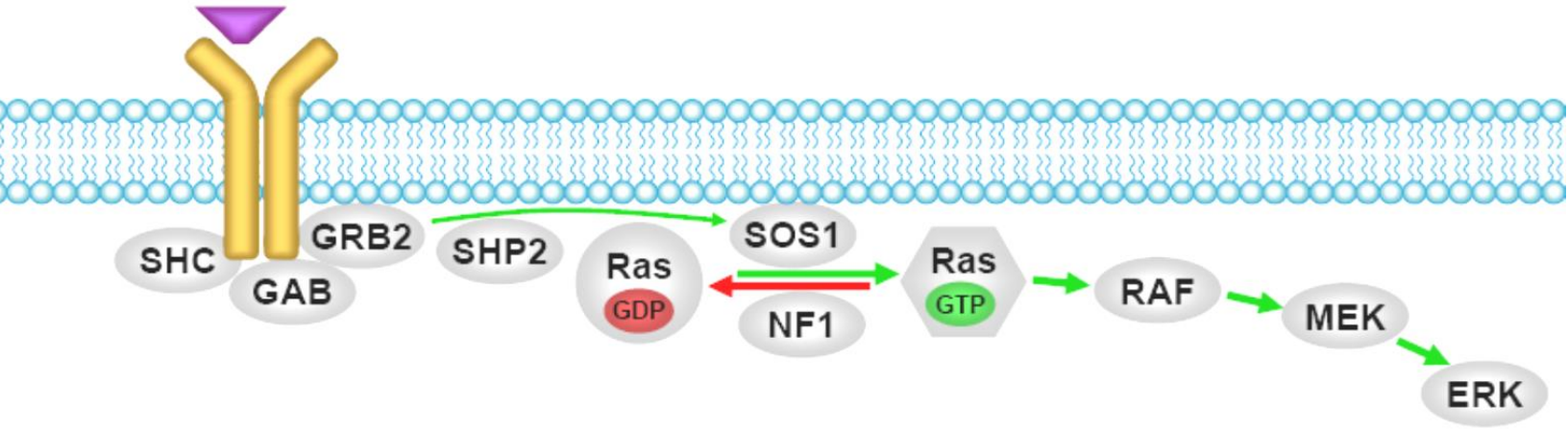

8th International Meeting on Rare Disorders of the RAS-MAPK Pathway

Virtual Meeting, November 10-12, 2022

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

Organized by: ERN-ITHACA

All given times refer to CET (Central European Time)

Program - *Day 1 (Thursday, November 10)*

14[30] **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

14[30] General intro on the "guidelines consensus group" activity
Emma Burkitt-Wright

14[45] Reports from the specialist work groups including:

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17[40] Prenatal aspects – **Alessandro de Luca**

Neurology and neurodevelopment – **Yves Sznajer**

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

Endocrine and growth – **Thomas Edouard** (*to be confirmed*)

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)

17[40] Discussion

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

14^{30}	**First Session: Nosology and diagnosis** **Chair: Martin Zenker and Alain Verloes**
14^{30}	RASopathy nosology controversy: lumping *vs* splitting (15 min + 5 discussion) **Martin Zenker** (Magdeburg, Germany)
14^{50}	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)
15^{30}	Patient advocacy perspective (10 min, each) **Lisa Schoyer** (RASopathies Network) and **Marcos Mengual Hinojosa** (Syngap Elternhilfe e.V.)
15^{40}	Short break
15^{50}	**Second Session: Mechanisms and signaling circuits** **Chair: Marco Tartaglia and Reza Amhadian**
15^{50}	The SPRED1-neurofibromin-KRAS module (15 min + 5 min discussion) **Frank McCormick** (University of California, San Francisco, CA)
16^{10}	The MRAS-SHOC2-PP1C module (15 min + 5 min discussion) **Dhirendra K. Simanshu** (Frederick National Laboratory for Cancer Research, Frederick, MD, USA)
16^{30}	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)
17^{00}	Short break

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

17[10] **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 cafè-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)

19[00] End of program day 2

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

14^{30}	**Fourth Session: Cardiovascular and lymphatic aspects** **Chair: Bruce D. Gelb and Jos Draaisma**
14^{30}	Lymphatic problems in RASopathies (15 min + 5 min discussion) **Sahar Mansour** (St George's University Hospitals NHS Foundation Trust, London, UK)
14^{50}	Lymphatic imaging in RASopathies: patterns of abnormalities (15 min + 5 min discussion) **Claus Christian Pieper** (University Hospital Bonn, Germany)
15^{10}	Natural history of hypertrophic cardiomyopathy in NSML (15 min + 5 min discussion) **Giuseppe Limongelli** (University of Campania "Luigi Vanvitelli", Naples, Italy)
15^{30}	Short presentations (selected abstracts) (10 min + 5 min discussion each)
	Atypical cardiac defects in RASopathies. **Paolo Versacci** (Università “La Sapienza”, Rome, Italy)
	LZTR1 oligomerization drives Noonan syndrome-linked cardiac pathology. **Lukas Cyganek** (University Medical Center Göttingen, Germany)
16^{00}	Short break
16^{05}	**Fifth Session: Neurodevelopmental / psychosocial aspects** **Chair: Yves Sznajer and TBD**
16^{25}	RASopathies: pathomechanisms in the nervous system (15 min + 5 min discussion) **Anna Fejtova** (University Hospital Erlangen, Germany)
16^{45}	Functional imaging in RASopathies (15 min + 5 min discussion) **Jennifer L. Bruno** (Stanford University School of Medicine, Stanford, CA, USA)
17^{05}	Cognition, psychopathology and clinical management in Noonan syndrome spectrum disorders (15 min + 5 min discussion) **Ellen Wingbermühle & Rene Roelofs** (Radboud University, Nijmegen, Netherlands)
17^{25}	Short break
17^{30}	**Sixth Session: Novel aspects on treatment** **Chair: Jeroen den Hertog and Gregor Andelfinger**
17^{30}	Research & drug development (15 min + 5 min discussion) **Bruce D. Gelb** (Icahn School of Medicine at Mount Sinai, New York, NY, USA)
17^{50}	Treatment for cardiologic disease/cardiomyopathy (15 min + 5 min discussion) **Cordula Wolf** (German Heart Center Munich, Germany)
18^{10}	Experience with MEK inhibitors for lymphatic disease (15 min + 5 min discussion) **Lotte Kleimeier & Jos Draaisma** (Radboud University, Nijmegen, Netherlands)
18^{30}	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)
18^{50}	Closing remarks