

International Meeting on Genetic Syndromes of the Ras/MAPK Pathway
R13 HL108432, P.I.: Bruce D. Gelb, MD

Meeting Co-Chairs: Bruce D. Gelb, MD, Amy E. Roberts, MD, and Lisa Schoyer, M.F.A.

The scientific meeting entitled “International Meeting on Genetic Syndrome of the Ras/MAPK Pathway: Finding Our Way Back to the Bedside” was held at the Westin O’Hare Hotel in Chicago, IL from July 29-31, 2011. Attendance was nearly 100 individuals, including 53% scientists, physician-scientists and physicians, 18% trainees, and 29% affected individuals, family members and other syndrome advocates. There were 25 professional speakers and moderators, and presentations from 10 syndrome advocates. The keynote address, delivered by Dr. Leslie Gordon, herself a parent advocate, described the successful collaborative effort by scientists, physicians and families concerned with the genetic disorder progeria to develop novel therapies and move them into clinical trials. The meeting featured five plenary sessions on the following topics: recent gene discoveries for Ras/MAPK pathway disorders, advances in clinical care, Ras pathway biology, cell and animal models of RASopathies, and clinical trials/resources for the Ras/MAPK pathway disorders. Time was given for group discussion after each presentation. The invited talks for those sessions were delivered by experts from North America, Europe and Asia. Trainees and junior faculty were major contributors to the meeting, which featured a Young Investigator Competition with oral presentations by the three finalists and a poster session with 21 presentations. Advocates, comprising people affected by a RASopathy and parents of such individuals, attended the sessions and were active participants. Representatives from four family support and advocacy organizations made a formal presentation at the first plenary session and led a panel discussion near the meeting’s end.

The final portion of the meeting was devoted to developing next steps in organizing the scientific and physician-scientific communities toward developing therapies for RASopathies as well as optimizing care using our current knowledge. The attendees divided themselves into four working groups with the following themes: *preclinical consortium*, *RASopathies resource network*, *clinical network* and *clinical trials consortium*. The working groups then reported to the entire meeting at the closing discussion session. Based on those efforts, several concrete steps were developed. The *preclinical consortium* planned resource sharing between research groups (reagents, animal models, preliminary results), to focus on animal model testing of drugs that show promise for treatment of humans with RASopathies, and on developing preclinical measurements that are clinically relevant when designing experimental trials. The *RASopathies resource network* working group discussed the importance of developing a centralized genotype repository with complimentary phenotypic data as well as data sharing regarding mutation informatics. The *clinical network* agreed to a nomenclature change for one RASopathy (changing the diagnostic label of LEOPARD syndrome to Noonan syndrome with multiple lentigines), to re-evaluate previously developed diagnostic criteria, to update currently published management guidelines, and to consider establishing centers of excellence in the research of and care for people with RASopathies. Finally, the *clinical trials consortium* began to strategize how to structure and fund a multicenter clinical trial of rapamycin in people with Noonan syndrome with multiple lentigines, a multicenter clinical trial of the effect of statins on learning and memory in people with Noonan syndrome, and a formal clinical trial of the effect of melatonin on disordered sleep in people with a RASopathy syndrome.

A publication summarizing the presentations and conclusions from the working groups is in preparation.