

# 5<sup>th</sup> International RASopathies Symposium: When Development and Cancer Intersect

Renaissance Orlando at SeaWorld, Orlando, Florida ~ Friday, July 28 to Sunday, July 30, 2017

## AGENDA

Chairs: Katherine A. Rauen, MD, PhD and Frank McCormick, PhD, FRS

Co-Organizers: RASopathiesNet - Lisa Schoyer, MFA, Lisa Schill, BS, Beth Stronach, PhD

### DAY 1 – FRIDAY 7/28/17

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| 8:00-10:00 pm | <b>Dessert and Scientific Poster Session</b> (Scientists and advocacy/family groups)<br>Goal: Encourage collaboration between researchers and families in a nonclinical setting |
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### DAY 2 – SATURDAY 7/29/17

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| 7:00-8:00 am        | <b>Breakfast</b>  |
| 9:00 am-5:00 pm     | <b>Family Photo Shoot</b> in and around meeting areas - Rick Guidotti   |
| 8:00-10:00 am       | <b>Session 1: What Defines a RASopathy?</b><br>Moderator: <b>Martin Zenker, MD</b><br>Goals: Hear from patients and families about their experiences living with a RASopathy.<br>Lay the scientific foundation for a comprehensive and accurate understanding of the current definition of a RASopathy. |
| 8:00-8:30 am        | <b>Four Individuals/Caregivers:</b> Perspectives from the Home Front  |
| 8:30-9:00 am        | <b>Frank McCormick, PhD, FRS:</b> Molecular primer on the Ras signaling pathway   |
| 9:00-9:30 am        | <b>Katherine A. Rauen, MD, PhD:</b> The RASopathies   |
| 9:30-10:00 am       | <i>Discussion</i> (Clinical Diagnosis, Phenotype-Centered vs. Molecularly Defined)  |
| 10:00-10:10 am      | <i>Break</i>  |
| 10:10 am -12:00 pm  | <b>Session 2: Syndromic and Sporadic Cancers of the Ras Pathway</b><br>Moderator: <b>Karen Gripp, MD</b><br>Goal: Examine cancer types and mechanisms in individuals with RASopathies   |
| 10:10-10:50 am      | <b>KEYNOTE: Nancy Ratner, PhD:</b> Preclinical studies to guide NF1 clinical trials   |
| 10:50-11:10 am      | <b>Corinne Linardic, MD:</b> Pediatric sarcomas, rhabdomyosarcoma   |
| 11:10-11:30 am      | <b>Hélène Cavé, PharmD PhD:</b> Myoproliferative neoplasms (JMML) in RASopathies  |
| 11:30-11:50 am      | <b>Brigitte Widemann, MD:</b> Clinical trial updates, NF1 Plexiforms and MPNSTs   |
| 11:50 am – 12:00 pm | <i>Discussion</i>   |
| 12:00 – 1:00 pm     | <b>Lunch and Learn: Rick Guidotti: Positive Exposure</b>  |
| 1:00-4:30 pm        | <b>Session 3: Human Development: Effects on Organ Systems</b><br>Moderator: <b>Bruce Korf, MD, PhD</b><br>Goal: Learn how RASopathy mutations affect developing tissues, organs, and body systems   |
| 1:00-1:40 pm        | <b>KEYNOTE: Marco Tartaglia, PhD:</b> RASopathy genetics, new mutations, congenital defects   |
| 1:40-2:40 pm        | <b>NERVOUS SYSTEM</b>   |
| 1:40-2:00 pm        | <b>Erika Yeh, PhD (Weiss lab):</b> From skin cells to neurons   |
| 2:00-2:20 pm        | <b>Erik Ullian, PhD:</b> How do astrocytes affect brain function in RASopathies?  |
| 2:20-2:40 pm        | <b>Giuseppe Zampino, MD:</b> Penn MDBR 2015 Grantee - Pain in RASopathies: new investigative techniques and treatments  |
| 2:40-2:50 pm        | <i>Discussion</i>   |
| 2:50-3:00 pm        | <i>Break</i>  |
| 3:00-3:40 pm        | <b>CIRCULATORY SYSTEMS</b>  |
| 3:00-3:20 pm        | <b>Bruce Gelb, MD:</b> Human inducible pluripotent stem cells for the study of heart defects  |
| 3:20-3:40 pm        | <b>Max Itkin, MD:</b> Imaging of the central lymphatic system in patients with Noonan syndrome using Dynamic Contrast Enhanced MR Lymphangiography  |
| 3:40-4:00 pm        | <b>GASTROINTESTINAL SYSTEM</b><br><b>Cheng Sun, PhD (Kontaridis lab):</b> Penn MDBR 2014 Grantee - Using human inducible pluripotent stem cells to delineate the cause of gastrointestinal abnormalities in RASopathy disorders   |
| 4:00-4:10 pm        | <i>Discussion</i>   |
| 4:10-4:20 pm        | <i>Break</i>  |

**5<sup>th</sup> International RASopathies Symposium: When Development and Cancer Intersect** Agenda, continued

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| <b>4:20-5:50 pm</b> | <b>Session 4: Developmental Perspective: Modeling RASopathies in Animals and in Silico</b><br><b>Moderator: Suma Shankar, MD, PhD</b><br><b>Goal:</b> Discuss nonhuman model experimental systems and how they are used to study RASopathies |
| 4:20-4:40 pm        | <b>Stanislav Shvartsman, PhD:</b> Quantitative biology of RASopathies  |
| 4:40-5:00 pm        | <b>Ethan Perlstein, PhD (Perlara):</b> Rare disease drug discovery using whole animal disease models   |
| 5:00-5:20 pm        | <b>Edward Stites, MD, PhD:</b> Computational analysis of pathological Ras mutants  |
| 5:20-5:40 pm        | <b>Annette Schenck, PhD:</b> Habituation learning in <i>Drosophila</i> - a high-throughput platform to identify drugs that ameliorate cognitive and behavioral problems in Rasopathies   |
| 5:40-5:50 pm        | <i>Discussion</i>  |
| 5:50-6:30 pm        | <i>Break</i>   |
| <b>6:30-8:30 pm</b> | <b>Networking Dinner with Cash Bar</b>   |

**DAY 3 – SUNDAY 7/30/17**

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| <b>7:00-8:00 am</b>   | <b>Breakfast Meeting: How Do You Define a RASopathy?</b>  |
| <b>8:00-9:30 am</b>   | <b>Session 5: Ras Pathway Mechanics</b><br><b>Moderator: Martin McMahon, PhD</b><br><b>Goal:</b> To discuss molecular mechanisms of Ras pathway signaling: How do crystal structures and dynamic imaging shed new light?            |
| 8:00-8:20 am          | <b>Jay Groves, PhD:</b> Membrane signaling dynamics   |
| 8:20-8:40 am          | <b>John Albeck, PhD:</b> Quantifying the cellular effects of Ras pathway mutations with live-cell imaging   |
| 8:40-9:00 am          | <b>Deborah Morrison, PhD:</b> Divide and Conquer: Targeting Raf Regulatory Interactions   |
| 9:00-9:20 am          | <b>Marc Therrien, PhD:</b> Allosteric control of RAF activation by dimerization   |
| 9:20-9:30 am          | <i>Discussion/Break</i>   |
| <b>9:30-11:00 am</b>  | <b>Session 6: Potential Therapeutics</b><br><b>Moderator: David Stevenson, MD</b><br><b>Goal:</b> Discuss promises and challenges of Ras pathway therapeutic drug development   |
| 9:30-9:50 am          | <b>Brage Andresen, PhD, FRCPATH:</b> Splice switching oligonucleotides (SSOs) for HRAS exon 2 skipping  |
| 9:50-10:10 am         | <b>Pascal Fortin, PhD (Relay Therapeutics):</b> Allosteric inhibition of the SHP2 phosphatase: suppressing RAS-ERK signalling in RTK-driven cancers   |
| 10:10-10:30 am        | <b>Christopher Gibson, MD, PhD (Recursion Pharmaceuticals):</b> Image-based high throughput screens for rare disease therapeutics   |
| 10:30-10:50 am        | <b>Philip Stork, MD:</b> Penn MDR 2016 Grantee - What can Ras-dependent cancers teach us about Rasopathies?   |
| 10:50-11:00 am        | <i>Discussion/ Break</i>  |
| <b>11:00-12:30 am</b> | <b>Session 7: Next Generation: Junior Investigator Poster Session Abstracts and Closing Keynote</b><br><b>Moderator: Bronwyn Kerr, MBBS</b><br><b>Goal:</b> Attract and highlight research on RASopathies from junior investigators |
| 11:00-11:30 am        | <b>Junior Investigator Poster Finalists:</b> Three 10-minute presentations, winner announced  |
| 11:30-12:20 pm        | <b>KEYNOTE: Frank McCormick, PhD, FRS:</b> Targeting Ras and NF1-related malignancies   |
| 12:20-12:30 pm        | <i>Discussion and Next Steps</i><br><b>Frank McCormick, PhD, FRS, Katherine A. Rauen, MD, PhD, Lisa Schoyer, MFA</b>  |
| <b>12:30-1:30 pm</b>  | <b>Breakout Sessions with RASopathy Family Groups:</b><br><b>CFC:</b> Katherine A. Rauen, MD, PhD<br><b>CS:</b> Karen Gripp, MD, David Stevenson, MD, and Bronwyn Kerr, MBBS<br><b>NS:</b> Bruce Gelb, MD, and Amy Roberts, MD      |
| <b>12:30-6:00 pm</b>  | <b>NF Network's Post-Symposium Family Meeting</b>   |
| <b>2:30-6:00 pm</b>   | <b>Post-Symposium Events</b> for CFC and NS families  |