Request for Proposals: 2024 IASLC/LCRF Team Science Award (TSA) on Advancing Therapies Towards Curing Oncogene-Driven Lung Cancers

1. Program Summary

Lung cancer is responsible for more deaths worldwide than any other cancer, accounting for an estimated 130,180 deaths annually in the United States alone.[1] The last 10-15 years have seen accelerated clinical trials and FDA approvals of targeted therapies for non-small cell lung carcinoma in part due to advances in molecular profiling of tumors. Many of these targeted therapies are directed against oncogenic drivers.

EGFR was one of the first oncogenic drivers that was successfully targeted with the use of tyrosine kinase inhibitors. Shortly thereafter, EML4-ALK rearrangements were identified as molecular markers and tumors harboring these alterations could successfully be treated with molecularly targeted agents.

Subsequently, additional oncogenic driver alterations in BRAF, RET, KRAS G12C, HER2, MET, NTRK, and ROS1 were identified along with corresponding therapeutic options for treatment. Despite substantial progress in this area, available treatments are not curative, and resistance invariably develops. Patients are usually treated with tyrosine kinase inhibitors (an antibody-drug conjugate in the case of HER2) but at some point, chemotherapy is utilized to control the disease. Immunotherapy in the form of PD-1/PD-L1 inhibitors has revolutionized the treatment of many forms of lung cancer but has not proven effective in the treatment of most oncogene-driven lung cancers.

Given that therapeutic options available to date are not curative, there is a need for novel approaches to treat these lung cancers and improve outcomes for patients with the ultimate intention of cure. This grant mechanism will focus on furthering the development of novel therapies, including immunotherapeutic approaches, for patients with oncogene-driven lung cancers.

Work supported through this mechanism will address important mechanistic questions and developmental therapeutics across the care continuum and have the immediate potential to increase survivorship. Given the specific interest in the development of novel therapies that could benefit this group of patients in the relatively near-term, a clinical trial must either be initially incorporated into the project or be an immediate result of the outcome of the research. It is expected that a program of correlative, translational research will be proposed that will enhance the understanding of these oncogenic-driven lung cancers.

Working in conjunction with IASLC, we will encourage applications on a wide variety of topics related to oncogene-driven lung cancer, including but not limited to the following:

- The proposal must include studies in patients and/or patient samples with oncogene-driven lung cancer.
- A proposal that is associated with a clinical trial either as part of the project or planned as a result of the research will be favorably looked upon. Funding from this grant cannot be used to support an ongoing clinical trial. The trial can investigate novel treatment approaches, new therapies (i.e., next generation drugs or agents with novel mechanisms of action, antibody-drug conjugates, etc.), immunotherapy, vaccines, cell therapy, and novel combinations if there is a strong rationale

[1] American Cancer Society. Cancer Facts & Figures 2022. Atlanta: American Cancer Society; 2022.

supporting the investigation. The associated clinical trial cannot be an early phase dose-seeking trial. There is a particular interest in investigator-initiated phase IB/II trials.

- The proposal must have a program of 2-3 projects. These projects must be closely integrated and should consist of clinical, basic and/or translational work. Topics of interest can include but are not limited to mechanisms of resistance, studies on the immune landscape and tumor microenvironment, biology and mechanisms of tumor progression, identification of biomarkers to predict sensitivity to specific therapies, methods for optimizing treatment, etc.
- The proposal must have a central, important theme. Projects associated with the proposal must address various aspects of this theme.
- Cancer researchers must be affiliated with an academic/research institution. The research team can include industry partners. The industry partner should support the clinical trial and/or have researchers that have the expertise necessary to the success of the project.

2. Eligibility Criteria

- Eligible teams must be comprised of independent faculty-level researchers providing complementary interdisciplinary expertise, each of which will make separate but closely integrated contributions to the research being done.
- Investigators must be affiliated with a non-profit academic or research institution.
- One team member should be designated as the Team Leader or Principal Investigator (PI) of the program. This individual will be responsible for the administrative leadership of the project. There should be one Project Leader per project. An individual can serve as both the PI of the proposal and as Project Leader of a project.
- All project leaders must show clear evidence of an independent research program, be investigators past the initial five years of their first academic appointment and must hold a full-time faculty position at the level of assistant professor or higher.
- Team members may be working within the same institution or at several institutions. Teams or team members from international sites are highly encouraged. There is no limit on the number of team members.
- Applicants may only apply for one LCRF grant per cycle.
- Applicants are prohibited from applying if they are currently receiving funding from IASLC or LCRF.
- Ineligible investigators with these or other special circumstances may request review by contacting the LCRF grants office (see Inquiries section below).

3. Budget Requirements

The maximum award amount is $2,500,000 for a period of 4 years. Additional budget requirements and considerations include the following:

- The IASLC/LCRF grant must be the primary source of research support for the proposal. Since a clinical trial may be part of the project, it is suggested that additional funding be obtained from a funding partner to help support the clinical trial costs. Additional secondary funding (e.g., for core services support) is also permitted. Proposed projects may not have other funding. Potential overlap with other funding should be discussed.
- Direct patient care costs reimbursable by other sources may not be included.
- At least 70% of the grant (i.e., $1,750,000 over 4 years) should be allocated to support the scientific translational work associated with the proposal, particularly if a clinical trial is part of the project.
- There is a 20% limit on the amount of salary support that may be requested. However, appropriate justification for all budget items is required. Any salary requests more than 20% of the budget for a particular project must be explicitly justified.

- Any major equipment costs must be justified and directly applicable to the research. Equipment is any article of nonexpendable, tangible property having a useful life of more than one year and an acquisition cost of $5000 or more per unit.
- Material, supplies, and consumables: The budget justification for supporting material and supply (consumable) costs should include a general description of expendable materials and supplies.
- Travel and publication costs are permitted. Travel can include project-related scientific presentations and in-person meetings that are vital to the grant.
- Up to 10% of the funding from this award may be used to support institutional indirect / facilities and administrative costs.

4. Data Sharing and Open Access Policy

IASLC and LCRF are committed to promoting open science by helping to increase access to investigators' findings and improving collaboration and data sharing among the lung cancer research community. Accordingly, it is a condition of IASLC/LCRF funding that all peer-reviewed articles supported in whole or in part by IASLC/LCRF funds must be made available in the PubMed Central online archive no later than twelve months after publication. In addition, IASLC/LCRF grantees must indicate explicitly in all reports, publications, and other research communications whether the data, methods used in the analysis, and materials used to conduct the research will be made available to any researcher for purposes of reproducing the results or replicating the procedure. At the time of submission of the full proposal, all investigators must indicate if they will or will not make their data, analytic methods, and study materials available to other researchers.

5. **Application Instructions and Requirements**

a. Go to https://proposalcentral.com/ and login under the "Application Login" section. After logging in, complete your Professional Profile before starting an application If you are already registered with ProposalCentral, access the site and log in with your Username and Password. If you do not have an account yet, please click on "Need an account?" and follow the instructions.
b. Click on the "Grant Opportunities" Tab.
c. A list of applications will be displayed. The list of applications can be filtered for just this organization by clicking "Filter by Grant Maker" at the top and selecting "Lung Cancer Research Foundation" in the drop-down menu. Find the "IASLC/LCRF Grant" and click the "Apply Now" button in the "Apply Column".
d. See the deadlines for the LOI stage, if applicable, and the Proposal stage. **All deadlines are in US Eastern Time**. If a document icon is showing, you can click on it to download it. This includes necessary information about the deadline from the grant maker.
e. Click the link or download the document in the Contact Information column. Clicking the link opens an email to the program administrator. If a document is provided instead, it includes the grant maker's contact information.

All applications for funding must be submitted online at Proposal Central through a two-stage process consisting of a letter of intent (LOI) and full proposal. Applicants may only apply for one LCRF grant per grant cycle. Upon submission and review of the LOI, applicants whose submission is reviewed favorably will be invited to complete a full proposal. Any applications for an extension of a previously awarded grant require resubmission as a new complete application (LOI and subsequent full proposal) and must include an update describing the progress made during the prior award period. Specific Aims at the LOI stage do not require references, and should not exceed 1 page. Text should be Arial, Times New Roman, Palantino Linotype, Courier New, Georgia, or Helvetica 11-point font or higher. Margins should not be less than 0.5" on standard letter paper (8 ½" x 11"), and you must verify the margins on the documents that you upload.

The following application components are required for a complete submission:

Letter of Intent	Full Proposal

• General Information / Demographics
• Specific Aims (one page in length per project)
• Team Summary
• Collaboration Commitment Statement (one page in length)
• NIH Biosketch for PI and all Project Leaders (NIH Biosketch Instructions)
	• General Information*
	• Demographics*
	• Eligibility Statement from all team member institutions
	• NIH Biosketch for PI and all Project Leaders*
	• Lay Summary
	• Team Summary*
	• Collaboration Commitment Statement (one page in length)*
	• Specific Aims (one page in length per project)*
	• Narrative (six-pages maximum per project):
	  ○ Background and Significance
	  ○ Preliminary Data
	  ○ Experimental Approach
	  ○ References (not included in page-limit)
	• Clinical Trial Protocol (if applicable)
	  ○ Patient Consent Form
	  ○ Patient Impact Summary (half page in length)
	• Success Factors (half page in length per project)
	• Timeline
	• Future Plans (half page in length per project)
	• Budget
	• Letter(s) of Support
	  ○ Cancer Center Director or Chief of Hematology/Oncology or Department Chair for PI institution
	  ○ Team members
	  ○ Funding source for clinical trial, if applicable

**Documents required in both LOIs and Full Proposals may be the same*

Additional Considerations:

- All LOIs must include the NIH biosketch (five pages maximum length) of the primary investigator, project leaders, and key personnel involved in the project.
- At the full proposal stage, applications must include at least one letter of support from the principal investigator and each project leader's institutional leadership affirming the following statements:

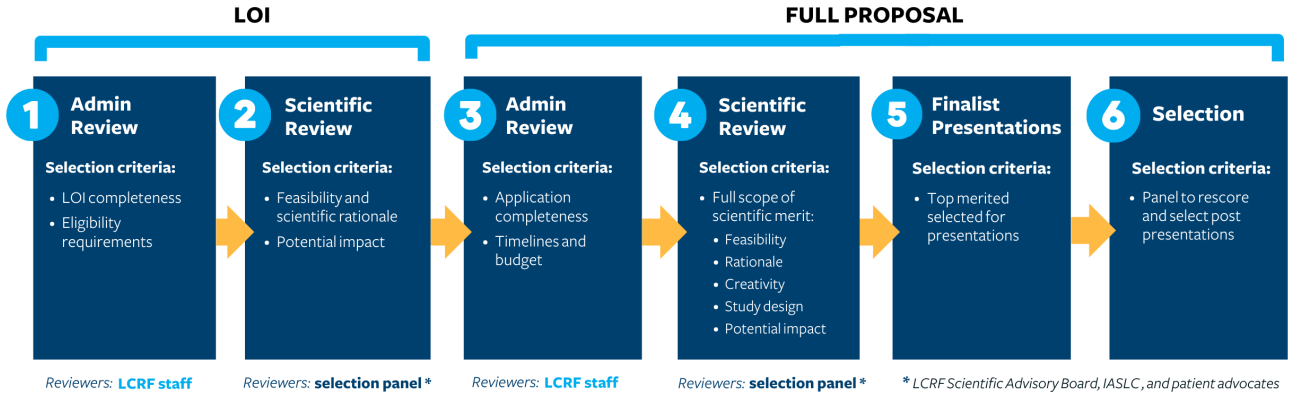
- The applicant will be officially affiliated with or employed by the institution during the grant period.
- There is adequate institutional space and equipment to accomplish the proposed project.
- Institutional leadership confirms his/her commitment to and provision of institutional space and equipment for the grantee.

6. Timeline

- LOI submission deadline: March 4, 2024
- Applicants notified of LOI decision: April 19, 2024
- Full proposal submission deadline: August 12, 2024
  - Finalist Selected for Presentations: September 20, 2024
  - Finalist Presentations[2]: Week of October 7, 2024
- Notification of award: November 2024
- Project start: December 1, 2024

7. Evaluation of Applications

All applications will be evaluated using a two-stage review process that includes review of LOIs and select full proposals. Only applicants whose LOI is reviewed favorably will be invited to submit a full proposal. At each stage, the evaluation consists of an administrative review followed by a comprehensive review by LCRF and IASLC affiliated experts. At the LOI stage, evaluations will focus on high-level aspects of the research proposal including overall rationale, feasibility, and potential impact on the lung cancer field. At the full proposal stage, submissions will additionally be evaluated for sound scientific rationale, study design, feasibility, and creativity/innovation.[3] Similar to an NIH R21 award, reviewers at the full proposal stage will be asked to provide an impact score reflecting their assessment of the likelihood for the project to exert a sustained, powerful influence on the field of lung cancer research and/or reducing disparities in lung cancer outcomes. At the full proposal phase finalists will be selected to present to a panel of experts and will be rescored based on information provided.



[2] Finalist will be selected based on highest merit, utilizing the NIH Scoring System. A report with feedback will be provided to each finalist prior to the presentations. Finalists are expected to prepare a presentation that brings clarity to any constructive feedback and overall scope of project. More information will be provided to finalists upon selection.

[3] Note regarding preliminary data: A grant application need not have extensive background material, and preliminary data are preferred but not required. Reviewers focus their evaluations on the conceptual framework, the level of innovation, and the potential to significantly advance our knowledge or understanding. Appropriate justification for the proposed studies can be provided through literature citations, data from other sources, or, when available, from investigator-generated data.

8. Award Notification and Announcement

All applicants will be notified of their award status by the date specified in the Timeline section above. Regrettably, due to the high volume of submissions, LCRF is not able to provide feedback on LOIs or proposals that are not selected to receive an award.

9. Post-award Reporting Requirements

During the funding period, all investigators are required to submit reports including the following:

Report Type	Due Date
6-month Progress Report	At conclusion of 6-months of funding
Year 1 Annual Report	At conclusion of year one of the grant term
18-month Progress Report	At conclusion of 18-months of funding
Year 2 Annual Report	At conclusion of year two of the grant term
30-month Progress Report	At conclusion of 30-months of funding
Year 3 Annual Report	At conclusion of year three of the grant term
42-month Progress Report	At conclusion of 42-months of funding
Final Report (includes financial summary report)	Within sixty days of conclusion of the grant term

Additionally, a check-in call with IASLC and LCRF is required upon completion of all progress and annual reports.

All reporting is required to be done in ProposalCentral, and additional reports may be assigned when project terms are amended (e.g., in the case of a no-cost extension or institutional transfer). Receipt of the second, third and fourth year of funding is contingent upon submission and approval of the interim progress report at the conclusion of the first and second years of the grant term.

10. Inquiries

For questions, please contact the LCRF office at grants@lcrf.org or via phone at +1 (212) 588-1580.

If you have any difficulties registering, logging in, or creating your application, contact ProposalCentral Customer Support at: 800-875-2562 (Toll-free U.S. and Canada), +1-703-964-5840 (Direct Dial International).