REQUEST FOR APPLICATIONS

Rising Tide/LUNGevity Award for
Improving the Early Detection of Lung Cancer through biomarkers and imaging

Rising Tide Foundation for Clinical Cancer Research ("RTFCCR") and LUNGevity Foundation ("LUNGevity") are issuing a request for applications (RFA) to support **interventional clinical trials** or **clinical validation studies** aimed at **Improving the Early Detection of Lung Cancer through biomarkers and imaging**.

Awards totaling up to USD 1,000,000 (USD 500,000 from LUNGevity and USD 500,000 from Rising Tide) for will be funded for a duration of up to 3 years. We anticipate funding at least one award through this mechanism.

RTFCCR and LUNGevity advise applicants to read the entire RFA, before starting an application. An applicant who is deemed ineligible for this award and/or does not follow the instructions for the application and the patient partners involvement plan will be disqualified and the application not reviewed.

This award application process will be managed through the RTFCCR online platform SmartSimple[SmartSimple | Rising Tide Foundation].

RISING TIDE FOUNDATION FOR CLINICAL CANCER RESEARCH
RTFCCR is a charitable, non-profit organization established in 2010 and located in Schaffhausen, Switzerland. RTFCCR's primary consideration in granting support is given to truly innovative, unique, patient-centered clinical research. With patients at the core of the mission, the foundation strives to support clinical trials resulting in the creation of less toxic therapeutic approaches, better disease burden management, earlier cancer detection, and innovative intervention strategies that will lead to increased survival and quality of life. For more information about Rising Tide, please visit Clinical Cancer Research - Rising Tide Foundation (risingtide-foundation.org)

LUNGEVITY FOUNDATION
LUNGevity Foundation is a 501(c)(3) philanthropy specifically focused on funding research for the early detection and effective treatment of lung cancer. LUNGevity's mission is to improve mortality rates of lung cancer patients through the development of protocols and tools for early detection of lung cancer, early intervention in the disease progression, and treatments, including targeted therapy and immunotherapy. LUNGevity focuses on translational science. For more information about LUNGevity Foundation, please visit www.LUNGevity.org.

BACKGROUND FOR GRANT

Lung cancer is the principal cause of cancer death for over 230,000 individuals in the US each year,[1] and almost 1,800,000 worldwide,[2] making it the leading cause of cancer death in the US and globally.[1,2] In the US, the 5-year survival rate traditionally hovered around 10%-15% for decades, but it has improved substantially in recent years due to substantial innovations in reducing tobacco exposure, lung cancer control and targeted treatments.[3] Despite the progress seen in lung cancer, only 22% of cases are diagnosed at the localized stage with a 5-year relative survival rate of 64%.[4] Conversely, the majority of lung cancer (53%) is diagnosed as metastatic disease with a 5-year relative survival of 9%.[4] When the incidence of lung cancers detected in late stage is decreased through regular screening tests, the mortality rate decreases.[NLST ref] Therefore, early detection of lung cancer to detect in early stage significantly more of the 78% of lung cancers that otherwise are detected in late stage continues to be an unmet need.

Lung Cancer Screening By Low-Density Computed Tomography:

In the last 10 years, lung cancer screening (LCS) using low-dose computed tomography (LDCT) has emerged as an evidence-based[5,6] and policy-supported tool[7,8] to reduce mortality by identifying early malignancy. When paired with early treatment, LCS has tremendous potential to transform lung cancer care outcomes.

Based almost entirely on the results of the National Lung Screening Trial (NLST)[5], but partially validated by results from the NELSON and MILD[11] trials, there has been broad support for implementing LDCT throughout the US in high-risk subjects with many years of tobacco exposure. Despite the value of LCS, as of 2023, only 5% of the screen-eligible population received LDCT screening in the United States.[12] LDCT is currently available to high-risk individuals defined as those between ages 50-80 (50-77 on Medcare), who have a pack-year smoking history of 20-pack years (a pack-year as defined as the equivalent of smoking one pack of cigarettes a day for one year), and who currently smoke or have quit within the past 15 years.

Currently, 50% of lung cancers are diagnosed in the high risk population but leaving the remaining 50% of lung cancers occurring in the ”not high risk population” according to the current definition. These data stress the need for identification of new and improved stratification criteria for the “at risk” population and the validation of more readily acceptable screening tests with follow-up for a positive test by LDCT.

Lung Cancer Early Detection Outside of the Screening Setting:
Several reports have shown that lung cancer is detected in individuals with lung nodules incidentally detected outside of lung cancer screening. Such individuals often do not meet the current screening criteria and have lung nodules that are referred to as indeterminate pulmonary nodules or IPNs.[14] IPNs are nodules that are 6–30 mm in size, not calcified, and have features suggestive of being cancerous.[15] However, most IPNs are not malignant and currently, there are no methodologies for clearly stratify the risk of development of a malignancy in presence of IPNs. . Therefore, a clear diagnosis can be achieved only with the use of invasive procedures such as lung biopsies. IPNs prognostication with non-invasive tests is an important unmet need in the early detection of lung cancer.

RTFCCR and LUNGevity Award:

Improving the Early Detection of Lung Cancer through biomarkers and imaging

As described above, two major unmet needs in early detection of lung cancer remain:

1. Suboptimal stratification criteria for the "at risk" population, and
2. non-invasive prognostication of IPNs and other incidental findings.

The Rising Tide Foundation for Clinical Cancer Research and LUNGevity Foundation are partnering to issue a Request for Applications to **Improve Early Detection of Lung Cancer through biomarkers and imaging.**

The request for application (RFA) **supports clinical trials and validation studies aimed at:**

- **improving current stratification criteria for of the high-risk population, or**
- **validating new early detection tests that are more acceptable than first line LDCT screening, or**
- **testing new methods for stratification risk of IPNs**

by utilizing new imaging, blood biomarkers, or monitoring algorithms, with patient partners involved in the study design and execution

Award eligibility:

Education and Experience: At the time of the award term, an applicant (who must be a principal investigator for the proposed research) must hold a doctoral degree and faculty appointment (or equivalent) with an academic institution, including research institutions that are not formally associated with a university and have completed a postdoctoral training fellowship. An applicant may be at any level of research experience.

An applicant must be an independent, self-directed researcher for whom their institution provides space and other resources customary for independent investigators. The application must convey the commitment of the institution to both the applicant and the proposed research activities. An applicant with an existing Rising Tide award or a LUNGevity award that would be concurrent with Rising Tide/LUNGevity Award is precluded from applying.

Geographical Restriction: International teams are highly recommended, and the Award Program does not have any geographical restrictions. **The application must be submitted in English**.

Award information:

Award Structure and Allocation:
Investigators may receive **up to** USD 1,000,000 per project, over three years.
Award funds may be used for the salary and fringe benefit costs of personnel other than the applicant. Fringe benefit costs may only be expended upon the stipulation that they cannot be obtained from another source. No more than 25% of the requested budget may be used for an investigator's salary and/or fringe benefits. Travel costs for investigators cannot be covered by this grant.
Please note that indirect costs, such as overhead, are not covered.

Allowable costs for clinical trials include: expenses related to subject recruitment (such as participation cost reimbursement, phlebotomy charges, etc.), clinical laboratory analyses of human subjects or their samples (such as clinical laboratory assays, imaging charges, etc.), and correlative validation studies. The award may be used to help with operational costs, The investigator is required to procure funding to cover the remaining cost of the trial, a fundraising plan will be requested as part of the application. **Drug costs will not be covered**.

Duration: The **Rising Tide/LUNGevity Award for Improving the Early Detection of Lung Cancer** may be granted for up to 3 years.

The following criteria must be met for the proposed clinical trial/ validation study:

1. The study may improve existing or identify newly developed tests, test methods, technologies, or devices.
2. The study should focus on populations at high risk of development, or progression of cancer or on identifying nodules or other structures detected on imaging (incidentally or on intentional search) which are likely to be malignant
3. Studies with a clinical intervention and a clinical endpoint will be prioritized.
4. Early development of a diagnostic tool without analytical validation in cancer populations or samples is not supported in this funding mechanism.
5. Patient research advocates or patient organizations (patient partners) must be involved in the proposed study from its beginning.

Note: Nation-wide population screening are not supported by this funding mechanism.

Factors considered in evaluating applications:

Some of the factors considered when reviewing applications include:

- **Innovation** – Does the project address the improvement of early detection of lung cancer?
- **Scientific merit and feasibility of the research plan**
- **Impact** – How will the research findings from the project move to the clinic and impact patients? What plans does/do the applicant(s) have for the clinical application of the findings of the project?
- **Study design and its burden on patient participation,** i.e., how difficult is it for study participants to participate in the proposed study? We recommend study designs that support the inclusion of a diverse group of patient participants
- **Research environment** Does the applicant have access to institutional resources required for the successful completion of the proposed project?
- **Appropriateness of the** requested **budget** to complete the proposed research project. Factors used to evaluate the budget include total costs of the trial, the amount requested and the plan to secure the remaining funds.
- **Patient Partners involvement activities:** How patient partners will be actively engaged in the study from the development of research questions through dissemination of study results. Specific guidance for preparing a Patient Involvement Plan can be found in this document and supplied upon request.

Final selection will be contingent on scientific review and availability of funds.

Application Instructions and Timeline

Applicants will be allowed to submit their letter of intent (LOI) from October 17th, 2024.

All applicants are invited to contact either of the foundations for any question or issue encountered during the application process.

Application process

The application process involves the following steps:

- Letter of Intent (LOI) are submitted online through our grant management system SmartSimple (SmartSimple | Rising Tide Foundation) with deadline **February 12th, 2025**. They will be assessed by internal staff and advisory board members of both foundations.
- Full Grant Application: the most promising LOIs that align with our RFA topic will be invited to submit a full grant application online.
- Grant Review Committee: full grant applications are reviewed by our grant review committee, a panel of external experts that carries out a comprehensive scientific review. Each application is independently analyzed and ranked by scientific peer reviewers, patient experts and biostatisticians on the panel.
- Recommendations made by the grant review committee are submitted to the RTFCCR's and LUNGevity's boards of directors for final funding approval. Upon approval recipients will be notified of the award, no later than a month after the board meeting. Declination letters will be sent to those who were not successful in their application.

Application requirements

Please note, all applications should include the following information as requested in the SmartSimple platform:

- The curriculum vitae (CV) of the principal investigator and co-investigators (max 2 pages each; please upload all CVs as PDF files in SmartSimple).
- A description of the proposed research project (organized in a manner similar to that required by the US National Institute of Health [PHS 398]), including:
  - Specific aims
  - Background and significance
  - Preliminary results and studies explaining the significance and potential for success
  - Experimental design and methods
  - Statement of objectives regarding how the study can change the current standard-of-care for today's patients or how it will create evidence to improve early detection of cancer
  - Detailed schedule of activities for patient participants in the study
  - Explanation of why the new early detection strategy may be helpful to patient participants
  - Description of criteria used in determining results (included quality-of-life measurements)
  - Statistical analysis section outlining approach taken to make study scientifically valid
  - Amount of time before the opening of the study upon approval for funding
  - Statement of next steps for research upon achieving positive or negative results
  - Description of how milestone achievements for the study are achieved
- Completed Patient Partners Involvement Plan (for more information please refer to instructions in this document).
- Current, active Institutional Review Board (IRB) or Ethical Committee (EC) approval letter for the study. If the IRB/EC has not been obtained at the time of proposal submission, please indicate the expected timeline for obtaining the approval [if applicable].

- Letter from department head stating institutional commitment to the project, no competing studies, and verification to accrue a valid patient participant population.
- Break-down of costs of the study, detailing the amount of the total costs, the amount requested (including costs related to patient partners involvement) and the plan for acquiring the eventual remaining funds (fundraising-plan).
- List of other sources of financial support for the project (include all sources applied – pending and/or active).
- Industry letter stating permission for the use of the investigational agent, who is supplying that agent for the study, and the in-kind amount of that contributed agent [if applicable].
- List of literature cited.

RFA Timeline

Tasks	Dates
Launch of Call	October 17th
Deadline for LOIs	February 12th 2025
Selected LOIs invited to submit Full Proposals	March 15th 2025
Deadline Full Applications	May 12th 2025
Approval / rejection	End of August 2025

Grant agreements and conditions of continued funding upon approval

- Once an award selection is made, LUNGevity Foundation and RTFCCR will each issue a separate funding award agreement that would cover 50% of the total awarded budget.
- The milestone table in the agreement will be agreed upon by the foundations and the grantee institution and will be used for demonstration of progress provided by progress reports twice/year.
- The payments are made twice a year upon demonstration of progress, as defined in grant award documentation
- Any modifications to the approved study, its Patient Involvement Plan, protocol, timeline, expectations, funding sources, patient participants status, and exact reason for any patient's discontinuation of study participation, etc. should be notified to the 2 foundation promptly
- RTFCCR and LUNGevity may require their grantees to talk to and meet staff, board members, or anyone else pertinent to the continued funding of the study (i.e. at the annual LUNGevity science meeting).

Royalties and Intellectual Property (IP)

The processes and approaches may differ between LUNGevity and RTFCCR, and as such, LUNGevity and RTFCCR will conclude separate grant agreements with the grantee, each using its own terms and conditions.

Application Assistance

For answers to questions regarding programs, eligibility, policies, terms and conditions, or instructions for the letter of intent or full application, please contact:

Upal Basu Roy
Executive Director of Research
ubasuroy@LUNGevity.org

Zoraide Granchi
Senior Scientific Program Manager
zoraide.granchi@risingtide.ch

For help with the Smart Simple electronic application process, please contact:

Zoraide Granchi
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Guidance for Planning your Patient Partner Involvement in Research

Throughout this document, we adopt the definition of Patient Partner provided by Patient-Centered Outcomes Research Institute (PCORI). PCORI's definition of patient partners includes patients(those with lived experience), family members, caregivers, and organizations that are representative of the population of interest in a particular study.

Early involvement of Patient Partners, based on co-design principles allows a better formulation of relevant research questions, more credibility of the knowledge produced, identifying, and solving potential challenges faced during the project, and better application of outcomes to specific contexts.

Here is a checklist to help you plan Patient Partner Involvement and complete our Patient Partner Involvement Plan table required to be submitted as part of the LOI. It encompasses points that should be considered for the application phase, during the implementation of the project, and beyond the project.

Patient Partner Involvement in Research

The checklist below is to help you plan Patient Partner Involvement and complete our Patient Partner Involvement Plan template required to be submitted with your Letter of Intent.

Before the project starts

- ☐ Patient Partner Involvement is planned across the entire project lifecycle
- ☐ The most appropriate Patient Partner Involvement model is selected
- ☐ The appropriate Patient Partners are involved early in formulating the concept, hypothesis
- ☐ Appropriate budget for patient partners involvement activities and compensation of Patient Partners is reflected in the Patient Partners Involvement Plan and the overall grant budget request

During the project

- ☐ Assessment of needs of trial participants by Patient Partners is included
- ☐ Adaptation of trial and procedures where necessary to meet trial participants' needs
- ☐ Assessment of the impact of patient partners involvement in your project at mid-term and at the end of the project is considered

Beyond the project

- ☐ Communication and dissemination activities involving patient / public partners is planned after project end
- ☐ Collaboration with patient community on trial outcomes is planned

For more information, please refer to: http://synapse.pfmd.org/resources/considerations-guide-to-implementing-patient-centric-initiatives-in-health-care-product-development/download

Note: Please consider the choice of your patient advocates that you engage in order to select the ones who can best add value to this project

Choice of Model of Patient Partner Involvement in Research Projects

Research teams should think carefully about the activities across the whole project lifecycle that the Patient Partners could undertake. Short term activities are easy to define upfront, but it is more challenging to think about sustained involvement across the entire project.

Therefore, depending on the research project, it is important to think about the most applicable role of a Patient Partner for contributing in a clinical research project:

Patient role	Examples	Involvement level
Team Member role	• Patient Partners provide a priori and continuous consultation on outcomes of importance, study design, etc. • Patient Partners are paid investigators or consultants • Patient Partners have a governance role – "a seat at the table"	High
Advisor role	• Patient Partners serve as advisory committee members or provide a priori consultation on outcomes of importance and study design, but have no leadership role or governance authority	Moderate
Reactor role	• Patient Partners input is collected distally through surveys, focus groups or interviews, but patients are not consulted directly or a priori on such things as study design and outcomes of importance • Patient Partners are asked to react to what has been put before them rather than being the origin of the concepts of interest	Low

Patient Partner Involvement Plan

We require you to submit a "Patient Partner Involvement Plan" as part of your LOI and Full Application. The plan should describe Patient Partner Involvement processes during the generation of the project application as well as during the implementation of your project. It describes Involvement e.g., how you engaged with the patient partner(s) when your research question was defined, while the proposal is written, when it is being submitted and resubmitted, and which patient partner involvement model you chose for the implementation of your project.

When developing your project budget, please make sure that adequate and realistic resources for Patient Partner Involvement are reflected in the Patient Partner Involvement Plan and the overall grant budget request. This could include e.g. appropriate budget for work time (staff or contractors in patient organizations) as well as project-related pass-through costs (e.g. travel expenses and meeting venue costs).

Different phases of research will need different activities to ensure patient partner involvement is implemented in the way defined in this document.

For the LOI and full application, please submit your Patient Partner Involvement Plan through the online submission platform.

- Each Patient Partner Involvement Plan should have activities proposed listed and properly described
- Activities proposed designed for patient partners and with patient partners
- The results of these activities are implementable in the clinical trial design or execution to ensure patient needs are met

Please be very clear at the outset about what you expect to achieve and what metrics – both quantitative and qualitative – you will use to measure progress against and achievement of both overall research goals and specific patient-centricity goals.

References:

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