One Goal. Prevent Cancer.

We are so proud of the impact RRP has achieved in such a short time, but there is still much to be done. Join us in our pursuit to find a cure and prevent cancer for RUNX1-FPD patients worldwide.

Tim Babich
Co-Founder & Director

Monica Babich
Co-Founder & Director

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As a rare disease nonprofit, we understand the challenge of having little information and no treatments. Our patient community are the educators themselves—with their family, their friends and with healthcare professionals.

RRP has been committed to raising awareness of hereditary hematologic malignancies (familial blood cancers), their prevalence, and the importance of early and regular genetic testing. Most importantly, RRP has invested close to $11M in research projects that aim to understand how inherited mutations in \textit{RUNX1} predispose individuals to blood cancers. This important work has far-reaching implications for the general population, as it can shed light on how cancer manifests and progresses in all of us.

In 2022, RRP continued to make history with a record of “firsts.” These achievements included:

- Receiving a $2M multi-institution grant from the Chan Zuckerberg Initiative (CZI) to support a four-year research project. This collaborative effort will be co-led by RRP and Drs. Alex Bick from Vanderbilt University, Anupriya Agarwal from OHSU and Esther Obeng from St. Jude’s.
- Launching the \textit{RUNX1} Patient Data Hub, which aggregates hard-to-collect patient information that will support new discoveries.
- Delivering our 2022 clinical webinar series, Hereditary Hematologic Malignancies—Not That Rare, which reached over 1,000 scientists, clinicians, nurses and genetic counselors.
- Holding an in-person patient meeting in Princeton, New Jersey, with over 30 patients and family members, and expanding our scientific conference in-person attendees to close to 100 individuals.

RRP is making history across the research continuum. After just five years of grantmaking, RRP-funded investigators are on track to launch the very first \textit{RUNX1}-FPD clinical trial in 2023. This groundbreaking study will test whether the drug imatinib can raise \textit{RUNX1} levels back to normal—to the same levels found in individuals without \textit{RUNX1} mutations. The idea is that by using a drug that can increase \textit{RUNX1} activity, platelet numbers and platelet function should improve, and reduce blood cancer risk. Additionally, since imatinib is a systemic treatment, it may have an impact on many parts of the body, not just the blood system, potentially reversing other signs and symptoms related to the disease.

These historical achievements are just the beginning of an upwards trajectory toward cancer prevention for those at greatest risk of developing blood cancer. With the ongoing support of our community, we are determined to continue to make inroads and fuel discovery.

RRP hopes to create a world without blood cancer. This goal is a lofty one, but as we know, transformative breakthroughs start with an unwavering dedication to a grand idea.

So, I ask that you join our efforts and help us prevent cancer.

Sincerely,

Katrin Ericson, Ph.D.
President & Executive Director
The RUNX1 gene provides instructions for making RUNX1 protein, which plays a vital role in the production of blood stem cells. RUNX1 Familial Platelet Disorder (RUNX1-FPD) patients have a hereditary mutation in one of the two copies of this gene that causes symptoms such as low platelet counts, poor platelet function and a predisposition to developing blood cancers.

Through our research partnerships we increased our research spend up to 180%. For every $10 we invest, our partners have committed an additional $8.

- Dr. Katrin Ericson

$2,142,750* Total RUNX1 research investments made with our partners in 2022 (by grant mechanism type)

*This includes $915,000 contributed by our partners.
The RUNX1 Team Science Excellence (RISE) Grant Program is a collaborative effort with the National Institutes of Health (NIH)'s National Cancer Institute (NCI) and National Institute of Allergy and Infectious Diseases (NIAID). The grant program supports research projects that bring together multi-disciplinary scientific teams to accelerate research focused on discovering cancer prevention treatments.

### 2022 RiSE Grant Awardees

**Alan Cantor, M.D., Ph.D.**
Boston Children's Hospital & Dana-Farber Cancer Institute

**Sung-Yun Pai, M.D.**
National Cancer Institute (NCI)

**Rescue of RUNX1 deficiency phenotypes in RUNX1-FPD patients treated with imatinib.**

Previous RRP co-funded research by Dr. Cantor and colleagues found that the activity of the RUNX1 protein can be controlled by a chemical modification called phosphorylation. When the RUNX1 protein is phosphorylated, it suppresses full RUNX1 activity. By preventing this naturally occurring chemical modification, it might be possible to boost RUNX1 activity back to healthy levels.

From these results and previous reports in the literature, the team hypothesized that using a drug that can block phosphorylation could boost the activity of existing RUNX1 protein levels in patients, thereby reducing the risk of developing a blood cancer.

There are several drugs already approved by the Food and Drug Administration (FDA) that can block phosphorylation, including a drug called imatinib. Drs. Cantor, Pai and collaborators are currently developing a Phase I clinical trial (a safety study) at the National Institutes of Health (NIH) to determine the safety and correct dosage of imatinib when taken by RUNX1-FPD patients.

Because blood cancer development is a long-term process, and fortunately doesn’t happen in all patients, it is not an ideal measure to determine whether imatinib is effective at reducing the risk of blood cancer. In this research project, Drs. Cantor and Pai will work to develop and optimize shorter-term measures for imatinib’s effectiveness in reducing blood cancer risk by deeply analyzing patient samples obtained during this Phase I clinical trial (as well as the NIH RUNX1 Clinical Study) in order to prepare to move into Phase II (a study designed to test efficacy of a drug).

**Imatinib has the potential to be the first therapy that addresses the root cause of RUNX1-FPD—that is, to bring RUNX1 back to healthy levels.**

- Dr. Alan Cantor
Defining clonal and metabolic alterations in the evolution of RUNX1-FPD.

Leonard Zon, M.D.  
Boston Children’s Hospital

Luigi D. Notarangelo, M.D.  
National Institute of Allergy and Infectious Diseases

All humans have stem cells responsible for continuously making blood cells. Each of these stem cells can be considered a clone, and in normal individuals, the clones are balanced and every clone functions relatively equally. However, in individuals with RUNX1-FPD, clones behave differently and acquire new cancer-causing mutations, which initiates the process towards developing blood cancer.

Currently, eliminating just the mutated clones is not possible as there is no way to tell one stem cell clone from another. In prior RRP co-funded research, Dr. Zon and his team used a method called cellular barcoding that can detect the clones from one another in runx1-deficient zebrafish, while simultaneously examining which genetic mutations are present in a mutated clone versus a healthy clone.

Drs. Zon and Notarangelo’s research project will apply this technology and another, newer technology developed by collaborator Dr. Vijay Sankaran to examine RUNX1-FPD patient blood samples to determine clone number as compared to healthy volunteer blood samples. Clones in RUNX1-FPD samples will also be evaluated for somatic mutations (acquired cancer-causing mutations) and further characterized using metabolomics (a novel tool that enables scientists to measure all of the metabolites produced by cells) to hone in on differences in metabolites between mutated clones (i.e., bad clones) and unmutated clones.

Any identified differences could uncover vulnerabilities in the bad clones that could be taken advantage of by using drugs that selectively target those differences and destroy the bad clones. Using the RUNX1-FPD zebrafish in Dr. Zon’s lab, drugs can be quickly tested for their ability to destroy bad clones. The hope is to use these studies to nominate FDA-approved drugs that could intervene and stop bad clones from multiplying and becoming blood cancer in RUNX1-FPD patients.

We are examining how the pool of blood stem cells (or ‘clones’) are affected in patients with RUNX1 mutations over time to uncover which stem cells are on the path to becoming cancerous. By identifying which stem cells are becoming cancerous (the ‘offending clones’) we can find methods to eliminate them.

- Dr. Len Zon

We are using innovative approaches to map all of the genes that RUNX1 controls within a cell. Having a map of all these genes will help the field begin to tease apart which genes may be critical in establishing blood cancer risk.

- Dr. Kristy Stengel

Delivering on the promise of germline genetic testing for RUNX1 variants.

Abbye McEwen, M.D., Ph.D.  
University of Washington

To date, there are 310 RUNX1 variants classified as variants of uncertain significance (VUS) reported in a large international database called ClinVar. These VUSes, which cannot be used for clinical decision-making, represent at least 310 different patients or families without a genetic diagnosis.

Dr. McEwen will help provide current and future patients harboring RUNX1 VUSes with a diagnosis, furthering our understanding of variants by defining which may be more severe than others. This can also help pave the way for studying other genes related to myeloid malignancy, possibly leading to a paradigm shift for interpreting variants in genes associated with rare diseases.

We are using "large-scale" laboratory experiments to test the effect of hundreds of RUNX1 gene variants in a single experiment. This will allow us to generate a map of the RUNX1 gene which clinicians can when interpreting RUNX1 variants found in patients.

- Dr. Abbye McEwen

Using chemical genetics to define the precise role of RUNX1 in transcription & beyond.

Kristy Stengel, Ph.D.  
Albert Einstein College of Medicine

The RUNX1 protein is a transcription factor, controlling a select group of genes that are critical for a normal healthy blood system, including the production of properly functioning platelets. Therefore, the ability to define the exact genes RUNX1 controls is critical to our understanding of how RUNX1 governs platelet biology and how loss of RUNX1 activity predisposes to blood cancers.

Dr. Stengel’s group has engineered a new cell line that can rapidly degrade RUNX1 protein levels within 1-2 hours. This cell line will allow the team to finally define the direct RUNX1 target genes in cells. Furthermore, her cell line will help determine what role RUNX1 plays in DNA damage response, a pathway that, when perturbed, can increase cancer risk.
Our patient community is at the core of our work. RRP is committed to providing multiple avenues for patients to become involved as advocates and experts. We place a priority on understanding their diagnostic journey, offer opportunities for peer-to-peer support, continuously develop useful educational tools and encourage engagement in co-designing research.

### RUNX1 Patient Data Hub

RRP launched the RUNX1 Patient Data Hub in December 2022. This centralized data hub allows us to remotely collect previously hard-to-gather health data from patients and identify opportunities for education and advocacy.

The RUNX1 Hub will provide insights about our patient population, revealing the breadth of patient experiences and perspectives, as well as clarify questions that remain about the disease.

Ongoing and planned data collection include:

- Medical history, including family medical history with longitudinal follow-up
- Patient-reported outcomes using validated instruments on topics such as fatigue, pain and mental wellbeing
- Molecular testing results (reviewed by genetic counselors)
- Patient preferences and risk/benefit analyses for therapeutic interventions

A core value of the Data Hub is to share findings continuously with our patient community.

### Age at RUNX1-FPD Diagnosis

Age at diagnosis ranges from 2-76 years, with a median age of 37.

I have been really encouraged by the data hub. I have so many questions about RUNX1-FPD and whether the commonalities in my family might be true for all families. I look forward to learning more when there are enough patients participating.

- Clarice, RUNX1-FPD patient

### Patient-Centered Outcomes Research Projects

RRP has been the recipient of two Eugene Washington Patient-Centered Outcomes Research Institute (PCORI) Engagement Awards.

The first award supported the formation of the Research Guided by Patients Committee (RGPC). The RGPC includes patients and caregivers, along with clinicians and researchers, dedicated to developing RUNX1-FPD research centered around patients’ defined priorities and preferred outcomes. This funding helped RRP to develop a training program to support RUNX1-FPD patients, caregivers, scientists and clinicians to effectively partner in this research endeavor.

The second PCORI project focused on convening these diverse stakeholders through a series of workshops with the RUNX1 community and co-developing a five-year strategic plan. The workshops and strategic plan will help shape RRP’s future research and educational programming in a way that ensures patients and their priorities remain central. Both PCORI projects have positioned RRP to identify and prepare patient research partners, ensure scientists value patients as research partners, collate patient-driven research questions and ensure these questions are incorporated into future grantmaking programs and research strategy.
Patients as Research Partners and Participants

The RRP Conference gave me the boost of confidence I needed to finally sit down with my family and discuss the disorder. It’s impossible to put into words how much it meant to have knowledge and hope that I could share with my children.

2022 Scientific Conference and Patient Meeting: Making Cancer History

The 6th Annual Scientific Conference and 3rd Annual Patient Meeting were held October 18 - 21, 2022 in Princeton, New Jersey. The overarching goal of these events is to foster collaboration across the RRP community by providing an opportunity to share knowledge and the latest research data with a diverse stakeholder audience.

It is the only convening of its kind internationally, and continues to be an important driver of discovery and future therapies for the disorder. It’s also an opportunity for early career investigators, postdocs and graduate students to present their research. RRP’s philosophy is to pull young leaders into the RUNX1 and cancer prevention field early so that they consider dedicating future years of their research efforts towards RRP’s mission.

This was the first live convening of patients, and attendees expressed great appreciation of both the opportunity to build relationships with one another and the RRP team, and to engage in varied contexts with scientists and clinicians.

Presentations included lay summaries of research findings to date, along with potential impacts for the patient community, stem cell transplant considerations from a transplant expert and a session on mindfulness for managing worry.

Two patients presented their stories to scientists, clinicians and the patient community. The scientific community conveyed an overwhelming level of appreciation for the impact that hearing directly from patients had on them and their teams.

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I was honored to speak at the Princeton meeting and took the opportunity to share my own experience with a genetic condition in the family, my somewhat unconventional experience developing a drug for a hematologic malignancy disease, and the personal perspective on how science can get to clinical solutions efficiently. But the most important feature of the Princeton meeting was to meet patients, their families and listen to their stories about their trials in life. The people they have lost and the hope that the Foundation fosters, not just for themselves but to their children, relatives and the unknowns that carry the same liability. Such meetings bring into sharper focus the needs of patients and the goals of biomedical research.

- Dr. Hugh Rienhoff, CEO, Imago BioSciences & Scientific Advisory Board Member

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- Melissa, RUNX1-FPD Patient

27 patients from five different countries met in-person for the first time

Breakout sessions during the 6th Annual Scientific Conference

Keynote presentation by Hugh Rienhoff, M.D.
RRP is dedicated to educating the medical community about the underappreciated prevalence of hereditary blood cancers, and the importance of early and regular genetic testing to improve patient care and health outcomes across inherited blood cancer predisposition syndromes and blood cancers.

2022 Medical Education Webinar Series

RRP reached more than 1,100 healthcare professionals with the Hereditary Hematologic Malignancies—Not That Rare webinar series conducted on May 23, May 25, September 19 and September 21, 2022. The webinar series aimed to educate the medical community (i.e., physicians, fellows, nurses, genetic counselors) on the importance of molecular profiling of hematologic malignancies, the high prevalence of pathogenic germline variants within hematologic malignancy populations, and how to implement routine genetic testing in clinical practice to improve patient outcomes.

RRP hosted the four-part webinar series with expert academic clinician Courtney DiNardo, M.D., of MD Anderson Cancer Center, who specializes in the diagnosis, management and care of patients with hereditary blood cancers. Following Dr. DiNardo’s presentation, each webinar had an expert panel of clinicians available to answer questions from the audience.

I commend RRP for their dedication to educating the medical community in order to improve patient outcomes. It was a privilege to collaborate on this impactful webinar series. - Dr. Courtney DiNardo
The RRP Scientific Advisory Board includes both academic and industry experts who span basic science, translational science, clinical research and clinical development.

Members offer advice and guidance on how best to propel basic, translational and clinical research forward with the goal of positively impacting our patients’ lives as quickly as possible. The SAB plays a critical role in defining our research agenda, reviewing grant applications and fostering collaborative relationships within the scientific community.

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The North American & Australian RUNX1 and Inherited Hematologic Malignancies Consortium brings together physicians and genetic counselors who care for RUNX1-FPD and similar inherited platelet disorder patients across the U.S. and Canada in order to drive collaboration and accelerate advancements in medical care for patients. This list of experts is available to both patients and medical professionals for consultation. Visit our website for direct contact information.
We are fortunate to have these organizations as partners and co-funders. Thank you for your support!

Chan Zuckerberg Initiative

The Chan Zuckerberg Initiative (CZI) awarded RRP and three partner institutions a four-year $2M grant to support RUNX1 research. This highly competitive award will fund the project, “Deciphering RUNX1-Familial Platelet Disorder at Single-Cell Resolution,” which aims to illuminate cellular-level processes in the body that are responsible for inflammation in RUNX1-FPD.

Using the single-cell data generated from patient samples, the research team below will work to advance the understanding of RUNX1-FPD and nominate high priority therapeutic targets to address inflammation in RUNX1-FPD patients.

Katrin Ericson, Ph.D. Patient Organization PI
Alexander Bick, M.D., Ph.D. Coordinating PI
Anupriya Agarwal, Ph.D. Co-Principal Investigator
Esther Obeng, M.D., Ph.D. Co-Principal Investigator

Financials

Beginning Assets: $3,085,066
as of 12/31/2021

Funding Received in 2022:
New Grants Received $670,178
Private Contributions $539,889
Government (PPP) $56,995
Events and Campaigns $56,145

Ending Assets with Pledges: $1,547,381
as of 12/31/2022

Total 2022 Expenses: $2,880,432

- Management and General 6%
- Fundraising 7%
- Research and Program Initiatives 87%
- Research and Support Grants $1,477,750
- Program Expenses $163,633
- Management and General $214,638
- Fundraising $1,026,411
- Total Expenses $2,880,432
HOW TO GIVE

Please contact Alex Gonzalez, Director of Development, at agonzalez@runx1-fpd.org if you have any questions or would like to support us.

Online
Giving online is easy! Scan the QR code.

By Mail
If you would like to send a donation via check, please make it out to the RUNX1 Foundation and address it to:
The RUNX1 Research Program
1482 E Valley Rd, Ste 137
Santa Barbara, CA 93108

Donor Advised Fund
A donor advised fund (DAF), which is like a charitable savings account, provides the flexibility to recommend how much and how often money is granted to RRP. You can recommend a grant or recurring grants at any time using your DAF.

Gifts of Stock
If you own stock or mutual funds, it may be more beneficial to contribute these shares than contribute cash. Gifts of appreciated stock or mutual funds provide a two-fold tax advantage: you avoid paying capital gains tax on the increase in the value of the stock or mutual funds, and you receive a federal income tax deduction for the full fair market value of the stock or mutual funds at the time of the gift.

Employee Matching Gifts
Have your donation make the most impact. Matching gifts and workplace giving programs are excellent ways to double the impact of your donation to the RRP. Ask your employer if they offer a matching program.

Planned Gifts
Leave a legacy and support cancer prevention research by including RRP in your estate plans.

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