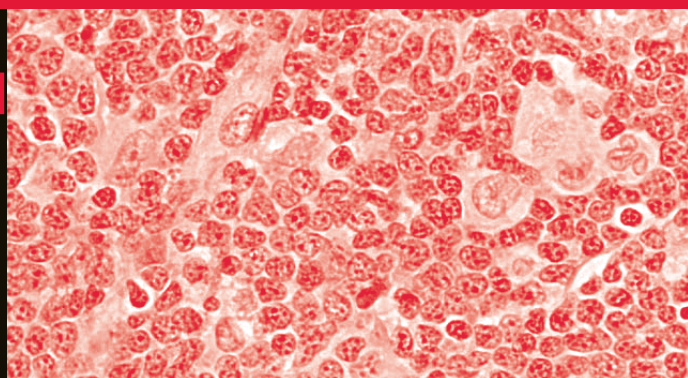


RESEARCH Report



Foundation Awards \$2 Million in Funding to Early-Career Lymphoma Researchers



2019 LRF Scholars at the Lymphoma Clinical Research Mentoring Workshop. (First Row, L to R) Rahul Lakhotia, MD, NIH NHLBI, Reid Merryman, MD, Dana-Farber Cancer Institute, Allison Rosenthal, DO Mayo Clinic, Arizona; (Second Row) Andrew Ip, MD, Emory University, Manali Kamdar, MD, University of Colorado, Paolo Strati, MD, MD Anderson Cancer Center, Brian Hess, MD, Medical University of South Carolina, and Yazeed Sawalha, MD, of Cleveland Clinic.

The Lymphoma Research Foundation (LRF) has announced the recipients of its early career research grants and mentoring program for 2019, representing 21 projects and \$2 million in funding. The Foundation's early career grants support clinical and postdoctoral fellows as well as junior clinical faculty pursuing research in lymphoma and chronic lymphocytic leukemia (CLL). Grants awarded for 2019 include four Clinical Investigator Career Development Awards (CDA), nine Postdoctoral Fellowship Grants, and eight

awards in conjunction with the Lymphoma Clinical Research Mentoring Program (LCRMP), and bring the Foundation's total awarded funding to \$62 million.

For the second straight year, more than half of LRF's grantee class are women, including three of four CDA recipients and seven of nine Postdoctoral Fellowship grantees. Projects awarded include early clinical trials of new novel therapies, investigations into the biology of virus-driven lymphomas, and new mechanisms for chimeric antigen

receptor (CAR) T-cell therapy. Of note, four projects, representing \$440,000 in funding, focus on T-cell lymphomas, LRF's largest commitment to T-cell lymphoma research in a single grant cycle.

"The Lymphoma Research Foundation is committed to funding the next generation of lymphoma researchers, whether that is in the laboratory or the clinic," said Thomas M. Habermann, MD, of Mayo Clinic, Rochester, Chair of LRF's Scientific Advisory Board. "Following rigorous review by the SAB, the number of high-quality grants was notable. The variety of institutions and lymphoma subtypes represented in this year's class demonstrate the Foundation's drive to supporting innovative research and promising young researchers that will drive new developments for patients of all types of lymphoma across the United States."

Recipients of this year's CDAs, awarded to advanced clinical fellows and clinical researchers in their first faculty positions, are Jean L. Koff, MD, MS, of Winship Cancer Institute at Emory University; Anita J. Kumar, MD, MSc, of Tufts Medical Center; Neha Mehta-Shah, MD, of Washington University in Saint Louis; and Raghuveer

[\[CONTINUED ON PAGE 3\]](#)



FEATURED IN THIS ISSUE: Profiles of New Grantees

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2019 Postdoctoral Fellowship Grantees (including Lena Lupey-Green, PhD, of Penn State College of Medicine, pictured), Clinical Investigator Career Development Award recipients, and Lymphoma Clinical Research Mentoring Program participants discuss their research.

LETTER FROM THE CEO



Dear LRF Friends and Supporters,

The Lymphoma Research Foundation (LRF) is pleased to announce our 2019 grant class in this edition of *Research Report*. This year, twenty-one exemplary grantees received \$2 million in funding through our Postdoctoral Fellowship Grant, Clinical Investigator Career Development Award, and Lymphoma Clinical Research Mentoring Program. We are excited by the variety of research represented in this year's class. We hope you enjoy learning more about these researchers and their innovative research, beginning on page 3.

As part of our commitment to identifying new lymphoma treatment options, we also highlight the results of the AUGMENT trial, recently published in the *Journal of Clinical Oncology*, which demonstrated significant results for relapsed/refractory follicular lymphoma and marginal zone lymphoma patients. Read more about this trial, including thoughts from the paper's first author, LRF Scientific Advisory Board member John Leonard, MD, of Weill Cornell Medicine, on page 14.

The support you have given to the Foundation has been instrumental in allowing us to fund this large and varied class of promising investigators. Thank you for your part in helping the Foundation fund life-saving research and support all those affected by this disease.

Sincerely,



Meghan Gutierrez
Chief Executive Officer

Team LRF Spotlight: Laps for Lymphoma

"Being in the Grizzly community means being a part of something a lot bigger than yourself and walking in Laps for Lymphoma is doing exactly that. There's nothing better than knowing we have the ability to make a difference." - Senior Audrey Baker, Student Council President of Grassfield High School in Chesapeake, VA.

On March 30th, the Grassfield community rallied for a world without lymphoma for its 10th consecutive year. The inaugural Laps for Lymphoma event was established as a school-wide event to remember Cliff Bernard - the husband of former Grassfield Principal Carolyn Bernard - and to raise awareness for lymphoma. That first year, 190 students and staff walked in memory of Cliff and their loved ones. Since then, Laps for Lymphoma has grown into a community-wide event raising over \$165,000 in support of LRF. Thank you Grizzly community for your commitment to our mission to eradicate lymphoma and serve those touched by this disease! To support their efforts, visit support.lymphoma.org/LapsforLymphoma.



New Grantees

[CONTINUED FROM PAGE 1]

Ranganathan, MD, of the University of North Carolina-Chapel Hill. Dr. Mehta-Shah, a 2017 LCRMP participant, is the seventh LCRMP alum to receive a Foundation CDA; four of the six members of her LCRMP class have received subsequent research grants from LRF.

Postdoctoral Fellowship Grants, awarded to postdoctoral and advanced clinical fellows pursuing laboratory, translational, and/or clinical research in lymphoma and CLL, are Elise A. Chong, MD, Antonia Rotolo, MD, PhD, and Rui Wu, PhD, of the University of Pennsylvania; Yuxuan Liu, PhD, of Columbia University; Lena Lupey-Green, PhD, of Penn State College of Medicine; Teresa Sadras, PhD, of Beckman Research Institute, City of Hope; Irene Scarfo, PhD, of Massachusetts General Hospital; Nathan Ungerleider, PhD, of Tulane University School of Medicine; and Gabriele Varano, PhD, of Icahn School of Medicine at Mount Sinai. Dr. Chong has been named the inaugural Bruce D. Cheson, MD Postdoctoral Fellow, a named fellowship in honor of the long-time LRF Scientific Advisory Board (SAB) member and past SAB Chair, his service to LRF programs, and founding of the Lymphoma Research Ride, which has raised more than \$6 million for LRF grants and programs. Dr. Sadras is this year's Oliver Press, MD, PhD, Memorial Postdoctoral Fellow, which recognizes one grantee annually in memory of Dr. Press, also a past SAB Chair, for his commitment to LRF and support of early career researchers throughout his career. Dr. Wu has been named the Carl Olsen Postdoctoral Fellow in memory of an LRF donor with interest in T-cell lymphoma research.

Lymphoma Clinical Research Mentoring Program (LCRMP) award recipients, called LRF Scholars, are advanced clinical fellows and junior faculty pursuing clinical research projects. LRF Scholars attended a week-long workshop in early March 2019, working with senior experts in lymphoma research to refine their research projects and further develop their skills in preparing effective research presentations and publications, working with the NCI cooperative groups, and managing clinics for complex therapies such as CAR T-cells. Scholars will attend follow-up programs over the next two years, including attending a grant review meeting and presenting their research at the North American Educational Forum on Lymphoma. This year's LRF Scholars are Brian Hess, MD, of the Medical University of South Carolina; Andrew Ip, MD, of Winship Cancer Institute at Emory University; Manali Kamdar, MD, MBBS, of the University of Colorado; Rahul Lakhotia, MBBS, of the National Institutes of Health (NIH) National Heart, Lung, and Blood Institute; Reid Merryman, MD, of Dana-Farber Cancer Institute; Allison Rosenthal, DO, of Mayo Clinic Arizona; Yazeed Sawalha, MD, of Cleveland Clinic; and Paolo Strati, MD of the University of Texas MD Anderson Cancer Center.



Elise A. Chong, MD
University of Pennsylvania
Perelman School of Medicine
*Bruce D. Cheson, MD,
Postdoctoral Fellow*

Predicting Patient Response to CAR T-cell Therapy

Chimeric antigen receptor (CAR) T-cell therapy has been an effective treatment for many patients with B-cell lymphomas who don't respond to other therapies, producing remissions in 30 to 40 percent of patients. Dr. Chong and her collaborators are seeking a way to better predict which patients will respond well to CAR T-cells before patients undergo the therapy. "To understand why CAR T-cells succeed or fail, we are studying patients' blood samples and tumor biopsies collected before and during treatment with CAR T-cells," Dr. Chong says. In the course of her LRF Postdoctoral Fellowship grant, Dr. Chong will study T-cell functional states (processes which occur inside the cell) in response to treatment and seek to identify ways in which patients' tumors may suppress their immune system or prevent immunotherapies from killing lymphoma cells. "This research will guide further approaches to improving immunotherapy for patients with lymphoma."

Dr. Chong is the inaugural Bruce D. Cheson, MD Postdoctoral Fellow, a named fellowship honoring Dr. Cheson, current LRF Scientific Advisory Board member and former SAB Chair, for his commitment to supporting the Foundation and lymphoma research. She first became interested in lymphoma after working as a research assistant in the lymphoma program at Abramson Cancer Center at the University of Pennsylvania. "The ability of research to improve patients' lives, the long-term relationships that patients and physicians develop, and the scientific questions being explored all were the impetus for my interest in lymphoma research," Dr. Chong says, adding that this experience prompted her to change her career path from laboratory research and apply to medical school. She received her MD from the Perelman School of Medicine at the University of Pennsylvania, where she has subsequently completed her residency and is now a third-year hematology/oncology fellow.

Dr. Chong is excited for the opportunity LRF funding gives her, both in being able to address research questions and advance her career as a researcher. "After years of clinical training, I am finally able to study the types of questions I envisioned over ten years ago prior to medical school," she says. "The LRF Award will allow me sufficient time to dive deeply into this translational research and provide essential support for both this current project as well as my future career aspirations and development."



Yuxuan Liu, PhD
Columbia University Medical Center
Postdoctoral Fellowship Grant

Understanding Potential Therapeutic Pathways for FL, DLBCL

Recent research has shown that genes encoding histone acetyltransferase (HAT) enzymes, EP300 and CREBBP, often become mutated in the malignant cells of follicular lymphoma (FL) and diffuse large B-cell lymphoma (DLBCL). HAT enzymes, which have the capability to switch genes on and off within cells, appear when inactive to drive the growth of malignant cells, however, because the mutations appear to occur in only one of each pair of chromosomes, it is possible that a therapy restoring HAT's normal level of activity could be effective. Dr. Liu and her colleagues have developed a small molecule that enhances HAT activity and appears to kill lymphoma cells that have HAT mutations. For her LRF Postdoctoral Fellowship grant, Dr. Liu will perform further evaluation of this molecule, hoping to find evidence that a HAT activating therapy would be truly effective in lymphomas featuring this mutation. "To date, there are no known HAT activators that have been studied clinically," Dr. Liu notes, "If successful, the findings will support IND enabling studies for first-in-class novel HAT activating compounds and clinical trials in patients with relapsed or refractory lymphomas."

Dr. Liu received an MS in pathology from Peking University in her native China before a PhD in pathology and medical biology from the University of Groningen in the Netherlands, where she began studying lymphomas in the lab of Anke van den Berg, PhD. "From that time, I have been particularly interested in targeting identified genetic lesions in lymphomas through the novel therapeutic approaches," she says. After earning her PhD, Dr. Liu spent time in the lab of LRF Scientific Advisory Board member Anas Younes, MD, of Memorial Sloan Kettering Cancer Center, as a postdoctoral fellow, and has since joined the lab of Drs. Jennifer Amengual and Owen O'Connor (also an SAB member) at Columbia University, where she was recently promoted to Associate Research Scientist.

Dr. Liu comes from a family of professors and research and development professionals and cites a lifelong interest in biological sciences and the evolution of human knowledge as inspiration for her own scientific work. She adds that the LRF funding will provide crucial support to her short- and long-term goals as a researcher. "In ten years' time," she says, "I hope to be an independent researcher with my own group of students and researchers, working together to elucidate the basic biology of lymphomas and consequently result in the development of new targeted therapies."



Lena Lupey-Green, PhD
Penn State College of Medicine
Postdoctoral Fellowship Grant

Furthering Understanding of Aggressive EBV-Lymphomas

Lymphomas that are associated with infection of the Epstein-Barr virus (EBV), which induces a chronic, latent infection in B-cells, present a unique therapeutic opportunity wherein the virus can be specifically targeted to treat the lymphoma, with potentially less significant toxicity than standard chemotherapeutic approaches that target the host. Dr. Lupey-Green's LRF grant project focuses on understanding a new function for a viral molecule that may contribute to EBV-associated lymphomas—the long non-coding RNA molecule BHLF1 (which carries signals from DNA but, unlike standard RNA, does not translate into protein). "Gaining insight into how BHLF1 regulates latency [the ability of a virus to be dormant within a cell] and the viral life cycle may reveal important therapeutic targets—both viral and human—to specifically treat these aggressive EBV-associated lymphomas," she notes.

Dr. Lupey-Green received her PhD in biomedical sciences from Lewis Katz School of Medicine at Temple University, with an emphasis on cancer biology and genetics. Initially interested in viral infections as a graduate student, laboratory research on EBV led her to learn more about its associated cancers, and from there cancer genetics. "I found a passion for cancer research that I never anticipated, and one that I have carried with me into my postdoctoral work," she says. Now a postdoctoral scholar at Penn State College of Medicine, "I bring my expertise in viral oncology and molecular biology to a lab that has historically worked to understand the basic mechanisms dictating viral latency and gene expression. With this work, I am integrating my knowledge of cancer and Epstein-Barr virus biology to identify the potential contributions of this complex BHLF1 locus to lymphomagenesis in hopes that it may one day lead to the development of EBV-specific treatment strategies."

Dr. Lupey-Green adds that LRF funding "will allow me to carry out basic molecular biology research for a virus that receives very little attention despite its oncogenic potential. EBV-associated cancers are particularly aggressive, and so any progress we can make in understanding virus biology is progress towards treating EBV-associated disease." She concludes, "Receiving this award is an acknowledgment of the importance of the contributions of basic science research to biomedical science and gives me both the ability and confidence to continue to work in virology, while asking questions and thinking in the context of cancer research."



Antonia Rotolo, MD, PhD
University of Pennsylvania
Perelman School of Medicine
Postdoctoral Fellowship Grant

Improving CAR T-cell Therapy for the Treatment of Lymphoma

Researchers are seeking ways to expand the effectiveness of chimeric antigen receptor (CAR) T-cell therapy to lymphoma subtypes for whom the most common type of CAR therapy, CD19 CAR T-cell, is not effective due to a lack of the CD19 biomarker. In T-cell lymphomas, the biomarker CD5 is extremely common; unfortunately, it is found not just on malignant T-cell lymphoma cells, but on normal T-cells in the immune system. In order to avoid eradicating both “good” T-cells and T-cell lymphoma cells with a CD5 CAR T-cell therapy, Dr. Rotolo and her colleagues have developed a process to remove the CD5 biomarker from the “good” cells, creating cells they call CD5 Knock Out (or CD5KO) T-cells. “We can tweak the ‘good’ T cells not to express CD5 (CD5KOT), thus making them ‘invisible’ to CART5 cells, and co-inject CART5 cells to eradicate the tumor with CD5KOT cells to ensure concomitant protection against pathogens,” Dr. Rotolo says. “Upon disease eradication, CART5 cells can be eliminated to allow recovery of the endogenous ‘good’ T cells and long-term restoration of normal T cell immunity.”

Dr. Rotolo received her MD from the University of Torino in her native Italy, where she also completed a residency and hematology fellowship before an additional fellowship at Imperial College London Hammersmith Hospital. While in London, she was offered an opportunity to study the development of novel therapeutic strategies for relapsed/refractory lymphoma patients. “It was 2013, a number of exciting reports were suggesting that CAR T-cells could potentially cure B-cell lymphoma patients where all available treatments had previously failed,” she says. “Hence, in 2014 I enrolled in a PhD program at Imperial College London and committed to research in the field of CAR immunotherapy.” Upon completing her PhD, Dr. Rotolo became a Postdoctoral Fellow at the University of Pennsylvania in order to work with CAR T-cell pioneer Carl June, MD, and her Fellowship sponsor, Marco Ruella, MD.

Dr. Rotolo says receiving the LRF Postdoctoral Fellowship Grant will aid her career development as an independent researcher. “Thanks to LRF support, I will be able to continue working at Penn and move forward my research project. Given the strong translational connotation of my project and the vibrant scientific environment of my Institution, I also anticipate that my LRF funded postdoc will be of great educational value and will enormously impact my academic career.”



Teresa Sadras, PhD
Beckman Research Institute
City of Hope
Oliver W. Press, MD, PhD, Memorial
Postdoctoral Fellow

Investigating the ZAP70 Protein for Therapies in CLL

Though chronic lymphocytic leukemia (CLL) patients with indolent (slow-growing) forms of the disease have a high rates of long-term survival, patients with more aggressive forms of CLL have significantly poorer outcomes. As a result, many CLL researchers have attempted to identify molecular and genetic proteins, or biomarkers, that can better identify which patients are at risk for more aggressive disease, and to develop therapies tailored to their biology. The T-cell associated tyrosine kinase (protein) ZAP70 is associated with other aggressive CLL markers, and correlates with a poor clinical outcome; though ZAP70 is known to play some role in the development of CLL and the BCR signaling pathways, its exact function has not yet been identified. Dr. Sadras’s LRF Postdoctoral Fellowship Grant project will investigate the role of ZAP70 within the BCR pathway in detail and test its response to targeted inhibitors of the BCR pathway, such as ibrutinib (Imbruvica). “I expect the work from my project will shed novel insight into the pathogenesis of high-risk CLL,” she says.

Dr. Sadras received her PhD from the University of Adelaide and Centre for Cancer Biology in Australia and worked as a postdoctoral researcher at the South Australian Health and Medical Research Institute before joining the Beckman Research Institute at the City of Hope, also as a postdoctoral researcher. Dr. Sadras has been designated the Oliver Press MD, PhD, Memorial Postdoctoral Fellow, a distinction given to one LRF Postdoctoral Fellowship recipient each year in memory of Dr. Press, a former LRF Scientific Advisory Board Chair who was committed to the mentorship and development of early career scientists in lymphoma research. “My father is also a scientist, and from a very young age I was immersed in biology, nature, and curiosity to understand how systems worked,” she says. Dr. Sadras notes she is particularly fascinated by how cancer cells “mis-use” normal cellular functions to grow and spread disease. “This same concept is the focus of my current research, as I aim to understand how B-cells from CLL patients utilize the T-cell associated kinase ZAP70 to promote lymphoma growth.”

Dr. Sadras says receiving an LRF grant will allow her to pursue her research and develop her skills as a researcher. “Receiving funding support from the LRF represents a critical step in my career towards becoming an independent investigator and opens ground for me to build collaborations with experienced clinicians and scientists in lymphoma research. I feel highly privileged to be an awardee of an LRF fellowship, and am excited about the research and discoveries that lie ahead.”



Irene Scarfo, PhD
Massachusetts General Hospital
Postdoctoral Fellowship Grant

Exploring New Possibilities for CAR Therapy

The majority of chimeric antigen receptor (CAR) T-cell therapies currently being tested in lymphoma, including both therapies that have received U.S. Food and Drug Administration (FDA) approval, target CD19 antigen, and rely on a patient's own T-cells, which must be extracted and modified. Dr. Scarfo's LRF Postdoctoral Fellowship Grant project seeks to develop a CART-cell therapy which targets CD37, an antigen expressed by B- and T-cell lymphomas, as well as using CRISPR gene-editing techniques to create CART-cells from healthy human donors rather than patients. As part of this project, Dr. Scarfo and her collaborators will also investigate whether natural killer (NK) immune cells, cells which perform similar functions to T-cells in the immune system, could be an alternative effective CAR product. "I'm focusing on developing new Chimeric Antigen Receptor T-cells to treat Peripheral T-cell lymphomas as my desire is to help those patients for whom current therapies are unsuccessful," Dr. Scarfo says, "We hypothesize that this novel construct will result in durable antitumor effects. These studies have the potential for direct clinical relevance defining a new therapeutic option for the treatment of T-cell NHL."

Dr. Scarfo received her PhD from the University of Torino in her native Italy before her current position as a postdoctoral fellow at Massachusetts General Hospital. Having had an interest in science since high school, Dr. Scarfo became interested in T-cell lymphomas during her graduate studies, originally identifying biomarkers and genetic mechanisms in a laboratory setting before moving towards a more translational research focus, helping move laboratory research into the clinical setting. "I believe that research is the foundation to fight incurable diseases. During these last few years I had the opportunity to work with Dr. Maus [her grant sponsor] at the interface of basic science and early phase I trials involving cellular therapy," she says. "Being directly involved in the development of next-generation therapies gives me inspiration and hope to help patients."

Dr. Scarfo adds that her LRF funding will be crucial to moving her research forward. "The Foundation's support is instrumental in carrying out further studies on CAR-37 cells and to advance this new type of therapy from the bench to bedside of lymphoma patients," she says. "I want to thank LRF and all the donors who make this possible and give us an opportunity to investigate our ideas."



Nathan Ungerleider, PhD
Tulane University School of Medicine
Postdoctoral Fellowship Grant

Understanding EBV's Role in Burkitt Lymphoma

The Epstein-Barr virus (EBV) has been shown to be linked to the development of Burkitt lymphoma, an aggressive B-cell lymphoma. EBV-infected cells are particularly efficient, capable of altering normal cells and promoting the growth of malignant cells while evading clearance by the immune system. Dr. Ungerleider's LRF Postdoctoral Fellowship Grant project will investigate which cell pathways the virus targets in order to promote lymphoma progression. "Understanding the human pathways targeted by the virus will teach us a) specifically how the virus promotes Burkitt Lymphoma progression, and more generally, b) lead us to critical pathways that, when dysregulated, can promote the out-of-control cell division that characterizes tumors," he says.

Dr. Ungerleider received his MS in molecular and cellular biology from the University of Massachusetts Amherst before receiving his PhD in pathology from Tulane University School of Medicine, where he is currently a postdoctoral fellow. Inspired to start studying how tumors form by his father, a survivor of colon cancer, his interest in lymphoma research was prompted by the wide-ranging impact discoveries in lymphoma have on cancer research and science in general. "Lymphoma research has contributed so much to our understanding of tumors, how they form, and how they progress," he notes. "Many advances made studying lymphomas have underpinned research progress in a broad range of tumor types, even improving our understanding of basic cellular biology."

Dr. Ungerleider adds that his LRF funding will assist with both this specific research project and his progression towards an independent research career. "The Lymphoma Research Foundation grant will contribute to my research progress by allowing me to study a topic that is of great interest and value to me. This will serve as an important opportunity for me to demonstrate that I am capable of being the principal investigator on a research fellowship and fulfilling my obligation to the LRF."



Gabriele Varano, PhD
Icahn School of Medicine
at Mount Sinai
Postdoctoral Fellowship Grant

Investigating FOXO1 Mutations in B-Cell Lymphomas

Researchers have found the protein FOXO1 is mutated in several types of aggressive B-cell Non-Hodgkin lymphoma, but the role these mutations play in lymphoma development is not fully understood. Dr. Varano's LRF Postdoctoral Fellowship Grant project builds on earlier research showing that FOXO1 mutations have an altered response to signals from the stress-activated protein kinase (SAPK) and will attempt to identify both the exact mechanism through which this occurs and its impact on lymphoma cells. Dr. Varano and his collaborators hope that identifying this mechanism will also lead to new avenues for targeted therapies. "This project is expected to identify important regulators of B-cell biology that may hold potential interests as novel targets for therapy of aggressive B cell lymphomas," he says.

Dr. Varano received his MS in medical biotechnology from the University of Florence and his PhD from the University of Milan in his native Italy. While pursuing his studies, Dr. Varano undertook an internship at the University of Cambridge, where he attended a lecture by his eventual PhD mentor on the identification of genetic factors promoting B-cell lymphomagenesis. Intrigued, Dr. Varano shifted his own research focus towards that concept, particularly as it related to cancer immunology, and joined the lab of David Dominguez-Sola, MD, PhD at the Icahn School of Medicine at Mount Sinai in order to further this line of research. "I believe that understanding why and how specific genetic mutations are acquired and selected in B-cell lymphomas represents a unique opportunity to understand the role of those genes in the biology of normal B-cells," he says, "as well as providing potential targets to exploit for therapeutic purposes."

Dr. Varano was inspired to begin a scientific career by his father, a medical doctor who instilled in his son a love of science and learning. "One of the things we would tell each other is that the beauty of being a researcher is that you are doing something that no one else in the world is doing, and that you will be the first one to witness or discover something," he says. As he continues his progress towards a career as an independent researcher, Dr. Varano is grateful for LRF's support. "Thanks to the LRF, I will have economic and educational support for the next 2 years of my postdoctoral training. This will allow me to work on not only this specific project, but will pave the way for the development of new projects, which will be essential for my transition as an independent scientist."



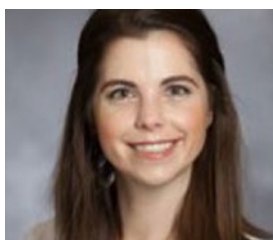
Rui Wu, MD, PhD
University of Pennsylvania
Perelman School of Medicine
Carl Olsen Postdoctoral Fellow

Understanding Treatment Resistance in ALCL

Anaplastic large cell lymphoma (ALCL) is a rare type of Non-Hodgkin lymphoma and one of the subtypes of T-cell lymphoma. While current therapies help many patients, as many as 30 percent will have disease which fails to respond to treatment or becomes resistant to therapy. This resistance in ALCL is at least in part caused by an oncogene (a gene capable of transforming a regular cell into a cancer cell) called NPM-ALK, which also appears to help ALCL cells evade detection by the immune system, thus allowing the cancer to progress. For her LRF Postdoctoral Fellowship Grant, Dr. Wu and her collaborators will investigate the mechanism by which NPM-ALK promotes immune evasion in ALK+ ALCL. "Successful completion of this project will provide significant insights into the immune evasion mechanism regulated by ALK and help design novel therapeutic approaches to reestablish innate immune response in ALK+ ALCL," Dr. Wu says.

Dr. Wu notes that she has a long-standing interest in lymphoma since the beginning of her medical studies, prompting her to complete a PhD from the University of Groningen in The Netherlands, and an MD from Shantou University Medical College in China. Currently, Dr. Wu is a postdoctoral fellow at the University of Pennsylvania, where she works in the lab of Megan Lim MD, PhD. "Using the experience of this lab my aim is to contribute to better understanding and to find alternative therapeutic strategies for treatment of specific types of lymphoma," she says.

Dr. Wu has been named the Carl Olsen Postdoctoral Fellow, in memory of an LRF donor with a particular interest in T-cell lymphoma research. She adds that the Foundation's funding is key to her goals for both her research and her career. "Lymphoma Research Foundation support will pave a way for me to pursue my research career in lymphoma with the hope of fulfilling my overarching goal to mitigate the therapeutic burden on at least one type of lymphoma," she says. "This is my first funded fellowship in the United States and will be instrumental to the establishment of my future research career as an independent investigator."



Jean L. Koff, MD, MS
Winship Cancer Institute
Emory University
CDA

Seeking Better Understanding of Outcomes for PTLD

Post-transplant lymphoproliferative disorder (PTLD) is a type of lymphoma that may occur in patients who have undergone stem cell or organ transplants. While some PTLD patients are cured simply with a reduction in their anti-rejection medication, others ultimately succumb to their disease despite aggressive chemotherapy. Dr. Koff's Career Development Award project will seek to identify common factors that can help identify patients at high risk of poor outcomes. "We will assemble a large group of PTLD patients and capture detailed clinical information and tumor specimens," she says. "We will then use next-generation genetic sequencing and characterize the immune cells of PTLD tumors to identify patient and molecular factors that contribute to poor survival."

Dr. Koff completed her MD, residency, and fellowship at Emory University's Winship Cancer Institute, where she is currently an Instructor. She also recently completed an MS in Clinical Research. Having an interest in lymphoid malignancies since medical school, Dr. Koff says that she was particularly drawn to understanding why some lymphoma patients respond to first-line therapy while others continually relapse or fail to respond, leading her to her current project. "A significant knowledge gap exists in the understanding of dysregulated [mutated] molecular pathways across PTLD subtypes. This limits opportunities to identify therapeutic targets or to explore prevention strategies," Dr. Koff notes. "My LRF-funded project seeks to fill these knowledge gaps and serve as a basis for developing treatment strategies that will improve PTLD patient outcomes."

Dr. Koff adds that, since so little is known about the molecular biology of PTLD and its relationship to patient outcomes, her LRF funding will help her generate data that could have a long-term impact on both her career and general understanding of this disease. "This project and its associated career development plan will allow me to cultivate expertise in assembling and analyzing large datasets across the key technologies that will impact lymphoma clinical and translational science," she says. "During my career, I expect to apply findings from these LRF-funded studies to inform new clinical trials aimed at improving outcomes for patients with PTLD."



Anita J. Kumar, MD, MSCE
Tufts Medical Center
CDA

Studying the Impact of Chemotherapy Modifications for HL

For most Hodgkin lymphoma (HL) patients, chemotherapy is the standard treatment. However, patients often have their initial treatment plan modified (through dose adjustment or delays in treatment) due to concerns over toxicity or other factors. "There is little data on incidence and reasons for dose modification and how dose modification impacts treatment response outcomes, particularly in the community setting [a healthcare facility not part of an academic or research institution] where the majority of patients are treated," Dr. Kumar notes. For her Career Development Award project, Dr. Kumar and her colleagues will examine patient data and interview doctors in both academic and community practice to both assess whether there is a correlation between chemotherapy modifications and poorer survival outcomes in HL, and better understand the factors behind doctors' decisions to modify chemotherapy. "This study will demonstrate how early treatment decisions impact response outcomes in real-world HL patients," she adds.

Dr. Kumar received her MD from Albert Einstein College of Medicine in the Bronx, New York, before residency and fellowship at the University of Pennsylvania, where she also received an MS in clinical epidemiology and biostatistics. She is currently an Assistant Professor at Tufts University School of Medicine, where she is working on a PhD in Clinical and Translational Research. While working in Tufts' survivorship clinic, Dr. Kumar became interested in the variety of experiences among patients who were treated in the community versus an academic medical center. "This drove me to better understand how care is delivered in both academic and community-based oncology settings, and what factors drive decisions about treatment in each of these settings," she says. She credits her mentor, Susan Parsons, MD, with inspiring her to pursue her own research in an attempt to answer the question "How can we improve the lives of patients?"

Dr. Kumar adds that she is excited to join the community of early-career investigators supported by LRF funding. "Through collaborative work, I have met several LRF scholars in the past twelve months, and I have realized what a special community LRF has created. I am excited to develop my work alongside other LRF grantees who have the same mission through their work!"



Neha Mehta-Shah, MD
Washington University in Saint Louis
 CDA

Measuring Residual Disease to Evaluate Patients for Transplant

Peripheral T-cell lymphomas (PTCL) are a rare group of lymphomas that are commonly treated with combination chemotherapy, followed by autologous stem cell transplant for patients with a good response. However, it is unclear why transplant results in a complete and durable response for some patients, while others relapse. Dr. Mehta-Shah and her colleagues will be using two new blood tests for minimal residual disease (MRD) in PTCL patients prior to transplant; these tests will allow them to determine whether MRD is correlated with poorer outcomes following transplant and to better understand the clonal evolution (how cancer cells evolve following treatment, often developing resistance to therapy). “We hope that these techniques will ultimately help us understand which patients benefit most from a stem cell transplant at the end of therapy,” Dr. Mehta-Shah says. “These techniques may also be used to develop liquid biopsies for mutational profiling of tumors or serve as a method to help us determine which patients are more likely to relapse.”

Dr. Mehta-Shah received her MD from the Feinberg School of Medicine, Northwestern University, before an internship and residency at Weill Cornell Medicine and chief residency and fellowship at Memorial Sloan Kettering Cancer Center. In her current position as Assistant Professor of Medicine at Washington University in Saint Louis, she was a participant in the 2017 class of the Lymphoma Clinical Research Mentoring Program (LCRMP). Inspired to a career in medicine by her mother (a pediatrician), Dr. Mehta-Shah became interested in lymphoma after a lecture by Steve Rosen, MD (a former LRF Scientific Advisory Board Member) at Northwestern University, and became specifically interested in T-cell lymphoma while working with SAB member Steven Horowitz, MD, at Memorial Sloan Kettering. “Patients with these rare diseases suffer from our lack of knowledge regarding how to tailor treatment to specific disease types,” Dr. Mehta-Shah notes. “We wondered if some of our patients were over-treated or under-treated. This is what gave birth to this project.”

Dr. Mehta-Shah says she considers herself fortunate both to have participated in the LCRMP and, now, received a Career Development Award. “The Lymphoma Research Foundation uniquely supports young investigators in lymphoma, connects them to other leaders in the field and develops opportunities for collaboration between generations of lymphoma experts,” she says, “The Foundation recognizes that improving our knowledge about lymphoma from all fronts is critical to advancing the field.”



Raghuveer Ranganathan, MD
University of North Carolina, Chapel Hill
 CDA

Exploring a CART T-cell Therapy with Fewer Toxicities

Though CART T-cell therapy has been successful for many patients with Non-Hodgkin lymphomas, the nature of the two versions currently approved by the FDA can have some severe side effects, as the CART T-cells are programmed to attack not just the malignant cancer cells, but normal B-cells in the immune system that also have the CD19 biomarker, which can leave a patient with a compromised immune system. Dr. Ranganathan’s Career Development Award project will evaluate a CART T-cell therapy that is programmed to target the light chain part of surface immunoglobulin B cells. This type of CART T-cell would eradicate all malignant cells, which express the targeted light chain, but would spare normal B cells, which don’t express the target, leaving a patient’s immune system relatively intact. “As a result, I hope to be introducing a more beneficial version of CART T-cell therapy where patients will still have the same chance of curing their lymphoma as current CART T-cell therapies, but they’ll instead keep their immune system relatively unharmed and minimize their risk for infection,” he says.

Dr. Ranganathan received his MD from Temple University and completed his Internal Medicine residency at Drexel University. He then underwent a research fellowship specializing in CART-cell therapy at the University of Pennsylvania prior to joining his current clinical Hematology/Oncology fellowship at the University of North Carolina. He became interested in lymphoma research because of the wide variety of subtypes and the breadth of knowledge required to understand and treat them. “What drew me to my particular CART-cell project,” he adds, “was 1) the chance to continue building upon my experience in CART-cell research and 2) the originality of how the project was targeting a unique antigen that can be applied across multiple lymphoma subtypes.”

Dr. Ranganathan further notes, “The time spent on the LRF Clinical Investigator Career Developmental Award will be hugely beneficial in terms of both my research progress and overall career development. First, it provides critical financial support to allow me to bring the preclinical research I’ve worked on over the past 3 years to the clinical bedside. Second, it will provide me protected time to focus on additional lymphoma-centric CART T-cell research which can also be translated to the clinic. I wish to mold my career into becoming one of the thought leaders for cellular immunotherapy directed at lymphomas, and the LRF will be playing an indispensable role in providing me with avenues to achieve that goal.”



Brian Hess, MD
Medical University of South Carolina
LCRMP

A New Agent to Improve Salvage Therapy for DLBCL

A common treatment for relapsed or refractory diffuse large B-cell lymphoma (DLBCL) is salvage chemotherapy followed by an autologous stem cell transplant (a transplant of a patient's own healthy cells). Though this treatment can lead to a cure, only a small proportion of these patients achieve this. Dr. Hess's LCRMP project adds novel therapeutic CC-486 (an oral version of the targeted agent azacitidine) to salvage chemotherapy in order to increase the chemotherapy sensitive of DLBCL, thus hopefully improving the rate of complete remission and subsequent cure.

After receiving his MD from the University of Missouri, Dr. Hess first became interested in malignant hematology as a resident at Loyola University Medical Center (Illinois), and narrowed his focus to lymphoma while working with Nancy Bartlett, MD (a LRF Scientific Advisory Board member) at Washington University in St. Louis during his fellowship. "During fellowship, the more experience I had with lymphoma, the more I was able to see the diversity of and nuance within each lymphoma subtype," Dr. Hess says, "I also found the research to be the most dynamic in the field of oncology and became involved in translational projects with my mentors, showing me first hand how interesting therapies can move from the bench to bedside."

Dr. Hess is currently Assistant Professor of Hematology and Oncology at the Medical University of South Carolina, where he is also the Hollings Cancer Center CAR-T Cell Adult Clinical Director and the Lymphoma Clinical Director. Noting that in his roles at MUSC he is attempting to establish the institution as a national presence in lymphoma, Dr. Hess is "very excited" to be a part of the LCRMP and establish collaborations both with his peers in the program and the LCRMP faculty. "I look forward to meeting so many experts in the field and not only collaborating with them during the Workshop by for many years to come."



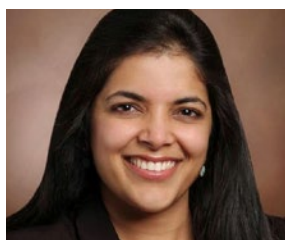
Andrew Ip, MD
Winship Cancer Institute
Emory University
LCRMP

Measuring the Effects of Exercise on Outcomes for Transplant

For many lymphoma subtypes, a bone marrow transplant is the recommended treatment strategy following relapse. Previous research has also suggested that lymphoma patients who engage in physical activity during their treatment have better outcomes. However, no one has yet studied whether physical activity during the period of a bone marrow transplant improves outcomes for lymphoma patients. Dr. Ip's LCRMP project will look at this question, asking patients to agree to a certain level of physical activity (including walking) during their transplant and providing smart watches to monitor and verify this activity. "This study will strive to show a cause and effect between physical activity, quality of life, and outcomes such as less time in the hospital, less complications after treatment, and improved immune system recovery," Dr. Ip says.

Dr. Ip received his MD from Jefferson Medical College in Pennsylvania before moving to Emory University for his residency. Currently a hematology/oncology fellow at Emory, Dr. Ip expects to complete an MSc in Clinical Research in May 2019. Inspired to a scientific career by his parents, who work in the pharmaceutical industry, he became interested in lymphoma research during residency, when assigned to a rotation with Drs. Chris Flowers (an LRF Scientific Advisory Board member) and Jonathon Cohen (a past LCRMP participant himself). He credits Dr. Flowers with inspiring his current project, saying, "I specifically remember Dr. Flowers telling me that he always had an interest in investigating the effect of exercise on lymphoma patients' outcomes, but never had time. As a junior investigator, I took that as an opportunity to seize!"

Dr. Ip adds that his participation in the LCRMP "has been a fantastic foundation to help jumpstart my career as a young lymphoma investigator. The connections I have made and the assistance in my project development has have been invaluable for my research progress. I believe this will set me up for future success in my career as most of cancer research is collaborative across institutions and in team science."



Manali Kamdar, MBBS
University of Colorado
LCRMP

Investigating Earlier Intervention for Indolent Lymphomas

Patients with indolent (slow-growing) lymphomas such as follicular (FL) or marginal zone (MZL) are chronic, frequently relapsing diseases which can vary widely in clinical presentation. Therapies are varied and can often include a “watch and wait” plan (where the patient receives regular monitoring and only receives treatment if their disease begins to spread) to antibody and/or chemotherapy treatments. Clinical trials have shown no difference between patients who go on watch and wait and those who receive early treatment. However, Dr. Kamdar notes, “Very few clinical trials have been conducted in the era of novel therapies, and thus one can hypothesize that offering treatment earlier... might improve outcomes in these lymphoma subtypes.”

Her LCRMP project was inspired by her indolent lymphoma patients who found “watch and wait” more akin to “watch and worry.” It proposes testing a new monoclonal antibody, ublituximab, in advanced stage indolent lymphoma patients. If patients enter complete response (no detectable disease) following ublituximab therapy, they will end treatment; patients without a complete response will receive a combination of ublituximab and a new non-chemotherapy pill called umbralisib. “If this novel treatment strategy shows excellent durable responses, I believe it will allow patients to have longer remissions, thus translating into fewer relapses and decreased need for future treatments,” Dr. Kamdar notes.

Dr. Kamdar is an Assistant Professor of Medicine at the University of Colorado Hospital, where she is also Clinical Director of Lymphoma Services. She began her training with an MBBS (MD equivalent) from K.J. Somaiya Medical College in Mumbai, India, before completing a residency and hematology/oncology fellowship at East Carolina University and a blood and marrow transplantation fellowship at Stanford. During her fellowship at ECU she was able to pursue electives in lymphoma clinics at Weill Cornell Medicine and Tata Medical Center in Mumbai. She credits all her mentors at those institutions as well as current advisor Sonali Smith, MD (an LRF SAB member) in supporting her early lymphoma career, and hopes her participation in the LCRMP will expand that support.

Dr. Kamdar hopes to advance towards a career as a senior lymphoma clinical researcher committed to developing targeted drugs that are less toxic, more efficacious, and affordable. “I see myself collaborating with lymphoma colleagues not just in the U.S. but worldwide, so that lymphoma care is standardized across the globe, giving every patient an equal opportunity to be cured.”



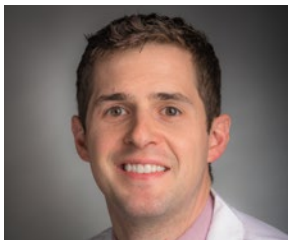
Rahul Lakhota, MBBS
*National Institutes of Health
National Heart, Lung, and Blood
Institute*
LCRMP

Combination Therapy with Macrophage Checkpoint Inhibitors

Indolent lymphomas frequently require multiple lines of treatment as the disease recurs; the frequency of treatment makes it important to balance efficacy with potential toxicities (side effects). Dr. Lakhota’s LCRMP project tests a new combination of venetoclax, a BCL2 inhibitor already approved for certain CLL patients, with rituximab (Rituxan) and Hu5F9-G4, a macrophage checkpoint inhibitor, which works by disrupting the function of macrophages, a component of the tumor microenvironment that play a role in cancer cell growth. “Being a macrophage checkpoint inhibitor, it doesn’t have the adverse effects associated with immune checkpoint inhibitors,” Dr. Lakhota says. “We hypothesize that this combination will be more effective than any of the drugs given individually, and due to their non-overlapping side effect profile, the regimen will be tolerated well.”

Currently a Hematology/Oncology Fellow at the National Institutes of Health, National Heart, Lung, and Blood Institute (NHLBI), Dr. Lakhota began his medical training with an MBBS (MD equivalent) from Seth G.S. Medical College and K.E.M. Hospital in Mumbai, India, before residency at Medstar Washington Hospital Center/Georgetown University Hospital, where he was also Chief Resident. He first encountered lymphoma during residency, when a patient who seemed to have a rare autoimmune disease turned out to have DLBCL in their ovary. “As I learned more about the disease, I was deeply intrigued with the varied clinical manifestations and the complexity and heterogeneity of the various lymphoproliferative disorders,” he says. Now managing a variety of B and T-cell lymphoma patients at the NIH, Dr. Lakhota works closely with Mark Roschewski, MD who he considers a role model for caring for lymphoma patients on various clinical research protocols.

Dr. Lakhota is hoping his participation in the LCRMP will be beneficial to both his project and his career. “The LCRMP research plan is my first treatment protocol which I am developing with my mentor. Since it is at an early stage, participation in the LCRMP will provide me with valuable feedback on how to maximize the potential of this combination therapy,” he says, adding “Working at the NIH... the fellows don’t get a lot of experience in grant writing. Participation in LCRMP small groups and coursework focusing on grant writing will further help me in advancing this skill, a necessary requirement for being an independent investigator.” He adds, “If in the next ten years’ time, the research I contribute to helps patients in a meaningful way, I would be overjoyed.”



Reid Merryman, MD
Dana-Farber Cancer Institute
LCRMP



Allison Rosenthal, DO
Mayo Clinic Arizona
LCRMP

Testing New Combination Immunotherapy for MZL

Marginal zone lymphoma (MZL) is a slow-growing B-cell NHL that has a relatively low number of new diagnoses each year. As a result, few clinical trials are available for MZL patients, including virtually none testing the novel immunotherapy treatments that have proven successful in other lymphoma subtypes. Dr. Merryman's LCRMP project seeks to test a combination of two therapies for MZL patients: duvelisib (Copiktra), a PI3K inhibitor recently approved for certain CLL and FL patients, and a newly developed immune checkpoint inhibitor that targets the protein OX40. "Duvelisib kills lymphoma cells by blocking signaling through proteins called PI3 kinase delta and gamma," Dr. Merryman says. "In addition, duvelisib stimulates the immune system and together with a drug targeting OX40, may be able to establish a long-lasting immune response that targets and kills lymphoma cells."

Dr. Merryman sees his project as filling a currently unmet need in lymphoma clinical research. "Despite the important role that immune dysregulation [a malfunction or mutation of human immune cells] plays in the development of many cases of marginal zone lymphoma, there have been few studies that have tested immune-based strategies for this lymphoma subtype. I am hopeful that this clinical trial can lead the way for new therapeutic approaches in this disease."

Dr. Merryman received his MD from Harvard Medical School and completed his residency at Brigham and Women's Hospital, before his current hematology/oncology fellowship at Dana-Farber Cancer Institute. He became interested in lymphoma because of its clinical diversity, both in terms of the difference between aggressive and indolent lymphomas, and the variety of ages of his patients. "My patients are a continuous source of inspiration for me," he says. "They are a daily reminder that more work is needed so that we can provide, safer, smarter, and more effective treatments for all of our patients with lymphoma."

Dr. Merryman hopes to develop as a clinical researcher with a focus on testing novel immunotherapy approaches in lymphoma, including personalizing treatment through the identification of biomarkers. He sees the LCRMP as an "amazing opportunity to learn from national leaders" in lymphoma research. He adds, "The program allows young investigators like me to build relationships with current and future leaders in the field that I hope will spur research collaborations in the future."

Validating a New Prognostic Tool for MCL

Mantle cell lymphoma (MCL) can present in a variety of ways, from slow-growing indolent to more aggressive forms with poorer outcomes. Currently a patient's treatment plan is largely based on patient age and overall health rather than biologic factors that predict the aggressiveness of their disease. A new tool, the MCL35 proliferation index, is being developed to risk stratify patients as being at low, intermediate, or high risk for poor outcome. Dr. Rosenthal's LCRMP project seeks to validate this assay as a prognostic tool in older patients with MCL and ultimately in a clinical setting in a risk adapted trial with the hope that it can better personalize therapy. "In many other types of lymphoma, a better understanding of disease biology has driven practice change when it comes to selecting what we hope is the 'best' treatment," Dr. Rosenthal says, "We have lagged behind in being able to do so for MCL. I'm hoping through this work ... to better identify patients who might respond well to standard treatments versus those that are high risk for progress or failure to respond and have novel therapeutic options available from the start."

Dr. Rosenthal received her DO from Midwestern University (Arizona) before a residency at St. Joseph's Hospital and Medical Center. She completed her Fellowship at Mayo Clinic's Arizona campus, where she also completed a special Advanced Fellowship in Lymphoma as a Mayo Clinic Scholar based at Memorial Sloan Kettering Cancer Center, and is currently an Assistant Professor with Mayo Clinic. Dr. Rosenthal says she is excited about participating in the LCRMP to improve her clinical research skills, as well as other skills such as grant writing and getting involved in collaborative research efforts. "I am certain that my participation in the LCRMP will serve as a springboard for my clinical research efforts and will be a setting in which I learn the important principles of designing and implementing a feasible clinical research project."

A leukemia survivor herself, Dr. Rosenthal cites her patients as her reason for her passion for lymphoma research. "Just as I looked to my oncologist for hope and the expertise to know what to do in an unpredictable and vulnerable situation, I want my patients to feel confident that I'm doing everything I can to give them the best care possible, she says. "While being a lymphoma doctor allows me to celebrate a lot of success, there are still failures and as long as there are, I will continue to push boundaries, ask questions, and continue doing the research."



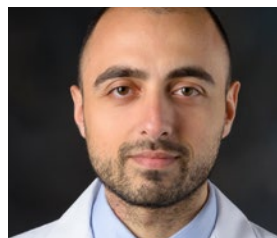
Yazeed Sawalha, MD
Cleveland Clinic
LCRMP

Novel Combination Therapy for Indolent NHL

Patients with indolent non-Hodgkin lymphoma who relapse or have refractory lymphoma that does not respond to treatment still have poorer outcomes, with many of the current available treatments having either limited benefit or significant side effects. Dr. Sawalha's LCRMP project is testing a combination of three newer novel agents – lenalidomide (Revlimid), umbralisib, and ublituximab – which have shown promise as individual therapies. “The purpose of this clinical trial is to find out whether we can achieve a safe and more effective treatment regimen in this patient population by combining these three drugs together,” Dr. Sawalha says.

Dr. Sawalha received his MD from the University of Jordan and completed a residency at King Hussein Cancer Center in Jordan before a residency and fellowship at Cleveland Clinic, where he is currently completing the final year of his fellowship. “I decided to become a clinical investigator focusing on lymphoma after I spent time during my residency and fellowship training taking care of patients with lymphoma,” he says. “I appreciated the need for more effective cancer treatments, and experienced firsthand the joy of enrolling patients with lymphoma on clinical trials and seeing the positive impact of investigational therapies on patients who otherwise had limited treatment options.”

Dr. Sawalha will be joining the lymphoma faculty at The Ohio State University in July 2019, and anticipates that his participation in the LCRMP will help him succeed as he moves into the next stage of his career as a clinical investigator in lymphoma. “It will allow me to expand my knowledge in topics pertinent to the development and conduct of this clinical trial and other future projects. In addition, this program provides me with an invaluable opportunity to connect with esteemed researchers and experts in the field, and develop relationships with new mentors and other scholars,” he notes. “I am very excited to be a part of this great opportunity and hope to be able to deliver cutting edge research and care for our patients.”



Paolo Strati, MD
The University of Texas
MD Anderson Cancer Center
LCRMP

Combination Therapy and the Tumor Microenvironment

Macrophages are large white blood cells that present antigens within the human immune system, an important step in signaling the immune system to attack disease. Researchers are developing therapies which help increase the activity of macrophages in hopes of inducing a more effective response to treatment. Dr. Strati's LCRMP project will test a combination of a monoclonal antibody targeting the protein CD47, which can increase the anti-tumoral activity of macrophages, with rituximab (Rituxan) and lenalidomide (Revlimid) in patients with relapsed or refractory B-cell lymphomas. Dr. Strati will also test tissue samples to identify the changes the therapy induces in the tumor microenvironment, in hopes of identifying additional therapeutic targets. “I believe this project will lead to a significant change for patients, opening the therapeutic horizon to novel, safer and more effective macrophage checkpoint inhibitors and combinations,” Dr. Strati says.

Dr. Strati received his MD from the University Vita-Salute San Raffaele in Milan, Italy, where he also completed a residency, before an initial fellowship in leukemia at MD Anderson Cancer Center. His initial studies focused on chronic lymphocytic leukemia (CLL). Further studies took him through a fellowship at Queen Mary University in London and a residency at Mayo Clinic, Rochester, before returning to MD Anderson for a clinical fellowship in hematology-oncology, and where he recently accepted a position as Assistant Professor. “Thanks to my current mentor, Dr. Sattva Neelapu, a world expert in the field of lymphoma microenvironment, I am now working on applying the expertise I developed in CLL/SLL to the treatment of more aggressive B-cell lymphoma,” Dr. Strati notes. He adds that Dr. Neelapu has been an immense source of inspiration. “I can relate to his experience, as an international medical graduate who immigrated to the U.S. and restarted from the bottom, driven by passion and commitment, to achieve his goal – to help patients with lymphoma.”

Dr. Strati expects that his participation in the LCRMP will be helpful not just to his current project, but the broadening of his expertise. “The field of macrophage checkpoint inhibitors is still new and largely unexplored, highlighting the importance of collaborative efforts and collegial study design. The experience and guidance from my LRF mentors will be invaluable to the study's development,” he says. “In addition this program will be crucial to extend my research from CLL/SLL to other lymphomas. This transition is a challenge, and I will need strong mentorship and continuous advice to be successful. As such, I consider myself blessed to be part of this program.”

News from the Field: AUGMENT Trial Demonstrates Promising New Combination for Relapsed/Refractory Indolent Lymphoma

Rituximab (Rituxan) has long been the standard of care for many lymphoma patients with relapsed follicular lymphoma (FL) and marginal zone lymphoma (MZL). Researchers on the AUGMENT trial, a large-scale, multicenter study, sought to improve outcomes for this group of patients by combining rituximab (Rituxan) with lenalidomide (Revlimid), after earlier stage clinical trials suggested this combination improved the efficacy of treatment over rituximab alone. Results of this trial were initially presented at the American Society of Hematology (ASH) Annual Meeting in 2018 and were published in the *Journal of Clinical Oncology* in March 2019.

The study was led by John P. Leonard, MD, of Weill Cornell Medicine, a current LRF Scientific Advisory Board and Board of Directors member and past SAB Chair, and included contributions from former SAB member Nathan H. Fowler, MD, of MD Anderson Cancer Center, and MCL Consortium member Ian Flinn, MD, PhD, of Sarah Cannon Research Institute.

The study enrolled 358 patients with FL or MZL who had relapsed after at least one prior treatment and at least two doses of rituximab alone. Patients were randomized into one of two arms: those treated with rituximab and lenalidomide in combination and those treated with rituximab and a placebo. Either lenalidomide or the placebo

were taken as an oral therapy with intravenous rituximab at scheduled intervals; patients continued therapy for 12 cycles or until their disease progressed or they had unacceptable toxicity (side effects). Follow-up was done for up to five years after the last patient was randomly assigned.

Dr. Leonard and his collaborators found statistically significant improvements of progression-free survival (PFS) for the lenalidomide combination group, with a median length of 39.4 months compared to 14.1 months in the placebo group, more than two years longer on average. Results were particularly significant for the FL patients who made up most of the study; the authors noted that no significant difference in PFS was found for the MZL cohort, but added that the small number of MZL patients enrolled (63, or 18 percent of the total) made it difficult to determine if these results would be similar for all MZL patients.

The authors did note an increase in severe-grade toxicities (side effects) in the lenalidomide group, particularly neutropenia (an abnormally low white blood cell count, which increases a patient's vulnerability to infection). However, because the lenalidomide combination was so effective, a larger percentage of that group was able to complete all 12 cycles of treatment compared to the placebo group. The researchers further suggested that for most patients, the increase



John Leonard, MD, of Weill Cornell Medicine, member of the LRF Scientific Advisory Board and Board of Directors, and first author on the AUGMENT study.

in toxicity (particularly in the case of neutropenia) was worth enduring in order to achieve the longer lasting responses and PFS possible with the rituximab-lenalidomide combination.

"The greater efficacy of lenalidomide plus rituximab, vs rituximab alone, seems to be clinically meaningful in the context of the side effect profile," said Dr. Leonard. "I believe that this combination represents an important new option that patients with follicular and marginal zone lymphoma (and their physicians) should consider as they choose therapy."

Disclosures: Dr. Leonard has served as a consultant for both Celgene and Genentech/Roche.

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The Lymphoma Research Foundation's volunteer Scientific Advisory Board, comprised of 45 world-renowned lymphoma experts, guides the Foundation's research activities, seeking out the most innovative and promising lymphoma research projects for support.

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RESEARCH • FOUNDATION

National Headquarters

Wall Street Plaza
88 Pine Street, Suite 2400
New York, NY 10005
(212) 349-2910

Helpline: (800) 500-9976
helpline@lymphoma.org

Website: lymphoma.org

Email: LRF@lymphoma.org



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About the Research Report

Research Report is a publication of the Lymphoma Research Foundation, providing the latest updates on our grantees and their progress, as well as on the work of the Foundation. The Lymphoma Research Foundation is the nation's largest non-profit organization devoted to funding innovative lymphoma research and serving the lymphoma community through a comprehensive series of education programs, outreach initiatives, and patient services.

LRF Helpline

The Lymphoma Research Foundation (LRF) offers a variety of support services to lymphoma patients, survivors, and caregivers. These programs include the LRF Helpline, which provides information about lymphoma and its treatment options, as well as the Lymphoma Support Network for peer support and encouragement. Individuals touched by lymphoma can also learn about novel and emerging therapies through our Clinical Trials Information Service. As part of this program, LRF staff can conduct individualized lymphoma trial searches for patients to assist them in making important decisions about their care. For more information about the Clinical Trials Information Service or any of LRF's support services, please contact the LRF Helpline at 1-800-500-9976 or helpline@lymphoma.org, or visit lymphoma.org/learn/supportservices.

Lymphoma Research Foundation
Wall Street Plaza
88 Pine Street, Suite 2400
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News from the Field

The AUGMENT trial demonstrates a promising new combination therapy for relapsed/refractory follicular and marginal zone lymphomas.

See page 14 for details.

WALK WITH TEAM LRF

Rally your friends, family and teammates to find a cure for lymphoma at one of our upcoming 2019 Lymphoma Walks, held across the United States.

Irish Whisper Walk of Hope

Saturday, April 27

Pinecliff Lake Club House, West Milford, NJ

Nebraska Lymphoma Walk

Saturday, April 27

Mahoney State Park, Ashland, NE

Houston Lymphoma Walk

Saturday, May 18

Stude Park, Houston, TX

Minnesota Lymphoma Walk

Saturday, June 1

Lake Nokomis, Minneapolis, MN

New York Lymphoma Walk

Wednesday, June 12

Hudson River Park - Pier 45, New York, NY

Chicago Lymphoma Walk

Saturday, August 4

Montrose Harbor, Chicago, IL

Arizona Lymphoma Walk

Sunday, October 20

Phoenix Zoo, Phoenix, AZ

TEAM LRF

JOIN THE TEAM. **FIND A CURE.**