Research Accelerator for Follicular Lymphoma – I (RAFL – I)

Translational Grant (TRL)
Guidelines and Instructions

Effective dates:
July 1, 2024 – June 30, 2025

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Application Compliance

- It is highly recommended to access the **LLS Research Portal, Fluxx**, at https://lls.fluxx.io to begin the application process well in advance of any deadlines. In addition, each stage of the application process (letter of intent/full application) should be completed well before the deadlines.

- No aspects of the application, except regulatory approvals, will be accepted past the deadline.

- All components of the application must be presented in the order indicated in these guidelines.

- Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template. Font must be black Arial 11 pt. including figure legends, which should be text boxes separate from the figure itself. **If character limits and font restrictions are not adhered to, or the preset margins are altered, the application may be administratively disqualified.**

- Line spacing is preset in the Word document. **Do not change this setting**. Pasting text from another document into the template may result in a change in the line spacing. Check the line spacing in the template before pasting, and if there is a change after pasting, return the line spacing to the original setting. Any modifications in line spacing, particularly if the change allows for more text to fit into the page, **may result in administrative disqualification of your application.**

- Do **not** attach documents to the application that are not specifically called for. **The application may be administratively disqualified if this rule is violated.**

- **The PI and/or Co-PI** may apply to more than one grant program during an application cycle if the aims do not substantially overlap with the aims of any other application across all programs.

- **Collaborators or Key Personnel** may be part of other RAFL projects or other grant program applications, **provided it is evident that the research to be conducted and aims differ**.

- All duplicate grant proposal submissions with substantially overlapping aims are subject to administrative disqualification, and such proposals will not be reviewed further or considered for funding. Contact researchprograms@lls.org with any questions about this policy or to discuss with LLS scientific staff any questions concerning potential overlap.

- Completion of several steps in the process initiates emails from the LLS Research Portal. LLS staff may also send emails during the application process. Spam filters should be monitored for these emails. Contact researchprograms@lls.org if expected emails are not received by the times indicated in these guidelines or if you have any questions not clarified in this document.

- Note that **there are two subprograms under the RAFL Research Initiative.** Please ensure that you are applying to the subprogram that best fits the goals and structure of your proposal.

About The Institute for Follicular Lymphoma Innovation

The Institute for Follicular Lymphoma Innovation (IFLI) is a global non-profit, private foundation dedicated to accelerating the development of innovative treatment options for patients with follicular lymphoma. IFLI supports cutting-edge research and technology to lead to the development and commercialization of novel therapeutics and/or biomarkers for the treatment of follicular lymphoma (FL), and to understand the biology of FL. The foundation deploys its budget across grants, project-based partnerships, and venture philanthropy investments to achieve its innovation goals. IFLI aims to promote data sharing among researchers and institutions working on different aspects of FL research, fostering collaboration, and enabling the exchange of knowledge and expertise. Learn more at i-fli.org.

About The Leukemia & Lymphoma Society, Inc.

The Leukemia & Lymphoma Society, Inc. (LLS) is a national voluntary health agency dedicated to the conquest of hematologic malignancies and relevant premalignant conditions. LLS supports research, patient aid, community service programs, advocacy, and public and professional education.

Program Description

Follicular lymphoma (FL), a type of non-Hodgkin lymphoma, is an indolent blood cancer for which there is no cure. FL patients may experience varied clinical courses. For many patients, FL will progress slowly and either not require therapy (a “watch and wait” situation) or respond well to chemoimmunotherapy. Many of these patients enjoy long survival times with no additional therapy. However, some patients either do not respond, or will relapse after a long period of remission. In its most aggressive form, some patients (3-8% within 10 years of diagnosis) will experience transformation of FL to a rapidly progressing disease (tFL) leading to mortality within a few years after transformation[i]. Therefore, better treatment strategies for long-term FL control are needed in each of these varied populations. Ultimately, the overarching goal is to achieve a cure in which FL is eradicated, and therapy can be discontinued.

To achieve this bold goal, scientists and clinicians must tap into the innovations and emerging technologies to solve three critical objectives. In this next era of FL research, we believe:

- The biology of non-responders and patients who relapse can be targeted for therapeutic effect. New technologies may elucidate the unique biology of indolent lymphomas and their tumor microenvironment (TME), pinpointing mechanistic vulnerabilities[ii].
- More durable response can be achieved. New diagnostic and monitoring strategies may optimize the sequencing of immunotherapy and precision medicine approaches[iii].

- Better methods to identify patients at risk of transformation of FL (tFL) can be developed, along with new targets and treatment regimens to reduce the burden of early mortality in tFL patients[i].
- Serendipitous observations will open new avenues of investigation.

To address these challenges and to encourage innovative research, The Leukemia & Lymphoma Society (LLS) and Institute for Follicular Lymphoma Innovation (IFLI) have joined forces in a strategic partnership called the Research Accelerator for Follicular Lymphoma (RAFL).

LLS and IFLI are jointly funding creative and ambitious research and development proposals under the RAFL program. International and US-based applicants are welcome to apply. Two funding cycles are anticipated (RAFL-I opening 2024, with funding commencing in 2025 and RAFL-II opening in 2026, with funding commencing in 2027), with total funds of at least $20 million US dollars available for meritorious research.

Innovative projects that have the potential for high impact in the field of FL may cover discovery, translational and/or clinical research. Successful candidates will be established investigators in FL or related fields with demonstrated track-records of significant contributions. Cross-disciplinary collaboration including industry partnership is encouraged. Teams may be strengthened with investigators who bring special expertise in epigenetic or apoptotic control, computational skills, data science/AI, animal model development, neoantigen discovery, and antibody treatment to the project in FL.

[i] Parry et al. DLBCL arising from indolent lymphomas: How are they different? Seminars in Hematology 2023; 60: 277-284.

[ii] Radtke et al., Multi-omic profiling of follicular lymphoma reveals changes in tissue architecture and enhanced stromal remodeling in high-risk patients. Cancer Cell 2024; 42: 444-463.

[iii] Friedberg, J. Update on follicular lymphoma. Hematological Oncology. 2023; 41(S1): 43-47.

Research Focus Areas

The development of new therapeutic options and monitoring strategies will address key unmet needs in FL. Potential areas of interest are described below.

- New Therapeutic Development – Development of new chemical entities and other therapeutic approaches is needed to address disease heterogeneity and resistance/relapse. Examples include:
  - New therapeutic modalities such as, but not limited to, BCL6 degraders, CREBBP controllers, transcriptional regulators.
  - Immunotherapy agents targeting novel antigens or leveraging the activity of other agents.
  - New therapies for transformed FL.
  - New therapeutic approaches that impact patient quality of life.

- Target Identification - Leveraging innovation in, for example, genomics, computational biology, and data science for identification of novel therapeutic targets.

- Follicular Lymphoma Biology - Research programs to identify and understand the cellular and molecular determinants of tumor heterogeneity driving FL progression, treatment resistance, and transformation. Examples include:
  - Common precursor cell – identification and demonstration by functional studies that disease and progression/recurrence are driven by a common precursor cell. Design of new therapeutic strategies to eradicate common precursor cells.
  - TME and immune biology – identification and demonstration of changes in TME that contribute to FL resistance and/or transformation.

- Biomarker Discovery and Development – Research programs to identify and validate surrogate or ancillary biomarkers for FL and tFL. Examples include:
  - biomarkers to improve diagnostic and disease progression prediction (e.g. POD 24, tFL) via patient stratification, to inform treatment selection, to allow response monitoring, and to decrease time on ineffective therapies.
  - biomarkers in non-relapsing patients to determine if functional cure is durable, complete cure.

- Monitoring and Diagnostics - Leveraging innovation in next-generation sequencing to diagnose relapse before clinical or radiological evidence, optimize treatment response, and inform treatment selection. Plasma-based methods have the potential to improve monitoring and enhance patient quality of life.

- Translational tools and technologies –
  - new disease models including preclinical animal models.
  - leveraging data science/AI to drive discovery and development of new personalized medicine approaches.

RAFL- I Grant Funding Mechanisms

LLS and IFLI are activating a global call for innovative proposals with potential for high impact in the field of FL. RAFL-I will support two types of awards, Synergistic Team Awards (STA) and Translational Grants (TRL):

- **Synergistic Team Award** —This multi-investigator grant is designed to support a coordinated, focused, and significant effort to understand the biology of follicular lymphoma and develop effective treatments for the disease. A team comprised of multiple investigators from the same or different institutions working collaboratively will be required for this grant.

- **Translational Awards** — These grants aim to support clinical and/or biological research. Activities supported by these awards should lead to initiation of a clinical trial by year three of the grant.

For the RAFL-I 2024-25 cycle, a single Synergistic Team Award and up to two Translational Awards will be awarded.

These guidelines are for the TRL subprogram. Please review the link below regarding the STA subprogram to ensure you are applying to the subprogram that best suits your research. If you are unsure, please contact researchprograms@lls.org.

STA Award: Guidelines and Instructions

Translational Awards (TRLs)

The overall goal of the TRL award mechanism is to reduce the time between laboratory findings and actual clinical utility, putting research on the bench-to-bedside fast track when it comes to finding better treatment and cures for follicular lymphoma. TRL awards will support translational research that moves potential therapeutic candidates toward clinical trials within 2-3 years of the 5-year award period. For example, completion of IND-enabling studies and IND approval are desirable goals for these projects on the path to a clinical trial.

LLS and IFLI specifically seek applications that propose novel approaches to the prevention, diagnosis, or treatment of follicular lymphoma, or bring a novel approach from a related field to FL. Proposals should be based on molecular, cellular, or integrated systems findings and be conceptually innovative.

The TRL grant is expected to be led by a single principal investigator (PI), but may have a Co-PI, if appropriate. A clearly outlined translational aspect is a plus for TRL proposals in basic research, but outstanding biological research proposals without a translational element will be considered.

The maximum total award is $1,750,000. The maximum total annual award is $350,000 for each year of the five-year grant. The maximum annual indirect cost is $35,000 (10% of total annual costs). An applicant may claim less than 10% indirect costs and apply those costs to the direct costs.

The budget must align with the actual costs of the research; this will be reviewed both by the IFLI/LLS Joint Leadership Group composed of IFLI and LLS scientific staff.

In addition to these funds, IFLI may in its discretion make up to $2.25M available in each grant cycle as awards to supplement funded RAFL Grants (“Supplemental Funds”). IFLI will not award any Supplemental Funds until at least the second year of the RAFL grants. Progress reports will serve as a means for Supplemental Funds to be requested and for such requests to be evaluated by IFLI and LLS.

Post Award Management

Annual TRL Progress Meeting
Each year, there is a mandatory, in-person Progress Meeting for representatives from the RAFL TRLs and all currently funded LLS Translational Award (TRP) teams. LLS and IFLI leadership will attend.

Professional Headshot for the TRL Principal Investigator
LLS requires submission of a photo (head shot) for the Principal Investigator. The photos will be used alongside the Biography and Lay Description which is collected at the full application phase for publicity and fundraising purposes and displayed on the LLS and/or IFLI websites. ***The photos are due prior to the start of funding.***

Annual Reports
Financial, Intellectual Property, Conflict and Other Disclosures, and Progress Reports are due annually while Publication Reports are due quarterly. The Progress Report will contain a summary of the year's research and is essential for staff evaluation of progress. Release of the next TRL funding payment is contingent on approval of satisfactory reports.

Progress Evaluation
A major Go/No Go decision will be made by LLS and IFLI at the end of two years, based on the Second-Year milestone included in the Full Application. Progress reports, teleconferences, and presentations at the Annual TRL meeting will form the basis for the evaluation and decision.

Who Can Apply?

Citizenship

The program welcomes applications worldwide from appropriate academic institutions and investigators of any nationality.

General Eligibility

Applicants must hold a PhD, MD, DVM, or equivalent degree and must be affiliated with a non-profit Institution at the time funding commences and for the duration of the award. Applications may involve multiple institutions.

Institutional Affiliation

Applicants (PI) must be independent investigators affiliated with a non-profit Institution. Individuals from non-academic organizations are not eligible to apply as the PI (but may participate as Collaborators).

Application Limitations

An applicant may submit one application per cycle as a STA Director or Principal Investigator in either or both RAFL grant mechanisms, provided that the project is unique. Applications from the same research lab that exceed the 1 + 1 limit will not be accepted. A PI or PD can serve on only one other application as a Project/Core Leader (STA) or as a Co-Principal Investigator (TRL). A Co-Principal Investigator or STA Project/Core Leader may serve as a Co-Principal Investigator or STA Project/Core Leader on a maximum of two applications. A Principal Investigator or Co-Principal Investigator can serve as a Collaborator on an unlimited number of applications.

Leadership

The TRL is led by a Principal Investigator who is responsible for writing and submitting the proposal including the budget, the conduct of the research project, and adherence with all stipulations made by IFLI and LLS in this document, and the Funding Agreement, if funded. Successful candidates will be established investigators in FL or related fields with demonstrated track records of significant contributions.

Leadership Limitations and Staffing

The Principal Investigator (PI):

- MUST be a person (companies or institutions are not eligible)
- MUST be an independent investigator at the time of the Letter of Intent, defined as a scientist who has dedicated laboratory space, directly hires, and supervises laboratory personnel (technicians, graduate students, postdocs, and staff scientists), and makes all decisions concerning research activities and use of the grant funds
- MUST be an established investigator, defined as a researcher with more than 3 years in an independent faculty appointment at the time of the Letter of Intent
- may only submit ONE application per cycle as PI or Co-Principal Investigator
- CAN serve as a Collaborator on other applications provided aims differ

NOT eligible to apply for a grant in this program:

- predoctoral scientists or postdoctoral fellows
- junior principal investigators (within the first 3 years of initial independent faculty appointment)

A Co-Principal Investigator (Co-PI):

- MUST be a person (companies or institutions are not eligible)
- MUST be an established, independent investigator with more than 3 years in an independent faculty appointment at the time of the Letter of Intent
- if the PI has the necessary track record in follicular lymphoma research, a co-PI may strengthen the proposal but is not required
- if the PI has no expertise or proven track record in follicular lymphoma research, an expert Co-PI is REQUIRED
- only ONE Co-PI is allowed
- at least one research aim of the proposal fully depends on the Co-PI expertise, typically performed in their laboratory and/or facility
- MUST be designated at the Letter of Intent phase detailing the nature and extent of the scientific interaction
- MUST be included in the “Interaction with Other Investigators” section as part of the Full Application
- the Co-PI MUST provide a letter detailing the scientific interaction as part of the Full Application

A Named Collaborator or Collaborators

- MUST be a person or persons (companies or institutions are not eligible)
- a maximum of TWO NAMED collaborators are allowed

- each Named Collaborator MUST provide a letter of support detailing the nature of the scientific interaction
- may strengthen the work proposed but is not required
- may supply the PI with a rare reagent that is not available commercially
- may provide expert insight, guidance, or feedback on research progress
- CAN serve as a Collaborator on other Applications in this program in the same cycle

An "unofficial" collaborator or collaborators

- may be a person, an institution or a company supplying practical support, such as access to a single rare reagent or an instrument
- may not provide scientific expertise, that role is reserved for the Co-PI and the Named Collaborator(s)
- may strengthen the work proposed but is not required
- there is no limit on the number of unofficial collaborator(s)
- may not be included in the "Interaction with Other Investigators" section, only provide a letter of support
- CAN serve as a Collaborator on other Applications in this program in the same cycle

Overlapping aims in grant proposals submitted to LLS

- **The PI and/or Co-PI** may apply to more than one grant program during an application cycle if the aims do not substantially overlap with the aims of any other application across all programs.

- **Collaborators or Key Personnel** may be part of other RAFL projects or any other grant program applications provided the aims differ.

Research Environment

Investigators must demonstrate that their research environment is equipped and suitable for all aspects of the work. Applications for projects that depend on clinical samples or drugs which are not commercially available must provide documentation confirming sample or drug availability. Collaborations between multiple investigators to strengthen the work proposed will be considered favorably but are not required. Applications may involve multiple institutions and collaborators; however, the applicant (principal investigator) will be responsible for signing off on all terms of the funding agreement.

Institution's Acceptance of the Terms and Conditions

Applicants who are offered a Translational Award will be sent a funding agreement. This must be accepted and signed by the Applicant and by responsible institutional officials. Currently, the NIH does not accept LLS's Terms and Conditions.

Relevance

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

Application Process & Applicant Notification

The application process will occur in two phases, the Letter of Intent (LOI) phase and Full Application phase.

Key Dates

Phase	Date
Call For Proposals	July 1, 2024
Letter of Intent Due	September 9, 2024, 3:00 PM ET
Notice of Full Application Invite	No Later than October 18, 2024
Full Application Deadline	January 13, 2025, 3:00 PM ET
Review Panel Meeting	March 2025
Notification of Awards	April 2025
Award Start Date	July 1, 2025

All submission deadlines will be enforced. Please note that all times are Eastern Time (ET). If any date falls on a weekend or US holiday, the deadline becomes the next business day.

It is highly recommended that submissions are done *prior* to the deadlines. Internet traffic may be slow near the deadlines, which may result in difficulties in submissions. In addition, LLS's response time to questions may be delayed by the high volume received near the deadlines. Therefore, it is imperative that any submissions or questions be posed to LLS well ahead of any deadlines.

Review Process for the Letter of Intent and Full Application

Letters of Intent for the RAFL-I TRL Program are reviewed and approved by IFLI/LLS after submission. The LOI stage is a competitive step; all LOIs will be reviewed for eligibility as well as for relevance and responsiveness to the goals of the program. If invited for full application submission, the applicant will be notified by email and will immediately have access to the application submission capability in the LLS Research Portal. If you have not received an email

regarding your LOI by **October 18th, 2024**, contact researchprograms@lls.org.

Full Applications received by the January 13, 2025, 3 PM ET submission deadline will be reviewed by the IFLI/LLS Joint Leadership Group for responsiveness to the RAFL program goals and adherence to the application guidelines. An application that does not meet the program goals, scope, or guidelines will be administratively disqualified.

Full applications will be reviewed by a peer review committee composed of a diverse group of external experts. Applications will be evaluated according to the Review Criteria listed below and assigned an initial score by the primary and secondary reviewers. Only applications that fall above a scoring level determined by program staff and the committee chair will be discussed in detail for final ranking by the entire committee. Once ranked by the peer review panel, the highest scoring proposals will be reviewed by LLS and IFLI research staff. LLS and IFLI will identify those proposals to be funded based on scientific merit, responsiveness to programmatic goals, and budget availability. Final approval of funding will be made by the Oversight Boards of the IFLI and LLS.

Review Criteria for Full Application

An application receives a Priority Score based on a 9-point rating scale (1=most meritorious; 9=least meritorious) using these criteria:

- the conceptual basis upon which the proposal rests
- the novelty of the concept and strategy
- innovation in focus and/or approach
- the quality and relevance of the preliminary data
- the feasibility of the proposed experimental approaches and research plan
- thoughtful and clear presentation
- the probability that the investigation will yield discoveries that can lead to clinical translation and a trial within 2-3 years into the 5-year award
- the feasibility and appropriateness of the proposed milestone to be completed by the end of year two (2)
- experience, qualifications, and track-record of investigators
- adequacy of resources and environment (facilities, access to patient samples if needed, data management, and data analysis)
- adequacy of provisions for protection of human subjects
- **DEI**: the applicant demonstrates understanding of any health disparities associated with the disease

Any Applicant selected for funding will be notified by the date indicated in the Key Dates section**.** Please do not call or email IFLI or LLS to determine whether the application has been received, when it will be reviewed, or the results of the review. Please check the LLS Research Portal for the status of your application. Final scores are confidential and are available only to IFLI Board of Directors and administrative staff, LLS staff, LLS's Medical & Scientific Affairs Committee and its Research Subcommittee, and LLS's National Board of Directors.

If there is a person that you would like excluded from reviewing your LOI and/or full application, please email researchprograms@lls.org no later than the LOI deadline of **September 9, 2023**. LLS will make every effort to accommodate these requests but cannot guarantee such exclusion(s).

General Application Instructions

All submissions must use the LLS Research Portal at https://lls.fluxx.io. It is recommended that you familiarize yourself with this portal well in advance of any deadlines.

Registration
Both the applicant and institution must be registered in the LLS Research Portal. If you have applied to LLS in the past, you do not need to create a new registration. Simply log in with your username and password. If you forgot your password, click the "reset or create password" link and enter your email address. The system will send your username and a link to update your password. Once updated, the applicant can begin the LOI. If you are a first-time user to the LLS Research Portal, please complete the intake form located at this link: Account Creation Request so an account can be created for you. Only LLS staff members have administrative permission to create new accounts.

Institutional Designation
Applicants should create their profile from the standpoint of where they will perform their research described in the application. The applicant must indicate the name of the institution as well as the name of the signing officials for that institution. If your institution is not displayed as an option under this field of the application, you may contact researchprograms@lls.org to have it registered in the system. Please provide the official's full name and email address.

Data Entry
Both the LOI and the full application may be accessed and changed multiple times as needed prior to the submission deadline. However, neither the LOI nor the full application can be changed once the respective deadlines have passed or the final application has been submitted. Moreover, some fields may not be modified in the full application following submission of the LOI.

Forms and Format
Applicants will provide information on the LLS Research Portal and downloadable templates at the LOI and full application phases. All information must be typed in English using commonly accepted grammar and punctuation. Some information will be captured when applicants populate fields on the LLS Research Portal. Fields in bold are required.

Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template.

Font must be black Arial 11 pt. including figure legends, which should be text boxes separate from the figure itself. *If character limits, font restrictions, margins and/or page limitations are not adhered to, the application may be administratively disqualified.*

In case there is a discrepancy between the application template and the guidelines document, the downloadable template supersedes the guidelines.

Contacting LLS
Questions that are not clarified in this document or the LLS Research Portal should be addressed to researchprograms@lls.org.

Beginning an application
The application will be completed in two phases: Letter of Intent and Full Application. Below are step-by-step instructions for applying:

1. Read these Guidelines & Instructions in full and familiarize yourself with the LLS Research Portal.

2. Log into the LLS Research Portal, and under "Information" in the left navigation bar, select Research Accelerator for Follicular Lymphoma program. Click "Apply to RAFL!" to begin the application process (well ahead of the deadline).

3. Click "Edit" and follow the instructions for each web form field. Bold font indicates required information.
    - Character limits include spaces. Character and other length limits are strictly enforced on the web form and the uploaded project description template. If character limits are not adhered to, the application may be disqualified.
    - You may save your work and return to it at any time by clicking "Save." Clicking "Submit" will lock your application and prevent further modification at that stage. Contact researchprograms@lls.org if you submit in error (must be before the deadline).

4. Once your LOI is submitted, you will receive an automated confirmation email within two business days from the LLS Research Portal. Consider that these emails may end up in your spam filter.

5. If your LOI is selected, you will have access to the full application. Click on your request, found in *New* or *Pending*, to continue with your application.

6. Please carefully follow the instructions on the LLS Research Portal and this document. Full applications require completion of both the web form and the application template, which should be downloaded from the *Project and Supporting Documentation* section of the LLS Research Portal. **Failure to follow all application instructions may result in administrative disqualification of your application.**

7. Submit your full application to the LLS Research Portal prior to the full application deadline. **We strongly recommend submitting well before the deadline, as site traffic on the day of and days leading up to the deadline will be heavy.**
    - Contact researchprograms@lls.org with any questions about the application phases that are not addressed in the LLS Research Portal or this document.

8. To create a fair process to all applicants, these Guidelines & Instructions and information on the LLS Research Portal must be followed. ***Do not ask for exceptions to these policies, including but not limited to exceptions to deadlines or making corrections to your document past the deadline.***

Carefully check every page of your application prior to submission. You are ultimately responsible for this submission, even if someone else submits your final application.

At any time during the application process, including after submitting your full application, you can check the status of your application by logging into the LLS Research Portal, selecting your application (under *Requests* in either "New or Pending" or "Submitted") and referring to the status in the yellow box at the top of the page.

If you have any technical difficulties with the LLS Research Portal, please contact researchprograms@lls.org.

Detailed Letter of Intent Phase Instructions

The LOI must be submitted by **September 9, 2024**, **at 3:00pm ET** via the LLS Research Portal or the following business day if this date falls on a weekend or a U.S. holiday. The Applicant should carefully craft the information requested in the LOI as this information is automatically populated into the full application and is subject to the Changes clause listed below.

The LOI will be evaluated by the IFLI/LLS Joint Leadership Group. If the LOI is approved, the Applicant will be notified by an automated email from the LLS Research Portal stating that they may proceed to the Full Application phase. Applicants may also check the status of their LOI on the LLS Research Portal.

There are two main aspects to the Letter of Intent Phase: all LLS Research Portal webform fields and the "Previous Studies/Preliminary Data" (2 pages maximum) downloadable template for completion.

Organization Information

(If the institution or officials are not listed, please contact researchprograms@lls.org with the name and email address for the official you need added)

Institution: Indicate the name of the institution where the research will be performed. If this institution is not listed, please contact researchprograms@lls.org with the institution name and address so an account can be created.

Location/Department: This field auto populates. Please do not change it.

Principal Investigator: The Principal Investigator is the applicant.

Institutional Signing Official (ISO): The ISO is the institutional representative responsible for signing and agreeing to the accuracy of the application and the terms and conditions of the award, should the application be selected for funding.

Financial Officer: The Financial Officer is the institutional representative responsible for the financial administration of externally funded research.

Additional Access (Admin/Assistant): Access may be given to personnel to assist in the application process. This is the institutional representative responsible for the day-to-day administration of externally funded research (or the Research Administrator).

Technology/Transfer Official (TTO): The TTO is the institutional representative responsible for overseeing Intellectual Property.

Additional Contact (Assistant): This is optional and may be a personal representative of the principal investigator, such as an administrator, an assistant, or a laboratory manager to be used as an additional point of contact, typically in the post-award phase. The Additional Contact will not have access to the application in Fluxx.

Zip Code of the Institution: Enter the zip code of the institution if located within the United States. You will need to select the zip code from the drop-down menu to ensure it is captured in the zip code field. If not located within the US, this can be left blank.

Co-PI: A designated Co-PI has a specific role and associated responsibilities in the proposed project. One Co-PI is allowed. The designated Co-PI cannot be changed after the Letter of Intent phase.

Project Information

Project Title: Provide a title adhering to the 150-character limitation (which includes spaces).

Project Summary (Public): Provide a short summary (approximately 2-4 sentences) in lay language. Charts and graphs cannot be included in the project summary section of the LLS Research Portal.

Brief Biography (for the PI only): A brief biography written for a lay audience (approximately 1,000 characters including spaces).

Structured Scientific Abstract: Briefly describe the overall proposed research in **6,000** characters (including spaces) or less using technical language in the following sections:

a. **Background and Preliminary Data**: Describe the background and overall purpose of your proposed study. Include a brief description of the preliminary data on which the study is based. (Maximum 1,500 characters)

b. **Goals and Objectives**: Provide a succinct project overview. Succinctly state the Specific Aims. Summarize your research plan: design, approach to analyzing your findings, and describe what you expect to find or achieve. (Maximum 1,500 characters)

c. **Expected Outcomes and Translational Significance**: Describe the potential impact of your study on follicular lymphoma. How will your study translate scientific

discovery into a solution for a problem in the diagnosis, prevention, or treatment of follicular lymphoma? (Maximum 1,500 characters)

d. **Role of the Co-PI (Optional):** If applicable, describe the role, responsibilities, and anticipated time commitment of the Co-PI, i.e., which research activities and specific aim(s) depend fully on the Co-PI and how. (Maximum 1,500 characters)

Once the LOI has been submitted, the Structured Scientific Abstract may not be changed without approval. If awarded, sections a-c will serve as a scientific abstract.

Lay Description (Public): Briefly describe the proposed research in lay language. Include a description of the proposed treatment, the patient population to be studied, the clinical problem/research question that will be addressed, and how the results will be measured. Describe the potential impact to patients and the timeframe in which the patient benefits might be realized. Clearly state how your study will progress into a solution for a problem in the treatment or prevention of a blood cancer or pre-blood cancer condition.

The Lay Description is essential for LLS to continue successful fundraising to support our current and future grantees, including the later years of ***your*** award, should it be funded. Thus, we require a well-written Lay Description, with sufficient detail and suitable language for non-scientists. Do not include confidential information, as the Lay Description (and Project Summary) will be shared with others. The Lay Description has a maximum of 3,000 characters, including spaces. Scientific/Greek characters or symbols must not be used.

Amount Requested: Enter the total amount of funding requested over the life of the grant (Maximum $1,750,000). The amount requested on the LLS Research Portal should match the budget section of the full application template. See Program Description section for annual maximums. Please note that LLS does not follow NIH guidelines for budgets. Please adhere to the LLS rules as outlined in this document.

Key Personnel: Include collaborators Key personnel (internal or external to your institution) may help strengthen your application. Please include their name(s) and institution(s). *This section helps LLS identify conflicts with reviewer assignments.*

Proposed Start Date: The start date for TRL grants is July 1, 2025.

Proposed End Date: The end date for TRL grants is June 30, 2029.

Previous Submission: Indicate whether you have previously submitted a similar proposal to LLS and indicate the date of any prior submission.

Previous Studies/Preliminary Data: Upload the Previous Studies/Preliminary Data (2 page maximum) to the “Project and Supporting Documentation” section of the web form. Text, figures, and references must be written single spaced in Arial size 11 font. Text figures should be easily readable without magnification. Please note that references are not required at the LOI phase but are required at the full application phase. Only one PDF is accepted in this section, so delete any other documents uploaded during the process. **Note**: When uploading this template to the LLS Research Portal, please ensure you choose the correct file name which should read

"Previous Studies/Preliminary Data" which you can choose from the document upload drop-down menu. If the file name is incorrect, you will not be able to submit the LOI. In addition, when you name your file, please only use underscores or spaces to separate words.

All LOI required forms must be consolidated into a single PDF file and uploaded to the Project and Supporting Documentation section of the LLS Research Portal**.**

LOI Save, Review, and Submit Instructions

Validation will automatically occur after clicking the "Save" button. Validation is a safety measure for the applicant to ensure that all required fields are complete. If required fields are empty or incomplete, the system notifies the applicant of fields that require information.

After clicking "Save" you will be directed to review your LOI. Please ensure all information is accurate, and then click the "Submit" button to submit your LOI to LLS.

Each applicant must submit the LOI by **September 9, 2024 at 3:00 pm ET** via the LLS Research Portal. After clicking the "Submit" button, the applicant will receive an automated email within 2 business days stating that your information was successfully submitted. If you do not receive the email from the LLS Research Portal within two business days of LOI submission, please e-mail researchprogram@lls.org. Signatures of the applicant and institution officials are not required for submission of the LOI.

The applicant is ultimately responsible for the submission, regardless of who actually is uploading information on the LLS Research Portal. Every year, LLS has a small number of people that notice problems with their letter of intent after the deadline. The solution to this problem is very simple and in the hands of the applicant:

- **Check your letter of intent prior to final submission.**
- **Submit well ahead of the deadline.**
- **We are not responsible if any applicants are unable to submit by the deadline if our system indicates that:**
  a. **the letter of intent procedure was started less than 24 hours before the deadline,** or
  b. **a previously started letter of intent file was then only picked up again less than 3 hours before the deadline.**

Changes
Information collected in the Letter of Intent Phase will automatically populate fields in the full application. Once submitted, changes may only be made after receiving prior approval from LLS. The applicant must email researchprograms@lls.org requesting any change and identifying the elements to be changed. Any changes made without the prior approval of LLS may result in the disqualification of the application.

Detailed Full Application Phase Instructions

Each invited applicant must submit a full application by **January 13, 2025, at 3:00 pm ET** via the **LLS Research Portal** at https://lls.fluxx.io or the following business day if this date falls on a weekend or a U.S. holiday. Most sections of the full application will carry through from the LOI Phase. Information that carries through must not be modified; changes cannot be made to the LOI components after the LOI Phase deadline. The remainder of the full application consists of web form components and elements to be uploaded as a ***single PDF***.

All sections in the full application template must use **Arial 11-point font**. Margins are pre-set and must not be changed.

Failure to submit as a single PDF in the order below may result in disqualification of the application.

1. Cover page (1 page)
- **Name of Applicant and Co-PI (if applicable)**
- **Project Title**
- **Specific Aims**

2. Graphical abstract (1 page, does not count towards maximum page limit)
Provide a single figure, which will provide a brief overview of the project. This is similar to the graphical abstract in a Cancer Cell paper.

3. Description of Models and Reagents (no page limit)
Provide information on the models, reagents, and trials described in your project description. This provides reviewers with an easily accessible reference source and demonstrates feasibility of your research plans.

4. Project Description (14 pages total)
Download and complete the project description template, including all required signatures, and upload to the "Project or Supporting Documentation" section of the web form. Margins are preset and must not be changed. Text, figures, and references must be written single spaced in Arial size 11 font. Embedded figures must be legible.

Only one application PDF is accepted at the full application phase (Project Description Template combined with biosketch(es) and all applicable appendix documents). Do not delete the LOI "Previous Studies/Preliminary Data/Trial Summary" PDF file.

The project description is limited to fourteen (14) pages or less (including figures and references).
- the described project must have a clear and strong connection to or implications for understanding and/or treating follicular lymphoma
- compelling preliminary data are required
- the proposal must contain a lucid and succinct description of how project success can be translated to clinical application

- proposals must include the description of a distinct and quantifiable milestone (goal) to be achieved by the end of the second grant year; the significance, appropriateness, and impact of this milestone will be a key rating criterion during the review of the proposal; if the grant is awarded, the subsequent years of funding will depend on the successful achievement of this goal

In addition, the project description must include the following sections in the following order (suggested length for each is indicated):

- **Title and Aims** (1/2 page)
- **Significance of the Work** (approximately 1 ½ pages) with the following sub-sections:
    - Clinical/Scientific significance
    - Innovation
    - Relevance to follicular lymphoma
- **Background and Preliminary Data** (up to 3 pages)
- **Research Plan and Timeline (1 page)**
- **Experimental Plan, Potential Pitfalls, and Alternative Approaches** (up to 4 pages) *Note: A Clinical Protocol Synopsis may be placed in the Appendix.*
- **End of Second Year Milestone** (approximately ½ page)
- **Interaction with Other Investigators such as Co-PIs and Named Collaborators (if appropriate)** (approximately ½ page)
- **Resources and Environment** (Major lab items or facilities) (approximately 1 page)
- **References** (2 pages maximum): Use the *Blood* citation format and Arial 11pt. font

5. Budget

The Budget and Budget Justification should provide itemized detail for each major category for all years of the project. The budget can be summarized in year one and extrapolated for the remaining four years. All totals and subtotals should be completed on the form.

The aggregate costs over five (5) years cannot exceed $1,750,000. The maximum annual total cost (direct and indirect) cannot exceed $350,000.

Permissible Direct Costs include the following with the specified limitations:

- Personnel Expenses including salary, wage, or stipend with fringe benefits.
- Supplies & Materials requests should be itemized by category.
- Equipment Purchase requests must identify each item of equipment with an acquisition cost of more than $4,000.
- Travel Expense requests cannot exceed $2,000 per year of the award.
- Other Direct Cost requests can include patient care costs.

Permissible Indirect Costs (often referred to as Institutional Overhead, IDC, M&A, G&A, or pooled costs) are those costs incurred for common or joint objectives that cannot be readily identified with a particular project (general maintenance, utilities, library, etc.) as defined in the Office of Management and Budget, Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards. ***Indirect costs are limited to 10% of annual total costs requested.*** For institutions that do not choose to use these funds for indirect costs, LLS allows the funds to be applied to the Principal Investigator's stipend or fringe benefits cost.

Subaward budgets should be included within the main budget line items. Indirect costs can be included in the total indirect costs. Please note, LLS will only pay the funded institution, and that funded institution will be responsible for all subcontracting and subsequent payments.

Impermissible Costs include membership dues, tuition, books, journals, and publication costs.

a. Budget Justification
2 page maximum.

b. Signature Page
This form must be completed, including the indicated signatures.

6. Appendix
The following sections must be attached in this order to the end of the project description template to create a single PDF. ***No other information may be provided in this section.***

a. Principal Investigator's NIH Biosketch (This document is not required for Senior Staff/Collaborators but is required for any Co-Principal Investigator(s) identified in the application).
Use the most recent NIH biosketch format found on the NIH website. Publications submitted and under review should be indicated on the biosketch. An eRA Commons Username is not required.

b. Principal Investigator's NIH Other Support Document (This document is not required for Senior Staff/Collaborators but is required for any Co-Principal Investigator(s) identified in the application).
Use the most recent NIH Other Support Document format found on the NIH website. Must contain all current and pending support from any source. **In addition, specific aims must be listed for current and pending grants that may overlap or appear to overlap with the LLS application.** This includes any grants or portions of grants submitted to any organization, including LLS.

c. Co-Principal Investigator's NIH Biosketch (if applicable)
Use the most recent NIH biosketch format found on the NIH website. Publications submitted and under review should be indicated on the biosketch. An eRA Commons Username is not required.

d. Co-Principal Investigator's NIH Other Support Document (if applicable)
Use the most recent NIH Other Support Document format found on the NIH website. This form must contain all current and pending support from any source. **In addition, specific aims must be listed for current and pending grants that may overlap or appear to overlap with the LLS application.** This includes any grants or portions of grants submitted to any organization, including LLS.

If funding decisions about potentially overlapping, pending grants become available

following submission of this application, LLS must be notified within five business days of the applicant's receipt of that information.

IFLI and LLS recognize that some investigations, particularly those involving clinical trials, may require multiple funding sources, so overlap of specific aims with another grant may be appropriate and acceptable. The need for and details about such overlap should be clearly explained in the application. However, IFLI/LLS will consider an applicant's other current grant support in its funding decisions. This may result in IFLI/LLS funding only part of the grant or none of the grant, depending on the level of overlap. In addition, IFLI/LLS reserves the right to adjust the level of funding of an awarded grant should another overlapping or potentially overlapping grant that was pending at the time of grant submission be awarded to the applicant.

Failure to abide by these rules on disclosure of current or pending support may jeopardize the funding of the current grant application.

e. Collaboration/Support Letters

Required if reagents critical for the research are to be obtained from non-commercial and/or commercial sources and are not currently available in your lab.

f. Clinical Trial Summary (required where applicable) and optional Clinical Protocol Synopsis (not to exceed 8 pages)

Provide a **one-page summary** and a link to the clinicaltrials.gov website for any clinical protocol essential to the proposed research. Include IRB approval date, IRB compliance number, and effective dates of approval. Projects for which IRB approval is pending must include a statement to that effect. The applicant should notify researchprograms@lls.org of IRB approval prior to the grant review. Optional: include a Clinical Protocol Synopsis. DO NOT include the full clinical trial protocol.

The applicant must provide information **if a trial is receiving funding from a sponsor,** specifically, how much money is to be received and what the funds will be used for.

Full approval for any IRBs that are necessary for the research must be obtained by the award start date.

g. Assurances (Required)

Human Subjects:

The applicant must indicate if human materials or subjects will be involved in the proposed research. The status (approved, pending, or exempt) of the Institutional Review Board (IRB or equivalent oversight entity) approval must be provided. The Human Subject Assurance Number (OHRP) must be included. If the research project has received IRB approval, the date must be provided, and documentation must be included in the single PDF of the application.

If a project is exempt from IRB review, the certificate of exemption must be included in the single PDF of the application.

Laboratory Animals:
The applicant must indicate if laboratory animals will be involved in the proposed research. The status and date of Institutional Animal Care and Use Committee (IACUC or equivalent oversight entity) approval must be provided. The Animal Welfare Assurance number must be included. Documentation of institutional approval must be included in the single PDF of the application. The application may be submitted with IACUC approval pending but an award will not be made without documented IACUC approval if it was pending at the time of application submission. It is recommended that the applicant notify LLS before the grant review if the IACUC status has changed.

Recombinant DNA:
The applicant must indicate if the proposed research involves the use of recombinant DNA. Documentation of institutional approval must be included in the single PDF of the application.

Biohazard Statement:
The applicant must indicate if the proposed research involves the use of biohazards. If the applicant indicates affirmatively, then an institutional statement of assurances regarding potential biohazards and safeguards must be included in the single PDF of the application.

Your institution is required to have assurance procedures in place, so please check with them if you are unsure how to obtain your assurance approval documentation.

No attachments besides those listed above can be included in the Appendix. Applications that include additional documents besides those requested may be administratively disqualified.

Uploading the project document and final submission
All documents must be combined into a single PDF in the order listed above. Failure to submit as a single PDF in the order above may result in disqualification of the application. Upload the full application components, as a single PDF, in the "Project and Supporting Documentation" section on the web form. The file upload should be labeled, "TRL Project Description/Application" which you can choose from the document upload drop-down menu. **Do not delete the LOI "Previous Studies/Preliminary Data/Trial Summary" PDF file.**

LLS Research Portal Webform Updates

- **Budgeting Information**
  Enter the budgeting information as required on the web form fields.

- **Assurances**
  Respond to the assurance questions and indicate if approvals are pending or the date of approval with the approval number.

- **Applicant Assurance**
  Check the box to accept the terms as stated on the web form field.

Save and Review
Validation will automatically occur after clicking the "Save" button. Validation is a safety measure for the applicant to ensure that all required fields are complete. If required fields are empty or incomplete, the system notifies the applicant of fields that require information.

Submission & Confirmation
After clicking "Save" you will be directed to review your application. Please ensure all information is accurate, and then click the "Submit" button to submit your application to LLS. Only one application document and one Letter of Intent request document should be present. If extra documents remain after submission and before the deadline, email researchprograms@lls.org and let us know which documents to remove. You will receive an automated email **within 2 business days** stating that your information was successfully submitted. **If you do not receive the email confirmation of submission, contact LLS at** researchprograms@lls.org.

Carefully check your PDF prior to submission. If you notice problems with your PDF after you have submitted, email researchprograms@lls.org, and we will help you upload the correct document or delete any incorrect documents. This email must be received, with the correct document, prior to the deadline; there are no exceptions to this rule.

The applicant is ultimately responsible for the submission, regardless of who actually is **uploading information on the LLS Research Portal.** Every year, LLS has a small number of people that notice problems with their application after the deadline. The solution to this problem is very simple and in the hands of the applicant:

- **Check your application prior to final submission.**
- **Submit well ahead of the deadline.**
- **We are not responsible if any applicants are unable to submit by the deadline if our system indicates that:**
  a. **the application procedure was started less than 24 hours before the deadline,** or
  b. **a previously started application file was then only picked up again less than 3 hours before the deadline.**

Once the deadline has passed, only the following updates may be made:

- Regulatory approvals
- Significant updates to clinical trials:
  - IRB updates
  - Opening of the trial
  - Patient enrollment
  - Opening of new clinical sites
  - Efficacy and/or safety updates
- Manuscripts that are accepted for publication; the following must be provided via email to researchprograms@lls.org:

  - Complete list of authors as they appear on the accepted manuscript with your name in bold
  - Manuscript title
  - Journal
  - Date of publication or online ahead of print (if known)
  - A copy of the acceptance letter from the journal

- Updates regarding any transfers to a new institution

If you plan to withdraw your application at any time during the application cycle, please inform staff of your decision by writing to researchprograms@lls.org.