7\textsuperscript{th} International Meeting on Rare Disorders of the RAS-MAPK Pathway
A workshop preceding the ESHG conference in Milan, 2018

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Registration limit: 100 participants.
Registration cost: 100 € (including buffet dinner on May 20), one day 50 €, students: free attendance.
Location: UNA HOTEL SCANDINAVIA, Via G. B. Fauché, 15, 20154 Milano, Italy.
Date: Friday, June 15, 2018 – Saturday, June 16, 2018.

Program - \textit{Day 1 (Friday, June 15)}

\begin{tabular}{|l|}
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\textbf{9\textsuperscript{00}} & \textbf{Noonan syndrome guidelines consensus meeting:}  
What can we do to promote further the development of international guidelines? Follow-up of the Barcelona meeting 2016  
(for guidelines consensus group members and interested participants of the main meeting)  
\textbf{Organisation and chair: Bronwyn Kerr} \\
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\textbf{9\textsuperscript{30}} & Diagnostic criteria for Noonan syndrome  
\textbf{Ineke van der Burgt} \\
\textbf{9\textsuperscript{40}} & Suggestions for a nosology of RASopathies  
\textbf{Martin Zenker} \\
\textbf{10\textsuperscript{00}} & Should all infants with cardiomyopathy have a RASopathy panel?  
\textbf{Bruce Gelb} \\
\textbf{10\textsuperscript{30}} & Prenatal screening: Guidelines for proper molecular screening based on the echographic prenatal assessment  
\textbf{Alessandro de Luca} \\
\textbf{10\textsuperscript{40}} & Coffee Break  \\
\textbf{11\textsuperscript{00}} & Minimum medical management guidelines for Noonan syndrome and results of a family survey  
\textbf{Bronwyn Kerr} \\
\textbf{11\textsuperscript{30}} & Minimum medical management guidelines for cardiofaciocutaneous syndrome and Costello syndrome  
\textbf{Giuseppe Zampino} \\
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\end{tabular}
Program - Day 1 (Friday, June 15) continued: Main Part of the meeting

1300 Registration
1345 Welcome addresses

1400 **First Session: Cancer predisposition**
  Chair: Marco Tartaglia

1400 RAS signaling and leukemogenesis  
Giovanni Cazzaniga

1430 Cancer surveillance and therapy in children with RASopathies and other cancer predisposition syndromes
Christian Kratz

1500 Genomic alterations in Costello syndrome-associated ERMS
Karen Gripp

1520 RASopathies: why are these rare spontaneous disorders so common?
Anne Goriely

1540 **From the patients' perspective: Living with with tumor risk.**
How to direct research to have a more effective surveillance?

1600 Coffee Break

1630 **Second Session: Cardiovascular system/hypertrophic cardiomyopathy**
  Chair: Bruce Gelb

1630 Cardiac defects, morbidity and mortality in patients affected by RASopathies - Update on the CARNET study
Giulio Calcagni

1650 Patient specific iPSC-derived cardiomyocytes reveal abnormal signaling pathways underlying hypertrophic cardiomyopathy in Noonan syndrome
Maria Kontaridis

1710 Heart defects in a genetic zebrafish model for Noonan Syndrome
Jeroen den Hertog

1730 Experiences with MEK inhibitor treatment in patients with RIT1-associated cardiomyopathy
Gregor Andelfinger

1750 Outlook on possible strategies of medical treatment for RASopathy-associated cardiomyopathy
Bruce Gelb

1810 **From the patients' perspective: Living with heart defect cardiomyopathy.**
How to direct research to have a more effective management?

1830 Dinner Buffet

1900 **Late session: new genes & mutations/gen-phen correlations/short reports**
  Chair: Marco Tartaglia and Martin Zenker

1900 - Functional dysregulation of CDC42 causes diverse developmental phenotypes (F. Pantaleoni)

1915 - LZTR1 and AD and AR inheritance of Noonan syndrome (M. Zenker)

Short presentations (7 min – 8 presentations maximum)
Two additional patients with NS-LAH caused by the recurrent PPP1CB mutation p.Pro490Arg (M. L. Dentici)
Phenotypes associated with concomitant mutations (A. De Luca)
NIPT assay to detect these selfish point mutations in maternal plasma (A. Goriely)

Selected abstracts

Participants are invited to present their data in this session (mainly for interesting case reports and genotype phenotype studies). Please send a brief abstract to the organisers.
<table>
<thead>
<tr>
<th>Time</th>
<th>Session</th>
<th>Title</th>
<th>Speaker(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>9:00</td>
<td>Fourth Session: Nutrition, energetic and bone metabolism</td>
<td>Energetic and bone metabolism in Costello and CFC syndromes: an overview</td>
<td>Chiara Leoni</td>
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<tr>
<td>9:20</td>
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<td>Chondrocyte differentiation during endochondral growth in Noonan syndrome</td>
<td>Thomas Edouard</td>
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<td>9:40</td>
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<td>Metabolic abnormlities in a mouse model of Costello syndrome</td>
<td>Ion Cirstea</td>
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<td>10:00</td>
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<td>The basis of nutritional and metabolic problems in RASopathies: Lessons from mouse models</td>
<td>Shin-Ichi Inoue &amp; Yoko Aoki</td>
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<td>10:20</td>
<td></td>
<td>Energetic metabolism in Costello syndrome</td>
<td>Elisabetta Flex</td>
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<tr>
<td>10:40</td>
<td></td>
<td>Metabolic dysfunctions in Noonan and NS-ML syndromes</td>
<td>Armelle Yart</td>
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<td>11:00</td>
<td>From the patients' perspective</td>
<td>The parents’ struggle with nutrition problems in RASopathies. How to direct research to have a more effective management?</td>
<td>Shin-Ichi Inoue &amp; Yoko Aoki</td>
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<td>11:20</td>
<td>Coffee break</td>
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<tr>
<td>11:50</td>
<td>Fifth Session: Nervous system - Lymphatics</td>
<td>Epilepsy in RASopathies</td>
<td>Domenica Battaglia</td>
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<td>12:10</td>
<td></td>
<td>Behavioral issues and cognitive profiles in RASopathies</td>
<td>Paolo Alfieri &amp; Dany Menghini</td>
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<td>12:30</td>
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<td>Update on lymphatic problems in RASopathies</td>
<td>Sahar Mansour</td>
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<tr>
<td>12:50</td>
<td></td>
<td>SOS2 mutation-related Noonan syndrome and its association with lymphedema</td>
<td>Christina Lißewski</td>
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<tr>
<td>13:10</td>
<td>From the patients' perspective</td>
<td>Living with lymphedema (Judith van de Meereakker). The parents’ struggle with epilepsy in cardiofaciocutaneous syndrome.</td>
<td>Judith van de Meereakker</td>
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<td>13:30</td>
<td>Closing remarks</td>
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<td>14:00</td>
<td>NSEuroNet – Kick-Off Meeting</td>
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<td>(NSEuroNet partners and external collaborators only)</td>
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</table>

Supported by:

[Supporting logos]
Speakers and Chairpersons:

Dr. Paolo Alfieri, MD, Department of Neurosciences, Ospedale Pediatrico Bambino Gesù, Rome, Italy
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