



8th International Meeting on Rare Disorders of the RAS-MAPK Pathway

Virtual Meeting, November 10-12, 2022

Scientific Board: Marco Tartaglia, Alain Verloes, Emma Burkitt-Wright, Martin Zenker

Organized by: ERN-ITHACA



Meeting Link:

[Click here to join the meeting](#)

Registrations still possible [here](#)

All given times refer to CET (Central European Time)

Program - Day 1 (Thursday, November 10)

14³⁰ **Noonan syndrome spectrum consensus management guidance: (session open to all)**
Updates from the specialist work groups: new evidence, advances on the 2010 guidelines and unresolved questions
 Chair: Emma Burkitt-Wright and Sixto Garcia Minaur

14³⁰ General intro on the “guidelines consensus group” activity
Emma Burkitt-Wright

14⁴⁵ Dyadic approach to the delineation of diagnostic entities in clinical genomics (15' + 5' discussion)
Leslie G. Biesecker (National Institutes of Health, Bethesda, MD, USA)

15⁰⁵ Reports from the specialist work groups including:

- Prenatal aspects – **Alessandro de Luca**

18⁰⁰ Neurology and neurodevelopment – **Yves Sznajder**

Feeding and gastroenterology – **Dagmar Tiemens and Jos Draaisma**

Endocrine and growth – **Thomas Edouard**

Oncology – **Hélène Cavé**

Cardiology – **Kathryn Chatfield and Bruce D. Gelb**

General and adult care – **Sixto Garcia Minaur**

(indicative 10-15 min presentation + 10 min discussion)

18⁰⁰ Discussion

Program - Day 2 (Friday, November 11) – Scientific program

14³⁰ **First Session: Nosology and diagnosis**

Chair: **Martin Zenker** and **Alain Verloes**

14³⁰ RASopathy nosology controversy: lumping vs splitting (15 min + 5 discussion)
Martin Zenker (Magdeburg, Germany)

14⁵⁰ Lumping vs splitting and classification of unusual presentations: selected RASopathies
(7 min + 3 min discussion, each)
MAPK1-related disorder. **F Clementina Radio** (Rome, Italy)
Mazzanti syndrome. **Laura Mazzanti** (Bologna, Italy)
Unusual presentation of *HRAS* mutations. **Tanja Frey** (Zürich, Switzerland) (selected abstract)
CM-AVM syndrome. **Emanuele Coccia** (Reggio Emilia, Italy) (selected abstract)

15³⁰ Patient advocacy perspective (10 min, each)
Lisa Schoyer (RASopathies Network) and **Marcos Mengual Hinojosa** (Syngap Elternhilfe e.V.)

15⁵⁰ **Short break**

16⁰⁰ **Second Session: Mechanisms and signaling circuits**

Chair: **Marco Tartaglia** and **Reza Amhadian**

16⁰⁰ The SPRED1-neurofibromin-KRAS module (15 min + 5 min discussion)
Frank McCormick (University of California, San Francisco, CA, USA)

16²⁰ The MRAS-SHOC2-PP1C module (15 min + 5 min discussion)
Dhirendra K. Simanshu (Frederick National Laboratory for Cancer Research, Frederick, MD, USA)

16⁴⁰ Short presentations (selected abstracts) (10 min + 5 min discussion each)

Mitochondrial proteostasis in Costello syndrome. **Didier Lacombe** (Bordeaux, France)

Pathways implicated in dysregulated energetic metabolism in Costello syndrome. **Elisabetta Flex** (Rome, Italy)

17¹⁰ **Short break**

Continued: Program - Day 2 (Friday, November 11) – Scientific program

17²⁰

Third session: Mixed presentations from selected abstracts

Chair: Helene Cavé and Giuseppe Zampino

Short presentations (selected abstracts) (7 min + 3 min discussion)

1. Deep phenotyping in fetal RASopathies. **Esther Dempsey** (London, UK)
2. SPRED2 LoF cause a recessive NS-like phenotype. **Marialetizia Motta** (Rome, Italy)
3. Clinical phenotype of NS due to *RRAS2* mutations. **Yline Capri** (Paris, France)
4. Adult “mild” presentation of the Thr68Ile *MRAS* change. **Manuela Priolo** (Reggio Calabria, Italy)
5. Mosaic RASopathies: Lateralized overgrowth with vascular malformation caused by a somatic *PTPN11* pathogenic variant. **Alessandro Mussa** (Turin, Italy)
6. *LZTR1* and isolated café-au-lait macules: are variants in this gene underestimated?
Gioia Mastromoro (Rome, Italy)
7. Children with isolated café-au-lait spots and heterozygous variants in *LZTR1*.
Claudia Santoro (Naples, Italy)
8. Trametinib treatment in a patient with *NRAS*-related cutaneous skeletal hypophosphatemia syndrome. **Diana Carli** (Turin, Italy)
9. Severe lymphatic disorder and multifocal atrial tachycardia treated with trametinib in a patient with NS (*SOS1* mutation). **Michele Lioncino** (Naples, Italy)
10. Germline and somatic *PTPN11* mutations confer diverse sensitivity to the SHP099 allosteric SHP2 inhibitor. **Luca Pannone** (Rome, Italy)
11. Abdominal pain & functional gastrointestinal disorders in RASopathies. **Valentina Giorgio** (Rome, Italy)

19¹⁰ **End of program day 2**

Program – Day 3 (Saturday, November 12) – Scientific program

14³⁰ **Fourth Session: Cardiovascular and lymphatic aspects**

Chair: Bruce D. Gelb and Jos Draaisma

- 14³⁰ Lymphatic problems in RASopathies (15 min + 5 min discussion)
Sahar Mansour (St George's University Hospitals NHS Foundation Trust, London, UK)
- 14⁵⁰ Lymphatic imaging in RASopathies: patterns of abnormalities (15 min + 5 min discussion)
Claus Christian Pieper (University Hospital Bonn, Germany)
- 15¹⁰ Natural history of hypertrophic cardiomyopathy in NSML (15 min + 5 min discussion)
Giuseppe Limongelli (University of Campania "Luigi Vanvitelli", Naples, Italy)
- 15³⁰ Atypical cardiac defects in RASopathies (15 min + 5 min discussion each)
Paolo Versacci (Università "La Sapienza", Rome, Italy)
- 15⁵⁰ LZTR1 oligomerization drives NS-linked cardiac pathology (selected abstract) (10 min + 5 min discussion)
Lukas Cyganek (University Medical Center Göttingen, Germany)

16⁰⁵ **Short break**

16¹⁵ **Fifth Session: Neurodevelopmental / psychosocial aspects**

Chair: Yves Sznajer and Tamar Green

- 16¹⁵ RASopathies: pathomechanisms in the nervous system (15 min + 5 min discussion)
Anna Fejtova (University Hospital Erlangen, Germany)
- 16³⁵ Functional imaging in RASopathies (15 min + 5 min discussion)
Jennifer L. Bruno (Stanford University School of Medicine, Stanford, CA, USA)
- 16⁵⁵ Cognition, psychopathology and clinical management in NS spectrum disorders (15 min + 5 min discussion)
Ellen Wingbermühle & Rene Roelofs (Radboud University, Nijmegen, Netherlands)

17¹⁵ **Short break**

17²⁵ **Sixth Session: Novel aspects on treatment**

Chair: Jeroen den Hertog and Gregor Andelfinger

- 17²⁵ Research & drug development (15 min + 5 min discussion)
Bruce D. Gelb (Icahn School of Medicine at Mount Sinai, New York, NY, USA)
- 17⁴⁵ Treatment for cardiologic disease/cardiomyopathy (15 min + 5 min discussion)
Cordula Wolf (German Heart Center Munich, Germany)
- 18⁰⁵ Experience with MEK inhibitors for lymphatic disease (15 min + 5 min discussion)
Lotte Kleimeier & Jos Draaisma (Radboud University, Nijmegen, Netherlands)
- 18²⁵ Short presentations (selected abstracts) (7 min + 3 min discussion each)
- Treatment of lymphatic malformations in Noonan patients with trametinib - the Bonn experience,
Andreas Müller (Universitätsklinikum Bonn, Germany)
- Targeting Src homology 2 domain-containing phosphatase 2 (SHP2) by inhibiting its protein-protein interactions,
Lorenzo Stella (Università Tor Vergata, Rome, Italy)

18⁴⁵ **Closing remarks**