The Clinical Roya Kabuki Program_Highlights of year 2020

Within the Genetics Department, Olaf Bodamer, MD, PhD, director of the Roya Kabuki Program; Jasmine Knoll, MD and genetic counselor Asma Rashid, MS, continue to conduct both pre-visit needs assessments and phone interviews with all new families—an important initial step to define and guide care management and coordination and to review families' unmet needs and expectations.

Our multidisciplinary team of specialists—Kabuki Champions—remains dedicated to treating, managing and innovating therapeutic strategies for children and adults with Kabuki syndrome who seek care at our Roya Kabuki Clinic.

During the past year, the Roya Kabuki Clinic has worked closely with Boston Children's Integrated Care Program, led by Richard Antonelli, MD, MS. By implementing tools to improve clinical care coordination across local and BCH team (e.g. Action Grid), developing a standard of care document and conducting both provider and patient surveys, they gained invaluable insight into the best ways to care for patients, allowing our team to continuously raise care standards and improve patient care.

The beginning of 2020 has brought unprecedented changes and challenges to our typical clinical practice. The majority of our outpatient staff had to adapt to work remotely and to support our patient families during the pandemic. The Roya Kabuki Clinic quickly adapted to implement an almost entirely virtual care model through the provision of telehealth services, which has led to an increase in out-of-state and international referrals.

Family Involvement and Outreach

Parent Advisory Board

The Parent Advisory Board continues to conduct bi-annual conference calls with Roya Kabuki team members to provide their input on a number of topics. Parent Advisory Board members have volunteered their time and have provided us with invaluable feedback and guidance as we pursue new clinical and research goals. Direct communication with community members allows us to best understand the unmet needs of patients and react accordingly. The patient resources, research goals and opportunities, and community events that are developed in response are then brought directly back to local communities.

Patient outreach activities

March 2020 – Virtual Roya Kabuki event: Share response to Covid-19 and engage community

June 2020 – Eversource Virtual Walk for Boston Children's Hospital: Team Kabuki Friends
|
September 2020 – Virtual Boston Marathon
|
October 23, 2020 — Kabuki Day: Halloween Cards and Candy, face masks sent out to 183 families
|
October 25, 2020 – Virtual Yoga Reaches Out: Team Kabuki Friends (open registration)

Clinical research

Natural History Study

To date 65 patients with genetically confirmed Kabuki syndrome are enrolled in the Natural History Study which evaluates the course of the disease by collecting nutrition, growth, muscle function, hearing, balance, speech, neurodevelopment and quality of life data. In addition, 63 patients with a Kabuki syndrome phenotype are enrolled who either lack genetic testing or carry a variant of uncertain

significance in either Kabuki gene. This Natural History Study for Kabuki syndrome is unique as it seeks to understand the natural evolution of phenotypes affecting different organ systems (e.g., brain, muscle, immune system and others) across the entire age spectrum to identify clinical trial endpoints and to prepare for clinical trial readiness. This study is in the process of being registered with the National Institutes of Health (NIH) Clinical Trials Website (www.clinicaltrials.gov). This website provides information on all ongoing clinical trials and registry studies worldwide.

Phenotype and biorepositories

The Kabuki syndrome phenotype and biorepositories based on a RedCap database continues to expand. To date, clinical information on 352 patients have been entered. These biorepositories are a central resource for collaborative clinical research among different centers. The scientific and clinical collaboration between the Roya Kabuki Program and two University Children's Hospitals in Shanghai and Shenzen in China also continued for its second year.

Laboratory research

Identification of novel genes associated with Kabuki and Kabuki-like syndromes

One novel gene (*ZMZ1*) has been identified in a patient with clinical features of Kabuki syndrome who was seen through the Roya Kabuki Program. The underlying mechanistic overlap between Kabuki syndrome and this new condition has been worked out in collaboration with investigators from Europe and the US.

KMT2D mouse model

We have established a kmt2d mouse colony in accordance with the Program's needs. This model will be used extensively to study the pathology of specific organ systems. In addition, the model will be used to test candidate drug compunds *in vivo* in pre-clinical studies.

Internet presence

Roya Kabuki Program website: http://royakabuki.org/
Boston Children's Hospital Internal Kabuki website: http://www.childrenshospital.org/ Bodamer Lab Website: http://bodamerlab.org/home/

Publications and lectures (members of Roya Kabuki Program in bold)

Carapito R et al, **Hung CY**, **Bodamer O**, Chelly J, Isidor B, Bahram S. ZMIZ1 variants cause a syndromic neurodevelopmental disorder. Am J Hum Genet 2019; 104:319-330.

Rosenberg CE, **Daly T, Hung C, Hsueh I**, Lindsley AW, **Bodamer O**. Prenatal and Perinatal History in Kabuki Syndrome. Am J Med Genet 2020; 182:85-92.

Daly T, Roberts A, Yang E, Mochida G, **Bodamer O**. Holoprosencephaly in Kabuki Syndrome. Am J Med Genet 2020; 182:441-445.

Wang Y et al. **Bodamer O**. The phenotypic spectrum of Kabuki Syndrome in patients of Chinese descent. Am J Med Genet 2020; 182:640-651.

Romeo-Luperchio T, Applegate CD, **Bodamer O**, Bjornsson H. Haploinsufficiency of KMT2D is sufficient to cause Kabuki syndrome. Mol Genet Genomic Med 2020 e1702.

Lectures and presentations:

Daly T, Bodamer O, King R. Poster Presentation at NORD Rare Diseases and Orphan Products Breakthrough Summit 2020: *Academic and community collaboration to accelerate Kabuki syndrome awareness, research, and clinical care.*