CUREBOUND

RESEARCH PORTFOLIO

2022-23


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CUREBOUND

2022-23 RESEARCH PORTFOLIO

CURE PRIZE, TARGETED GRANTS AND DISCOVERY GRANTS

CURES IN OUR LIFETIME

Dear Curebound Friends,

1 in 2 people will be diagnosed with cancer.

It's a staggering statistic. I have no doubt that you and your family have already been impacted by cancer. Every person on our staff, Board, research teams, and in our community has personally experienced cancer in some way, and together we are determined to change that number.

Curebound was founded with a deeply held belief that cures are possible. We live in an unprecedented time in the fight against cancer and have entered a transformative era in the way we are able to understand and treat this disease. The advancing technologies, treatments, and preventions, many of which are being pioneered by scientists here in San Diego, have shined a light on a future where cancer is managed and in many cases, cured. Over the next ten years, we will experience a period of game changing scientific discovery in which Curebound is committed to investing $100 million to accelerate innovative cancer research, bringing the best minds of San Diego's top institutions together with one vision: a world without cancer.

At the core of this vision is a commitment to collaboration. All Curebound grants demand collaboration among inter-disciplinary and cross-institutional specialized teams from our six research partner institutions, enabling the brightest minds to work together to drive the work faster and further, to achieve better results and producing better outcomes for patients.

This past year has been one of tremendous momentum for Curebound. We have made significant advancements in all areas of the organization, specifically in the development of our research department infrastructure. Thanks to the support of our generous community, in 2022 we were able to award 12 Discovery Grants for a total of $3 million and will award an additional $3 million in funding for innovative research in the Spring of 2023. This will be followed by a second wave of grants in the later part of this year. As part of this cycle, we are very proud to award the first Cure Prize, a million dollar grant for bold innovation in cancer research that aims to change the standard of care for ovarian cancer with patient application in 3-5 years.

We look forward to building on this momentum and charging forward with our mission to mobilize San Diego to accelerate cancer research into cures in our lifetime. Our heartfelt appreciation and gratitude to the members of our Founders Circle, Scientific Advisory Board, Board of Directors, Partner Institutions and the exceptional research scientists who drive this work forward. Together, we are charting a course to change the trajectory of cancer so that the next generation does not hear the words "you have cancer" in the way we do today.

Warm regards,

Anne Marbarger
CEO, Curebound

CUREBOUND IMPACT

$26 MILLION

AWARDED FOR CANCER RESEARCH SINCE 2013

95

RESEARCH GRANTS FUNDED

6

TOP INSTITUTIONS WORKING TOGETHER

21

DIFFERENT TYPES OF CANCER RESEARCH FUNDED

71

ADULT CANCER PROJECTS FUNDED

24

PEDIATRIC CANCER PROJECTS FUNDED

1

VISION: A WORLD WITHOUT CANCER

CUREBOUND GRANT FUNDING

Curebound is dedicated to accelerating cancer cures by funding the most promising, innovative research to collaborative teams from our six research partner institutions. For the 2022-23 grant cycle, we are proud to announce a $6 million investment in grant funding for leading oncology research in alignment with Curebound's five scientific pillars:

- Prevention and diagnostic tools
- Novel approaches and new therapeutic platforms
- Immunotherapies and personalized vaccines
- Cancer equities
- Pediatric cancers

This investment will fund 17 unique research projects spanning a broad range of translational research across many different disciplines, institutions, and types of cancer including:

- Ovarian
- Acute Myeloid Leukemia
- Melanoma
- Lung
- Prostate
- Pediatric
- Pancreatic
- Breast
- Myelodysplastic Syndrome
- Cancer vaccines

Curebound funds three levels of grant awards, each with a specific target and focus:

Cure Prize:

Curebound's highest award for bold innovation in cancer research. Cure Prizes are awarded to teams who present collaborative and/or inter-disciplinary solutions that show near-term promise of clinical breakthrough and represent "game changers" in the prevention, diagnosis, access or treatment of cancer patients. Grant funding of $1,000,000+ is awarded and administered over a period of 2-3 years. The first Cure Prize challenge is to develop an innovation that will improve the standard of care for a typically deadly cancer with patient application in 3-5 years.

Targeted Grants:

Larger gifts of $500,000 that aim to fund projects that are closer to clinical stages. Inaugural Targeted Grants require a clinical researcher to be part of the collaborative team in order to ensure the project is geared toward translational application. Priority is given to applications that have a high likelihood of significantly advancing detection, prevention, therapeutic development, access to patient care and/or clinical trials. Targeted Grants fund continuity of ideas from the investigators' past research, including research that builds upon previously funded Discovery Grants. Interdisciplinary collaboration is required and inter-institutional collaboration, while not required, is preferred.

Discovery Grants:

One-time seed grants of up to $250,000 for high-risk/ high-reward, translational research. Ideas are innovative and in the early phases where smaller grants can make a big impact in advancing research. Discovery Grants prioritize research that advances therapeutic development and/or has a high likelihood of leveraging extramural funding. Inter-institutional collaboration is required.

2023 CURE PRIZE

2023 Cure Prize

In Honor of the Koman Family

Screening for Ovarian Cancer with Advanced Diffusion MRI in Patients at High Risk for Ovarian Cancer

Scientists: Rebecca Rakow-Penner MD, PhD (UCSD), Anders Dale PhD (UCSD), Michael McHale MD (UCSD)
Pillars: Prevention and Diagnostic Tools, Cancer Equities

Ovarian cancer is the fifth-most deadly cancer in women in the United States with 60% of cases already metastasized at the time of diagnosis. Multiple screening programs have been attempted, but none so far have demonstrated survival benefit. This project intends to develop a robust screening technique, based on advanced diffusion- weighted MRI, that can non-invasively image ovarian cancers. This will decrease the need for surgical removal of ovaries from at risk women and while offering the promise of novel screening technique for early detection and treatment for all women.

"Our project, my passion, is to develop an innovative and advanced MRI protocol specifically tailored to detecting ovarian cancer in its earliest stages. By harnessing the power of cutting-edge technology, we aim to provide the information to at risk women so they can make informed decisions about their health and specifically about the very difficult decision they face with respect to prophylactic surgery. With the support of Curebound, we aim to significantly improve the outcomes for women facing this formidable challenge."

- Rebecca Rakow-Penner, MD, PhD
UC San Diego Health

2023 TARGETED GRANTS

1. Targeting the Proteostasis Network in Acute Myeloid Leukemia (AML)

In Honor of Anne Daigle, PhD and Rich Heyman, PhD

Researchers: Robert Signer, PhD (UCSD); Kentson Lam, MD, PhD (UCSD)
Pillar: Novel Approaches and New Therapeutic Platforms

AML is an aggressive and deadly cancer of white blood cells. Traditional chemotherapy has been used for the past 50 years, yet the survival rate is only 29%. This proposal is based on emerging evidence that AML cells are sensitive to drugs that interfere with the intracellular processes of "taking out the trash" and "recycling" (as known as proteostasis). The goal is to elucidate new strategies that can be used to more effectively treat AML and other cancers.

"Curebound's support is instrumental to expanding our studies to determine if this approach holds the key to eliminating AML within the body. This vital research has the potential to revolutionize AML treatment and pave the way for new therapies benefiting all cancer patients. Curebound's investment is propelling our mission to transform the lives of AML patients and make a lasting impact on cancer research."

- Robert Signer, PhD
UC San Diego Health

2. Advancing Immune Checkpoint Inhibition of PSGL-1 for Treatment of Malignant Melanoma

In Honor of the Whitworth Family

Researchers: Linda Bradley, PhD (SBP); Soo Jin Park, MD (UCSD)
Pillars: Novel Approaches and New Therapeutic Platforms, Immunotherapies and Personalized Vaccines

Despite recent advances, malignant melanoma still causes thousands of deaths in the US each year. The goal of this project is to develop a novel, monoclonal antibody-based therapy that can reactivate the tumor-killing properties of the patient's own immune system. This therapy has the potential to eradicate tumors that are refractory to existing therapy and thus save lives.

3. Targeting PI3Kg to Reverse Immune Suppression in Lung Cancer

In Honor of Sally and John Hood, PhD

Researchers: Judith Varner, PhD (UCSD); Mark Onaitis, PhD (UCSD); Sandip Patel, MD, PhD (UCSD)
Pillars: Novel Approaches and New Therapeutic Platforms, Immunotherapies and Personalized Vaccines

Lung cancer is a leading cause of death worldwide and there is a pressing need for new treatments that can cure the disease and promote long-term survival. The aim of this project is to investigate the effectiveness of Eganelisib, a first-in-class, immuno-oncology drug, in combination with standard-of-care chemotherapy and immune therapies in lab models. We predict that this project will directly inform the development of new treatments for lung cancer and has the potential to improve the survival rates and quality of life for those affected by this devastating disease.

"Curebound funding helps to foster innovative cancer discoveries for the benefit of patients during a time in which other funding sources have become increasingly limited and directed towards lower academic risk, but lower-reward, initiatives. Curebound's focus on transformative science with an eye to rapidly bringing these discoveries to the clinic to benefit patients helps bridge the grant divide and ensures that we continue to be leaders in biomedical innovation to help our cancer patients."

- Sandip Patel, MD, PhD
UC San Diego Health

4. Clinical Strategizing of PARP Inhibitors in Castration Resistant Prostate Cancer

In Honor of Cindy and Larry Bloch

Researchers: Ludmil Alexandrov, PhD (UCSD); Rana McKay, MD (UCSD)
Pillar: Novel Approaches and New Therapeutic Platforms

Prostate cancer is the most common cancer diagnosis in men. With more than 160,000 new cases each year in the United States, it remains the second-leading cause of male cancer death in the US. This collaborative bench-to-bed project will use next-generation sequencing to increase the precision and effectiveness of therapy for patients. By integrating state of the art bioinformatic and genomic analysis of patients enrolled in Phase 2 trails, this project expects to significantly improve outcomes by providing molecular tailored treatments for individuals with this disease.

2022 DISCOVERY GRANTS

1.Decoding the Role of the Long Non-Coding RNA PVT1 in Medulloblastoma

Researchers: Anindya Bagchi, PhD (SBP); Lukas Chavez, PhD (UCSD)
Pillar: Pediatric Cancer

Medulloblastoma (MB) is the most common malignant childhood brain tumor and is often associated with activation of the MYC gene. This Discovery Team uncovered a pathway that effectively regulates MYC. This grant investigates the elimination of the MYC protein that would, in turn, lead to effective treatment for medulloblastoma.

"Medulloblastoma is one of the dreaded childhood cancers. Our quest is to see that in our lifetime, no child suffers from this disease. The advances on the horizon in cancer research are already making its impact and the support from Curebound will directly help us to develop cures so that children afflicted with this cancer can live a full, happy, and healthy lives."

- Anindya Bagchi, PhD
Sanford Burnham Prebys

2. High Throughput-Screen for Inhibitors of Pediatric Ependymoma

Researchers: Michael Jackson, PhD (SBP); Lukas Chavez, PhD (UCSD)
Pillar: Pediatric Cancer

Ependymoma (EPN) is the third most common pediatric brain tumor and a leading cause of death in childhood cancer patients. This Discovery Team proposes to screen patient derived samples with drugs already approved by the FDA for other conditions. Once active drugs have been identified the team will also investigate their mechanisms of action potentially allowing further targeting of this deadly childhood disease.

3. Targeting Tumor-Associated Macrophages to Improve Immunotherapy in Neuroblastoma

Researchers: Shweta Joshi, PhD (Rady); Judith Varner, PhD (UCSD)
Pillar: Pediatric Cancer

Neuroblastoma accounts for over 15% of pediatric cancer deaths and the 5-year survival rate of these patients is very low. This Discovery Team's research will combine two inhibitors that activate macrophages with immunotherapy to ultimately allow macrophages to work with T-cells to attack tumor growth and target neuroblastoma.

4. Understanding the Biological and Clinical Role of ecDNA in Neuroblastoma

Primary Investigators: Ludmil B. Alexandrov, PhD (UCSD); Peter E. Zage, MD, PhD (Rady)
Pillar: Pediatric Cancer

Children with aggressive neuroblastoma tumors have poor rates of survival and cure despite intensive treatment, and better clinical management is needed. Interestingly, higher copies of the MCYN gene is associated with worse overall survival from neuroblastoma. In this project, the Discovery Team will examine large datasets from neuroblastoma patients as well as screen laboratory cell line and tumor models to improve the biologic and clinical understanding of neuroblastoma. These efforts will lead to improved therapeutic success and survival for children with neuroblastoma.

5. Determining the Impact of Regulatory Mutations and Dysregulated Transcription Factors in Neuroblastoma

Researchers: Graham McVicker, PhD (Salk); Peter Zage, MD, PhD (UCSD/Rady)
Pillar: Pediatric Cancer

Neuroblastoma is a tumor of developmental origin with high incidence of metastatic disease at initial diagnosis. There is an urgent need to develop innovative approaches to discover novel cancer dependencies and gene targets in neuroblastoma to improve patient outcomes. The main objective of this proposal is to use new molecular experiments to discover novel genetic mutations and cancer genes and determine their impact on neuroblastoma tumorigenesis (initial growth of tumor in the body). The long-term objective of this project is to discover prognostic biomarkers and therapeutic targets for early detection and treatment of neuroblastoma.

6. Pre-clinical Development of New Autophagy Targeting Drugs for Bone Metastatic Prostate Cancer

Researchers: Nicholas Cosford, PhD (SBP); Christina Jamieson, PhD (UCSD)
Pillar: Novel Approaches and New Therapeutics

One in six men will be diagnosed with prostate cancer. While patients are being diagnosed earlier and surviving longer, a growing number of patients have gone on to develop advanced prostate cancer. The main treatment for advanced prostate cancer (PCa) is androgen pathway directed therapy (APDT). Unfortunately, patients invariably become resistant to APDT, and their cancer metastasizes - most often to bone - for which there is no cure. This Discovery Team will examine a class of specific inhibitors in patient bone metastatic PCa cells and evaluate their ability to reduce PCa tumor burden in mouse models alone and in combination with ADPT. These studies will allow the development of a new drug therapy for the treatment of this deadly cancer and enhance patient outcomes.

7. Therapeutics to Overcome the Differentiation Roadblock in Myelodysplastic Syndrome (MDS)

Researchers: Michael Bollong, PhD (Scripps Research); Rafael Bejar, MD, PhD (UCSD); Arnab Chatterjee, PhD (Scripps Research)
Pillar: Novel Approaches and New Therapeutics

Myelodysplastic syndrome (MDS) is a pre-cancer condition involving mutations in the stem cells. This Discovery Team has identified a class of anti-malarial medications, called Artemisinins, which overcome these mutations. In this study, the Discovery Team will use medicinal chemistry to develop an Artemisinin derivative that can be orally dosed as therapy for this disease. Successful completion of this grant will deliver a preclinical candidate for the treatment of MDS, ready for IND-enabling safety studies, the next steps in advancing this candidate as a new drug.

8. Targeting Metabolic Vulnerabilities Unique to Pancreatic Ductal Adenocarcinoma

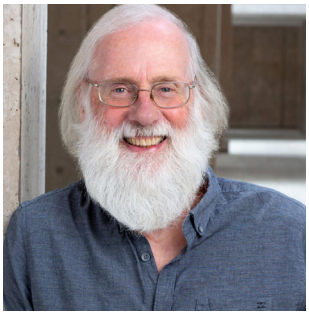
Researchers: Michael Karin, PhD (UCSD); Reuben Shaw, PhD (Salk)
Pillar: Novel Approaches and New Therapeutics

Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive cancer with a 5-year survival rate of 11%. We found that an FDA-approved antibiotic called tigecycline curtails PDAC metabolism and growth in preclinical models. This Discovery Team proposes to potentiate tigecycline's anti-PDAC activity by complementing it with inhibitors of an enzyme, ULK1, which is critical to repair of the PDAC mitochondria. This novel approach should be highly effective in blunting PDAC growth by cutting off tumor energy supplies.

9. Role of Histidine Phosphorylation in Breast Cancer Invasion

Researchers: Tony Hunter, PhD (Salk); Jing Yang, PhD (UCSD); Kay Yeung, MD, PhD (UCSD)
Pillar: Prevention and Diagnostic Tools

Breast cancer is the most common type of cancer amongst women in the world and led to 684,996 deaths in 2020. Our research has shown that an enzyme called LHPP is present at higher levels in triple-negative breast cancer (TNBC), which has the worst prognosis, and currently lacks an effective treatment. Combining cutting-edge molecular biology, cell biology and genetic techniques, we will investigate if this enzyme is important for breast cancer metastasis, aiming to identify key protein targets in this disease.



"This Curebound funding will play a key role in our efforts to understand the role of histidine phosphorylation in breast cancer. This is a new area of research for the group, and we hope our work can lead to identification of new drug targets to treat triple negative breast cancer, the deadliest form of the disease."

– Tony Hunter, PhD
Salk Institute

10. Neoantigen Driven Eradication of Immune-Reprogrammed Ovarian Cancer

Researchers: Dwayne Stupack, PhD (UCSD); Stephen Schoenberger, PhD (LJI); David Schlaepfer, PhD (UCSD)
Pillar: Immunotherapy and Personalized Vaccines

One approach to treating tumors uses intravenous therapies that boost the immune system. This works in many cancers, however, this approach does not always work, and can fail with time as tumors find ways to avoid the immune system – even shutting off its ability to attack tumors.

In ovarian cancer, studies showed that an oral drug called a FAK inhibitor helps to avoid a "shut down" of the immune system. FAK can also be combined with other immunotherapies. A second type of immunotherapy in development is a cell-based therapy that uses personalized vaccination against unique features of the tumor. While very precise, and potentially very potent, this approach is highly vulnerable to the "shut down" mechanism described previously. This proposal will test a new idea of combining these two strategies to ultimately improve outcomes in ovarian cancer.

11. Development and Optimization of Peptide-Based Nanoparticle NeoAg Cancer Vaccines

Researchers: Stephen Schoenberger, PhD (LJI);
Ezra Cohen, MD (UCSD); Aaron Miller, MD, PhD (UCSD)
Pillar: Immunotherapy and Personalized Vaccines

This Discovery Team explores natural immune responses that protect us from viral and bacterial infections that require the coordinated activity of two subsets of T lymphocytes known as CD4+ helper" T cells and CD8+ "killer" T cells. The team has found that this same idea applies to immune responses to cancer. Specifically, that our immune response to cancer is most effective when these two T Cells are engaged by a vaccine. The goal of this research is to develop a vaccine platform that will enable both CD4+ and CD8+ T cells against a patient's tumor-specific target antigens to be generated in a manner that is safe, effective, reproducible, and consistent with the regulatory and manufacturing constraints which necessarily govern what can be administered to a patient.

"Our work has placed us at the cutting edge of understanding the immune response to cancer in patients and how this can be therapeutically deployed by vaccines. Our new Curebound-supported work will enable us to develop more powerful cancer vaccines capable of producing deeper and more durable immunity by simultaneously engaging both the CD4+ and CD8+ arms of a patient's mutation-specific T cell response."

- Stephen Schoenberger, PhD
La Jolla Institute for Immunology

12. HERV env: A Targetable Surface Protein in Ovarian Cancer

Researchers: Erica Ollmann Saphire, PhD (LJI);
David Schlaepfer, PhD (UCSD)
Pillar: Immunotherapy and Personalized Vaccine

According to the American Cancer Society, ovarian cancer is the fifth leading cause of cancer deaths among women in the United States. However, there are few new treatments or diagnostic tools for ovarian cancer. This Discovery Team is focused on developing new tools to diagnose and treat ovarian cancer based on information derived hundreds of thousands of years ago. Before humans evolved from primates, another pandemic caused by viruses occurred. This pandemic was caused by retroviruses, which are viruses that can insert their own genetic information into the DNA of their hosts. Around 8% of human DNA is the remnant of viral genetic material from these ancient infections. These DNA remnants are called human endogenous retroviruses (HERVs). Endogenous means that these bits of viral DNA are now a stable part of our genetic make-up. These retroviral sequences were long thought to be silent 'junk' DNA, but recent research has uncovered the potential for these viral genes to start producing proteins in disease states, such as in cancer or autoimmune disease. For example, in ovarian cancer, researchers have seen that some retroviral proteins stud the surface of ovarian cancer tissues and ovarian cancer cells. In a mouse model of ovarian cancer, a monoclonal antibody treatment targeting a HERV protein slowed tumor growth. This project will approach HERV proteins as targets for drug discovery, with a focus on developing novel monoclonal antibodies to be used either to diagnose or treat ovarian cancer.

FOUNDERS FUND

The Founders Fund Campaign is Curebound's philanthropic effort to bring experts from San Diego's unique ecosystem of life sciences, research institutes and clinical settings together with the philanthropic community to ignite collaborative work for higher levels of discovery. To date, the campaign has secured over $23.5 million from 37 contributors. As our Founders Circle continues to grow, the campaign will provide substantial support for best-in-class research that has the power to save lives.

FOUNDERS CIRCLE

We are grateful for the visionary leadership of our growing circle of $50,000+ founding investors, all of whom believe firmly that cures are possible and together, we can change the trajectory of cancer for future generations. Curebound is made possible through the support and extraordinary generosity of these individuals and organizations.

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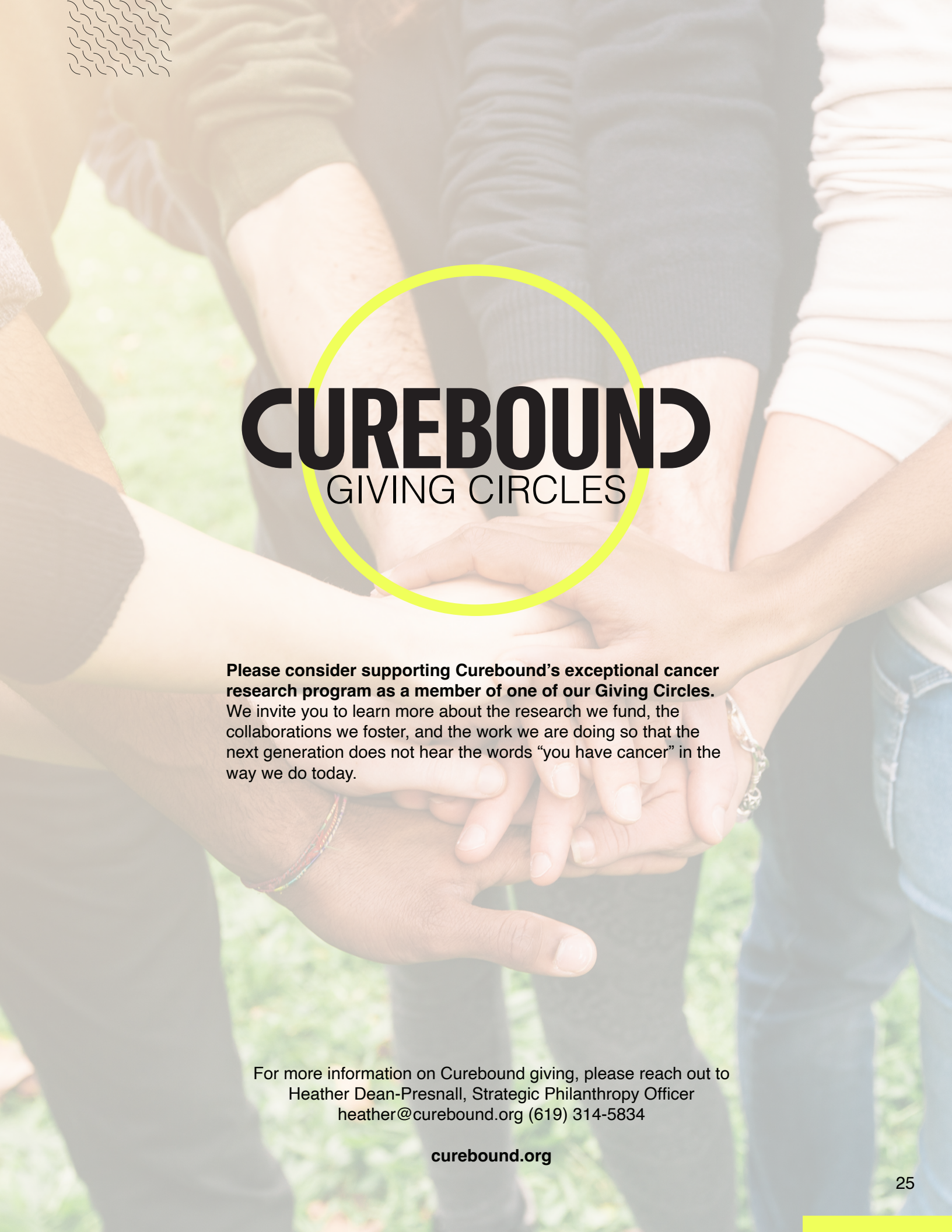

CUREBOUND
GIVING CIRCLES

Please consider supporting Curebound's exceptional cancer research program as a member of one of our Giving Circles. We invite you to learn more about the research we fund, the collaborations we foster, and the work we are doing so that the next generation does not hear the words "you have cancer" in the way we do today.

For more information on Curebound giving, please reach out to
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