



HCL2025: Expanding Research in Hairy Cell Leukemia to Better Characterize Its Biology, Develop New Therapies, and Optimize Outcomes for Patients

**An Initiative of
Hairy Cell Leukemia Foundation (HCLF) and The Leukemia & Lymphoma Society (LLS)**

Request for Proposals (RFP)

I. Hairy Cell Leukemia

Hairy Cell Leukemia (HCL) is a rare hematological malignancy characterized by the proliferation of morphologically aberrant (“hairy”) B-lymphocytes. Approximately 2,500 new cases of HCL are reported annually in the US and Europe, with a 4:1 predominance in males vs. females that is unusually high compared to other hematological diseases. Most HCL patients have the classical form (cHCL) of the disease and respond well to initial treatment, with an extended, progression-free period. Relapse and more rapid progression can occur after 5-15 years. However, up to 10-15% of patients have variant HCL (HCLv), a more aggressive disease with a limited remission period and less favorable prognosis. Neither of these forms of HCL are curable, and progress in addressing this unmet medical need will depend on a greater understanding of the disease and the development of more efficacious therapies.

A greater understanding of the disease was achieved when it was discovered that cHCL and HCLv cells have respective mutations in B-RAF and MEK, and these observations have led to therapeutic applications. While the BRAF V600E mutation is thought to drive the leukemic cell survival in most patients with cHCL, it is not found in the malignant cells of patients with HCLv. In contrast, mutations in MEK are found in some patients with HCLv and offer an opportunity for targeted therapeutic intervention. There is much more to learn about the respective diseases that ultimately may lead to improved treatment and possible cures.

For a more detailed description of HCL, as well as potential laboratory and clinical research avenues, please follow the link for the document entitled “[Statement on Future Research and Therapeutics for Hairy Cell Leukemia](#).”

I. **Goal of the RFP**

HCLF and LLS have joined forces to invest up to \$10 million over 5 years in targeted research to build a more comprehensive foundational understanding of the molecular basis of hairy cell leukemia, develop better therapies, and optimize outcomes for patients with HCL. This initiative is called The Hairy Cell Leukemia Foundation-Leukemia & Lymphoma Society HCL2025 Initiative (HCL2025).

II. **Research Focus Areas**

While investigators are encouraged to submit proposals in any clinical or biological topics related to hairy cell leukemia, certain research areas will be prioritized. On the clinical side, these include a) studies of innovative treatments for situations of high unmet medical need that require accurate diagnosis and characterization of the HCL-like disease spectrum, including classical HCL and HCLv; b) novel strategies to treat infections associated with HCL; and c) risk stratification and development of targeted treatments. Equally important, we also seek a deeper understanding of the disease and will support studies focused on a) uncovering novel features of HCL biology and cellular vulnerabilities; b) investigations into mechanisms of HCL relapse and therapy resistance; and c) efforts to establish and validate *in vitro* and *in vivo* models of the disease. Such fundamental studies should be focused toward translational potential and driven ultimately by the goals of improved patient outcomes and reduction or elimination of disease.

III. **Call for Proposals**

A. **Grant Funding Mechanisms**

HCLF and LLS are activating a global call for inventive proposals that have the potential for high impact in the field of HCL. Research funding during this first RFP will be allocated as stated below. Additional funding for projects that are successful may be granted in years 4 and 5 of the program. The grant programs are as follows:

Synergistic Team Award (STA). One will be awarded. This 5 year, \$2.5 million multi-investigator grant will focus on novel clinical trial(s) in HCLv or cHCL; the group may be from multiple centers. The group must have the knowledge and capacity to perform biomarker/PD assessment and/or basic HCL biology research.

Translational Grants (TRL). 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 will be considered.

Exploratory Awards (EXP). These 2 year, \$250,000 awards will support projects focused on both basic studies and/or therapeutic development. The award is designed for investigators who are currently working outside the HCL field but can add significant value toward understanding HCL.

B. **Eligibility**

HCL2025 welcomes applications from independent investigators (generally at least assistant professor-level or equivalent) of any nationality from appropriate academic institutions in any nation. An applicant may only be a Principal Investigator (PI), co-PI, STA Program Director (PD), and/or STA Project/Core Leader on a maximum of two grant applications, while there is no limitation on the number of collaborators.

The PI or PD must have a significant track record in the area of hematology and/or blood cancer research. If the scientific achievements and expertise of the PI or PD are in another scientific area, they must have a Co-PI (TRL and EXP) or at least one Project Leader (STA) who has the required significant track record in the area of hematology and/or blood cancer research.

The proposed research must be directly aimed toward advancing our understanding of and/or treatments for HCL. Projects must be concerned with understanding properties and vulnerabilities of HCL and/or focused on developing and testing novel HCL therapies. Applications that do not meet the relevance requirement will be disqualified.

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 eligibility, and all eligible applicants will be invited to submit a Full Application. Both LOI and Full Application submissions must be made electronically through the [LLS Research Portal](#).

Full Applications will be reviewed by a committee composed of experts in HCL, 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 HCL patients. HCLF and 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 HCL2025 Guidelines and Instructions documents available on the LLS website ([LLS Academic Grants](#)) or through these links:

[STA Guidelines & Instructions](#)

[TRL Guidelines & Instructions](#)

[EXP Guidelines & Instructions](#)

D. Key Dates

Phase	Date
Call For Proposals	November 2, 2020
Letter of Intent Due	January 29, 2021 at 3 PM ET
Notification of Full Application Invite	February 5, 2021
Full Application Deadline	April 16, 2021 at 3 PM ET
Review Panel Meeting	June 2021
Notification of Awards	August 1, 2021
Grant Term Begins	October 1, 2021