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

Annapolis Atrium, First Floor, Main Hotel

Dinner Sponsor: Sandra & Brian O’Brien
Monday, September 24, 2007

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

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**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

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**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 – 11:10 AM  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. Vidalas, 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

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 Saggar & 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 VI: Conference Wrap-Up
Regatta Ballroom, First Floor, Main Hotel

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

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