Pediatric Cancer Research Foundation — powering cures, realizing futures

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UNDERSTANDING PEDIATRIC CANCER

A DATA-DRIVEN RESOURCE GUIDE

Updated September 2022

pediatric cancer

Also referred to as childhood cancer, pediatric cancer describes cancers that occur between birth and 19 years of age.

While pediatric cancer cases are thankfully rare, cancer is the leading cause of disease-related death among children over the age of one in the United States[1].

Pediatric cancers are often very different from adult cancers in the way they grow and spread, how they are treated, and how they respond to treatment. There are over 12 major types of pediatric cancer and over 100 subtypes. The most common ones are leukemia, brain and spinal cord tumors, lymphoma, neuroblastoma, Wilms tumor (a type of kidney cancer), retinoblastoma, and cancers of the bone and soft tissue[2].

15,780

children are diagnosed with cancer in the United States each year[3]. Globally, this number is over 400,000[4].

1 in 6

patients do not survive childhood cancer. This can be attributed to a lack of research around certain types of aggressive cancers and the fact that many current treatments are decades-old and are too toxic for developing bodies[5].

10%

of all children with cancer have a genetic predisposition[6].

28%

of childhood cancer diagnoses are acute lymphocytic leukemia (ALL), the most common kind[5]. Thanks to research progress, it now has a 70% survival rate after five years following treatment[6].

500,000

is the current and growing population of childhood cancer survivors in the U.S. As survival rates increase, long-term health-related issues of treatments are becoming apparent[7].

95%

of childhood cancer survivors will have a significant issue by the time they are 45 years old. These long-term consequences are side-effects of either the cancer or more commonly, the result of its treatment, and range from secondary cancers, heart disease, and infertility to hearing loss and cognitive impairment[7,8].

6

While more than 200 cancer drugs have been developed and approved by the FDA for adults, today only six drugs are approved for use in the first instance of cancer treatment for children[8].

COLLABORATION IS THE KEY TO THE FIGHT AGAINST CHILDHOOD CANCER

Despite the tremendous progress in the treatment of some types of childhood cancer that has been made in the past 50 years, it is still the leading cause of non-accident related deaths in children.

New research is needed to develop new, more effective, and safer treatments for pediatric cancer, however, researchers face a series of unique challenges such as the following:

Understanding the causes

In adults, we know that lifestyle-related risk factors, such as smoking or being overweight, play a major role in many types of cancer. However, most childhood cancers have not been shown to have lifestyle-related or environmental causes. Rather, research suggests that most childhood cancers are caused by genetic mutations that happen early in a child's life, sometimes before birth. The causes of these DNA changes in most childhood cancers are not yet understood and present an ongoing challenge for researchers[9].

Finding safe targets

Pediatric cancers often lack the genetic targets for treatments that are used to treat adult cancers, and drugs for adult cancers may interfere with signaling pathways that are important for typical human development and therefore cannot be used in children[10].

Sourcing samples

Samples are hard to come by. Pediatric cancer represents less than 1% of all new cancer diagnoses in the U.S. each year and these patients are spread out at institutions across the country[10].

Limited funding

Pediatric cancer does not command the same level of funding as adult cancers. While the federal government is the largest single source of funding for childhood cancer research, only 4% of the national cancer budget is allocated to pediatric oncology[11].

Private philanthropies—which rely on the generosity of individual donors, foundations, and companies—fund at least half of all pediatric cancer research. The reality is that underfunding slows down advancement, and in the past two years, pediatric cancer research saw diminished funding, as other causes took priority during the pandemic.

Now more than ever, collaboration between research labs, funding institutions, and philanthropically minded companies and individuals is critical to advance knowledge and accelerate research breakthroughs in both diagnostics and treatments for pediatric cancer.

ELIMINATING ROADBLOCKS IN PEDIATRIC CANCER RESEARCH

Cancer immunotherapies save lives every day. It has become the standard of care for many adult cancers, and has shown success in treating several pediatric cancers including leukemia, lymphoma and neuroblastoma[12]. Yet many patients fall through the cracks when either their cancers do not respond to immunotherapies, or they have to halt treatment due to toxic side effects. Their hope for a cure is shattered.

Scientists at La Jolla Institute for Immunology (LJI) are committed to making cancer immunotherapies work for more patients.

INSTITUTE RESEARCH ADVANCES

A BETTER IMMUNE CELL ARMY

One danger for many pediatric cancer patients is a phenomenon called "T cell exhaustion"[13]. This occurs when the T cells that would normally fight cancer cells give up. They have used up too much energy fighting an enemy that is taking a long time to kill. T cell exhaustion is one reason some patients initially respond to immunotherapy only to have the immunotherapy stop working. LJI Professors Anjana Rao, Ph.D., and Patrick Hogan, Ph.D., have developed methods to engineer T cells resistant to T cell exhaustion[14]. "The idea is to give the cells a little bit of armor against the exhaustion program," says Dr. Hogan. "The cells can go into the tumor to do their job, and then they can stick around as memory cells to prevent cancer recurrence."

LJI Professor Sonia Sharma, Ph.D., is changing how we think of the innate immune system's role in cancer protection. The cells of the innate immune system are the body's first line of defense, and they can also produce molecules that may affect a patient's response to cancer immunotherapies[15]. Dr. Sharma is shedding light on these molecules, called metabolites, and she has established important partnerships with outside research groups that specialize in children's health[16].

THE ORIGINS OF PEDIATRIC CANCERS

Researchers in the laboratory of LJI Associate Professor Ferhat Ay, Ph.D., are investigating the very roots of pediatric blood cancers. LJI Instructor Abhijit Chakraborty, Ph.D., is working to understand how a healthy cell morphs into a cancer cell. He's shown how a "shattering" of the chromosome, an event called chromothripsis, drives cancer development. Dr. Chakraborty won funding from The Conrad Prebys Foundation to study pediatric iAMP21, a rare subtype of B cell leukemia with chromothripsis that leads to aggressive cancer with a high relapse rate[17]. For this work, Dr. Chakraborty established partnerships with Rady Children's Hospital and Children's Oncology Group[18].

LJI Assistant Professor Samuel Myers, Ph.D., is working closely with scientists at Yale University to shed light on mutations in a specific protein that appears to drive intellectual disabilities and potentially the development of certain brain cancers. Dr. Myers' very specialized expertise in proteomics—analysis at the protein level of cells—can give us important clues to why seemingly healthy cells go rogue and cause cancer[19].

REDUCING TOXIC SIDE EFFECTS

Then there's the problem of toxic side effects from cancer immunotherapies. In early 2022, LJI and University of Liverpool scientists shared the results of their investigation into why an experimental immunotherapy triggered harmful gut inflammation in clinical trial subjects. Their work showed that the immunotherapy allowed a harmful subtype of T cells to move unchecked in the gut. With this knowledge, study leaders Pandurangan Vijayanand, M.D., Ph.D., and Christian H. Ottensmeier, M.D., Ph.D., FRCP, tried using a smaller, slower dosing strategy in a mouse model. Their work suggests tweaking the timing of cancer immunotherapies may spare patients from some side effects[20].

NEW TOOLS TO ACCELERATE PEDIATRIC CANCER RESEARCH

Pediatric cancer research has entered a promising era thanks to new tools in the field. One important tool is the Cancer Epitope Database and Analysis Resource abbreviated and recognized as CEDAR, a new cancer research database developed at LJI. This database is the go-to site for researchers around the world to access data on cancer epitopes, the regions on cancer cells that can be targeted by the immune system. By sharing epitope data, researchers can develop new immunotherapies to target many cancer sites. CEDAR is directed by LJI Professors Alessandro Sette, Dr.Biol.Sci., and Bjoern Peters, Ph.D., and builds upon their experience organizing infectious disease data in a similar database, the Immune Epitope Database abbreviated and recognized as the IEDB[21].

Dr. Vijayanand is also pioneering new methods to track cancer development—and the effects of immunotherapies—in real time. His laboratory uses a method called single-cell sequencing to figure out how immune cell behavior changes in response to threats, such as cancers, and treatments, such as immunotherapies[22].

WHAT'S NEXT

These research discoveries, new tools, and new techniques are made possible by governmental and corporate support, as well as private philanthropy. Due to the pace and structure of traditional funding sources, the future of pediatric cancer research rests largely on individuals, foundations, and companies who are concerned about children's health and advancing trailblazing science. Only with increased investment in research will we gain the knowledge, diagnostic tools, and protocols that will enable more children with cancer to overcome their disease and live healthy, rewarding, and full lives.

In short, the potential impacts of investing in understanding pediatric cancer research cannot be overstated.

PEDIATRIC CANCER RESEARCH FOUNDATION

Since 1982, the Pediatric Cancer Research Foundation has been chasing one ambitious goal: to fund research that reduces the percentage of children who perish from cancer until that number reaches zero. The Foundation is determined to transform pediatric cancer care and make it possible for all children facing childhood cancer to beat their disease and realize their full potential. Overseen by scientific thought leaders, the Pediatric Cancer Research Foundation's rigorous and competitive process for awarding research grants has contributed to pivotal advancements in the areas of non-Hodgkin's lymphoma, immunotherapy/CAR T cells, osteosarcoma, juvenile myelomonocytic leukemia, and acute myeloid leukemia. The Pediatric Cancer Research Foundation is a GuideStar Platinum-rated charity. "Powering Cures, Realizing Futures," its inspiring motto, encapsulates the Foundation's motivation and commitment.

For more information, please visit PCRF-kids.org, and follow @PCRF_KIDS, or feel free to contact:

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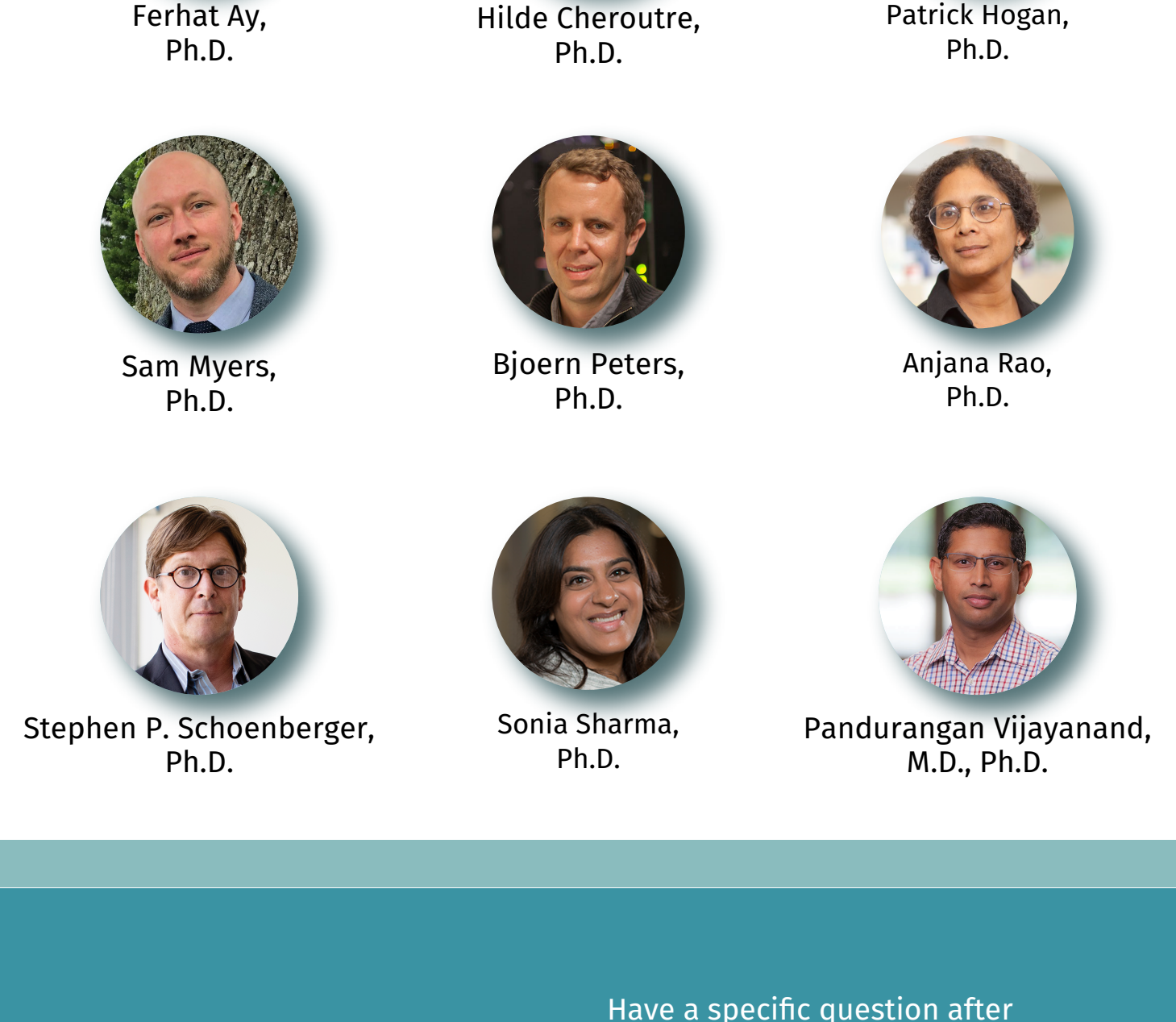

Ferhat Ay, Ph.D. | Hilde Cheroutre, Ph.D. | Patrick Hogan, Ph.D.

Sam Myers, Ph.D. | Bjoern Peters, Ph.D. | Anjana Rao, Ph.D.

Stephen P. Schoenberger, Ph.D. | Sonia Sharma, Ph.D. | Pandurangan Vijayanand, M.D., Ph.D.

inspired to learn more?

Have a specific question after reading this guide? Learn more at lji.org/center-for-autoimmunity or we welcome you to reach out to:

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1. Centers for Disease Control and Prevention. February 2022. National Center for Health Statistics: Child Health. Retrieved from: https://www.cdc.gov/nchs/fastats/child-health.htm

2. National Cancer Institute. NCI Dictionaries. Retrieved from: https://www.cancer.gov/publications/dictionaries/cancer-terms/def/pediatric-cancer

3. American Childhood Cancer Organization. US Childhood Cancer Statistics. Retrieved from: https://www.acco.org/us-childhood-cancer-statistics/#:~:text=Each%20year%20in%20the%20U.S.,cancer%20before%20their%2020th%20birthday

4. World Health Organization. December 2021. Childhood cancer. Retrieved from: https://www.who.int/news-room/fact-sheets/detail/cancer-in-children

5. Cancer.Net. February 2022. Childhood Cancer: Statistics. Retrieved from: https://www.cancer.net/cancer-types/childhood-cancer/statistics

6. Institutional Repository for Information Sharing/Pan American Health Organization. 2014. Early Diagnosis of Childhood Cancer. Retrieved from: https://iris.paho.org/handle/10665.2/34850

7. Science. March 2019. Treatments for childhood cancer can devastate lives years later. Scientists are trying to change that. Retrieved from: https://www.science.org/content/article/treatments-childhood-cancer-can-devastate-lives-years-later-scientists-are-trying

8. Coalition Against Childhood Cancer. 2021. Childhood Cancer Fact Library. Retrieved from: https://cac2.org/interest-groups/awareness/childhood-cancer-fact-library/

9. American Cancer Society. October 2019. Risk Factors and Causes of Childhood Cancer. Retrieved from: https://www.cancer.org/cancer/cancer-in-children/risk-factors-and-causes.html

10. National Cancer Institute. March 2022. Research on Childhood Cancers. Retrieved from: https://www.cancer.gov/research/areas/childhood

11. National Pediatric Cancer Foundation. 2019. Childhood Cancer Facts. Retrieved from: https://nationalpcf.org/facts-about-childhood-cancer/

12. Yale Medicine. Pediatric Cancer Immunotherapy. Retrieved from: https://www.yalemedicine.org/conditions/pediatric-cancer-immunotherapy

13. St. Jude Children's Research Hospital. February 2022. Young vs. old: How host environment affects immune response. Retrieved from: https://www.stjude.org/media-resources/news-releases/2022-medicine-science-news/young-vs-old-how-host-environment-affects-immune-response.html#:~:text=For%20pediatric%20cancer%20patients%2C%20that,published%20today%20in%20Science%20Immunology

14. La Jolla Institute for Immunology. July 2021. Preparing T cells for the long haul. Retrieved from: https://www.lji.org/news-events/news/post/preparing-t-cells-for-the-long-haul/

15. La Jolla Institute for Immunology. April 2021. Melanoma meets its match. Retrieved from: https://www.lji.org/blog/melanoma-meets-its-match/

16. La Jolla Institute for Immunology. June 2021. Sonia Sharma zeros in on metabolites. Retrieved from: https://www.lji.org/blog/sonia-sharma-zeros-in-on-metabolites/

17. La Jolla Institute for Immunology. March 2021. The Conrad Prebys Foundation grants more than $450,000 for studies into childhood cancer, cardiovascular disease. Retrieved from: https://www.lji.org/news-events/news/post/conrad-prebys-foundation-grants-more-than-450000-for-studies-into-childhood-cancer-cardiovascular-disease/

18. La Jolla Institute for Immunology. 2020 Tullie and Rickey Families SPARK Awards Winner Abhijit Chakraborty, Ph.D. Retrieved from: https://www.lji.org/support/giving-opportunities/spark-program/abhijit-chakraborty/

19. La Jolla Institute for Immunology. Myers Lab. Retrieved from: https://www.lji.org/labs/myers/

20. La Jolla Institute for Immunology. May 2022. Investigating cancer drug toxicity leads to a critical discovery. Retrieved from: https://www.lji.org/news-events/news/post/investigating-cancer-drug-toxicity-leads-to-a-critical-discovery/

21. La Jolla Institute for Immunology. June 2021. LJI launches new global cancer immunology resource. Retrieved from: https://www.lji.org/news-events/news/post/lji-launches-new-global-cancer-immunology-resource/

21. La Jolla Institute for Immunology. Vijayanand Lab. Retrieved from: https://www.lji.org/labs/vijayanand/

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