



LEUKEMIA & LYMPHOMA SOCIETY®

CMML Special Initiative

Expanding Research in Chronic Myelomonocytic Leukemia to Better Characterize Its Biology, Develop New Therapies, and Optimize Outcomes for Patients

Request for Proposals (RFP)

The purpose of the CMML Special Initiative is to establish a comprehensive research program to understand the unique characteristic of CMML, develop new targets and new therapies, and launch focused clinical programs needed to make significant progress toward cures for patients battling CMML. The grant program for the CMML Special Initiative will be comprised of two programs: a Synergistic Team Award (STA) similar to the LLS SCOR Program and a Translational Grant (TRL) similar to the LLS TRP Program.

I. Chronic Myelomonocytic Leukemia (CMML)

CMML is a disease that affects approximately 1,100 new people each year in the US. It is a disease characterized by a high monocyte count, genetic abnormalities, and mutations in genes involved in various molecular pathways that regulate gene expression and cellular pathways such as the spliceosome, epigenetics, signaling factors, etc. For most patients, CMML is an incurable cancer with a poor prognosis. There are only three FDA-approved therapies to attempt to control CMML. These are all hypomethylating agents with a similar mechanism of action, including azacitidine, decitabine, and more recently oral decitabine (plus cedazarzurdine). However, none of them enhance overall survival. The only curative option for CMML patients with advanced disease is a bone marrow transplant (BMT), which carries its own risks, especially since BMT in an elderly population (average age of a CMML patient is 72) has significant safety concerns.

Our understanding of the molecular basis for CMML has advanced considerably in the past 10 years. This is coupled by the realization that many of the mutations associated with CMML are also found in precursor conditions, in healthy individuals (that put people at higher risk of developing leukemia) as well as in AML and MDS patients. Therefore, there is an intense interest in the research community to identify and develop inhibitors for these new targets.

For a more detailed description of CMML, as well as potential laboratory and clinical research avenues, please see the attached document entitled “[Road Map to Cures For CMML.pdf](#).”

II. Goal of the RFP

LLS plans to invest up to \$13 million over five (5) years in targeted research to build a more comprehensive foundational understanding of the molecular basis of CMML, discover new therapeutic avenues, develop better therapies, and most importantly, **optimize outcomes in clinical research for the patient population already diagnosed with CMML.**

Priority will also be given to research that aims to deliver results on a timeline that can optimize outcomes for the patient population that has already been diagnosed with CMML.

III. Research Focus Areas

While investigators are encouraged to submit proposals in any clinical or biological topics related to CMML, certain research areas will be prioritized. On the clinical side, these include a) studies of innovative treatments using novel agents, pre-existing agents, or novel combination therapies; b) immunotherapies with high potential for clinical activity in CMML; or c) normalization of blood counts and relief of symptoms such as blood transfusions. Equally important, we also seek a deeper understanding of the disease and will support studies focused on a) uncovering novel features of CMML biology and cellular vulnerabilities; b) investigations into mechanisms of CMML relapse and therapy resistance; and c) identifying new targets and therapies. Such fundamental studies should be focused on translational potential and driven ultimately by the goals of improved patient outcomes and reduction or elimination of disease. Priority will also be given to research that aims to deliver results on a timeline that can optimize outcomes for the patient population that has already been diagnosed with CMML.

IV. Call for Proposals

A. Grant Funding Mechanisms

LLS is activating a global call for inventive proposals that have the potential for high impact in the field of CMML. Research funding during this first RFP will be allocated as stated below. The grant programs are as follows:

Synergistic Team Award (STA). Up to two will be awarded. These 5-year, \$5 million multi-investigator grants will focus on a program designed to include an understanding of the molecular basis of CMML, how to overcome resistance to existing therapies, and most importantly, clinical application of knowledge that may manifest as new clinical trials with novel agents or correlative studies with on-going clinical studies. The group must have demonstrated knowledge in the field as well as the ability to perform clinical trials, biomarker/PD assessment, and/or basic CMML biology research.

Support for core facilities may include the use of animal models, computational expertise, single-cell analysis, or other expertise required to advance new therapies. The grant program is designed to create a synergistic team that will work well together.

Translational Grants (TRL). Up to four will be awarded. These 3-year, \$750,000 awards will support clinical and/or biological research. A clearly outlined translational aspect is a plus for proposals in basic research, but outstanding biological research proposals without a translational element will be considered. The award is expected to support senior investigators, although young independent investigators with a proven track record will be considered.

All awardees will be invited to give a progress update at an annual in-person group meeting to be held in the autumn timeframe. This is complemented by an annual report of activities in the Spring timeframe. Awardees must attend or appoint a colleague to give the progress update.

B. Eligibility

The CMML Special Initiative welcomes applications from independent investigators (generally at least assistant professor-level or equivalent) worldwide from appropriate academic institutions and investigators of any nationality. An investigator may only be a PI, co-PI, and/or Project/Core leader on a maximum of one grant application. There is no limitation on the number of collaborations an investigator may have, and collaborators may be listed on more than one application so long as they are not in the leadership roles highlighted above.

The PI or co-PI must have a significant track record in hematology and/or blood cancer research. If the scientific achievements and expertise of the PI or co-PI are in another scientific area, they must have a Co-PI who has the required significant track record in hematology and/or blood cancer research with an emphasis on myeloid disease.

The proposed research must be directly aimed toward advancing our understanding of and/or treatments for CMML. Projects must be concerned with understanding properties and vulnerabilities of CMML and/or focused on developing and testing novel CMML therapies. Applications that do not meet the relevance requirement will be disqualified without full review.

C. Application Process

The application process has two phases. The first phase is submission and consideration of a Letter of Intent (LOI). The LOI will be evaluated for relevance and eligibility, and all applicants meeting the criteria will be invited to submit a Full Application. Both LOI and Full Application submissions must be made electronically through the [LLS Research Portal](#).

LOIs will be reviewed on a rolling basis prior to the due date. If accepted the full application template will be available immediately.

Full Applications will be reviewed by a committee composed of experts in CMML and myeloid diseases, blood cancer biology, and cancer therapeutics. Applications will be evaluated based on significance, scientific rationale, innovation, feasibility, experience and track-record of the investigators, and potential impact and benefit to CMML patients. LLS will make final funding decisions based on the committee evaluation, program priorities, and the availability of funds.

Detailed instructions for preparation of the LOI and Full Application can be found in the CMML STA and TRL Guidelines and Instructions documents available on the LLS website, <https://www.lls.org/research/cmml-special-initiative>, or through these links:

[STA Guidelines and Instructions](#)

[TRL Guidelines and Instructions](#)

D. Key Dates

Phase	Date
Call For Proposals	March 20, 2023
Letter of Intent Deadline	May 1, 2023, at 3 PM ET
Notification of Full Application Invite	No later than May 5, 2023
Full Application Deadline	June 30, 2023, at 3 PM ET
Review Panel Meeting	August 2023
Notification of Awards	September 15, 2023
Grant Term Begins	November 1, 2023