

Tuberous Sclerosis Complex: From Genes to New Therapeutics

September 23-25, 2007
Loews Annapolis Hotel
Annapolis, MD

Sunday, September 23, 2007

8:00 AM – 9:00 PM Conference Registration

Annapolis Atrium, First Floor
Main Hotel

Opening Session **Regatta Ballroom, First Floor, Main Hotel**

Session Chair: Hiroaki (Rocky) Onda, Jackson Laboratories, Bar Harbor, ME & TS Alliance Board of Directors

3:00 – 3:15 PM Conference Welcome
Kari Luther Carlson, Acting CEO, TS Alliance
Terry Elling, Chair, TS Alliance Board of Directors

3:15 – 3:45 PM Understanding the Function of the TSC1/2 Genes
Cheryl Walker, UT MD Anderson Cancer Center, Smithville, TX

3:45 – 4:15 PM Clinical Manifestations of TSC
Michael Frost, Minnesota Epilepsy Group, St. Paul, MN

4:15 – 4:30 PM Break

Session I: Regulation of Growth and Neoplasia in TSC and LAM **Regatta Ballroom, First Floor, Main Hotel**

Session Chair: Raymond Yeung, University of Washington School of Medicine, Seattle, WA

4:30 – 4:40 PM Living with TSC
TBD

4:40 – 5:10 PM Angiomyolipomas, Cysts, and LAM: Pathogenic Mechanisms
Elizabeth Petri Henske, Fox Chase Cancer Center, Philadelphia, PA

5:10 – 5:30 PM Signaling Through the mTORC1 and mTORC2 Pathways
David M. Sabatini, Whitehead Institute, Cambridge, MA

5:30 – 5:45 PM The LKB1 Tumor Suppressor is a Metabolic Checkpoint Regulating Cell Growth
Dana M. Gwinn, David B. Schackelford, Dan F. Egan & **Reuben J. Shaw**, Salk Institute for Biological Studies, La Jolla, CA

5:45 – 6:00 PM The Role of Tuberin for the Cell Cycle Regulation of Cytoplasmic and Nuclear mTORC1 and mTORC2 Activities
Margit Rosner and **Markus Hengstschläger**, Medical University of Vienna, Vienna, Austria

- 6:00 – 6:15 PM Control of Signal Transducer and Activator of Transcription-1 by the mTOR-Associated Phosphatase PP2A
Jill Fielhaber, Ying-Shan Han, Kwong-Bo Joung & Arnold S. Kristof, McGill University, Montreal, Quebec, Canada
- 6:15 – 6:35 PM Cell Migration Defects in TSC and LAM
Vera P. Krymskaya, University of Pennsylvania, Philadelphia, PA
- 6:35 – 6:55 PM The Biology of Hypoxia: The Role of Oxygen Sensing in Development, Normal Function, and Disease
M. Celeste Simon, University of Pennsylvania Cancer Center, Philadelphia, PA
- 6:55 – 7:15 PM Regulation of mTOR Function in Response to Hypoxia by REDD1 and the TSC1/TSC2 Complex
Silvia Vega-Rubin de Celis, Nicholas Wolff, Anh Tran, William G. Kaelin, Jr. & **James Brugarolas**
UT Southwestern Medical Center, Dallas, TX
- 7:15 – 7:35 PM Regulation of mTOR by Polycystin 1 – A Functional Link Between TSC and PKD
Thomas Weimbs, University of California, Santa Barbara, CA
- 7:45 – 9:00 PM Conference Dinner
Dinner Sponsor: Sandra & Brian O'Brien
- Annapolis Atrium, First Floor, Main Hotel

Monday, September 24, 2007

7:00 – 8:00 AM Breakfast Annapolis Atrium, First Floor, Main Hotel

**Session II: Signaling Defects in the mTOR Pathway and TSC
Regatta Ballroom, First Floor, Main Hotel**

Session Chair: Brendan Manning, Harvard School of Public Health, Boston, MA

- 8:00 – 8:10 AM Living with TSC
TBD
- 8:10 – 8:40 AM Angiogenesis in TSC Skin Hamartomas
Thomas N. Darling, Ji-an Wang, Shaowei Li, Sangeetha Rajesh, Gustavo Pacheco-Rodriguez & Joel Moss, Uniformed Services University of the Health Sciences and the National Institutes of Health, Bethesda, MD
- 8:40 – 9:00 AM The TSC-mTOR Pathway in Diabetes and Diabetic Nephropathy
Kun-Liang Guan, University of Michigan School of Medicine, Ann Arbor, MI
- 9:00 – 9:20 AM Regulators of the Nutrient-Sensitive mTOR Pathway
Richard Lamb, The Institute of Cancer Research, London, UK
- 9:20 – 9:40 AM Revisiting a Complex Relationship Between the TSC1-TSC2 Complex and the mTOR Complexes
Jingxiang Huang & **Brendan D. Manning**, Harvard School of Public Health, Boston, MA
- 9:40 – 9:55 AM Role of Autophagy in the Pathogenesis of Tuberous Sclerosis Complex
Victoria A. Robb, Andrey Parkhitko, Tasha A. Morrison, Elizabeth P. Henske, Fox Chase Cancer Center, Philadelphia, PA
- 9:55 – 10:10 AM Cellular Stress Response Pathways are Activated by Loss of the TSC Genes
Katrin Duevel, Alex Lipovsky, Jeff P. MacKeigan, Leon O. Murphy & Brendan Manning, Harvard School of Public Health, Boston, MA
- 10:10 – 10:30 AM Break

**Session III: Epileptogenesis and Neuropathology in TSC: Brain Development,
Cell Growth and Migration
Regatta Ballroom, First Floor, Main Hotel**

Session Sponsors: Joy & Chris Dinsdale and UCB Pharma

Session Chair: Elizabeth Thiele, Massachusetts General Hospital, Boston, MA

- 10:30 – 10:40 AM Impact of Epilepsy in TSC
Emily Johnson, Pleasanton, CA
- 10:40 – 11:10AM Developmental Pathogenesis of Brain Lesions in TSC

Peter Crino, University of Pennsylvania Medical Center, Philadelphia, PA

- 11:10 – 11:25 AM TSC1 and Rheb Control Orientation of Asymmetric Cell Division by Specifying Neural Progenitor Cell Fate in Drosophila
Magdalena Karbowniczek, **Damir Khabibullin**, Diana Zitserman, Fabrice Roegiers & Elizabeth Petri Henske, Fox Chase Cancer Center, Philadelphia, PA
- 11:25 – 11:40 AM Tuberin and Hamartin Coordinate Cytoskeletal Dynamics in Migrating Neurons
Tristan TJ Sands & Arnold R Kriegstein, Columbia University, New York, NY and UCSF, San Francisco, CA
- 11:40 – 11:55 AM Role of the *Tsc1* Gene in Neural Progenitor Cells
Peggy A. Winzenburger, Dominic Van Nielen & **Kevin C. Ess**, Vanderbilt University, Nashville, TN
- 11:55 – 12:15 PM The Role of Glia in Epileptogenesis in TSC
Michael Wong, Washington University School of Medicine, St. Louis, MO
- 12:15 – 12:35 PM Impaired Neuronal Function in TSC
Frances Jensen, Children’s Hospital and Harvard Medical School, Boston, MA
- 12:35 – 12:55 PM Magnetoencephalography, FDG-PET/MRI Co-Registration, and Diffusion-Tensor Imaging in TSC
Joyce Wu, UCLA, Los Angeles, CA
- 12:55 – 2:45 PM Lunch with Breakout Sessions – Powerhouse
Session I – Moderators: Ray Yeung & Lisa Henske – Thomas Point Room, Powerhouse First Floor
Session II – Moderators: Brendan Manning & Tom Darling – Windmill Point Room, Powerhouse – Second Floor
Session III – Moderators: Elizabeth Thiele & Peter Crino – Pont Lookout Ballroom, Powerhouse – Third Floor

**Session IV: Neurocognition in TSC: Neuronal Development, Synaptogenesis
and Behavioral Phenotypes in TSC
Regatta Ballroom, First Floor, Main Hotel**

Session Chair: Ann Hunt, Oxfordshire, UK

- 3:00 – 3:10 PM The Impact of Behavioral Issues in TSC
Celia Mastbaum, Marlboro, NJ
- 3:10 – 3:30 PM Can We Get a Molecular GRIPP on Cognition and Neurodevelopment in TSC?
Petrus J. de Vries & Christopher J. Howe, University of Cambridge, Cambridge, UK
- 3:30 – 3:45 PM Genetic Approaches to Study Cerebellum Development, Circuitry, and Disease
Mark Zervas, Brown University, Providence, RI
- 3:45 – 4:00 PM Loss of Tsc2 in Radial Glia Models the Brain Pathology of Tuberous Sclerosis Complex in the Mouse
S. Way, J. McKenna III & **Michael J. Gambello**, University of Texas Health Science Center, Houston, TX

- 4:00 – 4:20 PM Regulation of the ETS Transcription Factor *pointedP2* by the Insulin Receptor/TOR Pathway in Neuronal Differentiation in *Drosophila*
Aamna K. Kaul, Gavin M. Craig, Cedric Plachot, Helen McNeill & **Joseph Bateman**, Kings College London, London, UK & Samuel Lunenfeld Research Institute, Toronto, Canada
- 4:20 – 4:40 PM Regulators of Rho GTPases in Neuronal Development
N. Nadif Kasri, M. Watabe-Uchida & **Linda Van Aelst**, Cold Spring Harbor Laboratory, Cold Spring Harbor, NY
- 4:40 – 5:00 PM Break – Annapolis Atrium
- 5:00 – 5:20 PM Acute and Long-Term Regulation of Synaptic Glutamate Receptor Function and Expression and the Calcium Transients in Dendritic Spines by the TSC-mTOR Pathway
Veronica A. Alvarez, Jessica Saulnier and Bernardo L. Sabatini, Harvard Medical School, Boston, MA
- 5:20 – 5:40 PM Neuronal Connectivity in TSC
Mustafa Sahin, Children’s Hospital and Harvard Medical School, Boston, MA
- 5:40 – 6:00 PM Autism and TSC: What is the Link?
Diane C. Chugani, Wayne State University and Children’s Hospital of Michigan, Detroit, MI
- 6:00 – 6:20 PM Visuospatial and Executive Skills in Tuberous Sclerosis Complex
Deborah L. McCartney & Petrus J. de Vries, University of Cambridge, Cambridge, UK
- 6:20 – 6:40 PM Tuberous Sclerosis Complex: Behavioral and Psychiatric Aspects
Elizabeth A. Thiele, Carol and James Herscot Center for TSC, Massachusetts General Hospital, Boston, MA

**Poster Session
Annapolis Atrium**

- 6:40 – 8:00 PM Poster Session – Annapolis Atrium

**Conference Reception
Ridout House
120 Duke of Gloucester Street
Annapolis, MD**

- 7:30 – 9:00 PM Conference Reception @ Ridout House

Tuesday, September 25, 2007

8:00 AM – 9:00 AM

Breakfast

Annapolis Atrium, First Floor, Main Hotel

**Session V: Clinical Manifestations and Therapeutic Opportunities in TSC
Regatta Ballroom, First Floor, Main Hotel**

Session Sponsor: Wyeth Pharmaceuticals

Session Chair: John Bissler, Children's Hospital Medical Center, Cincinnati, OH

- 9:00 – 9:10 AM Living with TSC
Bonnie Gould Rothberg, Guilford, CT
- 9:10 – 9:40 AM Therapeutic Trials in Pre-clinical TSC Mouse Models
David J. Kwiatkowski, Lynsey Meikle, Kristen Pollizzi, Mustafa Sahin, Ioannis Kramvis, Michael Stumm & Heidi Lane, Brigham and Women's Hospital, Harvard Medical School, and Children's Hospital, Harvard Medical School, Boston, MA; and Novartis Corporation, Basel, Switzerland
- 9:40 – 9:55 AM The TSC1 and TSC2 Variation Databases
Rosemary Ekong, A. Texiera, S. Povey, C. Vidales, M. Feolo, S.T. Sherry, D. Maglott, P. Davies, J. Sampson, P. Roberts, D. Kwiatkowski, P.E.M. Taschner & J. den Dunnen, University College London, UK; Unidad de Genetica Molecular, Gipuzkoa, Spain; NCBI, National Library of Medicine, Bethesda, MD; Cardiff University, Cardiff, UK, Brigham & Women's Hospital, Boston, MA, Leiden University Medical Center, Leiden, The Netherlands
- 9:55 – 10:10 AM Long-Term Natural History of Renal Angiomyolipoma in TSC
JC Kingswood & **Jane A. Cox**, Royal Sussex County Hospital, Brighton, UK
- 10:10 – 10:25 AM Vigabatrin in the Treatment of Epilepsy in Tuberous Sclerosis Complex: A Retrospective Chart Review of Efficacy and Safety
Susana E. Camposano, Philippe Major & Elizabeth A. Thiele, Carol and James Herscot Center for TSC, Massachusetts General Hospital, Boston, MA
- 10:25 – 10:45 AM Break
- 10:45 – 11:05 AM Multi-Center Clinical Trials for Tuberous Sclerosis and Progress Towards a New Standard of Care
Sandra L. Dabora, Brigham and Women's Hospital, Boston, MA
- 11:05 – 11:25 AM TSC Clinical Trials in Europe: The TESSTAL Trial
Julian R. Sampson, D. Mark Davies, Simon R. Johnson, Anne Tattersfield, J. Christopher Kingswood, Jane A. Cox, Deborah L. McCartney, Tim Doyle, Frances Elmslie, Anand Saggarr & Petrus de Vries, Cardiff University, University of Nottingham, Royal Sussex County Hospital, University of Cambridge, St. George's Hospital, UK
- 11:25 – 11:45 AM TSC Clinical Trials in the U.S.A.
David Neal Franz, Children's Hospital Medical Center, Cincinnati, OH
- 11:45 – 1:45 PM Lunch and Breakout Sessions - Powerhouse

Session IV – Moderators: Ann Hunt & Petrus de Vries – Point Lookout Ballroom, Powerhouse, Third Floor

Session V – Moderators: John Bissler & David Kwiatkowski – Thomas Point Room, Powerhouse First Floor

Session VI: Conference Wrap-Up

Regatta Ballroom, First Floor, Main Hotel

Moderators: Cheryl Walker, Ph.D. & Michael Frost, M.D.

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| 2:00 – 2:15 PM | Breakout Session I Summary: Raymond Yeung, M.D. |
| 2:15 – 2:30 PM | Breakout Session II Summary: Brendan Manning, Ph.D. |
| 2:30 – 2:45 PM | Breakout Session III Summary: Elizabeth Thiele, M.D., Ph.D. |
| 2:45 – 3:00 PM | Breakout Session IV Summary: Ann Hunt |
| 3:00 – 3:15 PM | Breakout Session V Summary: John Bissler, M.D. |
| 3:15 – 4:00 PM | Discussion |
| 4:00 PM | Meeting adjourns |