Dear Friends,

This Winter 2020 newsletter marks our 12th quarterly newsletter. It’s promising to think about how much we have achieved in three, short years, and we thank you for being part of the RUNX1 Family. This Winter Newsletter includes a Patient Spotlight on patient and RUNX1-FPD advocate Georgie Blackburn and her family’s personal journey. As you might have heard, fall 2020 will mark our first-ever patient meeting, on the back of our 4th Annual Scientific Conference, and we are very excited to plan an intimate, thoughtfully-constructed meeting where patients and specialists can learn from each other and forge relationships. We expect this year’s Scientific Conference to expand upon previous years’ in scope and size. Next, our Executive Director, Dr. Katrin Ericson, will share her key RUNX1 takeaways from December’s American Society of Hematology (ASH) Meeting. We wanted to share news of an honor a long-standing member of our Scientific Advisory Board has received, and also introduce you to a new member of our RRP team. In terms of fundraising, we have received requests from patients to provide some grassroots resources in terms of fundraising how-to’s, and we would like to acknowledge those who donated to, and raised funds for, RRP in 2019. Finally, we would like to announce the news of several committees we are creating: the newly formed RRP Medical Advisory Board, the Patient & Family Advisory Council (PFAC), and to share some very exciting news with regards to our receiving a grant from the Patient Centered Outcomes Research Institute.

Patient Spotlight: Georgie Blackburn

“A RUNX1-FPD Advocate’s Journey - As a Patient and as a Mother,”
by Georgie Blackburn

I learned I had RUNX1 Familial Platelet Disorder (RUNX1-FPD) in a serendipitous way. Nearly two years ago, my grown son incurred a sudden and very serious arterial clot that ran the length of his leg to his foot. He underwent extensive emergency surgery to remove the clots, only to have to repeat the surgery two days later after the clot returned. We felt our faith in God prevailed because despite a 95% chance of losing the leg, it survived. My son had not presented with anything that could explain the extreme clotting, so genetic testing was recommended. One test required testing both of his parents. A few months later, he called to tell me the test had shown he has RUNX1-FPD. His doctor had told him about a historical study that had just commenced at the NIH and he decided to take part. I commented that I totally supported his decision, and he said, “Good Mom, because you have it too!”

And so the journey began! I researched all I could on-line and started to connect dots. My mother had died of AML in 1988 after having aplastic anemia for a few years. My grown daughter had developed global gastroparesis post a C-Section seven years earlier. Both my children had alopecia universalis, losing their hair at ages 5 and 9. None of these things had a logical explanation – until possibly now.
My children and I traveled to the NIH together and began our testing regimen last August. We three all have the same RUNX1 mutation but present differently. Interestingly, we all had been followed for idiopathic thrombocytopenia (ITP), and now we know why. As a family, we decided to be part of the solution as this puzzle is being unraveled. Our initial trip to the NIH, and meeting with Drs. Liu, Cunningham and Merguerian, proved we have made the right decision. We each have learned so much about our bodies and this looming “cloud”, yet we believe there is promised progress.

It is not easy to KNOW I have RUNX1-FPD and have passed it onto my children. And it is not easy for my children to decide whether or not to have their three children tested. It has been even more difficult for all of us to discover that I have smoldering multiple myeloma (SMM). I feel my son’s ordeal that led us to genetic testing and the NIH saved my life because SMM is not often discovered until it is very advanced. I’ve read that 30% of people diagnosed with SMM do NOT progress, so I’ve decided to stay within that category! I’ve always had a positive attitude about jumping the hurdles life puts before us, and both my children have the same optimistic view of life’s challenges. I would be less than honest, though, to say we don’t worry about what is ahead. That worry, though, is diminished by the research we know is underway.

Last fall I was invited to speak at the National Human Genome Research Institute’s Annual Symposium. I was part of a Doctor-Patient segment during which my care team and I discussed the diagnoses that have plagued the lives of my mother, my children and now me. I could sense the interest among the research audience - good minds are at work to unravel rare genetic mysteries like RUNX1-FPD. What an empowering, hopeful experience!

My 40-year career has spanned working with clinical teams to provide wheeled mobility and anatomical positioning for patients with spinal cord injury, head trauma and chronic illnesses to developing and overseeing a corporate compliance program, instituting policy and procedures. I have fought for improvements in health care policy, even testifying twice before congressional committees. It’s been a wonderful experience to have made a difference in many lives.

I believe all roads lead to the one being travelled, and so this year I retired from a career in health and policy, advocating for others. Now I advocate for my own health and that of my family! I believe this rare condition will someday be eradicated and those of us with RUNX1-FPD will not incur serious illnesses nor pass it on to loved ones. This can only happen with outcomes driven from research. My children and I will be part of putting this puzzle together!

**Fall 2020 RUNX1-FPD Patient Meeting**

Knowing that you are not alone in living with a rare disorder can be a life-changer for many individuals. Having the opportunity to forge relationships with peers, and to ask questions and learn from health-care specialists is a unique opportunity we want to afford our community. We have had the honor of getting to know many RUNX1-FPD patients and family members over the last few years, and are encouraged to learn of the relationships forming over the internet or via phone. However, we recognize there is no substitute for the depth of connection of an in-person meeting.
And so we are pleased to announce that our first-ever RUNX1-FPD Patient Meeting will take place this November. Patients, mark your calendars for:

November 7-8, 2020, in Charlotte, North Carolina


We are a small community, and though all patients and family members are welcome, we expect an intimate gathering that will bolster experience-sharing and relationship-building. We have heard from you that patients are eager to learn more about RUNX1-FPD and how to manage physical symptoms and the worry of the unknown. We plan to assemble panels of health-care specialists to present on a range of RUNX1-FPD topics and to answer your questions (see inset). We thank all those who completed our survey last fall to suggest topics, and we continue to welcome ideas. The ultimate goal is for patients to leave feeling empowered and equipped with the tools to self-advocate and manage their own RUNX1-FPD health care journeys.

As this is our first patient meeting, the RUNX1 Research Program has decided to pay for travel (economy class), food and hotel rooms for all attending RUNX1-FPD patients. We hope you will join us. Together we can prevent cancer. For more information and/or to register see: www.runx1-fpd.org/patientmeeting. To offer topic ideas or ask questions, please email our Patient Engagement & Clinical Program Manager, Dr. Amanda Eggen, at aeggen@runx1-fpd.org.

**RUNX1 CHARLOTTE 2020: 4th Annual Scientific Conference**

This year’s RRP Scientific Conference will be held, following our Patient Meeting, on:

November 8-10, 2020, in Charlotte, North Carolina
In the spirit of wanting to thoughtfully grow our scientific community, this year we are opening our annual conference to any and all who feel they have something to contribute to our conversation. RRP will cover room and meals on site for all attendees, and any attendee who is not presenting need only cover their transportation costs to and from the meeting. New this year will also be a poster presentation session and travel awards. The goal is to offer both career-training opportunities and financial support to junior researchers, women and minorities interested in RUNX1-FPD research. Please stay tuned for more information in the coming months both on our website and in our upcoming newsletter regarding abstract submissions for the poster session as well as travel award application guidelines. To register, visit: https://www.runx1-fpd.org/conference.

**December ASH Meeting Key Takeaways**

RRP and over 25,000 attendees in the field of hematology converged in Orlando, Florida, December 6-10, 2019, for the 61st annual American Society of Hematology (ASH) Meeting. On the meeting’s first day, an entire afternoon was dedicated to presentations on germline predispositions to blood cancer and bone marrow failure. In fact, there were four speakers who discussed ongoing research on RUNX1-FPD: Drs. Ravi Majeti, Anna Brown, Lea Cunningham and Yizhen Li.

Our very own SAB member, Dr. Ravi Majeti, presented research findings from his ongoing RRP/ALSF-funded project. The project involves evaluating how human blood stem and progenitor cells that are deficient in RUNX1 are different from “normal” cells. His lab used special culturing methods to coax stem and progenitor cells to generate all the different types of blood cells, which is what they naturally do in the body, in a dish. Then, they counted how many different types of blood cells were made to quantify their “stem cell” capacity. Dr. Majeti and his team found that RUNX1-deficient cells have a diminished capacity to make red blood cells and megakaryocytes (cells responsible for making platelets). As you know, the impact on megakaryocytes is not surprising since most patients with RUNX1-FPD have mild or moderate thrombocytopenia. Furthermore, when highly specialized tools like ATAC-seq and RNA-seq are used, they can uncover whether these RUNX1-deficient blood stem and progenitor cells are correctly following the instructions dictated by our DNA. If you imagine DNA as a cookbook with thousands of recipes, there are recipes for each cell type. Each cell must use the correct recipes in order to function properly and behave as it should. The Majeti Lab observed that RUNX1-deficient blood cells have altered their recipe. One of the key changes in the recipe is increased levels of inflammatory signals. These early findings suggest that having abnormal levels of RUNX1 may change the level of inflammation in RUNX1-FPD patient blood cells. Uncovering how the “recipe” has changed will help researchers determine whether those changes are linked to the health issues RUNX1-FPD patients face, including the development of blood cancer. Solving this puzzle will lead scientists, like the those in the Majeti Lab, to develop new treatments that could force RUNX1-deficient cells to use the correct “recipe.”
Dr. Anna Brown gave an update on the *RUNX1* database, the largest aggregation of *RUNX1*-FPD genomic data ever described. The data she shared was similar to her recent presentation at our annual conference. For details on these results please see our Fall 2019 Newsletter. Dr. Brown expressed sincere gratitude to the many international collaborators who shared sequencing data from *RUNX1*-FPD patients, highlighting the importance of numbers in order to understand this complex and rare disease. After her presentation she participated as a panelist, discussing the value of international collaboration to advance knowledge on rare predisposition syndromes. She was joined by one of our Medical Advisory Board members (learn about this below!), Dr. Akiko Shimamura, who spoke of her experience leading the establishment of the North American Pediatric Aplastic Anemia Consortium (NAPAAC). Dr. Shimamura will advise RRP on how to create the same kind of consortium for *RUNX1*-FPD. Building a consortium, a network of clinicians at academic institutions nationally, interested in improving the overall care and outcomes of *RUNX1*-FPD patients, is an important next-step for our community. If you are a clinician caring for patients and are interested in joining, please reach out to our Executive Director, Dr. Katrin Ericson, at kericson@runx1-fpd.org.

Dr. Lea Cunningham, Medical Director of the NIH *RUNX1*-FPD Clinical Research Study, was also a distinguished speaker during this session. She shared her experience and passion for her work on this important study and highlighted the criticality of collaboration across stakeholders in fighting rare diseases like *RUNX1*-FPD. In particular, she highlighted the patient voice and the RRP community’s concern about preventing blood cancer. Dr. Cunningham discussed the challenges she and the study team face regarding what to tell patients and their families about cancer prevention today. With limited data collected thus far, determining which *RUNX1*-FPD individuals are at greatest risk is still not possible. Today, the only curative therapy available is an allogeneic stem cell transplant; however, this treatment approach is not without significant risks, including transplant-related mortality. She and her colleagues at the NIH are developing a risk-score assessment to help the NIH, the families in the study and their primary hematologists determine the right time to transplant.

In recent years, the research community has learned that *RUNX1*-FPD is not merely associated with blood cancers called myeloid malignancies (cancers derived from a subset of cells within the blood system called myeloid cells), as previously believed. In fact, approximately 10% of blood cancers reported in germline *RUNX1* carriers (individuals with *RUNX1*-FPD) are lymphoid-derived, meaning the blood cancer cells come from cells of the lymphoid lineage type.

*Hematopoietic Hierarchy*

Legend: HSC, hematopoietic stem cell (blood stem cell); Thr, thrombocytes (platelets); Ery, erythrocytes (red blood cells); MC, mast cell; Bas, basophils; Neu, neutrophils; Eos, eosinophils; Mono, monocytes; Macro, macrophages; BC, B-cells; TC, T-cells; NK, natural killer cells. Adapted from - Bradshaw A, et al. (2016). Cancer Stem Cell Hierarchy in Glioblastoma Multiforme. Frontiers in Surgery. 3. 10.3389/fsurg. 2016.00021.
Dr. Yizhen Li of St. Jude Children’s Research Hospital was interested in understanding the prevalence of germline $\textit{RUNX1}$ carriers in pediatric patients with T-cell acute lymphoblastic leukemia (T-ALL). She and her colleagues performed genetic sequencing on 1,231 cases, part of the Children’s Oncology Group AALL0434 trial, and identified 13 pathogenic germline $\textit{RUNX1}$ variants in 16 individuals. This translates into a rate of 1.3% of T-ALL patients had an inherited pathogenic $\textit{RUNX1}$ mutation in this cohort. T-ALL represents approximately 10-15% of all pediatric ALL cases. Of note, 71% of $\textit{RUNX1}$ germline cases (only 7 of the 16 could be tested) showed co-occurring JAK3 mutations. This information provides insight into the predominant biology of these germline $\textit{RUNX1}$ T-ALL cancers and warrants further scientific research into the role of JAK3 and whether inhibitors of JAK pathways could be beneficial to T-ALL patients with germline $\textit{RUNX1}$ mutations and somatic JAK3 mutations.

After the initial session on inherited blood disorder syndromes on Friday, there were several other relevant presentations worth highlighting in the following days. Dr. Brian Estevez, from Dr. Morty Poncz’s lab, presented data from another RRP/ALSF-funded project. In his presentation, he showed that by using two different cell-based systems ($\textit{RUNX1}$-FPD hIPSCs [human-induced pluripotent stem cells] and sh$\textit{RUNX1}$ in CD34+ cells) that are deficient in $\textit{RUNX1}$ activity he could replicate the platelet production defect found in $\textit{RUNX1}$-FPD patients in a dish. Establishing these cell-based systems is important because they could be used to screen drugs that reverse the platelet production defect. Using these cell-based systems, Dr. Estevez showed that inflammatory pathways and cellular stress signals are higher in cells that have lower levels of $\textit{RUNX1}$ compared to cells that have normal levels. Furthermore, he demonstrated that chemical compounds that inhibit a specific inflammatory pathway called TGF-beta could increase platelet production to normal levels in $\textit{RUNX1}$-deficient cells. These results are exciting and the Poncz Lab plans to test the efficacy and safety of these compounds in mouse models of $\textit{RUNX1}$ deficiency.

Dr. Jennifer Towbridge’s lab at the Jackson Laboratory presented findings regarding the role of the bone marrow microenvironment in promoting the growth of blood stem cells that carry a ‘bad’ mutation in a gene called DNMT3a. As we age, our tissues, including our blood, accumulate mutations, most of which are not dangerous to our health. However, the probability of acquiring a “bad” mutation, meaning a mutation in a gene that can contribute to cancer, increases with age. Several seminal papers in the last decade have shown that 10-15% of healthy people above the age of 70 have “bad” mutations in their blood: this is called clonal hematopoiesis of indeterminate potential, or CHIP. People with CHIP are at greater risk of developing blood cancer. Using transplantation experiments, the Towbridge Lab showed that blood stem cells with DNMT3a mutations preferentially grew and expanded in old mice versus young mice. To understand why this was happening the researchers compared the bone marrow microenvironment (the tissue surrounding blood stem cells in the bone) of old and young mice. They found that old bone marrow had elevated levels of cytokines called TNF-alpha and M-CSF as compared to young bone marrow. Importantly, there are FDA-approved drugs that can directly target the TNF-alpha pathway. The Towbridge group suggested that perhaps in the future such medicines could be used to stop dangerous mutant stem cells from growing and transforming into a blood cancer in individuals with CHIP.
Why is this study important to our community? Because it demonstrates that the bone marrow microenvironment can influence which stem cells grow and which do not.

We know that individuals with RUNX1-FPD will only develop a blood cancer if “bad” somatic mutations occur in a blood stem cell and that the mutated blood stem cell is able to grow and expand into malignancy. This is why research projects led by Drs. Marc Raaijmakers, Anupriya Agarwal and others in our community are so critical. These groups are focused on determining whether the bone marrow microenvironment in RUNX1-FPD patients is different, and, if so, whether those differences are contributing to the development of cancer by promoting the growth of mutated stem cells over the growth of “healthy” stem cells. These research projects will help us determine whether we can slow or even stop blood cancer by blocking signals in the bone marrow.

Dr. Len Zon, ASH Mentor Award

On behalf of the entire RRP community, we would like to congratulate RRP Scientific Advisory Board Member Dr. Len Zon for his recent award from the American Society of Hematology for outstanding mentorship. Dr. Zon’s commitment to mentorship is a reflection of his sincere passion for science and his desire to cultivate that same passion in others. We are honored and grateful to have him as a member of our Scientific Advisory Board where he has served as an important mentor to us.

RRP Team: New Member!

After a long search, we have finally found someone permanent to fill the role of executive assistant/office manager at the RRP office, here in Santa Barbara. Houghton Hyatt, welcome to the team!

Originally from Louisville, Kentucky, Houghton graduated from Clemson University with a B.S. in Financial Management. She then spent the following eight years in Atlanta, working within the financial industry, before moving to Santa Barbara in 2009 with her husband, Ben. Houghton has grown strong roots in Santa Barbara and truly feels at home here. She believes in civic duty and has an enthusiasm for giving back to her community. She serves on the Board of the Montecito Association, on the Outreach Committee at All Saints by the Sea Episcopal Church, and volunteers at the Food bank, Direct Relief and the Montecito Union School where her children Jack (11) and Riley (7), attend. Houghton has been a strong supporter for cancer research - both of her grandmothers passed away from cancer, and her grandfather is a cancer survivor. She enjoys participating in the Santa Barbara Cancer Walk every year with her family. When in Atlanta, she and Ben raised over $6,000 and completed a 100-mile bike ride with “Team in Training” for LLS. In her free time, Houghton
enjoys spending time with family and friends at the beach, in wine country or hiking one of the many trails around Santa Barbara.

Fundraising Resources

We can’t fulfill our foundation’s mission and meet the great demand without the support of partners, families and friends to fundraise on our behalf. We have prepared some fundraising resources on our website to help you in these efforts, and we hope you find them useful. At www.runx1-fpd.org/fundraising, you will find a general how-to guide along with our brochure, a sample thank-you letter, a materials library of items you could borrow or request and our logo to download. Please reach out to us at info@runx1-fpd.org if you have any questions or issues and we would be happy to help. We are grateful for your efforts - thank you!

A Big Thank-You to our 2019 Donors!

We would like to acknowledge the many individuals who contributed to the RUNX1 Research Program in 2019 either by donating directly or developing a fundraiser for us. We will be creating a space on our website to more permanently express our gratitude.

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Although many have chosen to donate anonymously, we tried to contact everyone over the last two weeks for your permission to thank you publicly. Please let us know if you do not see your name above and would like to be, and we will recognize you in future communications. On behalf of the entire RUNX1-FPD patient community, we are extremely grateful. 100% of donations go toward funding important research and building and expanding our patient and clinician education programs, with all administrative costs covered by the RUNX1 Research Program.

Announcing the RRP Medical Advisory Board (MAB)

We have newly established a Medical Advisory Board comprised of a group of diverse international clinician experts who care for patients with RUNX1-FPD. The MAB offers us advice and guidance on how best to propel clinical research forward with the goal of positively impacting our patients’ lives as quickly as possible. We hosted our first live meeting together at the annual ASH meeting. As a result of the meeting, we came away with three actionable goals:

1) Build clinical research consortia for RUNX1-FPD
2) Develop focused education efforts for the medical community
3) Support the success of the NIH RUNX1-FPD Clinical Research Study through collaboration
We are deeply appreciative of their willingness to join us and dedicate themselves to our collective cause. Here are the members of the Board, and a link to their full bios can be found here: www.runx1-fpd.org/medical-advisory-board.

MAB Members from L-R: Drs. Lea Cunningham, Akiko Shimamura, Jane Churpek, RRP’s Katrin Ericson & Amanda Eggen, Marc Raaijmakers & SAB Chairperson/Scientific Director Nancy Speck. Dr. Courtney DiNardo was not present for the photo.

Patient & Family Advisory Council Announcement (PFAC)

At the RRP, our mission is to improve the quality of life and prevent cancer in patients with RUNX1-FPD. As we have a Scientific Advisory Board and now a Medical Advisory Board advising us, the natural next-step is to formalize the feedback and input we receive from patients and families in our community as well by launching the RRP Patient and Family Advisory Council (PFAC). We aim to assemble the PFAC to include patients and caregivers with diverse experiences and values, and the Council’s goals will be to ensure RRP’s mission, goals and activities are centered on the most pressing needs of our community. We anticipate a wider representation of the “patient voice” in discussing issues related to RUNX1-FPD diagnostics, management, treatment and research. The expectation is that we will meet at least four times per year to discuss current and proposed RRP initiatives, activities and materials, and to hear ideas for future initiatives. If you are interested in becoming a PFAC member, please contact Dr. Amanda Eggen, RRP’s Patient Engagement and Clinical Program Manager, at aeggen@runx1-fpd.org.

Patient Centered Outcomes Research Institute / Research Guided by Patients Committee

We are thrilled to announce that the RUNX1 Research Program has been selected for Eugene Washington PCORI Engagement Award funding. Dr. Amanda Eggen will lead this effort to help develop a community of patients, clinicians and researchers who can effectively work together as partners in designing, conducting and sharing results of RUNX1-FPD research. The two years of funding will support building the “Research Guided by Patients” (RGP) committee, providing training on effective ways these diverse members can work together to develop research questions, design research projects, share findings from research studies and serve as ambassadors to the wider
RUNX1-FPD multi-stakeholder community on the importance of these patient-centered outcomes research approaches.

PCORI (Patient Centered Outcomes Research Institute) is an independent, nonprofit organization authorized by Congress to fund comparative effectiveness research that can provide patients, their caregivers and clinicians with the evidence needed to make better-informed health and healthcare decisions. PCORI is committed to seeking input from a broad range of stakeholders to guide its work. This two-year funding will focus on building the RGP and developing and delivering a training program to prepare this committee. For more information on the Capacity-Building Award, visit http://bit.ly/1idlgt. If you are interested in serving on the RGP committee, please contact Dr. Eggen at aeggen@runx1-fpd.org.

In case you’re wondering how the Scientific Advisory Board, Patient & Family Advisory Council and Medical Advisory Board relate to the Research Guided by Patients Committee, here is a visual to give you a sense. The RGP will be comprised of members of each of the other committees and hence represents all stakeholders.

Finally, we wanted to mention that Dr. Alan Cantor’s RUNX1-ALSF grant on “Pharmacologic Enhancement of Residual Wild Type RUNX1 Protein Activity in RUNX1-FPD” has been renewed. We are looking forward to learning the results of his important research.

Thank you,

The RUNX1 Research Program Team
Dear Friends,

Little did we know, when we sent our last newsletter, how substantially the world was about to change. For all the upheaval, loss and uncertainty the past few months have brought, it is a comfort to know that we are all in this together. We hope this newsletter finds you healthy, and we long for the day when life can resume some of the normalcy we took for granted. Although much of the world has hit the pause button, we at RRP have been fortunate to be able to continue our work remotely. This newsletter will provide a brief summary of some pandemic-related RRP news, including recent videos we have filmed and uploaded to our website regarding COVID-19 and RUNX1-FPD and the state of potential treatment options. Over the past few months we have hosted a number of successful research webinars, and we have a few research and patient-oriented webinars upcoming. We would like to report on a number of patient peer-support efforts, such as a recent Patient Coffee Chat we hosted over the videoconferencing platform ZOOM, and a move from RareConnect to a private FaceBook RUNX1-FPD Patient Community Group as our secure patient discussion forum.

There are several honors to announce - our Executive Director, Dr. Katrin Ericson, has been elected into the inaugural class of the FasterCures LeadersLink Program, and RRP Medical Advisory Board member, Dr. Akiko Shimamura, has been awarded the 2020 Frank A. Oski Memorial Lectureship Honor by the American Society of Pediatric Hematology/Oncology. We are pleased to report that Dr. Uli Steidl has joined our Scientific Advisory Board, and have an update on Dr. Alan Cantor's grant extension and research progress. We have a moving Patient Spotlight of the Conlon family from Belfast, Northern Ireland, written by patient son, brother and uncle, Michael Conlon. The NIH has a RUNX1-FPD Clinical Research Study update, April 21st marked a successful Acute Myeloid Malignancy (AML) World Awareness Day, and, we are thrilled to launch our first-ever promotional item of a RUNX1 Signature Bracelet! As a lot happens at RRP between newsletters, we encourage you to follow us on social media, and to regularly check our website where we have included a new “RUNX1 Happenings” section at the top of the homepage where you can easily keep abreast of our announcements.

This newsletter is dedicated in memory of Debbie Trask, who passed away at 61 on March 27, 2020. She is the sister of Michele “Shelly” Couts Jauron, who our community also lost last October. Debbie’s family has endured more loss this past year than one family ever should. She is pictured here with daughters Sarah Couts Trask Higgins and Angela Couts Trask Sanford.
Fall 2020 Scientific Conference & Patient Meeting

As there still remains so much uncertainty in the world regarding COVID-19 and congregating in a large group, nevermind some of the associated research setbacks the community has had to endure due to social isolation, we have made the difficult decision to postpone this year’s Patient Meeting and Scientific Conference to a later date. We were coming upon vendor payment deadlines that would no longer allow us flexibility, and, ultimately, the consideration of everyone’s health is paramount. We share your disappointment, but in place of this fall’s meetings we will be hosting several virtual sessions for both our research community and our patients, and will let you know at the earliest our rescheduled in-person dates in 2021 for these two events.

The Pandemic & RRP

Our team has been working remotely in Santa Barbara for over eight weeks now. Using the ZOOM video platform, we have been able to proceed with little interruption (except for our children and pets!), meeting regularly as a team and communicating with all of you. In March we received questions from some of our patients regarding the potential impact of COVID-19 on families with RUNX1-FPD. In response, we produced several videos and FAQ’s to keep patients up-to-date and informed. You can find these on our social media sites and under RUNX1 Happenings, but for a direct-link to Dr. Ericson's COVID-19 & RUNX1-FPD video, visit www.runx1-fpd.org/rrp-happenings/runx1-fpd-covid19-faq.

As some severe COVID-19 cases can result in cytokine storms (extremely high levels of inflammatory factors), which can be life-threatening, and early evidence from Dr. Anupriya Agarwal's human data and Dr. Nancy Speck's mouse data indicate that there are likely heightened levels of inflammatory responses to infection with germline RUNX1 mutations, this suggests that our patients may have increased risk of severe illness. Additionally, since the virus causes a respiratory disease, and many of
our patients have been diagnosed with reactive airway disease, there are concerns that our patients may be at heightened risk for poor COVID-19 outcomes. For these reasons we caution our community to remain steadfast in taking every precaution to prevent exposure to the virus.

We continue to remain unaware of any RUNX1-FPD patients becoming ill with COVID-19, and thus have no data to share regarding actual outcomes. If you are a patient and believe you’ve had COVID-19, we would love to hear from you and know how you’re doing. Please reach out to Dr. Amanda Eggen, our Patient Engagement and Clinical Program Manager, at aeggen@runx1-fpd.org.

RRP Research Webinars

Since March, we have hosted two webinars by funded investigators: on April 1st, Drs. Nancy Speck and Dana Ballissimo presented on RUNX1 mutations and Inflammation, and on May 6th, Dr. Guy Savaugeau presented on glucocorticoids in RUNX1 mutated AML. Visit www.runx1-fpd.org/learn to view recordings of both of these past webinars, including a lay summary video by Dr. Ericson.

In an effort to build connections between our research and patient communities, we invite patients to join in these scientific presentations 15 minutes prior to the webinar to hear a lay summary given by the presenting scientist. The goal is for patients to learn some key terms and hear the impact of the study findings as a way to enable clearer understanding during the scientist-oriented presentation. At the end of the presentation, both scientists and patients are invited to join a Q&A
We are eager to hear from participants any and all feedback on what you found useful and what could be improved upon. We are grateful to Drs. Speck, Ballissimo and Sauvageau for presenting these to our community.

On Thursday, May 21st, we are hosting a webinar with Nationwide Children’s Hospital and former Governor John Kasich on “Inherited Hematologic Malignancies”. We will be discussing how genetic sequencing continues to uncover germline syndromes, like RUNX1-FPD, that predispose to hematologic malignancies, and discuss how health-care workers should identify, test and manage patients.

Upcoming, on May 28th, Dr. Anupriya Agarwal will present on the Role of the Inflammatory Microenvironment in RUNX1-FPD. Please register at: https://bit.ly/RRPWebinarMay28 by May 26th. And on June 18, Dr. Anna Brown will present on “Pre-leukemic states in RUNX1 Genetic Predisposition”. Please register at: https://bit.ly/RRPWebinarJune18 by June 16th.

RRP Patient-Support Efforts

On June 18th, fertility specialist Dr. Andy Huang and genetic counselor Ms. Kayla Hamilton will present a webinar entitled “Wanting (More) Children while Facing an Inherited Risk of Blood Cancer”. This webinar will explore family expansion considerations for individuals with genetic mutations that increase their risk of developing blood cancer. The discussion will provide an overview of basic genetics and inheritance before delving more into the reproductive options available to patients. They will also discuss fertility preservation options for those who are facing a blood cancer diagnosis and the possibility of treatment that could limit their ability to have children. RUNX1-FPD will be the primary focus, but the concepts discussed are applicable to other autosomal dominant predisposition syndromes. To register, please visit: https://bit.ly/FamPlanRUNX1.

On April 2, we held an informal “Coffee Chat” over ZOOM. Seven patients and caregivers met, along with our Patient Engagement and Clinical Program Manager, Dr. Amanda Eggen. Patients shared their RUNX1-FPD experiences with each other and discussed stories and similarities. Most indicated they appreciated the connection they made with others, so we plan to hold another of these in the coming months and hope to see more patients then! We are grateful that technology enables us to continue to connect, and, most importantly, to keep us on track towards achieving our mission. RUNX1-FPD will not slow down during a global pandemic, so neither will we.

RUNX1-FPD Patient Group

We have decided to shift our private patient and caregiver support community from RareConnect to a Private FaceBook Group. We had received patient requests to do so, and confirmed with similar patient organizations that their patients have found the FaceBook platform to be most valuable given wide familiarity. The group is quickly growing with members engaged in discussion and peer support. Note that this community is exclusively for patients and close family members and
caregivers, and excludes researchers, clinicians and industry representatives. We continue to offer our public page: www.facebook.com/fpdaml to share RUNX1-FPD relevant information for these wider audiences. If you are a patient, or close family member or caregiver, we invite you to join the conversation: www.facebook.com/groups/RUNX1PatientGroup.

Dr. Katrin Ericson selected for LeadersLink Program

We at RRP are committed to advancing on our mission as fast as possible. Fortunately, we now have a network of impressive non-profit leaders we can learn from to do just that. FasterCures, a Milken Institute program, has established the LeadersLink program to foster the development of emerging leaders of nonprofit biomedical research organizations, while allowing them to make connections that will catalyze their efforts in the future. Our very own Executive Director, Dr. Katrin Ericson, was selected to be a part of the 2020 inaugural cohort. She is thrilled to be joining this program and will bring back as much knowledge as possible to our community, and we are proud of her!

MAB Member, Dr. Akiko Shimamura Honor

RRP Medical Advisory Board Member, Dr. Akiko Shimamura, of the Dana-Farber/Boston Children's Cancer and Blood Disorders Center, has received the 2020 Frank A. Oski Memorial Lectureship Honor by the American Society of Pediatric Hematology/Oncology (ASPHO). This award is given only to outstanding clinical investigators in pediatric hematology/oncology whose cutting-edge research is of the caliber of the investigations made by Dr. Oski. Congratulations Dr. Shimamura, we are lucky to have you on our MAB!

Dr. Uli Steidl joins SAB

Dr. Uli Steidl of Albert Einstein College of Medicine has graciously accepted our invitation to join our Scientific Advisory Board. Dr. Steidl is a leader in the field of leukemia stem cell biology. His research paves the way towards developing treatment strategies to target these blood cancer-initiating cells, called leukemia stem cells. Dr. Steidl is Professor in the Departments of Cell Biology, and of Medicine (Oncology) and the Program Leader of the “Stem Cells, Differentiation and Cancer” program at the Albert Einstein Cancer Center, the Scientific Director of the Division of Hemato-Oncology within the Department of Oncology at Einstein/Montefiore Medical Center and a faculty member of the Ruth L. and David S. Gottesman Institute for Stem Cell Research and Regenerative Medicine. Outside of his impressive professional experience, Dr. Steidl is a wonderful, optimistic person filled with enthusiasm for life. Although we have benefited from his mentorship over the past several years, we look forward to having him join us as a formal advisor.

RRP/ALSF Grantee Research Spotlight & Update - Dr. Alan Cantor

Dr. Cantor, a Professor at Boston Children’s Hospital at Harvard, has received an additional two years of funding for his project entitled, “Pharmacologic Enhancement of Residual Wild Type RUNX1 Protein Activity RUNX1-FPD.” The Cantor lab has made significant progress. In fact, the team has helped our community achieve a significant milestone: the drafting of the first ever RUNX1-FPD clinical trial!

Dr. Cantor’s proposal is innovative in that it seeks to prevent the development of blood cancer by using FDA-approved drugs to enhance the activity of the residual, healthy RUNX1 protein activity. Remember, every patient has one healthy copy of the RUNX1 gene and one mutated copy. The
goal is to use drugs that exploit the known autoinhibitory mechanisms that normally turn down RUNX1 activity. Many proteins in our body have “on” and/or “off” switches to control the dosage of a protein’s effects. RUNX1 has an “off” switch controlled by enzymes that are druggable. In the first two years the Cantor Lab showed that oral FDA-approved abl inhibitors, like imatinib, dasatinib and nilotinib, can enhance residual RUNX1 protein activity by blocking the “off” switch. The team was able to show higher RUNX1 activity in cellular models of RUNX1-FPD. For example, RUNX1-deficient cells treated with one of these drugs were able to produce significantly more platelets.

This is exciting news, because of the three inhibitors, imatinib (Gleevec) is generic, it has a relatively clean safety profile and has been used for decades in 100,000’s of patients with blood cancers for long durations. This means the drug is easily accessible, has lower prices than an on-patent drug and the safety of the drug is very well understood, making it easier to evaluate the benefit/risk profile upfront. In fact, Dr. Brian Druker, an RRP SAB member, was a leading principal investigator in the clinical trials that led to the approval of imatinib in 2001 for chronic myeloid leukemia (CML) patients. Along with Drs. Cantor and Druker, we have pulled together a super team to initiate planning for an early-phase clinical trial including Drs. Lea Cunningham (NIH-NHGRI/NCI), Paul Liu (NIH-NHGRI), Hugh Rienhoff (RRP Advisor and CEO of Imago Biosciences) and Nancy Speck (SAB Chair). Each offers a unique and critical perspective and we will be sharing more with you soon as these efforts progress.

Patient Spotlight - The Conlon Family, in Michael Conlon’s words

In 1982, I was in year 3 of primary school in Belfast, Northern Ireland. One day my mummy picked me up early from school to take me to meet my sister Alicia, in Year 1, at her school. As a child I recall in those moments thinking, great, a day free of school, amazing!

But when we left Alicia’s school we went straight to our local hospital. We were put into a room and examined by a doctor. We were asked questions like, “do you have a lot of falls?” , “do you fight with your friends?” – my answer to all these questions was “no”. I remember the look of worry on my young, 24-year-old mummy’s face, and I will never forget the look of scorn the doctors and nurses directed at her. At the time, we were confused, we could not comprehend why such unusual questions were being asked - I was 7, and Alicia was 5! Then they asked me if my mummy ever hit me, well, I remembered laughing and replying with a big NO! I had never been physically punished.

Hours later, the nurses shared that our blood results had come back, and Alicia’s test showed a low platelet count. Though we did not understand what this result meant, we did learn that it meant we would no longer need to stay overnight at the hospital. It turned out that all of this questioning was the result of a social worker raising concerns after having visited Alicia’s school for a general check-in when she noticed Alicia had a lot of bruising. As an adult looking back, I know the social worker was doing her job and making sure we were safe. However, I can’t even begin to imagine the despair my mummy must have felt throughout the ordeal.

Thereafter, Alicia began to visit the hospital once a month for routine blood tests. For years she was being managed by a simple “watch and wait” approach for an unnamed platelet disorder.

When Alicia was about 12, her doctor suggested removing her spleen to help regulate the platelet count. He could not be sure this splenectomy would be effective, and it meant Alicia would be on medication for the rest of her life. There was lots of discussion in the house at the time and my
mummy ultimately decided that if they were not sure this would regulate her blood, then it was not worth the risk combined with life-long medication.

In 2000, not long after Alicia had her first son Pól, the doctors had a new treatment suggestion: a bone marrow transplant with me as the donor. In parallel, her doctor asked if we would give permission for our DNA sequencing results to be uploaded into a database at Great Ormond Street Hospital. Though the internet was in its infancy at this time, somehow the database in London was shared with other research hospitals around the world. Eight other families were identified with mutations in the \textit{RUNX1} gene. One Australian family’s doctor provided key, timely information to the doctors in London that stopped our potential bone marrow transplant in its tracks. A pair of siblings had undergone transplants and while they recovered and blood counts came into the “normal” range for a while, they both contracted a form of leukemia in their 40s.

To say my sister is an expert in the disorder would be an understatement. When her original doctor retired, he brought Alicia in so she could explain her case history to her new doctor. Over the years, Alicia has spotted many traits or irregularities. She has mentioned them to her doctors by saying something like “this might sound stupid, but have you checked this or noticed that...”. Many of her theories have proven to be new areas for investigation.

At some point, Alicia mentioned to her consultant that my daddy also had bruising, and he was then invited in for an examination. It turned out he had the same issue as Alicia, but still at that point the disease had no name; we were told it is just an unexplained irregularity. Our daddy was always sick. He did not have the best diet, was a recovering alcoholic and a heavy smoker. Health scares were the norm, so years later when he was diagnosed with Myelodysplastic Syndrome (MDS; which was then considered a pre-leukemia, but now considered a type of blood cancer in itself), we were not as shaken as one would expect. He was told that with his form of leukemia he could live to be an old man. That didn’t happen; within six months he had Acute Myeloid Leukemia (AML) and died at the age of 49.

A few years later, Alicia had another boy called Piaras. Piaras had the bruising. We were all still relaxed about Alicia’s blood disorder, having grown up with it. The only major side effect we connected to it was bruising, periods of tiredness and the fact that Alicia and Piaras had to attend the dental hospital rather than a regular dentist’s office. A routine appointment at the dental hospital for Piaras showed some bruising of his gums, and his dentist sent him directly to the hematology unit on site. It was then that we were told he had MDS, and given our daddy’s history, treatment was needed immediately.
A search for a bone marrow donor was instigated, and a match was found with relative ease. A transplant date was secured but required the family to move to Bristol, England, to be near the hospital. For the first time we were scared but had hope that this was perhaps the cure, and saw this as a great opportunity for a transplant at a young age while his body was at its strongest - an opportunity that his grandfather did not have.

The transplant was successful, and Piaras flew back home to Belfast. He seemed well for a while, but he picked up graft-versus-host disease which required his physicians to suppress his immune system. At this point, he picked up a virus that his body could not fight, and he passed away at eight years old. As he was passing, Piaras generously expressed with great maturity that he hoped his experience would help future children avoid similar suffering. You can only imagine the devastation and impact this had on our family. This blood disorder was now a great threat, to Alicia and any future children that might be born into our family.

Alicia did not think she would have any more kids, and this was certainly not on my radar. I’m 45 now and love the freedom of being a guncle (a gay uncle). I always look at people with kids in awe, as I just do not know how they do it, especially when their kids get sick.

Five years after we lost Piaras, Alicia unexpectedly became pregnant with a baby girl. Toni is now three years old and she too has the blood disorder. You can imagine that after losing a child, and then having a new one with the same disorder, Alicia does not get much sleep. She continues to advocate for Toni’s wellbeing; this includes a recent demand that Toni receive a platelet transfusion for a 10-hour surgery when the hematology consult did not think it was required. She knew even if Toni’s platelet levels were high, they would not function as expected.

Early last year, Alicia spent hours on the internet searching medical terms that she could not pronounce but could spell, in order to find not so much a cure, but hope. That is when she came across the RUNX1 Research Program. She could not believe it, we could not believe it: there were other families brought together through this program! Now we have hope again, not just for Toni but also Alicia and all the others that this program supports - once you have hope, you have a reason not to give up.

- Michael Conlon

“As he was passing, Piaras generously expressed with great maturity that he hoped his experience would help future children avoid similar suffering.”
We are grateful to Michael and Alicia Conlon for so openly sharing their family’s story, and especially for young Piaras, whose spirit lives through our collective efforts to push the science forward for all our patients’ benefit, current and future.  Thank you.

NIH RUNX1-FPD Clinical Research Study Update

You will be pleased to hear that the NIH study is still underway despite the pandemic.  The study team is working “safely, in social isolation” to continue processing large amounts of data, and to enroll and schedule patients for their campus visits.  They had to postpone in-person visits through June, but are aiming to reopen as soon as safely possible.  For currently enrolled patients, we encourage you to continue reaching out to the study team directly if you have questions.  You should also watch for communications from them.  They have begun scheduling virtual one-on-one discussions regarding your test results so far and how those fit into the bigger picture of the study.

To date, 51 RUNX1-FPD patients from 26 different families have enrolled in the NIH’s RUNX1-FPD Clinical Research Study, along with 45 additional unaffected family members.  33 have visited the campus at least once, and the rest are planning to visit or are participating remotely by sending samples.  We are thankful to all of these families and the NIH team who have contributed their time and energy to help further understanding of the disorder.

The NIH study team will be launching a twice yearly newsletter with study progress and initial results, and there are two other additional opportunities to learn more about the study.  First, the National Human Genome Research Institute has built a study page here:  https://bit.ly/RUNX1Study.  Secondly, we at RUNX1 Research Program are hosting a webinar in which the NIH study team will introduce the study and answer general questions.  This may be a good opportunity for those of you who have considered joining but would first like a few questions answered.  We will share the time and date through email and social media as soon as it is scheduled.

AML World Awareness Day

Thank you to all who participated with us in Acute Myeloid Malignancy (AML) World Awareness Day on April 21, 2020.  AML is the most common blood cancer diagnosed in RUNX1-FPD patients.  Each year our friends at KNOW AML rally people over the world to ensure that attention is paid to this rare and aggressive blood cancer.  From her home office, Dr. Amanda Eggen personally mailed 34 KNOW AML pins, and facilitated another 40 sent out by KNOW AML, to our community members.  Thank you to those who pinned these on themselves and their children, wore them on ZOOM with their colleagues and raised awareness through social media.  We are grateful.  Please take a moment to peruse the resources for patients and caregivers from our friends at www.know-aml.com.  Clinicians and researchers are offered vast resources on the team’s newly relaunched AML Hub:  www.aml-hub.com.

RRP Fundraising Resources

Now more than ever, we need your help.  We know there are so many financial burdens at this time, but you can imagine how the global financial contraction might impact philanthropic giving potential to foundations such as ours.  We wanted to remind you about several
resources we have on our website, should you find the time and ability to fundraise on our behalf. Over the coming weeks we will be adding more ways to give to our Donate page, where you can also find a link to our Fundraising page: www.runx1-fpd.org/fundraising. In light of much of the world’s physical distancing measures, congregating as a group is no longer really possible these days, but we have faith in the ingenuity of the human spirit.

Finally, we are pleased to announce that our first-ever promotional item has launched: the RUNX1 Signature Bracelet! Featuring our RRP colors in an easy-to-wear waxed nylon, the bracelet is fully adjustable and fits any wrist-size. It includes our “X” logo on a small, silver-colored metal charm. Show off your support for RUNX1-FPD while helping spread the word of our rare disorder. Proceeds go to supporting RRP programs! Visit www.runx1-fpd.org/shop/runx1-bracelet to purchase!

Thank you,

The RUNX1 Research Program Team
Dear Friends,

Amidst the “new normal” that is work and life during a pandemic, nevermind a roasting hot summer, our remote offices have been abuzz with activity. In this newsletter, we’ll update you on our latest Scientific Conference and Patient Meeting plans for this fall. Upshot: they ARE happening! Over the last quarter, we have hosted multiple webinars, both research-oriented and patient-focused, and have updates and highlights to share with you. Dr. Wenbin Xiao, of Memorial Sloan Kettering Cancer Center, is the recipient of the 2020 RUNX1-ASLF Early Career Investigator Grant, and we are now accepting applications for a 2021. As part of our growing efforts to bring expertise together in working groups to accelerate progress and create efficiencies, we are pleased to tell you about the new EU Network on Familial Platelet Disorders with Cancer Predisposition. One of our Medical Advisory Board Members has recently been awarded a distinguished prize, and we have been enjoying the help of a hardworking Berkeley undergraduate by way of a summer internship. Read on to learn more! This newsletter includes a special patient spotlight on the Johnston Family from Helensburgh, Scotland. We are grateful to patients and families like Mark Johnston’s who generously open up their lives to our community, helping fellow sufferers and the world to understand what a RUNX1-FPD journey can look like. Our Private Patient Facebook page is growing and thriving, and we have added two patient and caregiver advisory groups (with some overlapping functions) to help represent the “patient voice”, assisting us in maintaining patient-centered research and strategies. Finally, we have launched a new Patient Webpage. Please take a look as we would love to grow this space with more of your stories, videos and loved ones.

Fall Annual Scientific and Patient Conference - Now Virtual

It has been a year of adjustments and adversity for all of us, and making the decision to convert our fourth annual scientific meeting and our first-ever patient meeting to virtual formats was yet another disappointment. However, we have found that staying connected by whatever means necessary has become increasingly important during these times of limited social interaction, and that when done well, meeting virtually can sometimes be just as effective. Thankfully, many of our research community members have been able to return to their laboratories to continue their critical work, and, simultaneously, our patient community has continued to grow, with the level of engagement
intensifying substantially. In an effort to harness all of this momentum, we would like to bring us all together this fall - as planned, albeit virtually - to celebrate new learnings, forge new relationships and reinvigorate old ones, ready to tackle the challenges upon us.

We have developed a condensed agenda for both the scientific conference and patient meeting in November, in an effort to strike the balance between efficiency and effectiveness. We welcome all to join in and contribute, accelerating our understanding of RUNX1-FPD with the goal of ending patient and family suffering.

Please follow these links for more information:

- Patient Meeting: www.runx1-fpd.org/patientmeeting
- Scientific Conference: www.runx1-fpd.org/conference

**RRP Webinars**

We continue to host webinars on an array of topics relevant to our community members. Some are more research-focused, with RRP-funded investigators presenting their latest RUNX1-FPD relevant research findings. Others are more oriented to a clinician audience, such as our virtual seminars on inherited predispositions to hematologic malignancies, with clinicians and genetic counselors discussing the why, when and how of testing for genetic predispositions to blood cancers. We have also hosted webinars on topics requested by patients, such as “Family Planning” and “Introduction to the NIH’s RUNX1-FPD Clinical Research (Natural History) Study”.

**To learn about upcoming webinars**

- Receive email notifications: email info@runx1-fpd.org or subscribe at www.runx1-fpd.org/subscribe
- Follow our newsfeeds: FaceBook, Instagram, Twitter: www.runx1-fpd.org/connect
- View news & events: See RUNX1 Happenings Bar at top of homepage: www.runx1-fpd.org

**To view archived webinars & summaries**

- visit www.runx1-fpd.org/learn - Articles & Research
- Summaries describe the relevance of each research seminar for the broader RUNX1-FPD community & our mission
Q3 Research Webinar Highlights

In May and June we had Drs. Guy Sauvageau (University of Montreal) and Anna Brown (University of South Australia) present as part of our research webinar sessions. Below are some key takeaways from their respective presentations.

Dr. Guy Sauvageau’s Research Highlights (view the webinar here: https://vimeo.com/432887702):

- In a group of 430 AML samples, 10% had pathogenic RUNX1 mutations (consistent with many previous reports) but, importantly, 27% of those RUNX1-mutated samples were germline.
- If close to a third of RUNX1-mutated AMLs are in fact inherited, then that would translate into as many as 10,000 RUNX1-FPD patients diagnosed with AML each year across the world.
- AML blood samples with two RUNX1 mutations, meaning bi-allelic (one on each allele) are exquisitely sensitive to steroids like dexamethasone. This suggests that using dexamethasone alongside other AML treatments in patients with AML and two RUNX1 mutations could be effective. More studies need to be done to prove this.

Dr. Anna Brown’s Research Highlights (view the webinar here: https://vimeo.com/432362947):

- Analysis of 56 DNA-sequenced samples from RUNX1-FPD patients without leukemia showed that BCOR, TET2 and DNMT3a somatic mutations were the most common. Secondary somatic mutations in RUNX1 were not observed.
- But across 60 DNA-sequenced samples from RUNX1-FPD patients with leukemia, secondary RUNX1 mutations were the most common co-occurring somatic mutation, suggesting that a second hit to RUNX1 is a later event in the process of leukemic progression. This is important as we think about when to intervene because if a patient has evidence of secondary mutations in genes like TET2 and BCOR that are increasing in their blood over time (measured by variant allele frequency, VAF), and then suddenly a RUNX1 mutation is detected, this could be an indicator of leukemic transformation.
- The number of mutations and the number of cells with mutations (variant allele frequency, VAF) increase with age in pre-leukemic RUNX1-FPD samples. In fact, 36% (20/56) had evidence of mutations in leukemia-associated genes. Interestingly, no one under the age of 16 had a somatic mutation whereas everyone over the age of 70 did.
- What does this all mean? We know that in RUNX1-FPD, leukemic samples have 3+ mutations in addition to the germline RUNX1 mutation present in their blood. This suggests that you need at least that many mutations to transform to leukemia. One key leukemic-prevention approach to study is to discover and test targeted therapies that directly block the growth of blood cells that have somatic mutations.

Q3 Patient-Focused Webinar Highlights

Dr. Andy Huang and Ms. Kayla Hamilton’s Family Planning Webinar Highlights (view the webinar here: https://vimeo.com/432355547):

In June, Ms. Kayla Hamilton and Dr. Andy Huang presented the patient-requested Family Planning webinar. Ms. Hamilton introduced how genetic mutations pass through generations, and the role of somatic/acquired mutations in cancer development. She further introduced considerations patients
and their families with autosomal dominant inherited predispositions to blood cancer (like RUNX1-FPD) might make with respect to their values, cultural and religious beliefs, and preferences as they plan for family expansion. Dr. Huang followed with an introduction to in-vitro fertilization and the types of preimplantation genetic testing (PGD). He also stressed the value of self-reflection regarding all of the options for family planning, including natural conception and adoption.

NIH Study webinar highlights (view the webinar here: https://vimeo.com/438800162):

In July, we hosted key members of the National Institute of Health (NIH) team leading the RUNX1-FPD Clinical Research Study, including Dr. Paul Liu, Principal Investigator; Dr. Matthew Merguerian, Clinical Fellow; Ms. Natalie Deuitch, Genetic Counselor; and Dr. Lea Cunningham, Medical Director. The team reviewed the biology of RUNX1-FPD in health and disease along with the goals of the study. They dove into eligibility criteria, the enrollment process, what an NIH visit looks like and the various clinical and research studies conducted. Finally, they offered answers to frequently asked questions and took audience questions as well.

- The study currently includes 25 families with 49 RUNX1-FPD patient participants and 44 non-RUNX1-FPD family members for comparison. 29 individuals have visited the NIH. Some patient families have had to wait to be seen due to COVID-19 travel restrictions to the NIH campus that have since been lifted.

- Enrollees ages range from one to 95 with 35 being the average; the greatest proportion of participants are children and 56% of enrollees are female.

- Patients have presented well-known RUNX1-FPD symptoms including low platelets, platelet dysfunction, blood cancer and eczema.

- Many additional symptoms have also presented, though additional patient enrollment will help the NIH confirm linkage to RUNX1-FPD:
  - Pregnancy complications
  - Blood clots
• Cancers of the breast, uterine, colon, thyroid and skin
• Asthma or reactive airway disease
• Gastrointestinal issues

• Given the many allergy and immunology issues seen, an immunologist sees all patients who visit the NIH for this study.

The study is still open for enrollment, and patients are now being accepted for travel again. You can also learn more about the study and express interest in enrolling by visiting www.runx1-fpd.org/nih-study.

Announcing Dr. Wenbin Xiao, the 2020 RUNX1-ALSF ECI (Early Career Investigator) Grantee

Wenbin Xiao, M.D., Ph.D., of Memorial Sloan Kettering Cancer Center, has developed a project that aims to understand how a germline RUNX1 mutation cooperates with secondary, somatic mutations to drive the initiation and progression of leukemia. Dr. Xiao will use novel mouse models he generated in Dr. Ross Levine's laboratory that uniquely enable the sequential activation of somatic mutations in common leukemia-associated genes like TET2 and FLT3 in a mouse with a germline Runx1 mutation that can be reversed to a wild type state. This ability to reverse the status of the Runx1 allele from a pathogenic mutated allele to a wild type, functional allele will allow Dr. Xiao to determine what role a pathogenic Runx1 mutation has in the process of leukemia initiation, progression and maintenance. His research will provide insights into the underlying mechanisms that control clonal fitness and leukemic transformation in RUNX1-FPD. Such insights may help us identify which RUNX1-FPD patients are at highest risk of leukemia and inform the development of novel therapeutic approaches to prevent/intercept leukemic initiation.

Now accepting applications for 2021 RUNX1-ALSF ECI Grant

Together with our long-standing partners, Alex’s Lemonade Stand Foundation for Childhood Cancer (ALSF), we are accepting applications for the 2021 RUNX1-ALSF ECI (Early Career Investigator) Grant Program, due December 16, 2020.

This program aims to establish a new generation of scientists interested in tackling inherited hematologic malignancy predisposition disorders with a focus on RUNX1-FPD. ALSF and RRP believe that providing capital to early career investigators not only injects funding to where it is needed most, but also cultivates a new cohort of investigators who will be invested in an area of research that historically has had limited attention.

The RUNX1-ALSF ECI grant offers up to $180,000 over three years. Grants will be awarded to research proposals that will lead to the development of therapies aimed at preventing the transition from pre-leukemia to leukemia in patients with RUNX1-FPD.
Download application guidelines here: RUNX1 Early Career Investigator Grant Guidelines.

New! EU Network on Familial Platelet Disorders with Cancer Predisposition

This new network was launched in the late spring to unite the European clinical and scientific community working on familial platelet disorders with cancer predispositions, and, in particular, RUNX1-FPD. The network will function as a task force within the European Hematology Association’s Scientific Working Group (EHA-SWG) on Genetic Predisposition in Hematologic Cancer (chairs: Drs. Marc Raaijmakers, Austin Kulasekarara), with support from us at the RRP via the direct involvement of our Executive Director, Dr. Katrin Ericson.

Drs. Tim Ripperger and Jörg Cammenga are the co-leads of the network. On June 12th, they kicked off the first meeting (virtually, of course) during the annual EHA meeting. By the end of the meeting the group aligned on the following set of goals:

1. Formalization of a clinical knowledge/data-sharing hub
2. Establishment of data-collection processes and registries
3. Development of clinical guidelines/recommendations
4. Generation of a cohesive experimental and clinical research strategy

The network is well on its way, with 23 members involved and a plan to meet again in November. We are thrilled that this network has formed and are confident our RUNX1 community will learn much from this consortium of European experts.

Dr. Courtney DiNardo honored with ASH’s 2020 Ernest Beutler Lecture and Prize

Congratulations to Dr. Courtney DiNardo of MD Anderson Cancer Center and one of our Medical Advisory Board members! She will be honored at the 62nd Annual American Society of Hematology meeting with the Ernest Beutler Lecture and prize for her translational/clinical contributions to the treatment of acute myeloid leukemia through an improved understanding of epigenetics. To read more, visit: www.hematology.org/awards/honorific/ernest-beutler-lecture-prize-recipients/2020-ernest-beutler-lecture-and-prize.

Summer Intern - Jenna Rode

Jenna Rode joined RRP in June as our summer intern after completing her first year at the University of California, Berkeley. Jenna is a biology major who is exploring a variety of scientific careers including genetic counseling. She fit right into our team and rolled her sleeves up immediately, lacking any hesitation to jump in to learn and contribute. In her short time with us, Jenna has collaborated with several of our scientific community members and patients on projects designed to create patient resource materials. She worked closely with Katrin to develop plain language research summaries and organize scientific literature, and supported Amanda in several different group meetings with patients and researchers. Jenna has been a great addition!

Jenna Rode
Patient Spotlight: The Johnston Family

“An Accidental Discovery and Silver Lining”

Mark Johnston, of Helensburgh, Scotland, has had bleeding issues since he was a child. He bled out after tonsillitis surgery at age 10, flat lining and requiring a transfusion. Days later he was still vomiting blood. He continued to bruise easily, get nose bleeds and bleed moderately with cuts, but managed his injuries fine. He joined the military in 1997, and though his physicians noticed his tendency to bleed easily, they did not raise any real concern until 2009, as Mark was preparing to deploy to Afghanistan. His full physical revealed concerningly low blood counts, and they decided it would be unsafe for him to deploy to a warzone. A follow-up hematologist visit provided him a diagnosis of thrombocytopenia (low platelets), with only a plan for managing his injuries, as he had always had.

It was not until August of 2019 that Mark learned “by accident” that he had *RUNX1*-FPD.

Though normally fit and well, Mark had begun to feel increasingly ill over the course of the year. He had extreme fatigue, itching skin, burning rashes, nausea, abdominal pain, PR (perirectal) bleeding, gums inflamed and bleeding, migraines and dizziness. His white blood cells were low and his platelets fluctuated and dropped dramatically. Eventually he collapsed at work and was admitted to the hospital. A colonoscopy came back clear, and an endoscopy showed EoE (eosinophilic esophagitis) due to unknown cause. It turned out that Mark had pneumonia, and that many of his bleeding issues did not add up to his thrombocytopenia, so he was referred to a professor for further investigation. The professor suggested genetic testing for both Mark and his two-year-old, Amelia.

Next, Mark had full genome testing. While waiting for those results to return, he and his wife Sharyn took Amelia to the kids’ hospital for Amelia’s genetic testing. The doctor came in and said, “Do you know why we are here?”, and Mark and Sharyn said, “yes, for genetic testing for a blood disorder”. The doctor then said, “yes, *RUNX1* ... So you know that comes with an increased chance for leukemia...”. In stunned silence, Sharyn and Mark looked at one another, then their little 2-year-old and then at the doctor. He said, “Oh, you don’t know yet, do you?” Apologizing, he proceeded to attempt to answer their questions. He said not much was known about Mark’s germline *RUNX1* mutation, but that it can “develop into leukemia”. Mark and Sharyn quickly spiraled into worry that both Mark and Amelia were in a phase of pre-leukemia. They proceeded to walk their daughter through the testing process, stressed and unsure how they were going to remain strong for their daughter. Thankfully, Amelia did very well through the blood test with the pediatric team keeping her at ease with their “Elsa” (from the Disney film “Frozen”) numbing spray.

Upon arrival at home that evening, Sharyn searched online for more information that only served to heighten her worries. Then she came upon *RUNX1* Research Program’s Facebook page and sent a
message. Though it was very late in Scotland, it was the morning in the U.S., and Amanda responded immediately, offered support and walked through what is currently known. She clarified that RUNX1-FPD is a predisposition that confers an increased chance of leukemia, but is not the pre-leukemic state they feared. “That is why I often say that Amanda was the light on a very dark day”, says Sharyn, “because we were processing the possibilities of my husband having cancer and my child having cancer, and she helped calm us down from that.”

Mark describes the worry during the 3 months of waiting for Amelia’s test results as the darkest of his life, and the discovery that Amelia does not share his RUNX1 mutation as the brightest moment of his life. They admit they feel some guilt as they get to know other families in the private RUNX1-FPD Facebook group who are grappling with worry about their children’s experiences with RUNX1-FPD.

Mark felt less fazed by learning about his own RUNX1-FPD diagnosis, and saw it as more of a validation – clarity for many seemingly unrelated health issues added up. A key to this clarity was a trip to the NIH in Maryland, U.S., in early 2020 to participate in the RUNX1-FPD Natural History Study. The study team managed to secure additional specialist appointments for his ostensibly unrelated health issues. Though those extra appointments ate into Mark and Sharyn’s three extra days they scheduled for sightseeing in the Washington, D.C.-area following their visit to the NIH, they are extremely grateful that they accepted every additional appointment. In particular, Mark’s allergist appointment revealed extensive food allergies that have since been eliminated from his diet, leaving him feeling better than he’s felt in years.

The silver-lining Mark and Sharyn find from this diagnosis is that they now feel empowered to better manage Mark’s health, to watch closely for early signs of leukemia, and to help empower their family members with the same. Mark and Sharyn have recently returned to feeling a sense of some normalcy in their lives, dedicating their time to their children, many fur babies and launching a small online family business.

Private Patient Facebook Group

With 57 members and counting, our decision to move the private patient page from RareConnect to Facebook has been validated. We are pleased patients can now find an easy-to-navigate, familiar format to liaise with other patients and families about life with RUNX1-FPD. If you were hoping to join the private RUNX1-FPD Patient Group, but have not yet had a chance, go to www.facebook.com/groups/RUNX1PatientGroup to share your story, relate to others with similar experiences, explore how others approach challenges and decisions or simply just be somewhere where you know others will just get it.
Our two patient and caregiver advisory groups have launched: Meet the PFAC & RGPC

The Patient and Family Advisory Council (PFAC) includes a group of patients and caregivers who have committed to sharing their diverse experiences and perspectives to advise on the RUNX1 Research Program’s activities. RRP staff look to them to represent the “patient voice”, prioritizing education, advocacy and outreach initiatives. The PFAC officially kicked off in early April and met for a second time on Monday, August 3rd. The PFAC has thus far been instrumental in considering topics for our patient-oriented webinars and our first-ever patient meeting, selecting the best tools to support patient and caregiver involvement in research webinars, helping develop a RUNX1-FPD awareness day and reviewing patient resource materials developed by our intern this summer.

The Research Guided by Patient Committee (RGPC) similarly advises RUNX1 Research Program’s activities, with a focus on the research arm of our mission. The RGPC includes clinicians and researchers alongside patients and caregivers to facilitate breaking down traditional research silos to encourage a shift toward partnership between all of these stakeholders in RUNX1-FPD research development.

During its first year, the 13-member founding group has been focused on building a patient-centered outcomes research (PCOR) training program for any patient, caregiver, researcher or clinician who may want to be part of this endeavor. Next year, the group will expand and focus on building a system for members to share these patient-centered values with peers for the greatest possible patient-health impact. For the first two years of this effort (2020-2021), the RGPC is funded by a Patient Centered Outcomes Research Institute (PCORI) Eugene Washington Engagement Award - Capacity Building. For more information on the project and the PCORI award, see: www.pcori.org/research-results/2019/runx1-fpd-research-guided-patients-initiative.

To read more about the PFAC and RGPC committee members, visit our “About” page (www.runx1-fpd.org/about). If you are interested in getting involved in these groups as they expand, please email Dr. Amanda Eggen: aeggen@runx1-fpd.org.

New Patient Webpage: www.runx1-fpd.org/patient

We now have one dedicated page on our website where patients, old and new, and their families can learn about what we do to support you as patients directly, including how to navigate around and find information on our growing site. Excitingly, we are including patient stories and videos which have been made by you, patient families, and previously included in either our newsletters or other efforts. We would love to build out this page with more of your stories and videos as the feedback we’ve received is overwhelmingly positive and grateful. Not only does this content help patients feel less alone in their journeys and better able to understand what life with RUNX1-FPD can be like, but it gives faces and urgency to our cause.

Most importantly, we have added an “In Memoriam” section to pay tribute to those RUNX1-FPD patients who have lost their lives. We want to pay tribute to their memory, keep their families in our thoughts and stay motivated and driven to find a cure, dedicating our mission and efforts to those individuals. If you have a video or a written piece you would like to make of you or your family’s story, or if you have a loved one whose life you would like to have honored here, we would love to hear from you. Please email Dr. Amanda Eggen at aeggen@runx1-fpd.org.

As always, thank you for following our news and progress.

The RUNX1 Research Program Team
Welcome to our new short-form newsletter!
Love it? Hate it? Give us feedback here in a 2-question survey.

Has anyone else picked up some bad habits this pandemic they’d like to let go of? Well, here’s your chance! In honor of RRP’s 5th anniversary and in the spirit of cancer-prevention, we are launching the X-Out Cancer Challenge. Designed to spread awareness of RUNX1-FPD and to promote a healthy lifestyle, we’re asking you to X-Out (give up) a bad habit for the month of February. Have a friend who needs to give something up, too? Help us make our campaign go viral!
New Grant Programs

We continue to stimulate research on preventing cancer in *RUNX1*-FPD. Not only are we emphasizing the importance of investing in young researchers to further grow our research community through our ongoing RRP-ALSF Early Career Investigator award, but we have just launched two new targeted grant programs with two new, strategic partners: Evans-MDS and the Mark Foundation for Cancer Research.

Patient Meeting & Scientific Conference Re-cap

**Patient Meeting**

We were thrilled to see over 60 of our community members gather virtually for our very first patient meeting! We saw so much knowledge and value exchanged, and as there is power in numbers, we are excited to see where 2021 takes us as we build upon the connections made this year. Watch a short video summary of the meeting by Amanda Eggen.

**Scientific Conference**

Though our annual scientific conference was virtual this year, we were able to engage over 120 scientists from across the world, including a group of patients. This more than doubled the number of participants from our traditionally in-person meeting. The more people we have focused on *RUNX1* research, the greater our momentum. See a quick video by our ED on the most impactful key takeaways from the meeting.
**RUNX1 Cancer Disease Biology Video**

We’ve created a video that summarizes the biology of **RUNX1**-FPD and the processes by which scientists think germline **RUNX1** mutations create fertile soil for cancer development.

In parallel, we introduce how the research community is attempting to intercept the process of cancer development in the lab, and how translating such approaches from the lab into human studies could help inform the discovery of cancer prevention medicines.

We have already received great feedback, and version 2.0 is expected early next year.
New: Patient Resources

With input from our Patient and Family Advisory Council and our summer intern, Jenna, we have created patient resources that can be used to support communicating information about RUNX1-FPD to others.

Information has been assembled with the help of our medical expert advisors and from existing research findings.

The Patient Resources page can be found here, and other general resources (links, brochures, fundraising info and a glossary of terms) are on our Resources page.

Inherited Blood Cancer Roadshow

Raising awareness of RUNX1-FPD and of our work is always top-of-mind. In October, alongside scientific experts Drs. Ross Levine and Uli Steidl, we hosted a webinar to educate the greater New York City medical community on the prevalence of inherited blood cancers; including how to diagnose, provide counseling and manage patients.

For the full webinar, click here for Part 1 & here for Part 2.
Dr. Ericson @ Milken Institute

Not only do we provide educational opportunities to raise awareness, but we connect with other disruptive healthcare non-profits who are also fighting for cures for their patients. On December 7th, Dr. Ericson joined her peers for a panel discussion at the Milken Institute Health Summit. See a recording of the panel discussion here.

LIVESTREAM

2020 Future of Health Summit

Watch the best minds of the world confront the most significant health challenges of the day.

Director of Development

RRP is seeking a hands-on, impact-focused nonprofit fundraising leader with experience in a health-care-related (ideally rare-disease) nonprofit to lead, manage and implement an effective short- and long-term development strategy.

Know of a suitable candidate? Click here.
Thanks for following our progress and being a part of the RUNX1 community. Visit www.runx1-ffd.org to learn more and to keep up-to-date between newsletters.

The RUNX1 Research Program Team

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