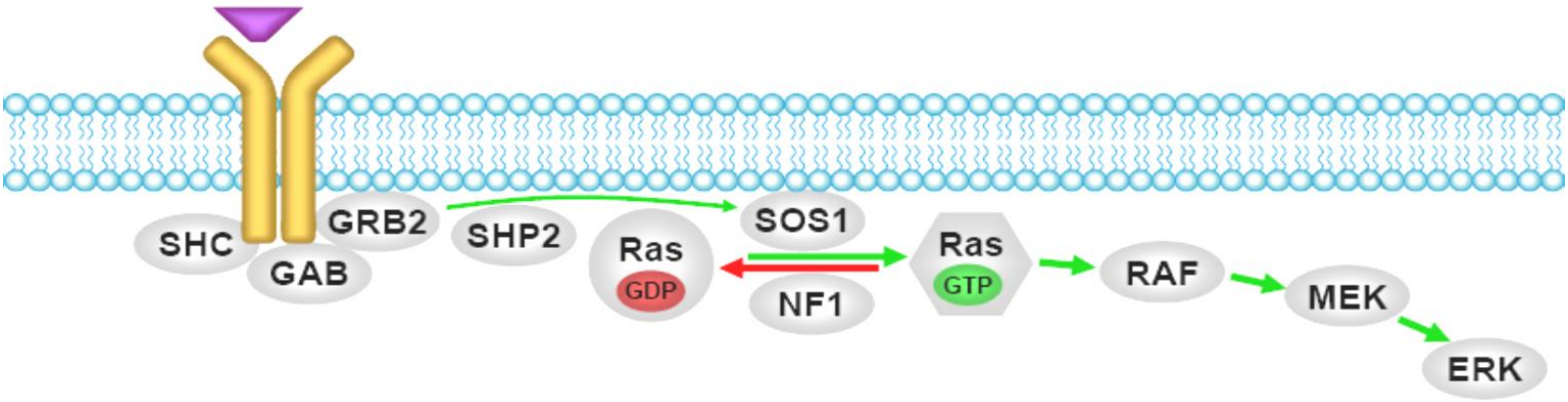

9th International Meeting on Rare Disorders of the RAS-MAPK Pathway

A workshop preceding the ESHG conference in Berlin, 2024

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

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Organized by: ERN-ITHACA

Date: Friday, May 31, 2024 – Saturday, June 01, 2024

Registration limit: 120 participants

Location: Novotel Berlin am Tiergarten, Str. des 17 Juni 106-108, 10623 Berlin, Germany

Pre-Programme - *Day 1 (Friday, May 31)*

8[15] Registration

9[00] **RASopathies nosology consensus meeting:**
To develop a nosological framework for RASopathies consented by medical experts and stakeholders
(Nosology expert panel and interested participants of main meeting)
Chairs: Emma Burkitt-Wright, Bruce Gelb, Marco Tartaglia, Alain Verloes, Martin Zenker

Topics/questions: What is a useful definition for the term RASopathies? How should these disorders be classified? What are the major disease categories? Which diseases should be included/excluded? How should diseases be named?

Expected result: A RASopathy nosology to be published after the meeting

9[00] Introductory remarks
Martin Zenker

9[15] Short statements by medical experts and patient advocacy representatives

Noonan syndrome: Michael Patton – Angelo Petroni/Michela Salin (15 min)

NSML: Bruce D. Gelb (15 min)

NSLH: Laura Mazzanti – Dagmar Tiemens (15 min)

CBL syndrome: Hélène Cavé (15 min)

CFCS: Giuseppe Zampino/Chiara Leoni – Troy Greisen (15 min)

Costello syndrome: Yoko Aoki – Lisa Schoyer, Kim Connor (15 min)

NF1 + Legius syndrome: Hilde Brems – NN (15 min)

SYNGAP1: Kirsten Eschermann - Verena Schmeder (15 min)

RASA1 and vascular mosaic RASopathies: Friedrich Kapp – Ruth Kerner (15 min)

Mosaic RASopathies: Alessandro Mussa (15 min)

other RASopathies / related conditions (MAPK1, ERF, RSK2, CDC42, phenocopies): Marco Tartaglia (15 min)

Additional panelists: Emma Burkitt-Wright, Alain Verloes, Christian Kratz (present); Miikka Vikkula, Veronica Kinsler, Karen Gripp (not available for the meeting but for further discussions after the meeting)

12[00] Discussion
All panel members and participants

12[30] Lunch Break

Programme - *Day 1 (Friday, May 31)*: Main Part of the meeting

13[00] Registration

13[45] Welcome addresses

14[00] **First Session: Hematology / Oncology**
Chair: Christian Kratz and Hélène Cavé

14[00] The nature of myeloproliferative disease in RASopathies (20 min incl. discussion)
Hélène Cavé

14[20] Brain tumors in RASopathies (20 min incl. discussion)
Pablo Hernáiz Driever

14[40] Solid tumours in RASopathies: unveiling high-risk genetic variants in a large monocentric cohort through an updated genotype-phenotype analysis (15 min incl. discussion)
Valentina Trevisan

15^{00} Importance of SPRED1 in cutaneous melanoma (15 min incl. discussion)
Charlotte Carton

15^{15} Modelling lymphoblastic leukemia in children with LZTR1 germline variants using fly avatars for Rasopathy detection (15 min incl. discussion)
Tobias Reiff

15^{30} Coffee Break

16^{00} **Second Session: New insights on molecular players & circuits**
Chair: Marco Tartaglia and Jeroen den Hertog

16^{00} SPREDs - Inhibitors of the Ras-MAPK Pathway or Promoters of its Inactivation? (20 min incl. discussion)
Kai Schuh

16^{20} Mechanisms of RIT1 variants in RASopathies (20 min incl. discussion)
Pau Castel

16^{40} Structure and regulation of BRAF: Insights into mechanisms of activation by RASopathy mutations (20 min incl. discussion) **Michael J Eck**

17^{00} Molecular bases of the phenotypic heterogeneity associated with YWHAZ mutations (20 min incl. discussion)
Marco Tartaglia

17^{20} Shp2 is essential for lymphangiogenesis during zebrafish development (15 min incl. discussion)
Daniëlle Woutersen

17^{35} A differential functional behavior of CDC42 underlies variable neurodevelopmental conditions, including a NS-like phenotype (15 min incl. discussion)
Simona Coppola

18^{00} Dinner Buffet

20^{00} **Late session: Mixed short contributions**
Chair: Alain Verloes and Emma Burkitt-Wright

Loss-of-function variants in ERF are associated with a Noonan syndrome-like phenotype with or without craniosynostosis (15 min incl. discussion) **Maria Lisa Dentici**

Recurrence risk in RASopathies (15 min incl. discussion) **Anne Goriely**

Congenital pulmonary airway malformations – a new class of mosaic RASopathies (15 min incl. discussion) **Christian Kratz**

Gastrointestinal pain and microbiome profiling in Costello syndrome (15 min incl. discussion)
Chiara Leoni

Autophagosomal dysfunction elicits neurodegenerative tauopathy in biallelic SPRED2 loss-of-function mouse models (15 min incl. discussion) **Sina Gredy**

Roles of senescence and inflammation in frailty associated phenotype in Noonan Syndrome (15 min incl. discussion) **Laurène Mazeyrie**

RASopathies and lymphatic malformation (15 min incl. discussion) **Yoko Aoki**

NF1 pleiotropic phenotype explained by rare variants (15 min incl. discussion) **Giulia Casamassima**

Preliminary Programme - *Day 2 (Saturday, June 01)*

9^{00}	**Fourth Session: Cardiovascular** **Chair: Cordula Wolf and Bruce D. Gelb**
9^{00}	Sudden cardiac death in childhood RASopathy-associated hypertrophic cardiomyopathy (20 min incl. discussion) **Olga Boleti**
9^{20}	Differentiating primary sarcomeric hypertrophic cardiomyopathy from RASopathic cardiomyopathy (20 min incl. discussion) **Cordula Wolf**
9^{40}	Specific RIT1 indels are associated with arteriovenous malformations (20 min incl. discussion) **Friedrich Kapp**
10^{00}	The RAF1:c.770C>T pathogenic variant is associated with a severe Noonan syndrome phenotype with hypertrophic cardiomyopathy and high mortality (15 min incl. discussion) **Andrea Gazzin**
10^{15}	Modeling LZTR1-related cardiac hypertrophy (15 min incl. discussion) **Lukas Cyganek**
10^{30}	Coffee break
11^{00}	**Fifth Session: Neuropsychology** **Chair: Anna Fejtova and Yves Sznajer**
11^{00}	Epilepsy in RASopathies – a comparison between CFC syndrome and SYNGAP1-related encephalopathy (20 min incl. discussion) **Kirsten Eschermann and Lorenz Kiwull**
11^{20}	Impacts of dysregulated RAS-MAPK signalling on functional development of nervous system (20 min incl. discussion) **Anna Fejtova**
11^{40}	Treatment of refractory epilepsy with MEK inhibitor in patients with a RASopathy (20 min incl. discussion) **Gianluca D'Onofrio**
12^{00}	Finding and treating hidden RASopathies among Drosophila models with habituation deficits (15 min incl. discussion) **Boyd van Reijmersdal**
12^{15}	Pathogenesis of cognitive and neurofunctioning impairments in Noonan syndrome patients: the potential role of RAS/MAPK signaling pathway gene disturbances (15 min incl. discussion) **Natalia Braun-Walicka**
12^{30}	Closing remarks
13^{30}	**NSEuroNet – Researchers Meeting** (NSEuroNet partners and external collaborators only)
15^{00}	**Chair: Marco Tartaglia**

Supported by:

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German Research Foundation

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