LYMPHOMA RESEARCH • FOUNDATION

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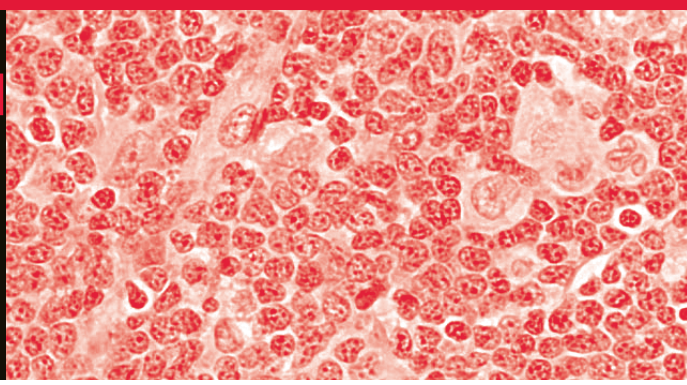
RESEARCH Report



Foundation Announces 25th Annual Class of Postdoctoral Fellowship Grants

2017 LRF Postdoctoral Fellowship recipient Mark Geyer, MD, of Memorial Sloan Kettering Cancer Center. Read more about Dr. Geyer's research in the area of immunotherapy on page 4.

The Lymphoma Research Foundation (LRF) has announced its 2017 Postdoctoral Fellowship Grantees. Part of LRF's Young Investigator Grants portfolio, Postdoctoral Fellowship Grants recognize innovative research conducted by postdoctoral and clinical research fellows in the first five years following the receipt of their doctorate. For many grantees, the Fellowship grant represents their first funding as a principal investigator on a project, and provides crucial protected time for their own research. This funding may also enable an early career researcher to develop or maintain a focus on lymphoma, establishing a new generation of clinicians and scientists pursuing research in this disease. The six grantees in the 2017 class represent a diverse array of bench, translational, and clinical research and more than $600,000 in research funding.

The 2017 Postdoctoral Fellowship Grantees include Ronan Chaligne, PhD, of Weill Cornell Medicine; Anja Deutzmann, PhD, of Stanford University; Mark Geyer, MD, of Memorial Sloan Kettering Cancer Center; Coraline Mlynarczyk, PhD of Weill Cornell Medicine; Jouliana Sadek, PhD of Weill Cornell Medicine; and Tai Wang, PhD of Memorial Sloan Kettering Cancer Center. Dr. Chaligne is the recipient of a named Fellowship grant, the Scientific Advisory Board Innovation Award. To learn more about LRF named research grants, see page 7.

Postdoctoral Fellowship Grants focus on clinical research projects, as well as laboratory-focused projects, such as identifying biomarkers, and translational research (projects which seek to move laboratory discoveries towards the clinic, such as developing mouse models or other in vivo tests of new therapies).

"LRF's Postdoctoral Fellowship Grants allow us to support early-career scientists who are making crucial contributions to our understanding of the biology of lymphoma, as well as identifying

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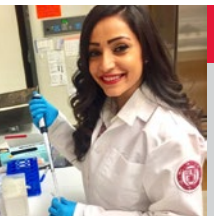
"We're not only supporting the best science in lymphoma, but providing support at a key time in the development of a lymphoma researcher's career."



FEATURED IN THIS ISSUE: Profiles of LRF's 2017 Postdoctoral Fellowship Grantees Page 4

The Foundation's 2017 Postdoctoral Fellowship Grantees, including Jouliana Sadek, PhD of Weill Cornell Medicine (pictured, left), discuss their research projects and the impact they will have on people with lymphoma and CLL.

LETTER FROM THE CEO

Dear LRF Friends and Supporters,

This issue of *Research Report* marks the second in our two-part series of our 2017 Young Investigator Grants class. In this edition, we explore our Postdoctoral Fellowship Grant recipients. (If you missed the profiles of the Clinical Investigator Career Development Awards and Lymphoma Clinical Research Mentoring Program in the Spring issue, please visit lymphoma.org/researchreport.) Profiles of these talented early career scientists begin on page 4.

In addition to celebrating this year's exemplary grantees, the 2017 class is the 25th Postdoctoral Fellowship Grant class to be awarded by LRF, our longest consecutively running grant program. The program now boasts a number of distinguished lymphoma researchers among its alumni, including seven current members of our own Scientific Advisory Board. Read more about the history of the program and alumni highlights beginning on page 3.

Every two years, the International Conference on Malignant Lymphoma (ICML) hosts one of the largest conferences specifically focused on lymphoid malignancies in the world. This year a number of researchers with LRF ties presented at ICML, including several LRF-funded projects. Highlights from the conference may be found on page 8.

Our Postdoctoral Fellowship Grant is truly supporting its second generation of researchers – something that would not be possible without your support. Thank you for all you do on behalf of LRF's mission to fund innovative lymphoma research and serve those touched by this disease.

Sincerely,

Meghan Gutierrez
Chief Executive Officer

New Grantees

[CONTINUED FROM PAGE 1]

potential new therapies," said Thomas M. Habermann, MD of Mayo Clinic, Chair of the LRF Scientific Advisory Board. "In doing so we're not only supporting the best science in lymphoma but providing support at a key time in the development of a lymphoma researcher's career."

Postdoctoral Fellowship Grants are LRF's longest-standing research mechanism. The 2017 Fellowship Grantees are LRF's 25th class in this program. For more on the outstanding lymphoma researchers who have received funding in these 25 years, see page 3.

"A key goal of LRF's early career awards, including the Postdoctoral Fellowship Grant, is to support accomplished young researchers and encourage them to remain in the field of lymphoma research," noted Meghan Gutierrez, LRF Chief Executive Officer. "It is gratifying to see so many distinguished names among our alumni – including seven who now serve on our own Scientific Advisory Board – and I have every hope that the 2017 grantees will match the accomplishments of our previous 24 classes."

Profiles of the 2017 Postdoctoral Fellowship Grantees begin on page 4. Information on past recipients of LRF Grants may be found on the LRF website at lymphoma.org/recentawards .

The 2018 grant cycle is now open for applications. Visit lymphoma.org/grants to view the RFPs and application instructions.

Celebrating a Quarter Century of Postdoctoral Fellowship Grants

In 1992, the Lymphoma Research Foundation of America (LRFA), one of two non-profit organizations that would later merge to become the Lymphoma Research Foundation, awarded its first scientific research grants. Designed to support early career researchers moving from fellowship to faculty positions, the organization awarded two fellowships to promising researchers Nancy Bartlett, MD, at Stanford University and Ann Mohrbacher, MD, of Dana-Faber Cancer Institute.

Twenty five years and over 200 grantees representing 70 institutions later, LRF's Postdoctoral Fellowship Grant program boasts a number of distinguished alumni, beginning with those first two grantees. Including the incoming 2017 class (see page 7), LRF's peer-elected Scientific Advisory Board has included seven former Postdoctoral Fellowship Grant recipients among its members.

"The goal of the Postdoctoral Fellowship Grant program has always been to support the next generation of lymphoma researchers," said Meghan Gutierrez, CEO of the Lymphoma Research Foundation. "It is clear in looking at our alumni and their accomplishments that this program has been incredibly successful in meeting this objective. I look forward to seeing names from our most recent classes when we celebrate the alumni 25 years from now."

The following profiles are only a selection of the over 200 researchers who have received LRF Postdoctoral Fellowship Grants, revealing where they are now and the impact the LRF Grant has had upon their career.

Dr. Bartlett is now at Washington University in Saint Louis, where she is a Professor of Medicine and the Koman Chair of Medical Oncology. She has been a member of LRF's Scientific Advisory Board since 2010; she is also the Chair of the Hodgkin Lymphoma Subcommittee for the National Cancer Institute (NCI) Lymphoma Steering Committee, and Vice-Chair of the CALGB/Alliance cooperative group Lymphoma Core Committee.

Nancy Bartlett, MD
Washington University in Saint Louis
1992 Grant-Stanford University

"Receiving an LRF grant as a third year oncology fellow at Stanford allowed me to extend my fellowship an additional six months, complete clinical research projects and prepare manuscripts that were critical to launching my career as a lymphoma clinical investigator. These awards provide encouragement and a sense of confidence to young lymphoma investigators, often fostering early professional success and hopefully leading recipients to choose lymphoma research as a career."

Dr. Michael Teitell is Professor in the Department of Pathology and Laboratory Medicine and in Pediatrics at the University of California, Los Angeles, where he also serves as Chief of the Division of Pediatric and Neonatal Pathology. He received both a Postdoctoral Fellowship Grant in 1997 and a Junior Faculty Award (an award which would later be merged with the Fellowship Grant) in 2001. He was elected into the American Scoeity of Clinical Investigators in 2004 Association of American Physicians in early 2017. Among his accomplishments are developing and integrating engineering and nanosystems technologies to facilitate pathways research and defining the role of TCL1 and co-regulated genes in normal B cell development and B cell lymphoma.

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NEW GRANTEE PROFILES

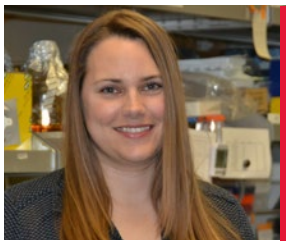
Ronan Chaligne, PhD
Weill Cornell Medicine
Scientific Advisory Board
Innovation Award

Identifying Epigenetic Alterations in CLL with CRISPR/CAS9

Approved by the U.S. Food and Drug Administration (FDA) for use on human cells in 2016, the CRISPR/CAS9 technology allows scientists to use a system of DNA proteins, called clustered regularly interspaced short palindromic repeats (CRISPR), to "edit" an individual cell's genome, removing and/or inserting segments of DNA. This technology offers immense possibilities in lymphoma research, where many therapies have had success targeting altered or mutated genomes that contribute to lymphoma growth. Dr. Chaligne and his collaborators will be using the CRISPR/CAS9 method as one part of his LRF grant project, which seeks to identify "epidrivers," or the epigenetic alterations that drive the formation of chronic lymphocytic leukemia (CLL) cells. "In this project, I aim to identify and validate the molecular events that allow the lymphoma cell population to evolve and escape therapy," Dr. Chaligne notes. "My ultimate goal is to use this information to identify novel therapies to directly address CLL evolution."

Dr. Chaligne received his PhD from the Institut Gustave Roussy / Faculté de Médecine Paris XI, in Villejuif, France, and did postdoctoral work at the Institut Curie in Paris before joining the lab of Dan Landau, MD, PhD, at Weill Cornell Medicine. During his graduate studies, Dr. Chaligne became fascinated by the process by which a normal human cell becomes cancerous, and has devoted his early career to working with expert researchers in cancer genetics and epigenetics, with a long-term goal of unraveling the complex biology of cancer and understanding cancer's evolutionary ability to adapt and grow in spite of initially effective therapies. He notes that the rapid rise of new technologies, such as CRISPR/CAS9, are providing enormous aid to researchers such as himself. "The pace of the biology is really extraordinary and every year, huge technical improvements allow the researcher to drive further the discoveries and understanding of cancer process."

Dr. Chaligne also notes that the funding provided by the Lymphoma Research Foundation is essential to his work. "The LRF grant is giving me the unique opportunity to spend the next two years of my scientific life at Weill Cornell in one of the most exciting and active research communities in the world," he says. "In addition to giving me time to concentrate on my work in the laboratory, it will also allow me to present my work in international conferences. Results of this project and scientific interactions created during its course will be of benefit to the whole scientific community as well as myself."



Anja Deutzmann, PhD
Stanford University
Postdoctoral Fellowship Grant

Developing a Screening Method for New Potential Inhibitors

Recent research has demonstrated that the oncogene (a gene which can cause and contribute to cancer growth) MYC is an important factor in the growth and proliferation of lymphoma cells. However, the pursuit of novel agents which could inhibit MYC's operation and thus eradicate lymphoma cells in humans has not yet yielded an effective therapy. Dr. Deutzmann's LRF Fellowship sponsor, Dean Felsher, MD, PhD, of Stanford University, in collaboration with Angela Koehler, PhD, at the Massachusetts Institute of Technology (MIT) have identified several potential novel compounds that could inhibit MYC. Dr. Deutzmann's project will develop a screening method to examine these compounds and identify the most potent for further laboratory testing. "The final goal of my project is to advance the development of a MYC-targeted pharmacological approach for the treatment of lymphoma," she says.

Dr. Deutzmann received her PhD in Cell Biology from the University of Konstanz in her native Germany. Though she began her career as a basic research scientist in cell biology, she was eager for the opportunity the Felsher lab at Stanford offered to shift her career towards translational research in cancer. "I am excited that I can focus my research efforts for the next two years on developing innovative ways to identify and further develop a novel MYC-targeted cancer therapy approach," she says, "My long-term goal is to contribute to the development of new therapeutic options for the treatment and ultimately cure of lymphoma."

Dr. Deutzmann recalls a recent visit of one of Dr. Felsher's former lymphoma patients to the lab to share his experience as a patient receiving treatment. "Ever since that lab meeting, he visits the lab regularly and supports us with his curiosity about our research, and his expertise from a patient's point of view. Cancer fighters such as him are an invaluable source of inspiration and motivation and I am grateful to be reminded that the ultimate goal of my research is to improve the lives of cancer patients." She further notes that LRF's support as a funder of early-career scientists is also crucial to her progress. "The successful development of a postdoctoral research project unfortunately does not only depend upon the passionate commitment of a scholar. It also requires adequate funding," she notes. "The LRF'sgrant funding provides me with the unique opportunity to work in a highly dynamic and interdisciplinary research environment, and to develop a translational research career in targeted therapeutics for lymphoma treatment."

Mark Geyer, MD
Memorial Sloan Kettering Cancer Center
Postdoctoral Fellowship Grant

"Tumor-Targeted" CAR T-cells in Relapsed CLL/B-cell NHL

Chimeric antigen receptor (CAR) T-cells have shown some promise as a novel therapy in lymphoma, but only a minority of patients with chronic lymphocytic leukemia (CLL) and B-cell non-Hodgkin lymphoma (B-NHL) have experienced deep responses. Researchers hypothesize that the tumor microenvironment, the broader cellular environment in which cancer cells and normal immune cells coexist, may limit the effectiveness of CAR T-cells. Dr. Geyer and his colleagues are exploring various strategies to modify CAR T-cells to counteract these effects. One strategy involves a CD19 CAR T-cell (a CAR T-cell which attaches to tumor cells expressing the protein CD19) which itself makes a cytokine (a molecule involved in cell signaling) called interleukin-12 (IL-12). In normal human immune function, IL-12 performs several functions that enhance the ability of T-cells and other immune cells to eliminate an infection. "We hypothesize that targeted delivery of IL-12 to the tumor microenvironment may enhance responses to CAR T-cell therapy while limiting side effects," Dr. Geyer notes. During his Postdoctoral Fellowship Grant, Dr. Geyer will conduct an early phase clinical trial designed to test IL-12 enhanced CAR T-cells in relapsed CLL and B-NHL. "We will assess safety, anti-cancer responses, the effects of IL-12 on CAR T-cell function, proliferation, and persistence, and the effects of these CAR T-cells on the immune system," he notes.

Dr. Geyer received his MD from Columbia University before a residency at Massachusetts General Hospital and a fellowship at Memorial Sloan Kettering Cancer Center, where he joined the faculty in July. "Since my days as an undergraduate, I have been fascinated by the intersection of the immune system and human cancers," he says, noting that he has been fortunate to study with some of the best researchers in this area, including Drs. Frederick Alt and John Manis of Harvard, and Dr. Mitchell Cairo of Columbia. His current project is an extension of that interest in immuno-oncology. "This project utilizes an innovative approach to overcoming the present limitations of CAR T-cell therapy in patients with lymphoma: delivery of an immunoregulatory cytokine to the tumor microenvironment."

Dr. Geyer hopes to become an independent investigator specializing in immunology, noting the encouraging pace of developments in the field. He adds that the hope and strength he derives from his lymphoma patients helps drive his commitment to research. "While I am pleased we can offer broader options to our patients than ever before, clinical care reinvigorates my commitment to understanding lymphoid neoplasia and developing safe and effective therapies."

Coraline Mlynarczyk, PhD
Weill Cornell Medicine
Postdoctoral Fellowship Grant

Detecting and Eradicating Dormant Malignant Cells in B-Cell Lymphoma

As researchers develop more targeted therapies for lymphoma, they are also tackling the problem of why certain patients remain resistant to treatment or prone to relapse. Dr. Mlynarczyk and her collaborators have found that a gene called BTG1 may hold the answer in B-cell lymphomas. BTG1 plays a role in "memory" B-cells, the immune cells which stay alive and dormant for a long period of time after an infection to "remember" how to fight that infection if it occurs again. When BTG1 becomes altered, it may transform memory B-cells into cancer cells that can go dormant and replenish themselves even after treatment. Dr. Mlynarczyk's Postdoctoral Fellowship Grant project seeks to both explain how BTG1 alterations contribute to lymphoma development as well as develop a way to detect and hopefully kill the dormant lymphoma cells, allowing patients to be cured.

Dr. Mlynarczyk became fascinated with cancer biology as a graduate student at the University Pierre and Marie Curie in Paris, ultimately completing a PhD in Hematology/Oncology at the University Paris Diderot/Saint-Louis Hospital before coming to Weill Cornell Medicine as a Postdoctoral Associate. "As I studied the stress response in cancer cells to improve treatment efficacy, I became eager to perform research at the translational level," she says. "This led me to join the laboratory of Dr. Ari Melnick (an LRF Scientific Advisory Board member) to elucidate the intricate mechanisms of lymphoma resistance to treatment and relapse." Dr. Mlynarczyk also has a personal connection to lymphoma, after losing her grandmother to the disease in 2004. "While her memory is a constant motivator, Dr. Melnick provides an outlet for stimulating discussions and encourages creative solutions to advance out research."

Dr. Mlynarczyk would like to eventually establish her own laboratory and become a faculty investigator in lymphoma research herself. She notes that support from LRF is a "strong driver" of her research progress. "This research forms the foundation of my career as a future independent investigator," she says, "and the LRF fellowship represents a major milestone in the pursuit of a successful and fulfilling scientific career."

NEW GRANTEE PROFILES

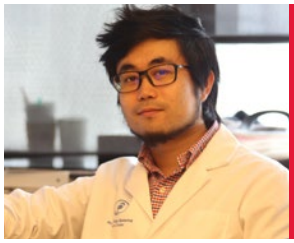
Jouliana Sadek, PhD
Weill Cornell Medicine
Postdoctoral Fellowship Grant

A Potential Prognostic Biomarker and New Novel Agent for Plasma Cell Malignancies

Hematological malignancies that occur in plasma cells, such as plasmablastic lymphoma (PBL) and primary effusion lymphoma (PEL) are most common in HIV patients and individuals with weakened immune systems. Current therapies have poor clinical outcomes with a median survival of less than a year. Multiple myeloma is a much more common plasma cell malignancy, for which therapeutic options have recently become available but with associated toxicities, and many patients eventually develop resistance. Dr. Sadek and her collaborators have discovered a novel nucleoside analog called 6- ethylthioinosine (6-ETI) (a class of therapeutic drugs commonly used as antiviral and chemotherapeutic agents) that can selectively target these cancers. 6-ETI is activated by the enzyme adenosine kinase (ADK), which occurs at high levels in PBL, PEL. As part of her LRF funded project, Dr. Sadek and her collaborators hope to further understand the role of ADK in tumor cell biology as well as assess potential combination therapies for 6-ETI in a laboratory setting. "Our studies suggest that our compound has a promising potential for the treatment of these aggressive tumors and that ADK expression can be used as a predictor of response to therapy," Dr. Sadek says.

Dr. Sadek's interest in cancer biology began when she volunteered at a pediatric cancer center in high school. "I realized then that I had an insatiable desire and commitment to be active in the fight against cancer." After completing her graduate studies at the University of Missouri-Kansas City, Dr. Sadek's interest in viral oncogenesis (how some viruses cause cancer) led her to a position as Postdoctoral Associate at Weill Cornell Medicine, in the lab of Ethel Cesarman, MD, PhD (a Foundation Scientific Advisory Board member).

Dr. Sadek notes that her LRF grant provides key support to her post-doctoral work. "The Foundation's support is instrumental in carrying out further studies to characterize the mechanism of action of our drug and identify effective anti-cancer drug combinations for plasma cell tumors, she says. "Our translational research seeks to advance our compound from the 'bench to bedside' and improve patient outcomes. This grant will help me establish myself as an independent young investigator and build my network with pioneers in lymphoma research."



Tai Wang, PhD
Memorial Sloan Kettering Cancer Center
Postdoctoral Fellowship Grant

Optimizing PU-H71, a Potential New Therapy for Lymphoma

Heat shock protein 90 (HSP90) is a protein within a cell's DNA that assists with a number of crucial functions. Unfortunately, in a tumor cell, HSP90 often stabilizes several functions needed for tumor growth; as a result, researchers have been looking at HSP90 inhibitors as potential candidates for targeted therapies. Dr. Wang and his colleagues have developed an HSP90 inhibitor, PU-H71, which showed success with some lymphoma cells, but was less responsive in others. The researchers discovered that the less responsive cells had lower levels of epichaperome, a structure made up of a tightly integrated HSP90 chaperome (a family of proteins) network. "However," Dr. Wang notes, "the level of epichaperome can be elevated by chemotherapy agents, whereby resistant cells become easier to be eradicated by PU-H71." Dr. Wang's Postdoctoral Fellowship Grant will thus test a new novel approach employing sequential treatment with chemotherapy agents and PU-H71 to improve the effect of the therapy on lymphoma cells.

Dr. Wang has been interested in HSP90 since he began his graduate studies at the University of Geneva, Switzerland, where he received his PhD in Biology, before joining Memorial Sloan Kettering Cancer Center as a Research Fellow. He notes that after seeing many HSP90 drugs rise and full, he hopes that PU-H71 can eventually become a therapy which will benefit lymphoma patients, adding that he joined the lab of Dr. Gabriela Chiosis at Memorial Sloan Kettering, the lab which discovered and developed PU-H71, to continue to pursue his interests. "I realized that improvement of lymphoma treatment requires not only discovery of new drugs, but also efforts to elucidate the best strategy that enables those drugs to fully exert their therapeutic potential," he says.

Dr. Wang notes that his LRF Fellowship Grant is the first grant of his postdoctoral research career. "It will play a pivotal role in determine the direction of my future research and the experiences that I will be able to acquire," he says. "I believe this project will be the opportunity to kick-start my career in translational science."

"Improvement of lymphoma treatment requires not only discovery of new drugs but also efforts to elucidate the best strategy that enables those drugs to fully exert their therapeutic potential."

A Living Legacy: LRF Research Grant Naming Opportunities

LRF's Named Research Grants Program enables a donor to fund innovative lymphoma research and name a specific research grant in their name, or in honor or memory of a loved one or the physicians and nurses who care for them. The 2017 Lymphoma Research Foundation grant class features two grants named by their underwriting donors. The Scientific Advisory Board Innovation Award (see page 4) is a Postdoctoral Fellowship Grant honoring the commitment of the physicians on LRF's advisory board to funding innovative research, while the Larry and Denise Mason Career Development Award (see the Spring 2017 Research Report) honors a long-time Foundation benefactor by recognizing a CDA recipient whose project will benefit a broad range of lymphoma patients.

Would you like to leave a legacy by supporting a research grant that bears your name? LRF staff can help you select a naming opportunity that is suited to your passion and personality or one that honors or memorializes someone special. Your gift to the Lymphoma Research Foundation provides significant resources to underwrite cutting edge cancer research that will benefit generations of Lymphoma patients.

Potential named grant opportunities include:

Young Investigator Grants, which attract and train early career scientists for lymphoma research through three distinct programs: Postdoctoral Fellowships, Clinical Investigator Career Development Awards, and the Lymphoma Clinical Research Mentoring Program:.

Disease Specific Focus Area Grants are awarded to senior researchers studying specific subtypes and/or patient populations. Award amounts for these grants vary depending on the scale and scope of the research projects funded.

To learn more about research grant naming opportunities at LRF, please contact: Dennis Chillemi, Sr. Director of Development at 212-349-2775 or email: dchillemi@lymphoma.org.

LRF Scientific Advisory Board Announces New Leadership

The Lymphoma Research Foundation's Scientific Advisory Board (SAB), a volunteer group comprised of 45 world-renowned experts in lymphoma research, announced new leadership on July 1, 2017. Thomas M. Habermann, MD, of Mayo Clinic, Rochester assumes the Chair of the SAB following the conclusion of the two-year term of Leo I. Gordon, MD, FACP of Robert H. Lurie Comprehensive Cancer Center of Northwestern University. Dr. Habermann, who has just completed two years as Chair-Elect, will also serve a two-year term as Chair through 2019.

Andrew D. Zelenetz, MD, PhD of Memorial Sloan Kettering Cancer Center, has been elected Chair-Elect and will assume the Chair role when Dr. Habermann's term concludes.

In addition, four new general members were elected to the SAB:

Catherine Bollard, MD, MBChB, of Children's National Medical Center and George Washington University

Steven M. Horwitz, MD, of Memorial Sloan Kettering Cancer Center

Kerry Savage, MD, of British Columbia Cancer Agency

Hans-Guido Wendel, MD, of Memorial Sloan Kettering Cancer Center.

Profiles of the new leadership and members will be featured in the Fall 2017 issue of the *Research Report*.

The Foundation and SAB would also like to thank Dr. Gordon for his service as Chair, as he steps down to become a general SAB member. In addition, the following general members are stepping down from the SAB, though they will still be active in various LRF activities. Departing members are:

John Chan, MD, City of Hope

Nathan Fowler, MD, MD Anderson Cancer Center

Neil Kay, MD, Mayo Clinic, Rochester

Louis Staudt, MD, PhD, National Cancer Institute

LRF thanks the departing members for their service on behalf of the SAB and the entire lymphoma research community.

News from the Field: ICML 2017 Edition

The biennial International Conference on Malignant Lymphoma (ICML), held June 14-17, 2017 in Lugano, Switzerland, is one of the premier conferences specifically devoted to lymphoid neoplasms. This expanded News from the Field highlights research presented at ICML 2017.

Foundation Scientific Advisory Board (SAB) Member Margaret Shipp, MD of Dana-Farber Cancer Institute, was invited to give the inaugural Gianni Bonadonna Memorial Lecture at ICML. Lecturing on the topic "Genetic Signatures and Targetable Pathways in Lymphoid Malignancies," Dr. Shipp discussed PD-1 signaling and the development of checkpoint inhibitors such as nivolumab and pembrolizumab, as well as questions the current clinical results for such therapies raise for future research.

Former SAB Member Ron Levy, MD of Stanford University, was invited to give the Henry Kaplan Memorial Lecture, for which he chose the topic "Immunotherapy Comes of Age to Treat Lymphomas." Dr. Levy discussed the history of immunotherapy in lymphoma, beginning with anti CD20 monoclonal antibodies (of which rituximab is an early example) through the CAR T-cells and checkpoint inhibitors of today.

Connie Batlevi, MD, PhD of Memorial Sloan Kettering Cancer Center, a 2016 LRF Scholar, gave an oral presentation of her Lymphoma Clinical Research Mentoring Program (LCRMP) project, an early phase clinical trial of ibrutinib (Imbruvica) and buparlisib in relapsed/refractory DLBCL, MCL, and FL. Based on prior research indicating that BTK inhibitors like ibrutinib and PI3K inhibitors like buparlisib were effective in combination in B-cell non-Hodgkin lymphoma, Dr. Batlevi and her colleagues enrolled 25 patients with at least one prior therapy, who received escalating doses once daily of each drug. The study established a potential baseline for dose levels of the combination that were effective without being excessively toxic; in addition, of the 20 evaluable patients at the time of reporting the overall response rates were 14 percent for DLBCL, 25 percent for FL, and 100 percent for MCL. Researchers concluded that the combination warrants further study, particularly in MCL. The study is currently enrolling additional patients.

➤*This study also included contributions from LRF grantee Anita Kumar, MD, former SAB member Craig Moskowitz, MD, and SAB members Steven M. Horwitz, MD, Andrew D. Zelenetz, MD, PhD, and Anas Younes, MD, all of Memorial Sloan Kettering Cancer Center.*

David Scott, MBChB, PhD, of British Columbia Cancer Agency, presented a poster with results from his LRF funded MCL Correlative Studies project, awarded in 2016. Dr. Scott's project uses a special assay (a process for measuring molecular levels within cells), the MCL35, that was developed to analyze a patient's "proliferation signature" (one of the most powerful biomarkers in MCL cells) and assign a level of low, standard, or high risk categories, to analyze samples from 62 younger MCL patients collected as part of a clinical trial in MCL. The MCL35 assigned the samples to one of the three risk categories, then the outcomes data for those patients were analyzed to determine if the MCL35 score effectively identified risk levels. Although progression free survival and overall survival rates were not significantly different for the low and standard level groups, the 11 patients identified as high risk did have significantly inferior outcome rates (3.5 years median overall survival compared to 7.6 for the standard risk and unreached for the low risk group).

Dr. Scott and his colleagues noted that this study not only verified the utility of the MCL35 assay as a prognostic tool, but given the poor outcomes for high risk patients despite intensive treatment in the clinical trial, new novel approaches should be developed for this patient population.

➤*This study also included contributions from SAB Members Nancy Bartlett, MD, of Washington University in Saint Louis, John Leonard, MD, of Weill Cornell Medicine, and Eric Hsi, MD of Cleveland Clinic.*

Gita Thanarajasingam, MD, of Mayo Clinic, Rochester, also a 2016 LRF Scholar, presented a poster of her LCRMP Workshop project, which developed a novel approach for analyzing adverse events (AE, or side effects) as they occur over the course of treatment in indolent lymphomas. The standard tables of severe AEs do not take into account the duration or escalation of severity over time, and also does not cover lower grade AEs that might persist over a long period of time for patients that receive continuous therapy for months or years. Dr. Thanarajasingam used data from a clinical trial of 94 patients with indolent lymphoma receiving lenalidomide and applied the Toxicity over Time (ToxT) measure she developed to show a more accurate description of how AEs such as cytopenia (anemia) and fatigue affect patients on a generally low

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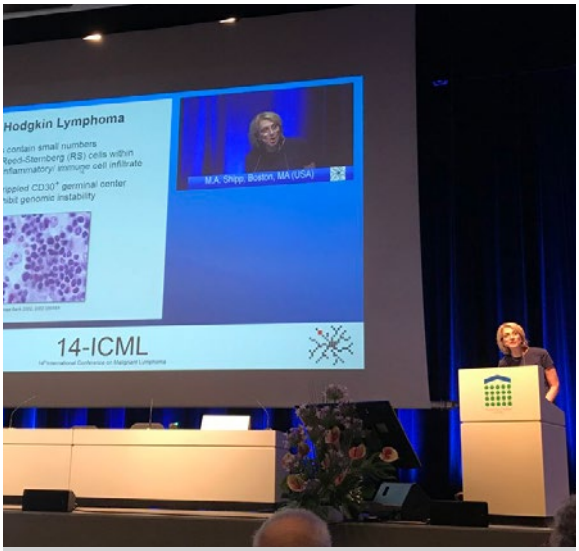
level, but for an extended period of time. Dr. Thanarajasingam and her colleagues noted that being able to accurately describe the time frame of a given side effect can give both patients and doctors reassurance about the symptoms patients experience during treatment as well as help guide future therapies to better address long-term side effects.

➤*This study also included contributions from SAB members Nancy Bartlett, MD of Washington University in Saint Louis, Kristie Blum, MD, of The Ohio State University, Christopher Flowers, MD, of Winship Cancer Institute, Emory University, John Leonard, MD of Weill Cornell Medicine, and Thomas Habermann, MD, and Thomas Witzig, MD, both of Mayo Clinic, Rochester.*

➤*This study also included contributions from LRF Scholars Carla Casulo, MD, of the University of Rochester and Connie Batlevi, MD, PhD of Memorial Sloan Kettering Cancer Center; LRF CDA recipient Paul M. Barr, MD, of the University of Rochester; SAB members Ranjana Advani, MD of Stanford University, Jonathan W. Friedberg, MD, MMSc of the University of Rochester, Anas Younes, MD and Andrew D. Zelenetz, MD, PhD, both of Memorial Sloan Kettering Center; and former SAB member Craig Moskowitz, MD, of Memorial Sloan Kettering Cancer Center.*



Margaret Shipp, MD of Dana-Farber Cancer Institute gives the Gianni Bonadonna Memorial Lecture at ICML 2017. (Photo courtesy American Association of Cancer Research)

Anita Kumar, MD, of Memorial Sloan Kettering Cancer Center a 2014 LRF Scholar and 2015 Career Development Award recipient, presented a poster of her LCRMP project, a pilot study examining a combination therapy of brentuximab vedotin (Adcetris) and AVD chemotherapy (doxorubicin, vinblastine, and dacarbazine) followed by involved-site radiotherapy (ISRT) for the treatment of early stage, unfavorable risk Hodgkin lymphoma (HL). Data presented at ICML represented the second cohort of the study, in which the dose of ISRT was reduced to determine whether it would decrease toxicity while remaining an effective therapeutic strategy. The 25 patients (of 29 enrolled) who completed the full therapy all achieved complete responses, with the duration of remission to date ranging from 2-13 months with no relapses yet recorded. Dr. Kumar and her colleagues suggested that their results suggest not only that the lower ISRT dose is effective while being safer for patients, but that the brentuximab vedotin/AVD/ISRT combination should be studied in a larger, randomized study for this patient population.

Several current LRF SAB members joined first author Christiane Pott, MD, PhD of University Hospital Schleswig-Holstein (Germany), a former LRF grantee in MCL, on a poster examining minimal residual disease (MRD) and its ability to predict outcomes in the GADOLIN study of relapsed or refractory follicular lymphoma. MRD refers to the very small amount of cancer cells that may remain in the patient during treatment or while in remission and is a potential cause of relapse. Recent advances in technology have allowed researchers to detect and measure MRD for the first time and explore its utility as a prognostic tool. The GADOLIN study, a randomized study of obinutuzumab and bendamustine (with maintenance obinutuzumab following treatment) vs. bendamustine alone, had 335 participants, 71 percent of whom had initial samples with the detectable clonal marker that is found in MRD. The patients with this marker tended to be at higher stage FL and have a worse prognostic index score. Dr. Pott and her colleagues also analyzed 88 samples at mid-treatment and 118 samples at the end of treatment, finding that the obinutuzumab/bendamustine arm achieved greater MRD negative responses (79 percent at mid-treatment and 86 percent at end of treatment) than the bendamustine arm (47 percent mid-treatment and 55 percent end of treatment). The researchers further noted that the obinutuzumab maintenance in the combination therapy arm also generally kept patients in MRD negative status, where some of the MRD negative patients in the bendamustine arm converted back to MRD positive status and relapsed. They concluded that using MRD status at the end of treatment was a good indicator of a treatment's effectiveness, while also demonstrating that the obinutuzumab/bendamustine combination therapy was significantly more effective than bendamustine alone at maintaining MRD negative status and thus preventing relapse.

➤*This study included contributions from SAB Members Bruce D. Cheson, MD, FACP, FAAS of Lombardi Comprehensive Cancer Center, Brad S. Kahl, MD of Washington University in Saint Louis, and Laurie H. Sehn, MD of British Columbia Cancer Agency.*

25 Years of LRF Fellowship Grants

[CONTINUED FROM PAGE 3]

Michael Teitell, MD, PhD
University of California Los Angeles
1997 and 2001 Grant - UCLA

"The LRF Junior Faculty Award was instrumental in supporting our lab's formative years and generation of a genetic mouse model for germinal center-origin B cell lymphomas and mature B and T cell leukemias, upon which much of our work to this day is grounded. LRF funds work at the most crucial stage of an investigative career, when new ideas abound and the return on investment is likely to be largest."

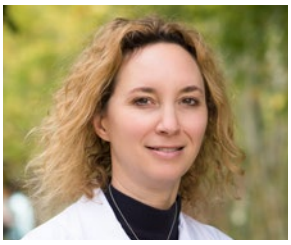
Dr. Eduardo Sotomayor is the inaugural director of the GW Cancer Center at George Washington University after many years at the H. Lee Moffitt Cancer Center and Research Institute in Tampa, Florida, where he was the scientific director of the DeBartolo Family Personalized Medicine Institute. His research specializes in basic and translational studies in lymphoma immunology and immunotherapy He has been a member of LRF's Scientific Advisory Board since 2013, currently serves on the Foundation's MCL Consortium Executive Committee, and is a co-Chair for the upcoming 2017 North American Educational Forum on Lymphoma.

Eduardo Sotomayor. MD
George Washington University
1998 Grant - Johns Hopkins

"As a former recipient of a LRF Fellowship Research Award and of a Junior Faculty Award, my academic career has been greatly influenced by LRF, an organization that I am proud of being part of, currently as a member of its SAB.

Back in the 1990's, I was in my last year of Fellowship at John Hopkins working in the emerging area of cancer immunotherapy. Then, cancer immunotherapy was not well regarded as currently is, and funding opportunities were scarce in particular for fellows or junior investigators interested in this field. I was however fortunate enough to receive a Fellowship research award from the LRF to study the mechanism by which lymphoma cells induced T-cell anergy. This was the beginning of a long-lasting relationship with the LRF that allowed me to successfully compete for a Junior Faculty award also from LRF, followed by a K08 and then my first R01 from the National Cancer Institute. LRF has had therefore a profound impact at the beginning of my academic career, when I needed support the most. I will be always grateful to LRF for its continuous investment in supporting innovative science, clinical research, educational programs, and by being at the forefront of patient advocacy and policy."

Dr. Leslie Popplewell is Associate Clinical Professor at City of Hope's Toni Stephenson Lymphoma Center. She specializes in clinical trials examining new therapies for lymphoma, including chimeric antigen receptor (CAR) T-cell immunotherapy, as well as developing advanced transplant techniques for patients with relapsed lymphoma. She has presented research multiple times at LRF's Mantle Cell Lymphoma Scientific Workshop and has also participated in grant review for later classes of LRF Postdoctoral Fellowship grants.



Leslie Popplewell, MD
City of Hope
2000 Grant-City of Hope

"Good ideas for improvement of lymphoma outcomes are more plentiful, but funding to make those ideas come alive can be scarce," Dr. Popplewell says. "The LRF grant arrived at a critical time in a research project and allowed me and my team to open a clinical trial using a new therapy for patients with aggressive non-Hodgkin lymphoma."

SCIENTIFIC ADVISORY BOARD

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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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.

Donor Spotlight

Donna and Paul Reinbolt of Houston, TX raised over $20,000 through the Kinkaid Lacrosse Six Game Challenge, a fundraiser to celebrate Donna's 10 years of remission from Hodgkin Lymphoma. Working with their son's lacrosse team at The Kinkaid School, Donna and Paul, as well as several other families on the team, contributed $50 each to LRF for each goal scored in a six game stretch. "We thought it would be fun to watch the guys rack up the points for a great cause!" says Donna.

Donna found LRF after her initial diagnosis in 2007, while looking for information on the internet. "Thankfully, I found trusted and up to date information on the LRF website." In 2009, Donna began working with LRF staff to start a Houston LRF Chapter, host an Ask the Doctor patient event, and start the Houston Lymphoma Walk in 2010. Today she is a member of LRF's Board of Directors.

LYMPHOMA
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25 Years of Fellowships

A history of LRF's longest running research grant program and highlights from its distinguished alumni. **Details on Page 3.**

APPLICATIONS OPEN FOR 2018 RESEARCH GRANTS

LRF's 2018 Research Grants are now open for applications. Visit lymphoma.org for RFPs and other application materials.

Application Deadline: September 6, 2017

For Early Career Investigators:
- Clinical Investigator Career Development Award
- Postdoctoral Fellowship Grant
- Lymphoma Clinical Research Mentoring Program

Disease Focus Area Grants:
- Adolescent/Young Adult Lymphomas Correlative Studies Grant
- Mantle Cell Lymphoma Therapeutic Studies Grant

lymphoma.org/grants