

Research ALKay+ve partnership with the Lung Cancer Research Foundation 2024 LCRF Research Grant on Early- Detection and Pre-Neoplasia in Lung Cancer

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<https://www.alkpositiveresearch.co.uk/our-team.html>. Accessed 24th October, 2024.

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Acknowledgements

On behalf of the trustees and committee members at Research ALKay+ve, we dedicate this research project to the courageous Kay Charlotte Murgatroyd. Kay's unwavering spirit has left an undeniable mark on the global ALK-Positive community. After her diagnosis with NSCLC (ALK-Positive) in May 2016, Kay battled for seven years until her death in July 2023. An avid and enthusiastic voice for research, Kay's determination into fundraising shall improve survival rates and treatment options for future patients diagnosed. We extend our thanks to those courageous patients who came before Kay, undertaking clinical trials that allowed her to live well with NSCLC for over seven years. Kay stated that she was "forever fundraising for ALK-Positive research" and we further that pledge in this partnership: our first ever research project. In July 2023, we renamed our charity to "Research ALKay+ve" to mark the profound legacy of this inspirational young woman. Our partnership with the Lung Cancer Research Foundation is a fully funded research grant in memory of Kay Charlotte Murgatroyd.

Also, we would like to extend our gratitude and acknowledge the significant impact of the late Cameron Millar, a fellow ALK-positive patient and committee member, who stated that "we need a big push to achieve results and fund the science for patients to live a full life". Cameron's positive outlook indicates how research can turn ALK-Positive NSCLC from terminal to chronic status whereby patients can live a normal, extended life. Thank you to Professor Matthew Hatton, Consultant and Honorary Professor in Oncology for your academic insight and encouragement. To those who have encouraged our fundraising efforts, we cannot put into words what this project means to us. Thank you for believing in us, it is with your continued support that we have been able to fund this innovative project.

Introduction

Lung cancer is the leading cause of cancer death worldwide; scholars estimate an annual 1.6 million deaths worldwide (20% of total cancer fatalities), alongside an estimated 1.8 million new cases.³ The outcomes for those diagnosed have remained relatively poor; the five-year relative survival rate for patients with metastatic non-small cell (NSCLC) were estimated to be just 6.1% for those diagnosed between 2009 and 2015.⁴ Yet, recent progress in the advancements of targeted therapies have extended survival outcomes for patients whose tumors harbor EML4-ALK translocations (ALK-positive).⁵

Next generation ALK tyrosine kinase inhibitors (TKIs; alectinib, ceritinib and brigatinib) have replaced the first generation crizotinib as initial treatment for patients with ALK-positive NSCLC. A study in 2020 by T. Mok et, concluded with mature PFS data confirmed a significant improvement in PFS for alectinib over crizotinib in ALK-positive NSCLC.⁶ OS data remain immature, with a higher 5-year OS rate with alectinib versus crizotinib. This is the first global randomized study to show clinically meaningful improvement in OS for a next-generation tyrosine kinase inhibitor versus crizotinib in treatment-naive ALK-positive.⁷

The importance of TKIs in the treatment of lung cancer control the growth and spread of cancerous cells. Newer generations of TKIs have produced better results in controlling the

³Ferlay J, Soerjomataram I, Dikshit R, et al. Cancer incidence and mortality worldwide: sources, methods and major patterns in GLOBOCAN 2012. *Int J Cancer*. 2015;136:E359–E386.

⁴National Cancer Institute. Surveillance, Epidemiology, and End Results Program (SEER) Cancer Statistics Review (CSR) 1975e2016. Available at https://seer.cancer.gov/csr/1975_2016/results_merged/topic_survival.pdf. Accessed February 25, 2020.

⁵Yuan M, Huang LL, Chen JH, et al. The emerging treatment landscape of targeted therapy in non-small-cell lung cancer. *Signal Transduct Target Ther*. 2019;4:61.

⁶T. Mok, D.R. Camidge, S.M. Gadgeel, R. Rosell, R. Dziadziuszko, D.-W. Kim, M. Pérol, S.-H.I. Ou, J.S. Ahn, A.T. Shaw, W. Bordogna, V. Smoljanović, M. Hilton, T. Ruf, J. Noé, S. Peters, Updated overall survival and final progression-free survival data for patients with treatment-naive advanced ALK-positive non-small-cell lung cancer in the ALEX study, *Annals of Oncology*, 2020.

⁷Ibid.

disease and extending patient survival.⁸ Current research suggests that understanding the biology of the tumor and the properties of the drugs could help treatment strategies and benefit patients with NSCLC.

Approved Proposal: 2024 LCRF Research Grant on Early Detection and Pre-Neoplasia in Lung Cancer

1. Program Summary

Lung cancer continues to be the number one cause of cancer deaths in the United States and worldwide, accounting for an estimated 127,070 deaths annually in the United States alone.⁹ When detected at early stage (Stage I), the prognosis is good for most patients. The current standard for detecting lung cancer is low-dose computed tomography (LDCT), with follow-up confirmation via biopsy. The U.S. Preventive Services Task Force (USPSTF) updated recommendations in 2021 to include annual LDCT screening for patients that are 50-80 years of age, have a 20 pack-year smoking history, and are either a current smoker or have quit within the past 15 years.¹⁰ While this has increased the number of people eligible for screening, it is still limited to people with a smoking history. Given the significance and need for early detection of lung cancer and advancements in molecular screening, LCRF continues this mechanism to support research projects that facilitate or advance the understanding and characterization of pre-neoplasia or approaches for early detection of lung cancer. Work supported through this mechanism addresses important questions in non-small cell and small cell lung cancer.

⁸Ilaria Attili, Carla Corvaja, Gianluca Spitaleri, Ester Del Signore, Pamela Trillo Aliaga, Antonio Passaro and Filippo de Marinis, New Generations of Tyrosine Kinase Inhibitors in Treating NSCLC with Oncogene Addiction: Strengths and Limitations, *Cancers*, 2023.

⁹American Cancer Society. Cancer Facts & Figures 2023. Atlanta: American Cancer Society; 2022.

¹⁰Lung Cancer Screening. US Preventive Services Task Force Website.

<http://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/lung-cancer-screening>. Published March 9, 2021. Accessed February 2, 2022.

This funding mechanism is focused on identifying, characterizing, and developing approaches and techniques that will allow early detection and/or prevention of lung cancer and gaining insight into preneoplastic processes in the lungs. The ultimate goal is to detect lung cancer at the earliest stages and subsequently increase survival and survivorship. While this list is not exclusive, general areas of interest include:

- Identification and characterization of new biomarkers for NSCLC and SCLC
- Liquid biopsy assays and related techniques
- Improvements in risk stratifying patients for screening
- Development of predictive, diagnostic, or prognostic biomarkers
- Genomic and histological approaches to improve early detection in tissue samples
- Novel imaging modalities to identify and risk stratify pre-neoplastic lesions
- Studies of pre-neoplasia and progression to lung neoplasia that may inform prevention strategies
- Development of pathways to increase uptake and utilization of lung cancer screening

2. Eligibility Criteria

Investigators must be affiliated with a non-profit academic or research institution and must be postdoctoral researchers, clinical fellows, or early-career and mid-career investigators with less than ten years' experience since their initial faculty appointment.

Applicants from US-based and international institutions are eligible to apply and may hold any residency/citizenship status. Applicants are prohibited from applying if they have received funding from the LCRF within the last 4 years. Senior investigators with more than ten

years' experience since faculty appointment are generally not eligible for funding and are encouraged to mentor a junior team member through the application process. However, exceptions will be made for investigators with more than ten years' experience in other disease areas or topics. Ineligible investigators with these or other special circumstances may request review by contacting the LCRF grants office (see Inquiries section below) before submitting an application.

3. Budget Requirements

The maximum award amount is \$150,000 for a period of two years (disbursed at \$75,000 per year). Additional budget requirements and considerations include the following:

- Funding from this award may not be used to support institutional indirect / facilities and administrative costs.
- The LCRF grant must be the primary source of support for the project. Additional secondary funding (e.g. for core services support) is permitted.
- There is no limit on the amount of salary support that may be requested. However, appropriate justification for all budget items is required. Any salary requests in excess of 20% of the total budget must be explicitly justified.
- Any equipment costs must be limited and directly applicable to the research project (i.e. large, general equipment costs are not permitted).
- Direct patient care costs reimbursable by other sources may not be included. • Travel and publication costs are permitted.

4. Data Sharing and Open Access Policy

LCRF is 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 LCRF funding that all peer-reviewed articles supported in whole or in part by LCRF funds must be made available in the PubMed Central online archive no later than twelve months after publication. In addition, 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 Proposal Central, 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 “LCRF Pilot 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 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
<ul style="list-style-type: none"> • General Information / Demographics • Specific Aims (one page in length) • NIH Biosketch (NIH Biosketch Instructions) 	<ul style="list-style-type: none"> • Lay Summary • Specific Aims (one page in length) • Narrative (six pages maximum): <ul style="list-style-type: none"> o Background and Significance o Preliminary Data (if applicable) o Experimental Approach o References (not included in page-limit)

	<ul style="list-style-type: none"> • Success Factors • Timeline • Future Plans • Budget • Letter(s) of Support
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Additional Considerations:

- All LOIs must include the NIH biosketch (five pages maximum length) of the primary investigator and any key personnel involved in the project.
- Funding will only be awarded to one PI, not to a team.
- At the full proposal stage, applications must include at least one letter of support from the principal investigator's program director/advisor affirming the following statements:
 - o The applicant will be officially affiliated with or employed by the institution during the grant period.
 - o There is adequate institutional space and equipment to accomplish the proposed project.
 - o The program director/advisor confirms his/her commitment to and provision of i institutional space and equipment for the grantee.

1. Timeline

- LOI submission deadline: March 4, 2024
- Applicants notified of LOI decision: April 19, 2024
- Full proposal submission deadline: June 10, 2024

- Notification of award: November 2024

- Project start: December 1, 2024

6. Evaluation of Applications

All applications are 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, a comprehensive review by LCRF's Scientific Advisory Board and a review conducted with patient advocates (see figure below). 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. Similar to an NIH R21 award, reviewers at the LOI stage and 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.

Figure 1.



7. 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.

8. Post-award Reporting Requirements

During the funding period, all investigators are required to submit at least two progress reports including the following:

Report Type	Due Date
Interim Report	At conclusion of year one of the grant term
Final Report (includes financial summary report)	Within sixty days of conclusion of the grant term

All reporting is required to be done in Proposal Central, 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 year of funding is contingent upon submission and approval of the interim progress report at the conclusion of the first year of the grant term.

9. Inquiries

For questions, please contact the LCRF office at grants@lcrf.org or via phone at +1 (212) 588-1580. OR. If you have any difficulties registering, logging in, or creating your application, contact Proposal Central Customer Support at: 800-875-2562 (Toll-free U.S. and Canada), +1-703-964-5840 (Direct Dial International).

10. Successful Applicant

Peggy Hsu, MD, PhD, University of Michigan

RESEARCH PROJECT:

Understanding the origin of ALK-driven lung cancer

SUMMARY:

ALK-positive lung cancer, often affecting non-smokers and diagnosed at advanced stages, has unclear origins. This research aims to uncover the earliest events driving ALK-driven lung cancer using advanced single-cell technologies. By studying patient samples, lung organoids, and mouse models, the team will map how ALK activation leads to tumor initiation. The findings could reveal novel molecular features, enhance our understanding of cancer cell plasticity, and pave the way for earlier detection and prevention strategies, improving survival rates for ALK+ lung cancer patients.

Figure 2.**Research ALKay+ve Fundraising Commitments**

“Lung cancer has a greater mortality rate than breast, prostate and bowel cancers combined but receives least government funding.”¹¹

¹¹Research ALKay+ve, <https://www.alkpositiveresearch.co.uk/index.html>. Accessed 24th October, 2024.

Lung cancer is shockingly underfunded relative to most other cancers. There is a misconception that lung cancer is caused by smoking, making it an unpopular cancer to donate to. Let us state that no one deserves lung cancer even if certain lifestyle choices were made.

Because lung cancer research is so underfunded, and ALK-Positive only affects 5% of lung cancer cases, research into ALK needs relies heavily on public fundraising if we can achieve the same groundbreaking advances and success rates as other cancer treatments.

So, at Research ALK+ve, our aim is a simple one – to raise much needed funds which will be used specifically for research into ALK-Positive lung cancer. The distribution of the money raised will be carefully considered by our trustees and committee members to ensure that it is targeted at research that is more likely to succeed, or make a greater impact, within a reasonable time frame.

Website: <https://www.alkpositiveresearch.co.uk/>

Email: research.alkpositive@gmail.com

LCRF Mission

The mission of the Lung Cancer Research Foundation (LCRF) is to improve lung cancer outcomes by funding research for the prevention, diagnosis, treatment and cure of lung cancer.¹²

LCRF is committed to improving lung cancer patients' quality of life and survival rates through advancing the best new research in the field. To accomplish this, LCRF has begun implementing strategies toward its goals for the next three years. LCRF intends to have funded a total of \$45 million in direct lung cancer research through 444 grants by 2024.

¹²Lung Cancer Research Foundation, Our Mission. <https://www.lungcancerresearchfoundation.org/about/>. Accessed 24th October, 2024.

We will achieve this by:

- Inviting the lung cancer community – patients, caregivers, patient advocacy groups, healthcare providers, family and friends – to join in achieving this goal.
- Communicating important scientific advancements in lung cancer with the community.
- Ensuring emphasis on health equity in our funding mechanisms, grantees, programs, policy, staff, and volunteer leadership.
- Evolving our scientific research programs to continue funding the best, most impactful research where it is needed most.
- Strengthening the Board of Directors by attracting and retaining active and engaged members who reflect the diversity of the lung cancer community.
- Ensuring operations are efficient and effective to maximize direct research investment.

Website: <https://www.lungcancerresearchfoundation.org/>

Email: nfinch@lcrf.org

Approval of Research ALKay+ve Trustees and Committee Member

Upon consideration, our trustees and committee members unanimously agreed to fund this research project. The mission and values of LCRF align with the fundraising commitments and ethos of Research ALKay+ve subsequently leading to the decision to fund the 2024 LCRF Research Grant on Early-Detection and Pre-Neoplasia in Lung Cancer.

LCRF has been subject to review with their scientific panel which includes Christine Lovly, M.D., Ph.D., a well-known ALK-positive oncologist.¹³ Professor Matthew Hatton has

¹³Lung Cancer Foundation of America, Christine Lovly, <https://lcfamerica.org/researcher/christine-lovly-md-phd/>. Accessed 24th October, 2024.

aply pointed out that peer review is important, and this project has been ranked highly by this esteemed group of researchers. Former Director of Public Health for Doncaster, Rupert Suckling, a fellow ALK-Positive patient indicates that the LCRF have clinical governance and accountability built into their process. The team at the University of Michigan, USA, are accredited by the global ALK-Positive community and are members of the Inter-university Consortium for Political and Social Research (ICPSR).¹⁴ This project, in collaboration with the University of Seoul, South Korea, ensures that the research is of academic merit.

In agreeance:

- Aileen Murgatroyd
- Colin Blackaby
- Kelvin Fitton
- Phil Murgatroyd
- Jenny Blackaby
- Nadine Fitton
- Ewan Murgatroyd
- Annie Fitton

Date: 22/10/2024

Conclusion

In summary, Research ALKay+ve are delighted to gift \$150,000 in this partnership with LCRF to fund this project in memory of Kay Murgatroyd. The LCRF research grants are global in

¹⁴ICPSR.

<https://www.icpsr.umich.edu/web/pages/membership/index.html#:~:text=What%20is%20ICPSR%3F.consortium%20of%20nearly%20800%20institutions>. Accessed 24th October, 2024.

scope, receiving applications from researchers in over 26 countries, and their advisory board selects projects based on the potential to make a significant impact on patient outcomes, regardless of geography. LCRF and Research ALKay+ve are confident that the advancements from this research will have a global reach.

Figure 3.

