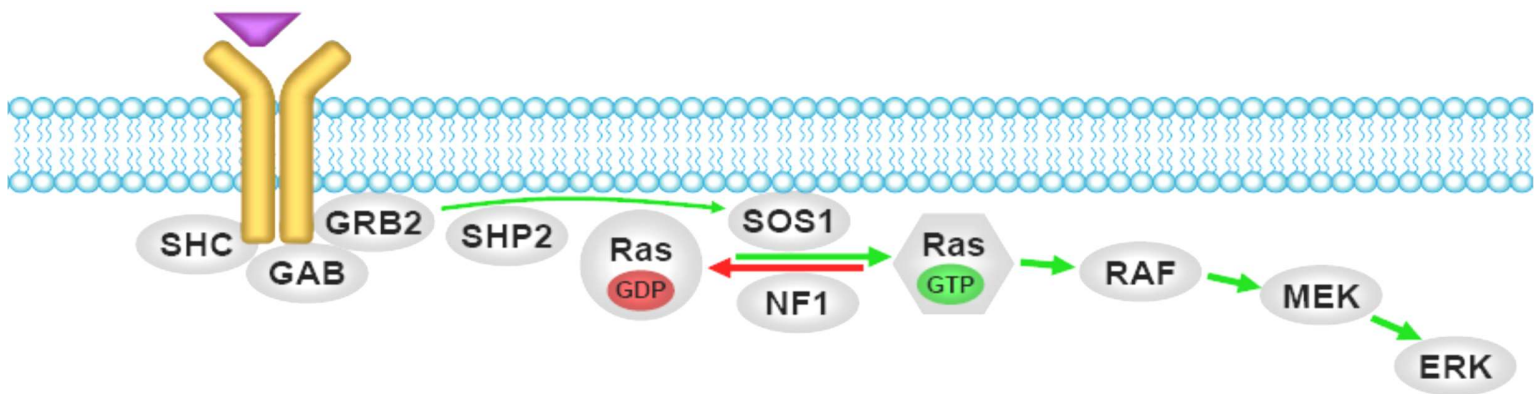




9th International Meeting on Rare Disorders of the RAS-MAPK Pathway

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)

8¹⁵ Registration

9⁰⁰ **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

9⁰⁰ Introductory remarks
Martin Zenker

9¹⁵ 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)

12⁰⁰ Discussion
All panel members and participants

12³⁰ Lunch Break

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

13⁰⁰ Registration

13⁴⁵ Welcome addresses

14⁰⁰ **First Session: Hematology / Oncology**
Chair: Christian Kratz and Hélène Cavé

14⁰⁰ The nature of myeloproliferative disease in RASopathies (20 min incl. discussion)
Hélène Cavé

14²⁰ Brain tumors in RASopathies (20 min incl. discussion)
Pablo Hernáiz Driever

14⁴⁰ 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

15⁰⁰ Importance of SPRED1 in cutaneous melanoma (15 min incl. discussion)
Charlotte Carton

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

15³⁰ **Coffee Break**

16⁰⁰ **Second Session: New insights on molecular players & circuits**
Chair: Marco Tartaglia and Jeroen den Hertog

16⁰⁰ SPREDs - Inhibitors of the Ras-MAPK Pathway or Promoters of its Inactivation? (20 min incl. discussion)
Kai Schuh

16²⁰ Mechanisms of RIT1 variants in RASopathies (20 min incl. discussion)
Pau Castel

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

17⁰⁰ Molecular bases of the phenotypic heterogeneity associated with YWHAZ mutations (20 min incl. discussion)
Marco Tartaglia

17²⁰ Shp2 is essential for lymphangiogenesis during zebrafish development (15 min incl. discussion)
Daniëlle Woutersen

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

18⁰⁰ **Dinner Buffet**

20⁰⁰ **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)

9⁰⁰ **Fourth Session: Cardiovascular** Chair: Cordula Wolf and Bruce D. Gelb

9⁰⁰ Sudden cardiac death in childhood RASopathy-associated hypertrophic cardiomyopathy (20 min incl. discussion)
Olga Boleti

9²⁰ Differentiating primary sarcomeric hypertrophic cardiomyopathy from RASopathic cardiomyopathy (20 min incl. discussion)
Cordula Wolf

9⁴⁰ Specific RIT1 indels are associated with arteriovenous malformations (20 min incl. discussion)
Friedrich Kapp

10⁰⁰ 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

10¹⁵ Modeling LZTR1-related cardiac hypertrophy (15 min incl. discussion)
Lukas Cyganek

10³⁰ **Coffee break**

11⁰⁰ **Fifth Session: Neuropsychology** Chair: Anna Fejtova and Yves Sznajder

11⁰⁰ Epilepsy in RASopathies – a comparison between CFC syndrome and SYNGAP1-related encephalopathy (20 min incl. discussion)
Kirsten Eschermann and Lorenz Kiwull

11²⁰ Impacts of dysregulated RAS-MAPK signalling on functional development of nervous system (20 min incl. discussion)
Anna Fejtova

11⁴⁰ Treatment of refractory epilepsy with MEK inhibitor in patients with a RASopathy (20 min incl. discussion)
Gianluca D'Onofrio

12⁰⁰ Finding and treating hidden RASopathies among Drosophila models with habituation deficits (15 min incl. discussion)
Boyd van Reijmersdal

12¹⁵ 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

12³⁰ **Closing remarks**

13³⁰ **NSEuroNet – Researchers Meeting**
(NSEuroNet partners and external collaborators only)
15⁰⁰ Chair: Marco Tartaglia

Supported by:

Funded by

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associazione italiana sindrome di costello
cardiofaciocutanea - rasopatie - onlus



Speakers and Chairpersons:

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Troy Greisen, CFRE, CFC International, USA

Ruth Kerner, Bundesverband Angeborene Gefäßfehlbildungen e.V., Germany

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