

Agenda

NNFF International Consortium for the Molecular Biology of NF1 and NF2

June 4-7, 2000

PRELIMINARY AGENDA

Hotel Jerome
330 East Main Street
Aspen, Colorado
Tel. 800-331-7213

Chairpersons

Andrea McClatchey, PhD
Harvard Medical School
Massachusetts General Hospital

Kevin Shannon, MD
UCSF

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Sponsors

The National Neurofibromatosis Foundation and the organizers gratefully acknowledge support from:

National Institute of Neurological Disease and Stroke

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Program

NNFF Consortium for the Molecular Biology of NF1 and NF2

Aspen June 4-7, 2000

4:00PM - 7:30PM **Registration and Reception**

Topic: Therapeutic Strategies and Clinical Results
Chairs: Jackson Gibbs, Merck, Inc. and Kevin Shannon, UCSF

Session 1: Sunday June 4, 2000 - 7:00 PM -10:10 PM

7:00-7:10 PM

Welcome:

Peter Bellermann
NNFF

Opening Remarks:

Kevin Shannon,
UCSF

7:10-7:40 PM

NF at the Millennium - A Retrospective and Prospective View

Jim Gusella,
Harvard/MGH

7:40-8:10 PM

Farnesyltransferase Inhibitors as Potential Anti-Cancer Agents

Jay Gibbs,
Merck, Inc.

8:10-8:25 PM

Phase 1 Trial of the Farnesyltransferase Inhibitor R115777 in Children with Refractory Solid Tumors and NF1 And Progressive Plexiform Neurofibromas

Wanda Salzer,
USAF Keesler
Medical Center

8:25-8:40 PM Break

8:40-9:05 PM

MEK Inhibitors: Targeting the MAP Kinase Pathway for the Development of New Anticancer Therapies

Judy Leopold,
Parke-Davis Research Laboratories

9:05-9:30 PM

CP-358,774: An Inhibitor of Epidermal Growth Factor Receptor Tyrosine Kinase in Phase II Clinical Trial

Jim Moyer,
Pfizer Central
Research Laboratories

9:30-9:55 PM
Preclinical and Clinical Evaluation of the Anti-Angiogenesis Kinase Inhibitors SU5416 and SU6668

Jerry McMahon,
SUGEN, Inc.

10:00 PM Beer Tasting Session

Topics: Animal Models and Genetics
Chair: Rick Fehon, Duke University

Session 2: Monday morning, June 5, 2000 - 8:30 AM-11:50 AM

8:30-8:40 AM
Introduction and update: US Army National Neurofibromatosis Research Program

Dr. Omar Hottenstein
Lt. Commander
U.S. Navy

8:40-8:50 AM
Opening remarks, chair

Rich Fehon
Duke University

8:50-9:40 AM
Keynote: Telomerase and Tumor Suppressors

Ron DePinho, Harvard/Dana-Farber
Cancer Institute

9:40-9:55 AM
Hyperproliferation of NF1 Heterozygous Mast Cells in Response to Stem Cell Factor Via Crosstalk Between the PI-3 and the RAS-RAF-ERK Kinase Pathway

Wade Clapp,
Indiana University

9:55-10:10 AM
Regulation of Neurofibromin by the Proteasome and its Effect on the Ras-Map Kinase Pathway

Karen Cichowski,
MIT

10:10-10:30 AM
Genetic analysis of Merlin/ERM Function

Rick Fehon,
Duke University

10:30-10:45 AM Break

10:45-11:05 AM
Non-autonomous, Ras-independent functions for NF1 in Drosophila

Andre Bernards,
Harvard/MGH

11:05-11:20 AM
NF1-Dependent Activation of Adenylyl Cyclase(S) in Invertebrates and Vertebrates

Hui-Fu Guo,
Cold Spring Harbor Laboratory

11:20-11:35 AM
Molecular Pathogenesis of NF1 Microdeletions

C. Lopez-Correa,
Center for Human Genetics, Belgium

11:35-11:50 AM
NF1 Gene Loss by Homologous Recombination at Flanking Hotspots

Michael Dorschner,
University of Washington, Seattle

Topic: Biochemical Functions of Neurofibromin and Merlin/Schwannomin
Chair: Jeff DeClue, NCI

Session 3: Monday evening. June 5, 2000 - 7:45 PM-10:10 PM

7:45-7:55 PM
Opening Remarks, Chair

Jeff DeClue,
NCI

7:55-8:45 PM
Keynote: The Role of the PI3K Pathway in Tumor Cell Proliferation and Survival

David Stokoe,
UCSF

8:45-9:05 PM
The Role of the EGF Receptor in NF1 Development and NF1 Model Systems

Tumor Jeff DeClue,
NCI

9:05-9:20 PM Break

9:20-9:35 PM
Neurofibromin Gap Related Domains (GRDs) Restore Normal Growth in NF1 $-/-$ Cells

Kelly Hiatt,
Indiana University

9:35-9:55 PM
A TBC Domain-Containing Protein Associates with the ERM-Merlin Interactor EBP50/NHERF

David Reczek,
Cornell University

9:55-10:10 PM
The NF2 Tumor Suppressor Merlin and Its Interactions

Thorsten Wiederhold,
Harvard/MGH

Topic: Molecular and Cell Biology 1
Chair: Andrea McClatchey, MGH Cancer Center

Session 4: Tuesday morning, June 6, 2000 - 8:30 AM-11:40 AM

8:30-8:40 AM
Opening Remarks, Chair

Andrea McClatchey
Harvard/MGH

8:40-9:30 AM
Essential roles for Rho GTPase Activating Proteins (GAPs) in Mammalian Neural Development

Jeff Settleman,
Harvard/MGH

9:30-9:45 AM
The TSC1 Tumour Suppressor Hamartin Regulates Cell Adhesion through ERM Proteins and the GTPase Rho

Richard Lamb,
MRC, London, UK

9:45-10:00 AM
Evidence that the Focal Adhesion Protein Paxillin Closely Interacts with Merlin in Primary Rat Schwann Cells

Jerome Ricard,
University of Central Florida

10:00-10:20 AM

The NF2 tumor suppressor gene product, merlin,
mediates contact inhibition and cell cycle progression through interactions with CD44

Helen Morrison,
University of Karlsruhe, Germany

10:20-10:35 AM Break

10:35-10:55 AM

The NF2 Tumor Suppressor, Merlin, is a Sensor of Rac-Mediated Signaling

Andrea McClatchey,
Harvard/MGH

10:55-11:10 AM

NF2 Tumor Suppressor Schwannomin Interaction with HRS Regulates STAT Signaling and Schwann Cell Proliferation

Daniel Scoles,
UCLA

11:10-11:25 AM

Merlin Selectively Binds F-but not G-Actin and Stabilizes the Filaments

Marianne James,
MGH

11:25-11:40 AM

N-Terminal Folding of the NF2 Tumor Suppressor Protein Regulates Subcellular Localization and Protein

Laurence Goutebroze,
INSERM U434 - CEPH,
Interactions Paris, France

Topic: Molecular and Cell Biology 2
Chair: Tyler Jacks, MIT

Session 5: Tuesday Evening, June 6, 2000 - 7:45 PM-10:05 PM

7:45-7:55 PM

Opening Remarks, Chair

Tyler Jacks,
MIT

7:55-8:15 PM

Modeling Cancer in the Mouse

Tyler Jacks,
MIT

8:15-8:30 PM
Analysis of NF1 Mutations and Cellular Defects in Neurofibroma-Derived Cells

Lynn Rutkowski,
University of Pennsylvania

8:30-8:45 PM
Schwann Cells are the NF1 (-/-) Cells in Neurofibromas

Eduard Serra,
Hospital Duran I Reynals, Barcelona, Spain

8:45-9:00 PM Break

9:00-9:20 PM
Mouse NF1 mutant Schwann Cells: Phenotype Plasticity and Signaling Abnormalities

Nancy Ratner,
University of Cincinnati

9:20-9:35 PM
The Role of the NF1 Gene as a Negative Growth Regulator for Astrocytes

David Gutmann,
Washington University, St. Louis

9:35-9:50 PM
CD44 Mediates Malignant Peripheral Nerve Sheath Tumor Cell Invasion and is Regulated by the Epidermal Growth Factor Receptor

Larry Sherman,
University of Cincinnati

9:50-10:05 PM
Evaluation of the Efficiency and Sensitivity of the PTT for the NF1 Gene in Familial and Sporadic Patients

L. Messiaen,
Ghent University, Belgium

Topic: Animal Models 2
Chair: Luis Parada, University of Texas, Southwestern

Session 6: Wednesday, June 7, 2000 - 9:00 AM-11:30 AM

9:00-9:10 AM
Opening Remarks, chair

Luis Parada,
University of Texas, Southwestern

9:10-9:50 AM
Mouse Models

Luis Parada,
University of Texas, Southwestern

9:50-10:05 AM
Astrocyte Specific ablation of NF1 results in Abnormal neural development and Tumorigenesis

Yuan Zhu,
University of Texas, Southwestern

10:05-10:20 AM
Evidence for Genetic Modifiers of Tumor Latency and Tumor Spectrum in a Mouse Model of NF1

Karlyne Reilly,
MIT

10:20-10:35 AM Break

10:35-10:55 AM
Mouse Tumor Models for Neurofibromatosis Type 2

Marco Giovannini,
INSERM U434 - CEPH,
Paris, France

10:55-11:10 AM
NF1 and Cytokine Signaling in Blood Cell Progenitor Expansion and Myeloid Leukemia

David Largaespada,
University of Minnesota

11:10-11:25 AM
Identification of Loci Involved in Progression of NF1 Associated Myeloid Leukemia

Susan Blaydes,
University of Florida

Adjunct Meetings and Sessions:

Poster Session #1: Monday, June 5, 2000 - 4:00 PM - 6:00 PM

Poster Session #2: Tuesday, June 6, 2000 - 4:00 PM - 6:00 PM

NINDS Workshop: Tuesday, June 6, 2000 - 3:30PM - 5:00 PM Ballroom

CCAB Meeting: Saturday, June 3, 2000 - 2:00PM - 4:00 PM - Aspen Club Lodge Room

Medical Policy Committee: Monday June 5, 2000 - 1:00PM - 2:30 PM - Hotel Jerome