestern University, Chicago, IL

The factors governing neuronal loss in Parkinson's disease (PD) are the subject of continuing speculation and experimental study. In recent years, non-cell autonomous factors, particularly genetic mutations and environmental toxins, have dominated public discussions of disease etiology. Although there is compelling evidence supporting an association between disease risk and these factors, the pattern of neuronal pathology and cell loss is difficult to explain without cell autonomous factors. This talk will focus on recent studies showing that the neurons at greatest risk in PD – substantia nigra pars compacta (SNc) dopamine (DA) neurons – have a distinctive physiological phenotype that could contribute to their vulnerability. The opening of L-type calcium channels during autonomous pacemaking results in sustained calcium entry into the cytoplasm of SNc DA neurons, resulting in elevated mitochondrial oxidant stress and susceptibility to toxins used to create animal models of PD. This cell autonomous stress could increase the negative consequences of non-cell autonomous factors that broadly challenge either mitochondrial or proteostatic competence. The availability of the hypertension medication isradipine, a well-tolerated, orally deliverable dihydropyridine antagonist of the L-type calcium channels underlying oxidant stress in SNc DA neurons, points to a novel neuroprotective strategy that could complement current attempts to boost mitochondrial function in the early stages of the disease.

SESSION VI

Case Studies

Chair — Brian Fiske, PhD, The Michael J. Fox Foundation for Parkinson's Research

Session Overview

Brian Fiske, PhD, The Michael J. Fox Foundation for Parkinson's Research

Neurotrophic Factor Mimetics: Target Validation to Lead Optimization

Frank M. Longo, MD, PhD, Stanford University

Development of Tysabri for Multiple Sclerosis

Ted Yednock, PhD, Elan Pharmaceuticals, Inc.

Novel Ways to Reduce Protein Aggregation

Alan D. Snow, PhD, ProteoTech, Inc.

Brian Fiske, PhD, The Michael J. Fox Foundation for Parkinson's Research



Dr. Brian Fiske is Director of Research Programs at The Michael J. Fox Foundation for Parkinson's Research. He earned his PhD in Neuroscience from the University of Virginia with a focus on the neurobiology of brain development. After a postdoctoral fellowship at Columbia University, Dr. Fiske joined the editorial staff of the journal *Nature Neuroscience*, before arriving at The Michael J. Fox Foundation in late 2004. Dr. Fiske's responsibilities include managing a large and growing grants portfolio, as well as developing strategies to facilitate and streamline research and drug development efforts in Parkinson's disease.

Frank M. Longo, MD, PhD, Stanford University



Dr. Longo received his MD in 1981 and PhD in Neurosciences in 1983 from the University of California, San Diego. Following an internship in medicine at NYU/VIA, he trained as a resident in neurology and fellow in neurobiology at University of California, San Francisco. While at UCSF he created the Neurogenetics Clinic which was the first West Coast site in the U.S. to offer DNA testing for families with Huntington's disease. He also led the creation of a national referral center for deep brain stimulation for Parkinson's disease and contributed to the development of programs in dementia, epilepsy and other areas. At UCSF he became professor and vice chair of the Department of Neurology and in 2001 he was recruited to become chair of the Department of Neurology at the University of North Carolina, Chapel Hill. While at UNC, Dr. Longo launched or expanded programs for Alzheimer's disease and other dementias, stroke, epilepsy, sleep disorders, multiple sclerosis and Parkinson's disease. In January 2006, Dr. Longo became chair of the Department of Neurology and Neurological Sciences at Stanford where he is focused on building and expanding multidisciplinary programs in neurology and neuroscience. In 2006 he was named a Stanford Fellow. Dr. Longo's research team focuses on elucidating novel mechanisms that prevent neural degeneration and promote regeneration. He and his colleagues have pioneered the development of small, drug-like, molecules that target neurotrophin receptors to delay onset of or slow progression of Alzheimer's and other neurodegenerative disorders.

Neurotrophic Factor Mimetics: Target Validation to Lead Optimization

Frank M. Longo, MD, PhD

Stanford University, Stanford, CA

In this Case Study Session, we will review the pathway taken, in an academic setting, starting at novel target validation and proceeding through small molecule screening, lead characterization and preclinical studies. We executed a series of studies indicating that the p75 neurotrophin receptor regulates fundamental signaling mechanisms relevant to synaptic dysfunction and degenerative signaling mechanisms occurring in Alzheimer's disease. Neurotrophins function as ligands for p75 and in a number of contexts promote death through p75 signaling. Based on our early work with synthetic peptides mimicking the neurotrophin loop 1 domain, we hypothesized that non-peptide, small molecule ligands of p75 might be created that would preferentially activate p75-induced survival signaling and counteract degenerative signaling. We used neurotrophin loop 1 domain features to design pharmacophores which were used to screen *in silico* small molecule libraries with the goal of finding non-peptide, small molecule p75 receptor ligands. Resulting hits were characterized for their p75 binding and signaling properties. Selected compounds were further characterized in *in vitro* Alzheimer's disease-relevant models. Compounds demonstrating the ability to inhibit A β -induced degeneration were submitted for ADMET evaluation. A lead and backup compound were applied in a number of mouse-based preclinical studies and found to demonstrate morphological and/or behavioral efficacy in aged mice, and in the Tg2675, hAPP-L/S and Ts65n AD models. We will discuss issues of *in silico* screening, lead characterization, ADMET and preclinical studies in an academic setting. Experiences with grant funding and options for moving academic-derived technology into the commercial sector will also be discussed. *This work has been funded by the ADDF and an NIA U01.*

Dr. Frank Longo is a founder of Pharmatropix, a company focused on the development of neurotrophin receptor small molecule ligands.

Ted Yednock, PhD, Elan Pharmaceuticals, Inc.



Dr. Yednock is Executive Vice President, Head of Global Research for Elan Pharmaceuticals. During Dr. Yednock's tenure at Elan, he initiated research on Multiple Sclerosis which led to the development of Tysabri as a drug for treatment of MS and Crohn's disease. Since that time, Dr. Yednock has contributed to the invention or progression of more than a dozen drugs in the areas of Alzheimer's, Alzheimer's immunotherapy, Parkinson's disease, Rheumatoid Arthritis, and Crohn's disease. He earned his BS in Biology and Chemistry from the University of Illinois, his PhD in Anatomy and Cell Biology from UCSF as well as postdoctoral work in Immunology from the same institution.

Development of Tysabri for Multiple Sclerosis

Ted Yednock, PhD

Elan Pharmaceuticals, Inc., South San Francisco, CA

Relapsing forms of Multiple Sclerosis are characterized by migration of auto-reactive lymphocytes into the CNS, resulting in demyelination and neuronal loss. An antibody screen looking for inhibitors of lymphocyte adhesion to inflamed brain endothelium revealed a critical role for $\alpha 4\beta 1$ integrin in immune cell infiltration of the CNS. These observations lead to the development of TYSABRI® (Natalizumab), a humanized monoclonal antibody against $\alpha 4$ integrin, which has been approved for treatment of patients with relapsing forms of Multiple Sclerosis. Over 75,000 patients with relapsing forms of MS have been treated with TYSABRI, and it has been shown to delay the accumulation of physical disability and reduce the frequency of clinical exacerbations. TYSABRI has a rare but serious side effect: It increases the risk of Progressive Multifocal Leukoencephalopathy (PML), an opportunistic viral infection of astrocytes and myelin-producing oligodendrocytes by the polyoma JC virus that usually leads to death or disability. An assay has been developed to help identify patients infected by JCV. While approximately half of the patient population carries antibodies to the JC virus, as of December 2010 all patients with plasma samples available prior to onset of PML have been serum antibody positive (n=22). The assay has been submitted to regulatory authorities for review as a potential tool to stratify the risk of PML in patients treated with TYASABRI.

Alan D. Snow, PhD, ProteoTech, Inc.



Dr. Alan D. Snow is Chairman, President and Chief Scientific Officer of ProteoTech Inc., a private Company that is developing a pipeline of drugs targeting amyloid diseases including Alzheimer's, Parkinson's, systemic amyloidosis and type 2 diabetes. He previously served as a Research Associate Professor of Pathology at University of Washington (Seattle, WA) and is a world-recognized authority on amyloid diseases. He holds a BS degree in Biology/Chemistry from Bowling Green State University in Ohio, a MS degree in Anatomy from University of Western Ontario (Canada), and a PhD in Pathology from Queen's University (Canada). His PhD research led to new discoveries

pertaining to the pathogenic role that proteoglycans play in amyloid diseases. Dr. Snow founded ProteoTech and left the University of Washington in 1999 to serve as the Company's first CEO. Currently, two small molecule drugs are in human clinical trials that were developed at ProteoTech: 1) Exebryl-1[®] targeting both beta-amyloid protein and tau protein for Alzheimer's disease and 2) Systebryl[™] targeting AA amyloid for systemic AA amyloidosis. Other drugs in ProteoTech's pipeline in late pre-clinical development include the small molecule Synuclere[™] targeting alpha-synuclein aggregates in Parkinson's disease, and the small D-amino acid peptide, Pepticlere[™] targeting beta-amyloid protein for Alzheimer's disease. Since being at ProteoTech Dr. Snow has acquired over \$15 million in grant funding, and is an inventor on over 100 issued patents pertaining to the development of new drugs for different amyloid diseases.

Novel Ways to Reduce Protein Aggregation

¹Alan D. Snow, ¹Joel Cummings, ¹Marisa-Claire Yadon, ¹Tom Lake, ¹Michael Hudson, ¹Eric Jacobson, ¹Qubai Hu, ¹Judy Cam, ²Manfred Weigele, ³Anil Kumar, ⁴Eliezer Masliah, ⁴Edward Rockenstein, ⁵Ben Wolozin, ¹Steve Runnels, ¹Luke Esposito

¹ProteoTech Inc., Kirkland, WA; ²Boston, MA; ³MedChem Source, Federal Way, WA; ⁴University of California-San Diego, San Diego, CA; ⁵Boston University, Boston, MA.

Parkinson's disease (PD) is a neurodegenerative disorder pathologically characterized by the presence and accumulation of a protein known as alpha-synuclein. Mutations in alpha-synuclein have been directly linked to familial PD, and alpha-synuclein aggregation and persistence in dopaminergic neurons is associated with the loss of these cells in the brains of people with PD. Inhibition or reduction of alpha-synuclein aggregation in dopaminergic neurons is an important therapeutic target for the treatment of PD and related disorders. Similarly, Alzheimer's disease (AD) is a neurodegenerative disorder pathologically characterized by the accumulation of amyloid plaques (containing beta-amyloid protein) and neurofibrillary tangles (containing tau protein). A reduction of beta-amyloid protein and tau protein aggregates are believed to be important therapeutic targets for the treatment of AD and related disorders.

ProteoTech scientists in conjunction with some of the leading researchers in the PD and AD fields have developed a small molecule library that specifically target different amyloid proteins. Identification and design of this small molecule library based on lead optimization, SAR studies and molecular modeling will be discussed. Our approach to identifying the most efficacious lead drugs for these diseases included *in vitro* and cell culture/cell model screening, safety and drugability testing, and efficacy testing using appropriate transgenic animal models. From these studies, we have developed Exebryl-1[®], a small molecule targeting beta-amyloid protein and tau protein currently in Phase 1 human clinical trials; and Synuclere[™], a small molecule targeting alpha-synuclein aggregates that is in late pre-clinical development. These drugs are postulated to be disease-modifying therapeutics for the treatment of AD and PD, and related disorders.

Funded by ProteoTech Inc. and a LEAPS Award from The Michael J. Fox Foundation for Parkinson's Disease Research.

SESSION VII

Resources and Services for Advancing Drug Discovery

Chair — Suzana Petanceska, PhD, National Institute on Aging

Session Overview

Suzana Petanceska, PhD, National Institute on Aging

Academic Models of Drug Discovery Services and Utilizing CROs

Marcie Glicksman, PhD, Harvard NeuroDiscovery Center

Resources at the National Institute of Health

Rebecca Farkas, PhD, National Institute on Neurological Disorders and Stroke

Neil S. Buckholtz, PhD, National Institute on Aging

Suzana Petanceska, PhD, National Institute on Aging



Dr. Suzana Petanceska received a BS degree in molecular biology and physiology from the University of Belgrade, Yugoslavia and a PhD degree in Pharmacology from New York University. Following her postdoctoral training at Rockefeller University (1995-1998) and at the Nathan Kline Institute of NYU (1998-2000) she became an Assistant Professor of Psychiatry and Pharmacology at the Nathan Kline Institute of NYU (2001-2005). Her research focused on the role of disrupted sterol metabolism in the development of Alzheimer's disease amyloidosis and the mechanisms by which estrogens and cholesterol-lowering drugs might exert neuroprotection. In 2005 she joined the Neuroscience and Neuropsychology of Aging Program at the National Institute on Aging where she serves as a Program Director covering research areas that address the role of metabolic and vascular factors in normal brain aging and in Alzheimer's disease. She also facilitates the development of NIA's drug discovery and preclinical drug development initiatives for AD, mild cognitive impairment and age-associated cognitive decline.

Marcie Glicksman, PhD, Harvard NeuroDiscovery Center



Marcie Glicksman is Senior Director, Leads Discovery Group at LDDN. Dr. Glicksman has extensive experience in assay development, high throughput screening, chemical databases, animal pharmacology and preclinical development. Her bachelor's degree is from Brown University and PhD from Washington University. Before joining LDDN in 2004, she had been in industry for thirteen years. Previously, she was at the start-up company, Descartes Therapeutics focused on imaging techniques. Before this, she was Director of Leads Discovery at Cubist. Before this, she was at DuPont-Merck and at Cephalon, Inc. She led the assay development and screening program for a cell-based protease project, and numerous G-protein coupled receptors, many of which were continued when Bristol Myers Squibb bought DuPont Pharmaceuticals. At Cephalon, she was co-inventor of CEP1347, a neuroprotective agent directed at a novel kinase, currently in Phase III clinical trials. She also consults for industry. She is a board member of the non-profit drug discovery organization Society for Biomolecular Screening and currently serves as the Chairman.

Academic Models of Drug Discovery Services and Utilizing CROs

Marcie Glicksman, PhD

Harvard NeuroDiscovery Center, Boston, MA

The model of drug discovery is changing. As the pharmaceutical industry looks for later stage projects to fill their pipeline and decrease their research efforts, there is a gap that has formed between basic research and the identification of drug candidates. The Laboratory for Drug Discovery in Neurodegeneration (LDDN) at the Harvard NeuroDiscovery Center works with academic labs around the world in a collaborative model of drug discovery focused on approaches that are not commonly found in the pharmaceutical industry. Our primary mission is to accelerate the development of therapeutics for neurodegenerative diseases. As a small group of fifteen that covers biology, medicinal chemistry, informatics and computational chemistry, we use some external resources for needs not covered internally. Unexpectedly, the vendor community is a rich source for collaboration that allows the academic community access to new technologies. Details will be provided on the academic models of drug discovery and the use of Contract Research services.

Rebecca Farkas, PhD, National Institute on Neurological Disorders and Stroke



Dr. Rebecca Farkas is a program director in the National Institute of Neurological Disorders and Stroke (NINDS) at the NIH. Dr. Farkas oversees the Medicinal Chemistry for Neurotherapeutics Program, which is part of the NIH Blueprint Neurotherapeutics Network. The Blueprint Neurotherapeutics Network provides researchers with their own “virtual pharma,” offering research funding and access to a full range of industry-style drug development services and expertise. Dr. Farkas also provides leadership on translational research training initiatives and efforts to advance translational projects toward commercialization. Dr. Farkas received her PhD in Developmental Biology at

Stanford University School of Medicine and her BA in Molecular Biophysics and Biochemistry from Yale University. She served as a science policy analyst in the NINDS Office of Science Policy and Planning for seven years before joining the NINDS Office of Translational Research.

Resources at the National Institute of Health

Rebecca Farkas, PhD

National Institute on Neurological Disorders and Stroke, Bethesda, MD

The translation of basic science into patient therapies is a critical mission of the National Institutes of Health. The Office of Translational Research (OTR), within NINDS, manages multiple initiatives in drug discovery and preclinical development of neurological therapeutics. These initiatives include: Exploratory Projects in Translational Research, Cooperative Agreement Program in Translational Research, Anti-Convulsant Screening Program, Small Business Program, Spinal Muscular Atrophy Project, Blueprint Neurotherapeutics Grand Challenge, CounterACT, NIH RAID (Rapid Access to Interventional Development) and certain programs within the NIH Roadmap. An overview of OTR activities in drug discovery will be presented and the funding mechanisms available to these programs will be discussed.

Neil S. Buckholtz, PhD, National Institute on Aging



Neil S. Buckholtz, PhD, is Chief of the Dementias of Aging Branch of the Neuroscience and Neuropsychology of Aging Program at the National Institute on Aging (NIA), National Institutes of Health (NIH), Bethesda, Maryland. This involves overall programmatic responsibility for development, coordination, and implementation of basic and clinical Alzheimer's disease research. Specifically Dr. Buckholtz is the program administrator for the areas of diagnosis and treatment and management of Alzheimer's disease. Dr. Buckholtz holds a doctorate in physiological psychology from the University of Wisconsin, Madison and was a faculty member at the Medical University of South Carolina, Department of Psychiatry, from 1970-1983, before coming to NIH.

Resources at the National Institute of Health

Neil S. Buckholtz, PhD

National Institute on Aging, Bethesda, MD

Dr. Buckholtz will give an overview of the National Institute on Aging's Alzheimer's disease translational research program and the current NIA funding opportunities for drug discovery and preclinical drug development. He will also highlight translational research resources at the greater NIH-level and provide practical advice on how the extramural community can best take advantage of the above funding opportunities and resources.