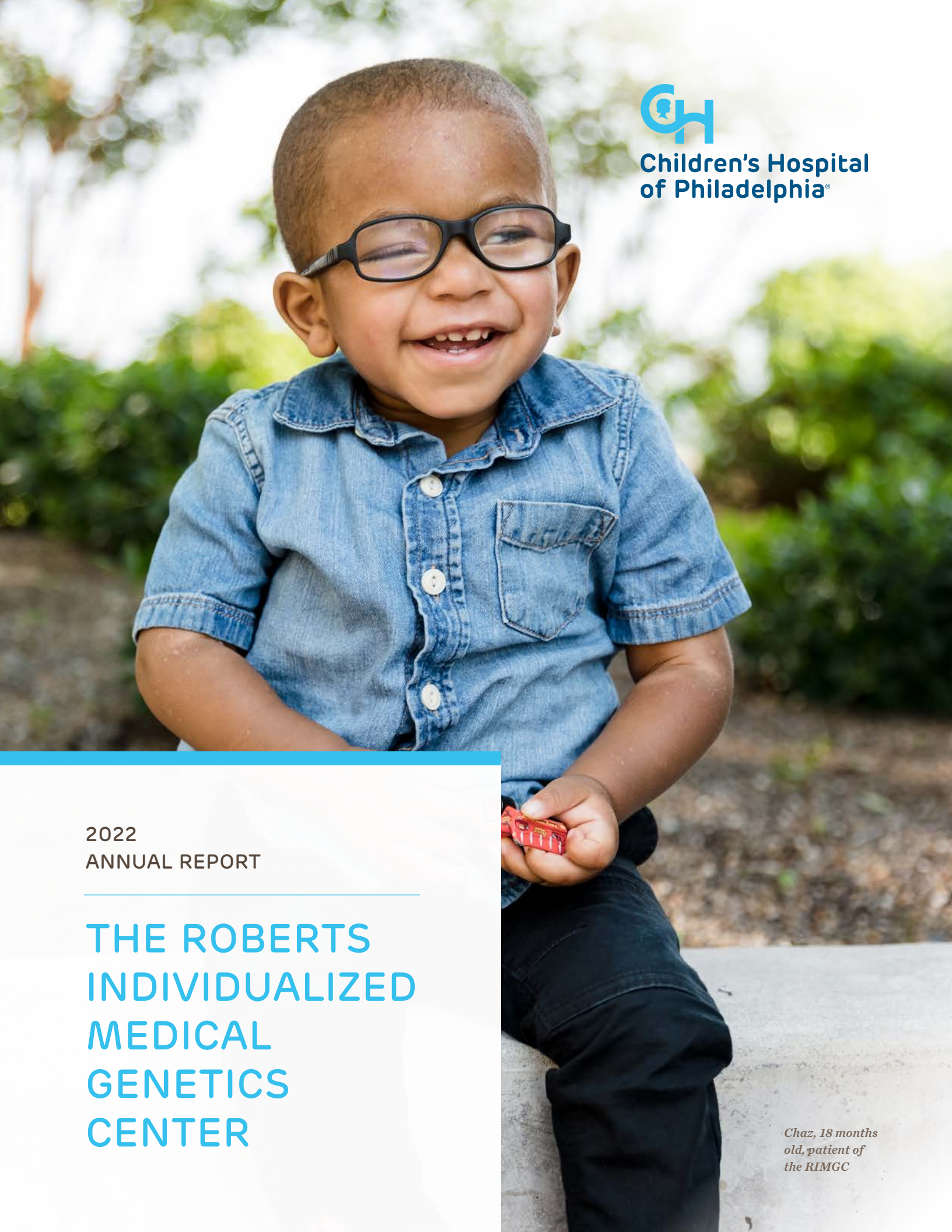


Children's Hospital of Philadelphia®

2022
ANNUAL REPORT

THE ROBERTS INDIVIDUALIZED MEDICAL GENETICS CENTER

Chaz, 18 months old, patient of the RIMGC

Emma Bedoukian, MS, LCGC, Co-Director of the Roberts Individualized Medical Genetics Center, connects with 22-month-old Edguardo, a patient with albinism.

our mission

To **facilitate access** to state-of-the-art individualized genetic testing and management for children, families and clinicians and to **promote integration** of phenotypic and genomic information into the diagnostic and research efforts at CHOP.

Latricia Lewis-Bunch, medical laboratory scientist II, uses a microscope to analyze cytogenetic samples in the Genomic Diagnostics Laboratory.

Maninder Kaur, MS, Research Laboratory Manager, (center) extracts patient-based cell lines and samples from liquid nitrogen in the RIMGC Sample Repository to help drive research. Looking on are interns Grace Araya (left) and Emma Lo (right).

LETTER FROM THE DIRECTORS

The year 2022 has been one of growth, new directions and collaborations for the Roberts Individualized Medical Genetics Center (RIMGC). It's shown RIMGC's ability to adapt and be resilient in the face of change and the ever-evolving technical challenges of the advancing field of genomic diagnostics. We are proud of our team in responding to these challenges — excited by our new team members and appreciative of the accomplishments of those who have moved on to other positions (and yet still support the RIMGC). This report provides some insight into the amazing work our team has accomplished to further our mission: to facilitate access to state-of-the-art individualized genetic testing and management for children, families and clinicians, and to promote integration of clinical and genomic information into the diagnostic and research efforts at Children's Hospital of Philadelphia (CHOP).

Due to increasing demand for genetic support services this year we welcomed four new genetic counselors — **Victoria Dortenzio, MS, LCGC, Emily Krauss, MS, LCGC, Anna Platt, MS, LCGC,** and **Jacob Squicciarini, MS, LCGC** — as well as a new Program Manager in the Research Core, B**ridget Gottlieb, BS** (see page 3).

We also experienced some transitions in our leadership with the promotion of **Livija Medne, MS, LCGC,** a founder and co-director of the RIMGC since its inception in 2014. She is now Systems Director for Genetic Counseling at CHOP. Medne now collaborates with medical and administrative leaders, and with CHOP's nearly 50 genetic counselors, to help address system-level opportunities and challenges. Without Medne's skill and dedication, the RIMGC would not be where we are today. Our patients and families are lucky that Medne continues to practice clinically within RIMGC, and the genetic counseling community is lucky to have a high-level advocate focusing on sustainability, innovation and strategic planning. **Emma Bedoukian, MS, LCGC,** a genetic counseling specialist in the RIMGC, was promoted to co-director. (see page 2).

We also saw the transition of **Tiffiney Hartman, PhD,** a genetic counselor who led RIMGC's Research Core, to Associate Director of Advanced Research Training for the Genetic Counselors Masters' Certificate Program at the Perelman School of Medicine at the University of Pennsylvania. While Hartman continues to play a role in the RIMGC to further our research mission, she will now also help shape the educational landscape of future genetic counselors by advancing their research expertise and working towards establishing additional graduate research programs for genetic counselors.

There are several research initiatives that the RIMGC has been involved in that are innovative, exciting and underscore the translational impact that genomics is having in the field of pediatric medicine including:

- Participating in several projects as part of CHOP's broad "Omics" initiative such as the Baby Eagle project (bringing rapid genome sequencing to infants in the neonatal and cardiac intensive care units)
- Projects to understand pediatric birth defects through our collaborative work on congenital diaphragmatic hernia and esophageal atresia studies
- The first clinical trial using gene therapy to treat hearing loss for a rare form of congenital hearing loss (OTOF-related auditory neuropathy)
- The RIMGC research biobank resource of clinical and genomic data linked to biosamples in the CHOP biorepository, which has surpassed 3,500 enrolled subjects and is available to all CHOP researchers.

Over the course of the year, we have seen how being creative and adaptable are key attributes to our successful team. We have developed roles for genetic counselors in divisions who previously had not had genetic counseling support. We have accommodated patient preferences by adopting ticket scheduling for some clinic and appointment types. We have increased our bandwidth for genomic testing as first-line testing increasingly shifts towards large scale tests, like exome and genome sequencing. We have advanced the clinical care of our patients and forwarded the research mission to lay the groundwork for tomorrow's clinical advances. We've worked hard and worked together; we can't wait to see what next year brings! ■

Ian Krantz, MD
Co-director

Emma Bedoukian, MS, LCGC
Co-director

Emma Bedoukian, MS, LCGC, (left) and Ian Krantz, MD, co-directors of the Roberts Individualized Medical Genetics Center.

contents

Grady, 6, patient of the RIMGC

[Photo on next page] The RIMGC Core Team includes (from left): Sarah E. Raible, MS, LCGC; Livija Medne, MS, LCGC; Jasmine Montgomery; Emily Krauss, MS, LCGC; Anna Platt, MS, LCGC; Audrey Lawrence; Alexandra Heck, BS; Jake Squicciarini, MS, LCGC; Tiffiney R. Hartman, PhD; Tyrah Williams; K. Taylor Wild, MD; Ian Krantz, MD, Co-Director; Emma Bedoukian, MS, LCGC, Co-Director; Cara M. Skraban, MD; Bridget Gottlieb, BS; Christopher Gray, MS, LCGC; Maninder Kaur, MS; Tomoki Nomakucki, MD, PhD; Victoria Dortenzio, MS, LCGC; Paul Deppen, MS; and Jacqueline Leonard, MSc, MS, LCGC.

Team members not pictured are: Priyanka Adusumalli, MHA; Justin Blair, MS; Brandon Calderon, MBA; Kosuke Izumi, MD, PhD; Deborah McEldrew, BS; and Louisa Pyle, MD, PhD.

OUR TEAM

Ian Krantz, MD
Co-director
Attending physician, scientist

Emma Bedoukian, MS, LCGC
Co-director
Genetic counselor

Priyanka Adusumalli, MHA
Business administrator

Justin Blair, MS
Bioinformatics scientist

Brandon Calderon, MBA
Administrative director

Paul Deppen, MS
Clinical and research coordinator

Victoria Dortenzio, MS, LCGC
Genetic counselor

Bridget Gottlieb, BS
Clinical and research coordinator

Christopher Gray, MS, LCGC
Genetic counselor

Tiffiney R. Hartman, PhD
Genetic counselor

Alexandra Heck, BS
Clinical and research coordinator

Kosuke Izumi, MD, PhD
Attending physician, scientist

Maninder Kaur, MS
Research laboratory manager

Emily Krauss, MS, LCGC
Genetic counselor

Audrey Lawrence
Clinical research assistant

Jacqueline Leonard, MSc, MS, LCGC
Genetic counselor

Deborah McEldrew, BS
Research technologist

Līvija Medne, MS, LCGC
Genetic counselor

Jasmine Montgomery
Practice manager

Tomoki Nomakucki, MD, PhD
Attending physician

Anna Platt, MS, LCGC
Genetic counselor

Louisa Pyle, MD, PhD
Attending physician, scientist

Sarah Raible, MS, LCGC
Genetic counselor

Cara Skraban, MD
Attending physician

Jake Squicciarini, MS, LCGC
Genetic counselor

K. Taylor Wild, MD
Attending physician

Tyrah Williams
Office coordinator

INTRODUCTIONS

Meet the new Co-Director of the RIMGC

With the transition of our founding co-Director, Livija Medne, MS, LCGC, to a new leadership role within Children's Hospital of Philadelphia (CHOP), we were delighted to be able to recruit **Emma Bedoukian, MS, LCGC**, to take the reins as the new co-Director of the RIMGC.

Bedoukian obtained her BS from Queen's University in Ontario, Canada, and her MS in Genetic Counseling at the Mount Sinai School of Medicine in New York.

Bedoukian is no stranger to the RIMGC, having been hired as our first full-time genetic counselor at the inception of the RIMGC in 2014. Bedoukian has been instrumental in building and growing the RIMGC from our initial patients and research initiatives to a thriving program with more than 1,400 annual patient encounters and multiple educational and research initiatives with a team of nine genetic counselors, four physicians, three administrators and other staff members.

Bedoukian has deep expertise in providing clinical services and counseling to families with a wide range of genetic diagnoses. She has a specific interest in ophthalmic genetics and has worked closely with the Department of Ophthalmology Children's Hospital of Philadelphia (CHOP) to provide genetic services for their retinal programs and to help coordinate gene therapy treatments in this population. Driven by her passion for this population she has established — and chairs — the Ophthalmology and Hearing Loss Special Interest Group, through the National Society of Genetic Counselors.

Bedoukian is passionate about patient care, optimizing administrative and clinical pipelines, mentoring junior counselors, the education of trainees and development of educational materials for the families we care for. She has been a tireless driver in carrying out the mission of the RIMGC to deliver state-of-the-art diagnostics and individualized care to patients and families from across all Divisions and Programs at CHOP.

Emma Bedoukian, MS, LCGC, new Co-Director of the Roberts Individualized Medical Genetics Center

While Bedoukian is a stellar genetic counselor, she is also a great colleague, collaborator, tireless runner and exceptional social planner — strongly believing in the philosophy that a team that is expected to work hard and be held to an extremely high standard should also be able to play together every now and then! All these attributes make Bedoukian an exceptional leader and the right person to guide the RIMGC into the next phase — we truly are incredibly fortunate to have her in this leadership position! ■

Welcome to our new hires of 2022!

RESEARCH

Bridget Gottlieb, BS

Hi, I'm Bridget, and I started as a program coordinator with the RIMGC in December 2022! I am originally from California and moved to the East Coast for college, where I went to Johns Hopkins University. After graduating, I moved to Philly and started at CHOP as a research assistant for three years at the Center for Autism Research. I'm really excited to continue working at CHOP and being in such a versatile role where my day-to-day ranges from enrolling families in genetic research to helping organize the Philadelphia Concours d'Elegance. It's special to get to be a part of all steps of the RIMGC from fundraising to working with families at the Cornelia de Lange Syndrome clinic to being a part of the research efforts.

CLINICAL

Victoria Dortenzio, MS, LCGC

Hi, I'm Victoria Dortenzio and I'm one of the new genetic counselors! I'm a recent graduate from Mount Sinai's genetic counselling program in NYC. I'm excited to be one of the first genetic counselors to join CHOP's hematology team and I look forward to joining the hearing loss clinic in RIMGC!

Emily Krauss, MS, LCGC

Hi, I'm Emily Krauss and I'm one of the new genetic counselors! I graduated from Jefferson's genetic counseling program in 2020. Prior to joining our team at CHOP, I was the ophthalmology genetic counselor at Duke Eye Hospital. I am beyond excited to continue genetic counseling in the field of Ophthalmology here at CHOP! I am also thrilled to be one of the first genetic counselors to join the Cystic Fibrosis team and expand in other areas of RIMGC with our hearing loss clinic.

Anna Platt, MS, LCGC

Hi, my name is Anna Platt, and I am a genetic counselor with the RIMGC at CHOP. My main focus is genetic counseling in the in-patient setting, especially the NICU and CICU, which has been one of the most rewarding experiences, as I am able to empower parents to make informed decisions about their child's future care, while providing psychosocial and emotional support during these time-sensitive and life-changing situations. I also am the genetic counselor with the multidisciplinary Immune Dysregulation Frontier Program (IDFP). Working with the IDFP has taught me the importance of centralized care for patients with complex immune dysregulation disorders and the critical role genetic testing and counseling can play.

Jake Squicciarini, MS, LCGC

Hi, I'm Jake Squicciarini and I'm one of the new RIMGC genetic counselors! I'm a recent graduate from the University of Pennsylvania Genetic Counseling Program and I was lucky enough to rotate with the RIMGC during my training. I'm excited to explore the impact of genetics in our RIMGC and hearing loss clinics and help extend the reach of the RIMGC into hematology as one of the first genetic counselors on the CHOP hematology team as well! ■

RIMGC: AN INTRODUCTION

The Roberts Individualized Medical Genetics Center (RIMGC) had another successful year providing clinical services and access to large-scale genomic testing to patients at Children's Hospital of Philadelphia (CHOP).

In 2022, there were nearly 1,400 patient encounters between the inpatient and outpatient settings. Telemedicine services continue to be utilized after expansion of the service at the beginning of the COVID-19 pandemic, providing patients access to care on a remote basis.

Genetic counselors continue to be a vital component to the success of the RIMGC. RIMGC genetic counselors are currently embedded within:

- **Ophthalmology** (Emma Bedoukian, MS, LCGC, and Emily Krauss, MS, LCGC)
- **Endocrinology** (Jacqueline Leonard, MSc, MS, LCGC)
- **Neuromuscular Undiagnosed Program** (Livija Medne, MS, LCGC)
- **Hematology** (Victoria Dortenzio, MS, LCGC, and Jake Squicciarini, MS, LCGC)
- **Cystic Fibrosis Program** (Emily Krauss, MS, LCGC)
- **General Genetics** (Christopher Gray, MS, LCGC, and Jacqueline Leonard, MSc, MS, LCGC)
- **Immune Dysregulation Program** (Anna Platt, MS, LCGC)

Sadie, 13, has a rare, genetic muscle condition and is treated by CHOP's RIMGC.

A benefit for our genetic counselors being part of the RIMGC is that they maintain the support of genetics colleagues throughout the hospital. Other counselors from the team can cover these clinics when the counselor is unavailable, and they can rely on the expertise of their colleagues when working through difficult genetic or psychosocial cases. Our counselors do not work in isolation. ■

STRIVE FOR KIDS

Support for youth with differences of sex development

The **STRIVE for Kids Program** (Supportive Team approach to ReproductIVE variations) was founded at CHOP in 2019 and named in 2022, with the goal of providing comprehensive care to children and families — with support from Endocrinology, Psychology and Genetics.

We focus on providing comprehensive diagnostic, management and treatment services, with an emphasis on tailoring care to specific patient and family needs. The program was formed at CHOP when healthcare providers determined they could — and should — do more to support families of children born with differences of sexual development (DSDs), intersex traits, differences of the gonads or genitalia at birth, or those who develop endocrine or urologic conditions later in childhood.

Differences of sexual development, or intersex traits, is an umbrella term describing a group of conditions that occur early in pregnancy in which sex development may not be typical. Sex development toward either a typical female path or a typical male path occurs as a function of sex hormones including testosterone or estrogen that act as chemical messengers during gonadal and/or genitalia development, and importantly the genetic factors that point the body down one path or the other during development.

A DSD occurs when there is an alteration in any of the factors needed for sex development, and therefore the reproductive body parts may develop differently. There are many intersex traits, and these can present as differences in external genitalia that are noticed at birth, or differences in internal reproductive body parts or sex hormones that are noticed later in childhood, in adolescence, or even in adulthood.

With the aid of the Divisions of Endocrinology, Psychology and the Roberts Individualized Medical Genetics Center, ***CHOP developed this specialized clinic to support multidisciplinary care for those with DSDs and endocrine differences.***

Visit **www.chop.edu/strive** learn more about the STRIVE for Kids Program at CHOP.

These differences can affect puberty, hormones, fertility and carry other health risks.

The reasons for people to be born with an intersex trait is that they have a biological difference that involves all or one of the following:

- Sex chromosomes
- Gonads (such as testicles, ovaries, ovotestes, and streak gonads)
- External genitalia
- Sex hormones, most often driven by an underlying genetic cause

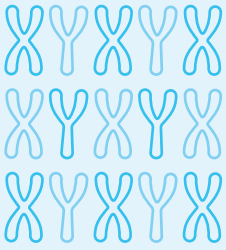
Genetics through the Roberts Individualized Medical Genetic Center (RIMGC) can therefore aid in the diagnosis of a specific DSD, the origin of that DSD within families, and can provide prognostic, and recurrence information.

Currently, our STRIVE program has seen and evaluated more than 200 patients, helped consult and counsel families with a variety of endocrine and DSD-related genetic conditions, medically manage these conditions, and determine and coordinate genetic testing as appropriate. Visits are comprehensive evaluations that include genetics, endocrinology, psychology, social work and urology, as needed.

The physicians, nurses, clinic support staff, psychologists, social workers, and genetic counselors in the STRIVE for Kids Program all have significant expertise in this field and share the goal of helping families as they navigate the medical, genetic and psychosocial care their child and family needs.

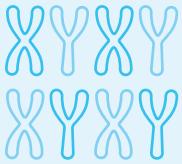
We saw significant growth in 2022: seeing an average of eight patients in our monthly clinic. We established monthly multidisciplinary case conferences including genetics, endocrinology, psychology, urology, radiology, pathology, oncology and ethics. We look forward to further growth in 2023! ■

STRIVE for Kids Program



Has evaluated

200+ patients



Sees an average of

8 patients each month

Multidisciplinary visits include:

Genetics, Endocrinology, Psychology, Social Work and sometimes Urology

TRANSPARENCY IS KEY

A 2021-2022 RIMGC Administrative Reflection

The Roberts Individualized Medical Genetics Center (RIMGC) recognizes that fiscal and clinical transparency with patient families is an essential first step to equitable, holistic care and continues to be at the forefront of administrative efforts to uphold this standard. The administrative core of the RIMGC welcomes patient families with prompt communication, equips families with knowledge about the recommendations for their child's care, and the options available to them. The goal of the RIMGC administration has always been for families to be included and informed, from the moment they are referred, through their clinical exam, and beyond.

New federal laws and statutes continue to shape the ways these goals are achieved. The **21st Century Cures Act** and the **No Surprises Act** — all or portions of which were both enacted during the past fiscal year — promote patient access to electronic health information and prevent unexpected medical bills. The RIMGC administrative core worked consistently with Finance leadership at Children's Hospital of Philadelphia (CHOP) to embrace these standards and to vocalize both provider and patient perspectives throughout the process of obtaining prior authorizations and cost estimates for genetic testing. Through the pioneering work of the RIMGC, hospital-wide protocols for genetic testing authorization obtainment were established. This workflow integrates family awareness and assent, seamless communication with financial counselors, and efficient updates to families — all while prioritizing the clarity of updates to clinicians and families.

As leaders in CHOP-wide practices of prior-authorization, the RIMGC is constantly reflecting on how to improve the patient experience, minimize burden to families, and optimize our workflow. We recognize the importance of empowering patient families with estimates and expectations before their clinical visit and are wholly dedicated to support them at every step.

RIMGC Practice Manager Jasmine Montgomery is constantly geared for innovation. From increasing patient access opportunities to daily streamlining of clinical operations, Montgomery consistently advances the mission of the RIMGC. Tyrah Williams, office coordinator, and Audrey Lawrence, clinical research assistant, complete the team, driving communication with families and clinicians. The trio works tirelessly to ensure families feel welcomed, informed and respected.

The RIMGC administrative core continues to advance with patient-facing goals and innovative approaches to optimizing patient communication, transparency and access. ■

RESOURCES

21st Century Cures Act
bit.ly/21CCA

No Surprises Act
cms.gov/nosurprises

The Administrative Core of the RIMGC is held together by its capable and supportive team including (from left) Tyrah Williams, Jasmine Montgomery and Audrey Lawrence.

CLINICAL AND RESEARCH SPOTLIGHT

Cornelia de Lange syndrome, Pallister-Killian syndrome and Kabuki syndrome

The Rare Diagnoses Core of the Roberts Individualized Medical Genetics Center (RIMGC) was established to provide a comprehensive medical and research home for children with multisystemic genetic diagnoses. The rare diagnoses core has clinical and research programs focused on providing medical care for those with **Cornelia de Lange syndrome (CdLS)** and related diagnoses, **Pallister-Killian syndrome (PKS)** and **Kabuki syndrome.**

Specialty multidisciplinary clinics are held for each of these diagnoses where ***patients and families can meet with a team of clinicians who are leading experts in their child's diagnosis.***

Clinical and research leadership

Our team is committed to serving not just local families, but national and international families as well. The **Center for Cornelia de Lange Syndrome and Related Diagnoses** has evaluated more than 1,000 individuals with CdLS and related diagnoses making it the largest program of its kind. We are proud to announce the CdLS clinical team has grown this year with the addition of occupational therapy services to further enhance our families multidisciplinary care experience with a focus on fine motor, visual/motor and visual/perceptual development. Our program is also the first to have developed a PKS clinic which exists as the only clinic in the world for children with this diagnosis.

In addition, our **Kabuki Syndrome Clinic**, which was established in 2021, is one of few established clinics in the country and continues to expand with increasing demands from growing patient volumes. Patients have traveled from all over the country and the world to attend the monthly multidisciplinary clinics to receive expert advice from our specialists — with the ultimate goal of improving the lives of children and adults with these rare diagnoses.

The clinical and research team of the rare diagnoses core is composed of an internationally recognized team committed to children with conditions affecting growth, cognition, and multiple body systems. Many of our team members have traveled to national meetings during the past year to collaborate and share scientific developments and breakthroughs in the field.

Cornelia de Lange syndrome

RIMGC members including **Justin Blair, MS, LCGC; Maninder Kaur, MS, LCGC; Sarah Raible, MS, LCGC; Anna Platt, MS, LCGC;** and **Ian Krantz, MD;** were invited to present at the National Cornelia de Lange Syndrome Foundation meeting in June 2022. Topics presented ranged from genomic analysis in CdLS, a novel candidate gene, a multidisciplinary clinic model, retrospective experience of returning research results and advancements in clinical trials.

Kennedi, 7, patient with Cornelia de Lange syndrome treated at CHOP.

Pallister-Killian syndrome

In addition, **Kosuke Izumi, MD, PhD,** and Dr. Krantz, along with Sarah Raible, MS, LCGC, presented at the **PKS Kids** foundation meeting in July 2022. The trio provided an overview on Pallister-Killian syndrome, the genetic basis of the diagnosis, and research updates. Additionally, Dr. Izumi and members of the research team at Children's Hospital of Philadelphia (CHOP) were available to provide patient consultations and enroll interested families in the RIMGC research protocol.

The CdLS Center is also an international leader in research. Not only are we committed to further understanding the mechanisms involved with these diagnoses, but we are also focused on therapeutics. The Center offers the opportunity to translate clinical and basic science research into improved management and treatment for individuals with these complex diagnoses in a setting where they can receive comprehensive care and coordinated services. Our CdLS team recently had a manuscript accepted for publication that reviews our 25 years of experience with CdLS including:

- Detailed genomic analyses
- Novel candidate genes
- Common mechanisms
- Genotype-phenotype correlations

Our team received a National Institutes of Health (NIH) X01 award which we are using to analyze genome-wide RNA sequencing data on a cohort of patients without a genetic etiology for their CdLS diagnosis. In addition, Dr. Izumi was recently awarded an NIH R21 grant to support his work on Pallister-Killian syndrome, specifically focused on elucidating the effects of extra chromosome elimination in mosaic aneuploidy syndrome, using PKS as a model.

Our research efforts continue to yield new insights into the clinical and basic science issues relevant to the children we care for and to support investigators interested in building careers focused on rare genetic diagnoses.

Our teams research efforts are funded by the CdLS Center Endowed Funds at the CHOP, the NIH, the PKS Kids Foundation and Cool Cars for Kids, Inc. ■

CHOP GENOMICS AND GENETIC PROGRAMS

Learn about specific CHOP programs in the links below.

Roberts Individualized Medical Genetics Center
www.chop.edu/IMGC

Center for Cornelia de Lange Syndrome and Related Diagnoses
www.chop.edu/CdLS

Kabuki Syndrome Clinic
www.chop.edu/kabuki-clinic

‘EYEING’ EARLY CLUES TO RARE GENETIC CONDITION

“... CHOP has helped us get this far and I know Chaz is going to do great things.”

— Jazmin, Chaz’s mom

Jazmin cuddles her son, Chaz. during a visit to the rooftop gardens at the Buerger Center for Advanced Pediatric Care at CHOP.

Nance Horan Syndrome: Chaz’s Story

Chaz was only two months old when his family learned he was nearly blind. Though the infant could track light, he couldn’t recognize familiar faces. His pediatrician referred the family to Children’s Hospital of Philadelphia (CHOP) for additional testing, where they learned Chaz had congenital cataracts and would need immediate surgery.

“Learning our baby couldn’t see was torturous,” says Jazmin, Chaz’s mom. “But we had no idea his condition would lead to answers to medical issues my family has had for generations.”

Early development

Chaz was born full-term at a community hospital outside Philadelphia. Though a healthy 6 lbs. 8 oz. at birth, his family noticed he didn’t open his eyes much at the hospital — or even after the family returned home to Glenside, PA.

"His eyes looked gray — like smoky," Jazmin recalls. When she and Chris, Chaz's dad, asked the pediatrician about it, the doctor wasn't concerned at first. But at 2 months old — at Jazmin's insistence — the pediatrician referred the family to a pediatric ophthalmologist at CHOP.

They met with **William Anninger, MD,** who performed a detailed eye examination, conducted tests, and confirmed Chaz had extremely limited vision in both eyes due to congenital cataracts. This condition, which produces a cloudiness in the lens of the eye, is rare in infants — only affecting about two to three babies per 10,000 — but is treatable.

However, to give Chaz the best chance at healthy sight, he would need immediate surgery.

"We were scared, but Dr. Anninger was so reassuring," Jazmin says. "He told us he sees babies with cataracts all the time. 'We can fix this,' he told us. 'After surgery, I'm confident he'll be able to see.'"

Cataract surgery

Within a week — and right before Christmas 2021 — Chaz underwent cataract surgery at CHOP's Main Hospital in Philadelphia. Jazmin and Chris waited anxiously through the nearly two-hour surgery to treat both of Chaz's eyes.

"When Dr. Anninger came out to see us after surgery, he told us everything went great," Jazmin said. "It was such a relief."

The couple was able to take Chaz home the same day. The baby had cones covering his eyes to protect them while they healed. "He looked like a little bumble bee," Jazmin says. The family was given instructions on how to care for Chaz's eyes until a follow-up visit with Dr. Anninger a few days later.

"We were at the hospital when the cones came off and Chaz opened his eyes. He fast blinked a few times, and immediately reached out to touch our faces," Jazmin said. "We were talking to him, and you could tell he was really seeing us for the first time. It was such a beautiful moment."

Though surgery treated the cataracts, Chaz's vision was still limited. He would need contacts — and later glasses — to help him see more clearly. Caring for an infant with contacts was challenging, but thankfully, CHOP staff coached the parents on how best to care for Chaz and his contacts, including removing them weekly for cleaning.

New symptom leads to more testing

At Chaz's second follow-up visit with ophthalmology, eye tests revealed the pressure in Chaz's eyes was abnormally high. High eye pressure can cause pain in and around the eye, blurred vision, blind spots, irritation, and headaches. It can also be an early sign of glaucoma.

Because Chaz was too young to say how he was feeling or what he could see, his parents and doctors had to rely on the baby's outward symptoms — like rubbing his eyes and fussiness — as well as testing to touch the surface of his eye to flatten the cornea and measure the pressure.

Troubled by the results, Dr. Anninger referred Chaz to **Monte D. Mills, MD,** Senior Surgeon in the Division of Ophthalmology, and the team at the Roberts Individualized Medical Genetics Center (RIMGC).

Dr. Mills examined Chaz and discovered an excess build-up of fluid behind the baby's corneas. Chaz would undergo three procedures to safely drain the fluid behind his eyes until a tube could be implanted to consistently prevent the fluid buildup.

Continued >

Family history provides clue to rare genetic disorder

At the RIMGC, Chaz and his family met with **Emma Bedoukian, MS, LCGC,** Genetic Counselor Manager and then-Associate Director, now Co-Director of the RIMGC, and **Cara M. Skraban, MD,** an attending physician in the Division of Human Genetics and clinical core leader in the RIMGC.

After talking to Chaz's family, the CHOP team learned Chaz was not the first in his family to have congenital cataracts — Jazmin was also diagnosed with congenital cataracts as an infant. So was her brother — Chaz's uncle, now in his 50s — who's been legally blind since childhood; and her uncle, who's 70 and is now completely blind. Jazmin only needs glasses.

This dramatic family history made Bedoukian and Dr. Skraban suspect there was a genetic basis behind Chaz's condition — and perhaps that of his family members. They ordered blood and genetic tests for Chaz; revealing the baby had Nance Horan syndrome.

Nance Horan syndrome is a rare genetic diagnosis characterized by teeth differences, cataracts, poor vision, and other eye issues. While the range and severity of symptoms can vary, the cause is the same: a genetic change in the NHS gene that is inherited as an X-linked dominant trait. The diagnosis can also be associated with physical abnormalities and, in some cases, intellectual disabilities.

While both boys and girls can be affected by the NHS gene, boys often exhibit more severe symptoms because they have only one X chromosome, while girls have two. The inheritance pattern also explains why Jazmin's vision was not as severely affected as her brother or uncle.

Answers and acceptance

While Bedoukian and Dr. Skraban educated Jazmin and Chris about Nance Horan syndrome, Chaz's parents couldn't help doing their own web searches about the condition and fearing worst-case scenarios for their baby's future.

Parents Chris and Jazmin support Chaz's early development and encourage him to try new things.

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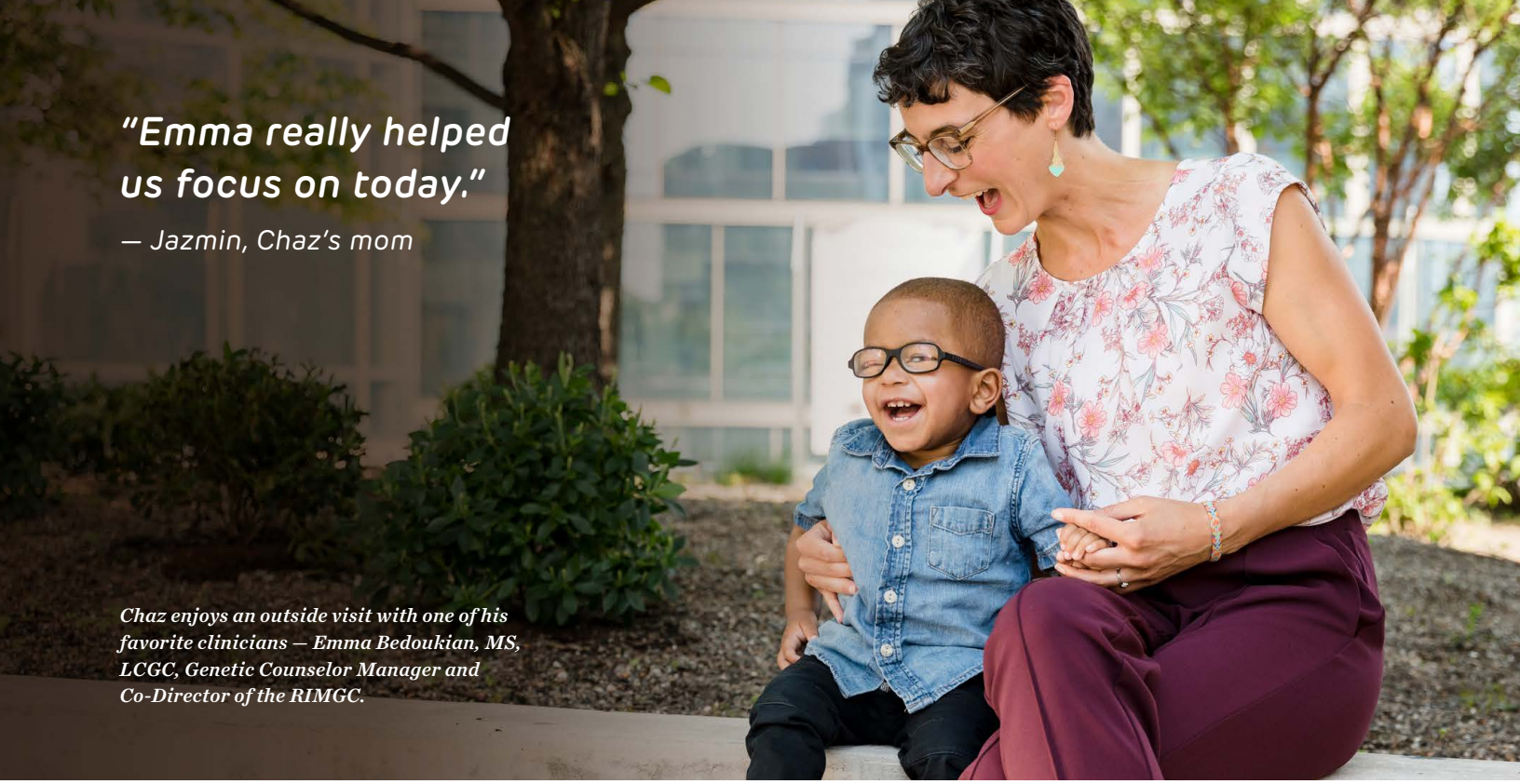


Chaz enjoys an outside visit with one of his favorite clinicians — Emma Bedoukian, MS, LCGC, Genetic Counselor Manager and Co-Director of the RIMGC.

The team at CHOP helped the family put the diagnosis in perspective, to understand that while Chaz's condition would likely create some developmental and learning challenges, it would not progressively worsen over time. Instead, Chaz would be able to learn, grow and develop — just in his own time.

There were many ways Chaz's family, medical team, psychosocial and early intervention team could support his growth and development, Bedoukian added, and better prepare him for the future.

"Emma (Bedoukian) really helped us focus on today," Jazmin says. "My brother is legally blind, but he gets around fine. He went to college. He's living his life ... and there's no reason to think Chaz won't be able to do that too."

Chaz got his first pair of glasses at 6 months of age and started early intervention services including physical and vision therapy. At 9 months, he began occupational therapy to improve his eye-hand coordination. As Chaz has gotten older, the ways to motivate him to actively participate in his therapy have changed — but food remains a consistent lure, Jazmin said.

"He loves all food and is very food-motivated," she adds. "But he also loves music and light-up toys and toys that vibrate or move. It's been fun trying to find the next best thing to get him excited."

Hope for Chaz's future

Today, Chaz is a bubbly and happy 19-month-old who enjoys couch-cruising, loves Cookie Monster and reading with his "Da Da." While he doesn't say a lot of words yet, it's obvious to his parents that he understands them when they talk to him.

Chaz recently started daycare, is enjoying being around the other kids, and having more people to interact with and pay attention to him. A trip to the Please Touch Museum in Philadelphia revealed Chaz also loves funhouse mirrors, carousel rides and waterplay.

"I don't know what the future holds for Chaz, but I do know what I want for his future: to be happy, to be productive, to live a normal life," Jazmin says. "I want people to treat him well, to get the support he needs and to be challenged to be all he can be. CHOP has helped us get this far and I know Chaz is going to do great things." ■

RARE CARS FOR RARE DISEASES

The Philadelphia Concours d'Elegance, initiated in 2017, is an annual local fundraising and awareness event to support the Rare Diagnoses Core of the Roberts Individualized Medical Genetics Center (RIMGC). The event is presented by Cool Cars for Kids, Inc. (CCfK), a nonprofit organization that aims to increase awareness of the issues faced by families of children with rare genetic diagnoses. Funds raised by CCfK are focused toward delivering care, providing support and driving research for children with rare genetic diagnoses with the goal of contributing a brighter future through development of novel treatments and cures.

The 2023 event

The annual Concours d'Elegance event was a two-day classic car show and competition held at the Simeone Automotive Museum in Philadelphia. The 6th event, "Porsche-delphia," highlighted Porsche as its feature marque. The gala preview dinner was held **Friday, June 23,** and included a wine tasting with Coach Dick Vermeil, a Concours preview and silent auction.

The main Concours d'Elegance event took place on **Saturday, June 24,** and included an invitation-only assembly of American and European classic and historic automobiles and race cars. The day-long event included professional judging and awards for cars and their owners, as well as music, local food vendors and family-friendly activities. A panel of world-renowned Porsche celebrities was in attendance.

For more information about Cool Cars for Kids and the Philadelphia Concours d'Elegance, please visit **coolcarsforkids.org** and **philadelphiaconcours.com.**

ABOUT THE PHILADELPHIA CONCOURS D'ELEGANCE

Established in **2017**

+$300k raised to support RIMGC to-date

Event has funded the:

- Skraban-Deardorff syndrome family meeting
- Congenital Hyperinsulinism Family Conference
- Ongoing research into Pallister-Killian syndrome and a novel pediatric neurodevelopmental syndrome caused by variants in Histone H3.3

*Over $300,000 has been **donated** to support the cause through these events since 2017.*

Supporting CHOP's RIMGC Since 2017

Since the inaugural Philadelphia Concours d'Elegance event in 2017, Cool Cars for Kids, Inc. has donated more than **$300,000** to Children's Hospital of Philadelphia (CHOP) and the RIMGC Rare Diagnoses Program to support clinical and research operations.

With the money donated this past year, Cool Cars for Kids released a request for applications (RFA) to the CHOP community providing funding opportunities for patient and community outreach, as well as basic science research in rare genetic diagnoses. ■

CCfK'S IMPACT AT CHOP … AND BEYOND

Skraban-Deardorff Family Meeting

Funds were awarded to **Cara M. Skraban, MD,** attending physician in the Roberts Individualized Medical Genetics Center, to support a family meeting for a novel genetic diagnosis, **Skraban-Deardorff syndrome.** The Skraban-Deardorff family meeting was held in July 2022 at Children's Hospital of Philadelphia (CHOP) and consisted of short patient evaluations, scientific and clinical updates from clinicians and researchers, professional networking, and family-friendly activities. This was the third family meeting for this condition and was the largest gathering of patients and families todate, with 22 families in attendance throughout the three-day event.

Cara M. Skraban, MD

Skraban-Deardorff syndrome was first described in 2017 by two then-CHOP physicians, Dr. Skraban, who is still at CHOP, and Matt Deardorff, MD, PhD, now at the Children's Hospital of Los Angeles.

With the invaluable support of **Christopher Gray, MS, LCGC,** genetic counselor at CHOP, and Katie Grand, MS, LCGC, genetic counselor at Cedars-Sinai Medical Center, the family meeting brought together the team of clinicians and scientists working to further elucidate the clinical spectrum of the condition and the underlying molecular mechanism — with the ultimate goal of improving the lives of the children.

Congenital Hyperinsulinism Family Conference

A second grant was awarded to **Diva De León-Crutchlow, MD, MSCE,** director of the Congenital Hyperinsulinism Center, and chief of the Department of Endocrinology, to support the 2023 Congenital Hyperinsulinism Family Conference April 14-16, 2023. The HI Family Conference is a joint effort of Congenital Hyperinsulinism International and the Congenital Hyperinsulinism Center at CHOP. The event brings together world-renowned physicians, researchers and specialists, along with patients, families and advocacy leaders.

Diva De Leon-Crutchlow, MD, MSCE

Continued >

Katelyn, age 6, was one of the first children diagnosed with Skraban-Deardorff syndrome, a disorder identified by CHOP physicians in 2017.

Ongoing research into PKS and novel pediatric neurodevelopmental syndrome

Kosuke Izumi, MD, PhD

Ramakrishnan Rajagopalan, PhD

The remaining two grants support ongoing research efforts at CHOP for rare diseases, specifically Pallister-Killian syndrome and a novel pediatric neurodevelopmental syndrome.

Kosuke Izumi, MD, PhD, attending physician in the RIMGC, and **Ramakrishnan Rajagopalan, PhD,** director of Translational Bioinformatics in the Division of Genomic Diagnostics, were awarded a grant to test the utility of DNA methylation profiling in Pallister-Killian syndrome (PKS) to support development of a novel clinical genomic test for PKS.

Laura Bryant, MD, and **Emily Durham, MD,** senior postdoctoral scholars in the laboratory of **Elizabeth J.K. Bhoj, MD, PhD,** an attending physician with the Division of Human Genetics, were awarded funds to support their investigation of a novel pediatric neurodevelopmental syndrome caused by de novo heterozygous missense variants in Histone H3.3. The funds are being utilized to validate craniofacial and neurological phenotype of a mouse model and determine the mechanism of action of a specific missense variant in H3.3 to help gather data for future funding.

Each of the awardees were given funds for a one-year period to support their work and further our broader mission of raising awareness and accelerating research in the rare disease community. ■

Hilde, 2½, a patient with Pallister-Killian syndrome (PKS), interacts with Kosuke Izumi, MD, PhD, at Children's Hospital of Philadelphia, while her mom, Jennifer, looks on.

A COMMITMENT TO THE NEXT GENERATION

The Roberts Individualized Medical Genetics Center (RIMGC) continues its commitment to the education and training of the next generation of geneticists, genetic counselors, and scientists. Our clinics regularly host rotating fellows, genetic counseling students, and observers, where we provide exposure to clinical and research initiatives with a focus on pediatric genomics and individualized medicine.

While the RIMGC continues to closely support local training programs including Clinical and Laboratory Genetics Programs at Children's Hospital of Philadelphia (CHOP), and the University of Pennsylvania's Master of Science in Genetic Counseling Program, we are pleased to see the return of in-person rotators coming from across the country and around the world as we transition out of the pandemic era.

This year, we were pleased to host Noura Abul-Husn, MD, PhD, (pictured) for the 2021-2022 CHOP Pediatric Grand Rounds RIMGC Lectureship. Dr. Abul-Husn is an Associate Professor of Medicine and Genetics, founding Chief of the Division of Genomic Medicine, and Clinical Director of the Institute for Genomic Health, all at the Icahn School of Medicine at Mount Sinai in New York City.

Dr. Abul-Husn's research includes the investigation of how biobanks embedded within electronic medical records can provide clinical insights and inform therapeutic discovery. She is also principal investigator of the eMERGE (electronic MEdical Records and GEnomics) Network, which seeks to integrate polygenic risk information into the clinical care of diverse populations. Dr. Abul-Husn's important work illustrates how genomic data can be leveraged to inform approaches to medical care at both the individual and population levels, and we were thrilled to be able to host her this year.

As we continue to see the rapid incorporation of genomics into the clinical care of our patients and families, the RIMGC remains dedicated to supporting the continued education and training of tomorrow's clinicians and scientists. ■

> *"Keeping people as healthy as possible for as long as possible."*
>
> *- Noura Abul-Husn, MD, PhD*

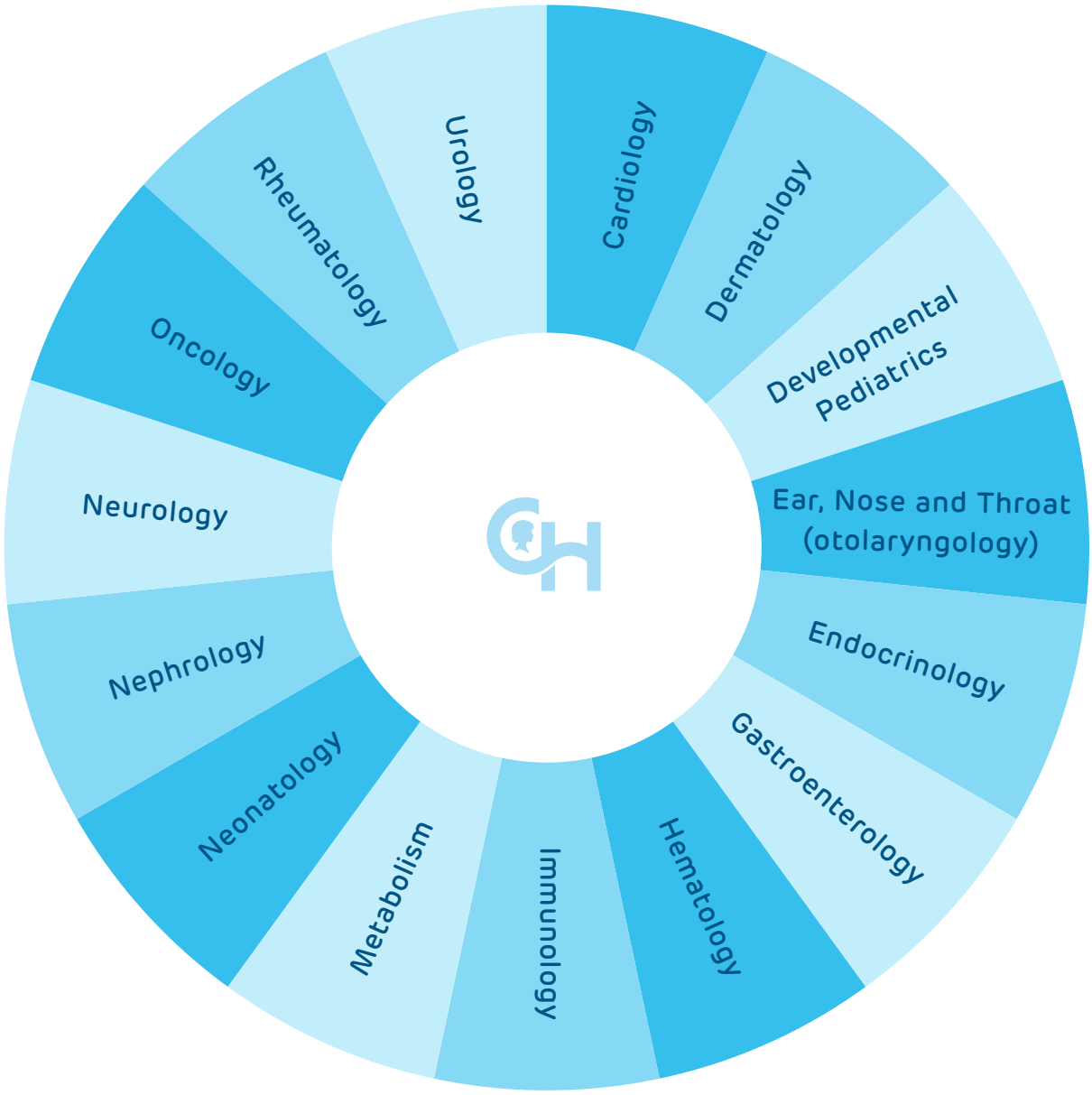
Alice Tran, BS, a genetic counseling assistant in the Genomic Diagnostic Lab, reviews patient data on a stored DNA sample.

GENETIC CHAMPIONS AT CHOP THROUGH THE RIMGC

When the Roberts Individualized Medical Genetics Center (RIMGC) was established, the genetic champion system was created to identify specialist physicians and providers across the different practice areas at Children's Hospital of Philadelphia (CHOP) who could be RIMGC advocates and experts in the genetic associations within their field.

These genetic champions have been invaluable resources of expertise across the variety of specialties at CHOP, both for the interpretation of genetic results, and referrals to and from our center for evaluation.

As of 2022, we have identified 45 genetic champions at CHOP across the specialties of:



In December 2022, the RIMGC hosted our annual Breakfast of Champions. This annual event updates our genetic champions on the current updates from the RIMGC and the Genomic Diagnostic Laboratory (GDL).

This year, we highlighted:

- Exciting updates regarding the transition to the genome platform at the GDL in 2023 (see page 27)
- The reporting criteria and categories of variants on the exome analysis testing
- Updates for our champions on the process of the genetic test utilization team
- News from the RIMGC, including the hiring of new counselors and growth of genetic testing at CHOP

These sessions help ensure our champions are up to date on our actions and the work the genomics diagnostic lab and the RIMGC has accomplished. It was an exciting morning full of discussions and questions from our champions!

If you're a physician at CHOP who is interested in becoming a RIMGC genetic champion, please do not hesitate to reach out to us at **imgcclinic@chop.edu.** ■

Emma Bedoukian, MS, LCGC, Co-Director of the RIMGC and a genetic counselor, meets up with 22-month-old patient Edgardo, who was born with albinism and other genetic differences.

GOING BIG WITH OMICS

Translational genomics is impacting pediatric medicine

There are several new research initiatives that the RIMGC has been integral to at CHOP. These are not only innovative and exciting, but underscore the translational impact that genomics is having in the field of pediatric medicine.

The RIMGC is playing a key role in the exciting broad "Omics" initiative that CHOP has embarked on — with a goal of positioning CHOP as the leader in integrating genomics (and other omics approaches) into the clinical care and research programs across the institution in an integrated and comprehensive manner.

Some of the initiatives that we are excited to play a part in include:

- The CHOP Biobanking initiative
- The Baby Eagle project (bringing rapid genome sequencing to infants in the neonatal and cardiac intensive care units)
- The Undiagnosed Disease Program
- Translation projects to understand pediatric birth defects through our collaborative work on congenital diaphragmatic hernias (CDH) and tracheoesophageal fistula/esophageal atresia studies

Our RIMGC research biobank resource of clinical and genomic data linked to bio samples in the CHOP biorepository has surpassed 3,500 enrolled subjects and we are merging this resource with the Division of Surgery's Birth Defects Biorepository (BDB). We are also integrating all this data into the broader CHOP Arcus data library, a group of tools that seamlessly links biological, clinical, research and environmental data. Our goal is to make these invaluable resources — generously contributed by our patients and their families — available to all CHOP investigators to support tomorrow's breakthroughs in diagnostics, clinical care and therapeutics.

K. Taylor Wild, MD, a dual fellow in neonatology and genetics, is helping to expand genetic testing for newborns at CHOP through a pilot "Baby Eagle" project. Here, she talks with Penelope and her 9-month-old daughter Eliana, a patient in CHOP's Newborn/Infant Intensive Care Unit.

Because most genomic diagnoses are so rare, collaborating with other large research institutes enables sharing of de-identified data to combine otherwise very small sample sizes into larger cohorts available for research and discovery. The CHOP RIMGC is involved in a large collaborative initiative called the Genomics Information Commons (GIC) that fosters teamwork between multiple institutions inspired by the common vision of accelerated genomic research discovery, collaboration and improved clinical outcomes.

Continued >

The GIC was initially established between CHOP, Boston Children's Hospital and Cincinnati Children's Hospital Medical Center with the creation of policies, highly scalable technologies and procedures for sharing de-identified genomic and phenotypic data and biospecimen metadata on consented individuals. The GIC has grown to include several additional large children's hospital networks around the country and has led to multiple novel projects for CHOP investigators.

John A. Germiller, MD, PhD

We have recently helped spearhead the first-ever gene therapy clinical trial for hearing loss. Working in close collaboration with **John A. Germiller, MD, PhD,** Director of Clinical Research in the **Division of Otolaryngology** (ENT) and his team at CHOP, and with industry partner Akouos Inc., we have embarked on a natural history study and gene therapy trial for the treatment for OTOF-related auditory neuropathy (a rare form of congenital hearing loss). With the Genetics of Hearing Loss Clinic being a major clinical part of the RIMGC since its inception, we are excited to be a part of this study that promises to take us from cutting edge molecular diagnostics for hearing loss to a potential new future of treatment. ■

RESOURCES

Visit link below to submit a request for RIMGC research enrollment.

bit.ly/IMGCredcap

Enter the RIMGC Research Portal

www.chop.edu/IMGC-research

A goal of positioning CHOP as the leader in integrating genomics into clinical care and research programs.

Allison, 8, a patient with optic neuropathy treated at CHOP.

UNLOCKING GENETIC CLUES

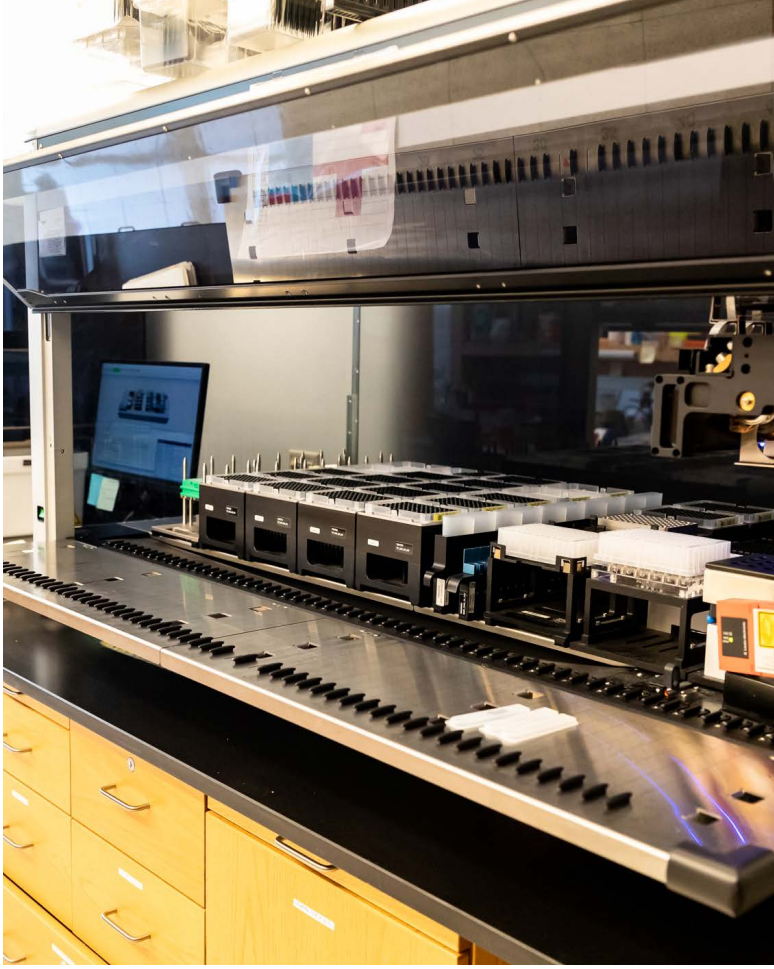
Genome-based tests support clinical decision-making

The Roberts Individualized Medical Genetics Center (RIMGC) works with the Genomic Diagnostic Laboratory (GDL) in the Department of Pathology to provide clinical expertise for complex test interpretation and to optimize the utilization of diagnostic genetic testing at CHOP.

These collaborative efforts greatly impact new test development in specialized areas of medicine and ensure that the benefits of these tests are fully realized by our patients.

The RIMGC and GDL continued to collaborate in the hospital's genetic test utilization program including the development of algorithms to guide somatic testing and a new policy to guide the use of rapid genomic testing. While the primary focus has been on genetic tests ordered during an inpatient admission, in some cases the review of outpatient tests has helped limit unexpected out-of-pocket costs for patients and families. The program continues to reassess its processes to facilitate transparent communication with families and support excellent patient care, ensuring that every patient receives the right genetic tests at the right time.

In June 2022, the GDL implemented the Epic Genomics module in collaboration with the RIMGC, Genetics, Oncology and Lab Information Services. This application supplies provider education of clinically significant genomic results within the EHR (electronic health record) and utilizes just-in-time clinical decision support.



Researchers use the liquid handler machine (pictured) to prepare patient samples for next generation sequencing, whole genome sequencing, SNP identity checks, and automated PCR set ups.

The GDL built an interface to deposit structured genomic data directly into Epic (the EHR) to drive clinical decision support and build a variant database for quality improvement and clinical research activities. The initial launch of Epic Genomics focused on 28 cancer predisposition syndromes targeted as secondary findings on the CHOP Medical Exome, utilizing genomic indicators to initiate consults with the Cancer Predisposition Clinic and to display best practice advisories to avoid or minimize ionizing radiation exposure to patients diagnosed with retinoblastoma or Li Fraumeni syndrome. We are currently building additional genomic indicators and advisories to assist in the care of patients with clinically significant findings in genes associated with cardiovascular-related conditions.

Continued >

In February 2023, the GDL transitioned to a new genome-based platform for constitutional multi-gene tests, including the CHOP Medical Exome. These multi-gene panels are now able to capture both sequence variants and copy number variants through a single technology, which serves to reduce the costs of these tests to patients and makes ordering more streamlined for clinicians. This technology change also lays the groundwork for GDL to offer customizable multi-gene panels. While the initial genome-based CHOP Medical Exome will be similar in scope to the previous version of the test, this technology change will provide the infrastructure to develop a genome analysis encompassing more types of variants in future versions of the test.

Looking ahead, the GDL is thrilled to partner with the RIMGC on project "Baby Eagle," a research study which will assess the utility of rapid genome sequencing for patients in CHOP's Neonatal/Infant Intensive Care and Cardiac Intensive Care units. This study will evaluate how rapid sequencing technologies can be used to speed diagnoses in these critical care settings, and how the use of this technology may benefit patients compared to current standard of care genetic testing.

More new tests are on the horizon thanks to ongoing work with our clinical partners, including development of a liquid biopsy circulating tumor DNA test with our partners in Oncology.

The GDL looks forward to another year of collaboration and innovation with the RIMGC and our clinical partners throughout CHOP to provide the best diagnostic care for the patients and families we serve. ■

[From top to bottom] ***Image 1:*** *In the research lab, a centrifuge is used to separate the contents of a blood sample.* ***Image 2:*** *Dried blood spots from patients are used to identify several inherited and metabolic diseases that can impact a child's growth, development and health.* ***Image 3:*** *An electric pipetter, like the one pictured, is used to transfer liquids (like blood and plasma) in the lab for testing and evaluation.*

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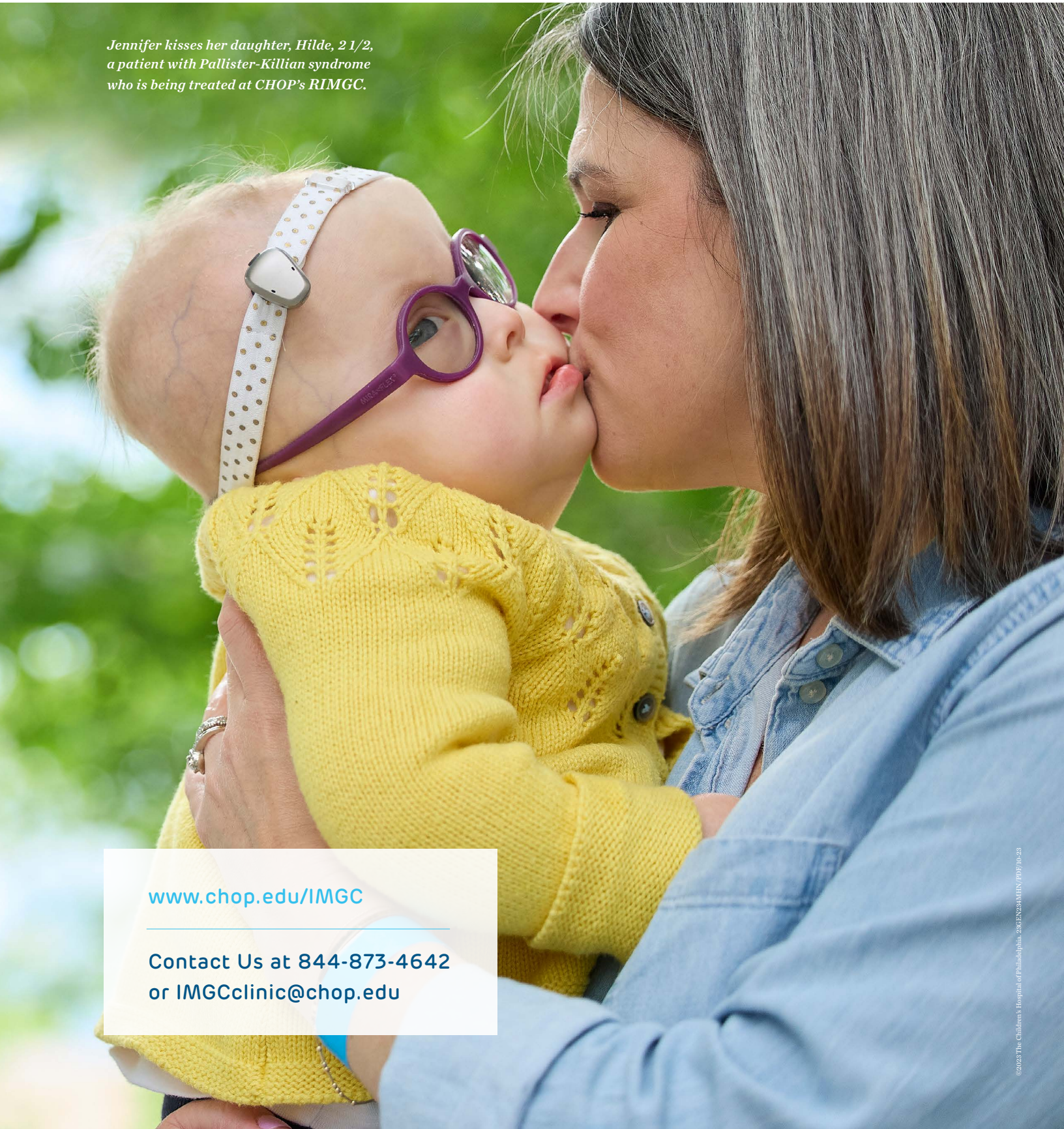

Jennifer kisses her daughter, Hilde, 2 1/2, a patient with Pallister-Killian syndrome who is being treated at CHOP's RIMGC.

www.chop.edu/IMGC

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