

The Society of MSK Campaign 2023–2024

# Advancing Lymphoma Research at MSK

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# Advancing Lymphoma Research at MSK

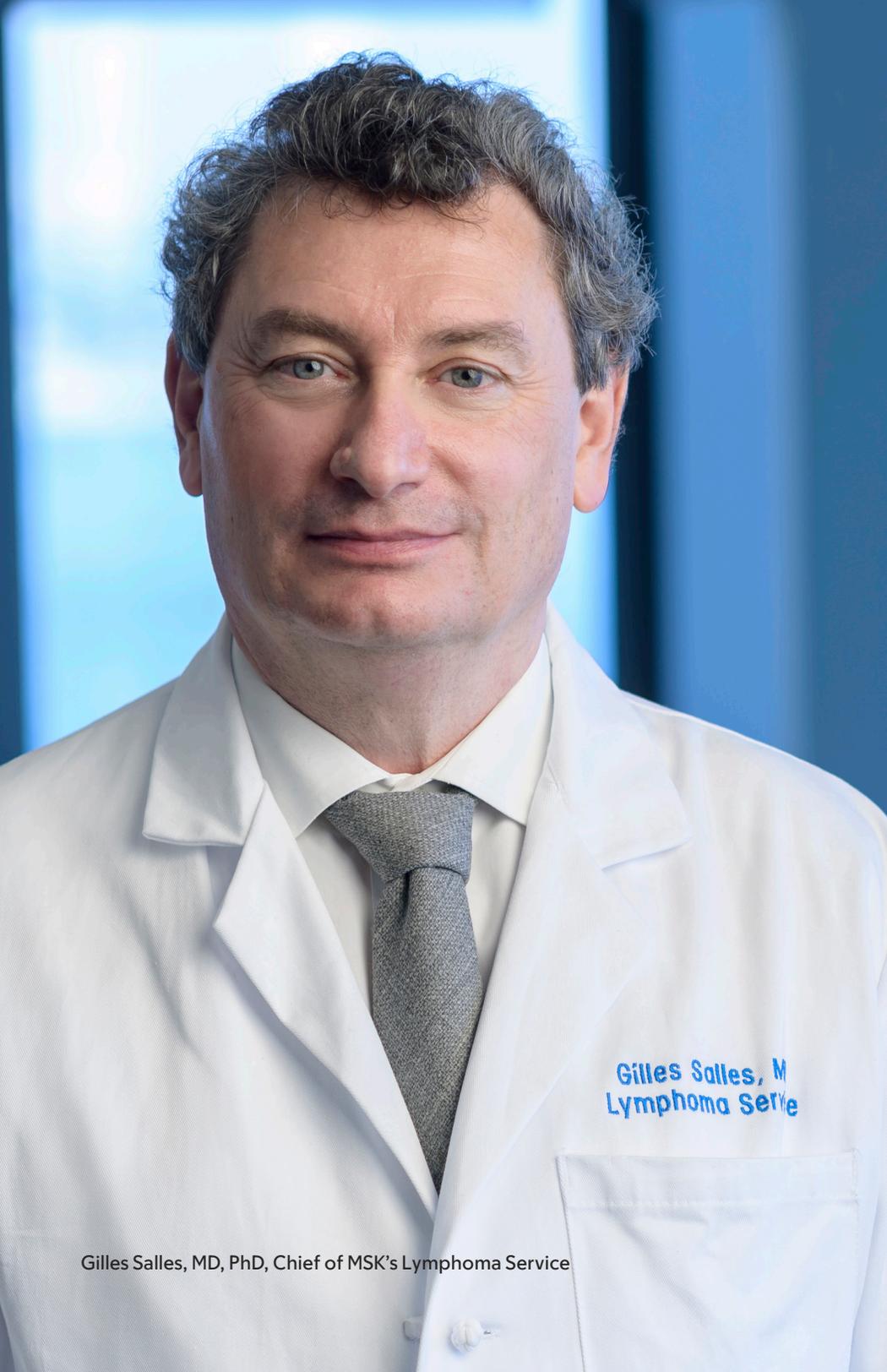
**Memorial Sloan Kettering Cancer Center (MSK) is home to one of the world's largest and most innovative research and clinical trial programs focused on lymphoma, a cancer that develops in the lymphocyte, a type of white blood cell essential to fighting infection.** As research has accelerated over the past two decades, more than 80 subtypes of lymphoma have been discovered and an array of new drugs has been approved to treat the disease. Despite this recent success, there is still an urgent need for effective treatments across the full spectrum of this complex cancer.

As a world-class academic medical center dedicated exclusively to the understanding and treatment of cancer, MSK is uniquely positioned to answer the most difficult questions and uncover new therapies that improve outcomes for people with lymphoma.

## Enhance Immunotherapies

Lymphomas are broadly divided into two groups: Hodgkin lymphoma, a less prevalent diagnosis that is distinguished by the presence of a type of B cell called Reed-Sternberg cell, and non-Hodgkin lymphoma, a more common form that arises from B cells or T cells. The cancer can be aggressive and require immediate treatment, or it can be slow-moving, may not need medical attention right away, and can be monitored attentively, sometimes for many years. Non-Hodgkin lymphoma is the seventh most common cancer in men and the sixth most common in women. It is responsible for approximately 20,000 deaths every year in the United States.

The diversity of subtypes in lymphoma is one of the greatest challenges for physicians and scientists when it comes to determining treatment plans. Recognizing even the smallest differences is essential to improving lymphoma drugs and prolonging survival.



Gilles Salles, MD, PhD, Chief of MSK's Lymphoma Service

## Recent Innovations

Lymphoma research has flourished in the last 20 years, and MSK has been at the forefront of the field. Leading the effort is Steven A. Greenberg Chair Gilles Salles, MD, PhD, Chief of MSK's Lymphoma Service. An international leader in the development of novel therapeutics for lymphoma, Dr. Salles has been involved in many large multinational clinical trials that have led to FDA approval of new treatments.

Dr. Salles cites immunotherapy, the revolutionary approach that uses the body's own immune system to fight cancer, as key to recent breakthroughs in treatment. It is especially effective in people with B cell lymphoma, which accounts for 80% of non-Hodgkin lymphoma cases. Monoclonal antibodies, man-made proteins designed to bind to a specific target on a cell and trigger an immune response to destroy cancer, have drastically improved outcomes for people with aggressive B cell lymphoma and extended the lives of people with slow-moving or indolent B cell lymphoma. Chimeric antigen receptor (CAR) T cell therapy, a breakthrough pioneered by MSK scientists that involves genetically engineering a patient's own immune cells to recognize and kill cancer cells, has shown success in treating people with aggressive B cell lymphoma who have failed two lines of therapy. CAR T cell therapy is effective in other lymphomas and blood cancers as well.

Discoveries made at MSK are also improving quality of life for people with lymphoma. Physicians now look at the whole patient, considering personal factors like their age and overall health, and treatments are moving away from harsh chemotherapies toward immune-based and targeted therapies that are more effective and less toxic.

"Our research is an ongoing story," Dr. Salles says, "one that continues to develop and bring new insights every day about a very complex cancer."

# Exploring the Next Breakthrough

MSK scientists are changing the landscape for lymphoma. Investing in lab-based and clinical research at MSK will accelerate innovations and support our researchers as they:

## Enhance Immunotherapies

Immunotherapy is one of the most promising ways to treat and ultimately cure cancer, and MSK is a world leader in the field. While many people benefit from CAR T cell therapy, some experience severe reactions that impact their health or interfere with the completion of treatment. MSK scientists are developing the next generation of CAR T cells to improve efficacy and diminish the frequency of harmful side effects.

In addition, our experts are exploring a subclass of drugs called bispecific antibodies, which target tumor cells while harnessing powerful components of the body's immune system. MSK research has been instrumental in the FDA approval of three bispecific antibody drugs since December 2022. Our scientists are continuing to pursue a deeper understanding of the characteristics of bispecific antibodies, specifically how they activate immune cells in the body and what leads some people to be resistant to them.

## Seek to Understand Tumor Response to Cancer Therapies

Researchers in labs across MSK are gaining new insights into the genetic makeup and progression of lymphoma and are determined to use this information to craft more effective treatments for every form of the disease.

One of their biggest resources is MSK-IMPACT® Heme, a sequencing test that analyzes 400 genes found in blood cancers. MSK scientists have used the test to analyze more than 2,300 lymphoma tumors in patients. The data collected helps them to evaluate tumors' vulnerability to cancer drugs, shape individualized and targeted treatment plans, determine if a patient is a good candidate for a clinical trial, and further their understanding of the different classes of lymphoma.

In addition, MSK scientists are exploring the epigenetic code in cells and its relation to cancer development. Epigenetic factors influence how genes prompt cells to acquire certain functions, and abnormalities in this process can have adverse effects and cause cancer. Knowing the epigenetic code is damaged in people with lymphoma, MSK researchers are investigating how new drugs or new combinations of drugs can target this pathway.

## Expand Clinical Trials

Clinical trials determine the safety and efficacy of a treatment, provide information on potential side effects, advance knowledge around a disease, and ultimately lead to new drug approvals. As one of the most active clinical trial programs in the world, MSK has helped to develop most of today's FDA-approved lymphoma drugs.

Dozens of clinical trials for a diverse range of lymphomas are underway at MSK. One such trial is a phase 1 study for people with diffuse large B cell lymphoma, the most common type of non-Hodgkin lymphoma, that tests CAR T cells made with the genome-editing tool CRISPR/Cas9, a technology that allows researchers to precisely target and modify specific genes to further enhance the effectiveness of CAR T cells.

In another phase 2 clinical trial, MSK scientists are exploring a bispecific antibody in people with follicular lymphoma, a type of indolent non-Hodgkin lymphoma, to replace the classical cytotoxic chemotherapies used for decades. This novel therapy may enhance the ability of the patient's own T cells to destroy cancer cells.

Multiple other phase 1 and phase 2 studies are evaluating combinations of bispecific antibodies with other drugs that may enhance their activity, to increase the proportion of patients who can be cured.



Marc Ladanyi, Molecular Geneticist;  
Chief, Molecular Diagnostics Service,  
and Ryma Benayed, Molecular Geneticist

# How You Can Move Progress Forward

The Society of Memorial Sloan Kettering Cancer Center will once again champion extraordinary breakthroughs in science. Philanthropy drives innovation and impacts every phase of the research process, from its earliest stages in the lab to its later investigations in clinical trials.

A gift to this year's campaign, "Advancing Lymphoma Research," will accelerate progress at MSK and support scientists as they gain a deeper understanding of the diverse biology of lymphoma and discover more effective treatments for people at MSK and beyond.



Urvi A. Shah, MD, Hematologic Oncologist,  
Myeloma Service

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