Translational and Basic Science Research in Early Lesions (TBEL) Webinar

***RFA-CA-21-054** Research Centers (U54)*

***RFA-CA-21-055** Coordinating and Data Management Center (U24)*

(A DCB-DCP Partnership Program)

NIH NATIONAL CANCER INSTITUTE

September 24, 2021

https://www.cancer.gov/about-nci/organization/dcb/funding/resources
https://prevention.cancer.gov/funding-and-grants/tbel-funding-opportunities

TBEL: A DCB-DCP Partnership

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Early Lesion Clinical Dilemma & Biological Challenges

- Increasingly sensitive diagnostic technologies exist that readily detect pre-cancers, early cancers and incidentalomas
- No effective means to phenotypically distinguish between lesions that are likely to progress and pose a threat to the patient and those that are indolent and unlikely to be lethal
- Insufficient biological studies on the role of stroma/microenvironment as a co-organizer of early lesion fate
- Inability to organically coordinate/bridge basic and translational research gaps/challenges in order to characterize and distinguish phenotypically and biologically between indolent and aggressive early lesions

TBEL Overarching Objectives

A new program that aims to develop a comprehensive mechanistic understanding of early lesions and the determinants of their clinical trajectory to improve their management:

- Support multi-disciplinary studies that bridge the basic biology-translation gaps
- Gain biological insights on early lesion-specific blockers and drivers of disease progression
- Build upon established predictive markers, retrospective data/samples and computationally-derived and biologically-backed leads
- Improve the understanding of early lesion fate for better risk stratification
- Identify tumor and stromal targets that may improve existing screening methodologies, inform the development of new screening approaches to unscreened tumors, and establish biology-backed data to guide “precision prevention”

Some Areas of Programmatic Interest in Need of Integration

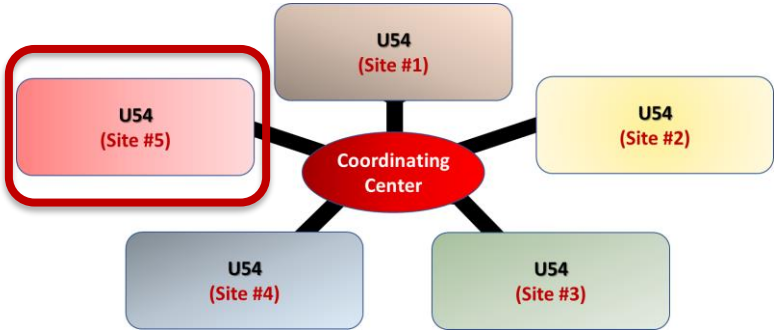
Basic Biology

- Tumor & stromal landscape of lesion drivers and suppressors based on position-dependent functional organization/heterogeneity/reciprocal interactions.
- Mediators of chronic inflammation, metabolic crosstalk, and/or phenotypic switching/cellular plasticity.
- Development of novel or repurposed early lesion platforms (and companion human resources) to interrogate complex ECM-stromal cell-nascent tumor cell interactions in malignant progression.

Translational Science

- Molecular “-omic” evaluation of recurrent and non-recurrent screen-detected lesions, interval lesions and incidentalomas to identify unique and/or shared aggressive or indolent features.
- Integrating phenotypes of the cellular and stromal components in early lesions with molecular signatures that may predict a lesion’s clinical trajectory toward indolence or malignancy.
- Adopting sequential imaging approaches to elucidate dynamic changes in progressive disease to provide insights into molecular and cellular events linked to lethal cancer versus non-lethal disease.

TBEL Program Framework



- Broad focus: Applicants welcome to propose tumor(s) type(s) – and accompanying rationale/justification – to be studied
- Identify unique and/or common pathways & determinants of indolence/aggressiveness

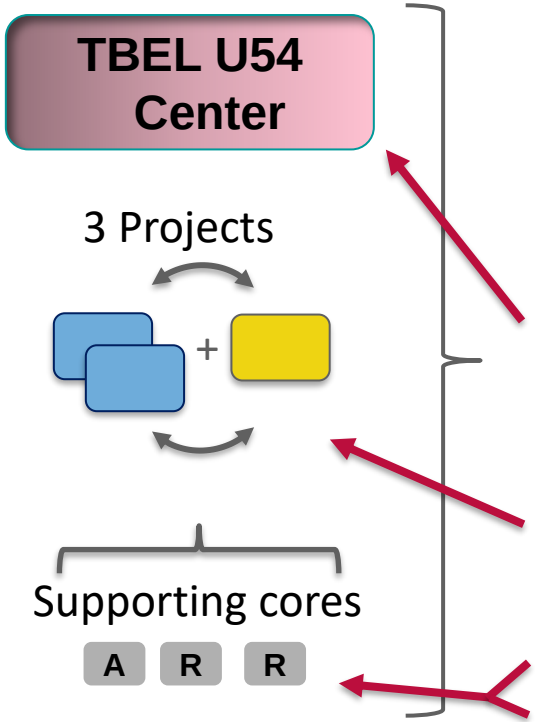
Structure:

- 5x U54 Specialized Centers
- 1x U24 Coordinating & Data Management Center
- U54: Complementary Multi-PI & integrated Projects
  - **2** Basic + **1** Translational projects
    OR
  - **1** Basic + **2** Translational projects
  - Dedicated core(s) for unique resources, tool development/optimization

Networking and Synergy:

- **Restricted funds** (years 2-5) for inter-U54 collaborations
- **Working group** activities to address common goals, challenges and opportunities
- **Sharing** of tools, reagents and resources
- Required **Steering Committee-led meetings**
- Inclusion of **Associate Members**

Research Center (U54) Objectives and Structure



U54 objectives: Integrate basic and translational cancer research studies – unified by a central hypothesis – to iteratively examine direct causal relationships and interactions of an early lesion, its microenvironment, and host-systemic factors as "co-organizers" of tumor initiation (or suppression) and malignant progression in conjunction with the clinical characteristics of the lesions.

U54 Components:

- *Overall*: Each proposed TBEL Center must articulate an overarching scientific theme that defines it. The proposed Research Projects must be aligned with the theme in testing hypotheses that address compelling questions in early lesion research
- *Projects*: 3 required (2 basic and 1 translational or 1 basic and 2 translational)
- ***A****dministrative Core*
- ***R****esource Core(s):* 1-2

Each U54 application is expected to be classified *by the* ***applicant*** as either **basic biology research emphasis** or **translational research emphasis**

Non-Responsive Applications *(RFA-CA-21-054)*

Research Centers will be considered non-responsive to the TBEL RFA if applications fail to:

- **Focus on early lesions**
- **Propose a combination of basic & translational projects** – *refer to RFA Part 2/Section IC (**Research Center Structure and Research Objectives**) for examples*
- **Integrate (and iterate) basic and translational projects**

Application "General Pointers"
(RFA-CA-21-054)

Please observe the following:

- In the initial planning, look for the **"must" have components**
- When writing, look for the **"Describe the…" prompts** within each sub-section
- Place emphasis on what the reviewers are looking for in the **Scored Review Criteria** section
  "Specific to this FOA: Will the…"
  "Specific to this FOA: How well does…"

U54 Thematic unity:

- **Strive for integration within a Center**
- **Center design should show synergistic potential between projects to address the overarching hypothesis**

RFA-CA-21-054 PHS 398 Research Plan: Page Limits

Component Types	Research Strategy Page Limits
Overall	12
Administrative Core	6
Research Project (each)	12
Resource Core (each)	6

RFA-CA-21-054 PHS 398 Research Plan: Significance

- Does the U54 Center address **basic/mechanistic AND translational challenges** in early lesions to better understand early lesions, their microenvironments and their reciprocal interactions that drive early lesion fate and biologically inform lesion stratification and clinical outcomes?
- Is there a **central hypothesis** for the U54 Center program, and sub-hypothesis for each individual research project that demonstrate integration and iteration to other proposed research projects within the TBEL site?
- Will the **Shared Resource Cores** support the proposed basic and translational projects within the U54 Center?

RFA-CA-21-054 PHS 398 Research Plan: Approach

- ***For basic cancer biology emphasis Centers***: Are criteria for the early lesion designation provided and relevant disease-appropriate models proposed? Are human platforms available to test initial proof-of-concept translational potential?
- ***For translational research emphasis Centers***: Are early lesions defined within a clinical context and detailed cohort/clinical information available? Are complement preclinical model systems used to probe underlying mechanisms?
- **Strength and complementarity of multidisciplinary team** design and approaches to iteratively bridge basic and translational research in each U54 site?
- How well matched are the **Core Capabilities** to the needs of the overall Site?

RFA-CA-21-054 PHS 398 Research Plan: Environment

- How well does the **scientific environment** at the participating site(s) stimulate multi-disciplinary research collaborations; and the iterative flow between basic/mechanistic and translational researchers?
- Are the **Resource Sharing plans** conducive for the sharing of data, model organisms, human and non-human specimens, tools, reagents, therapeutics, genomic data, IP, know-how and proprietary techniques and inventions, especially with other members of TBEL?

Mechanisms of Support & Funding (U54s)

Mechanism of support: U54 – Specialized Center Cooperative Agreement
Accommodate substantive programmatic involvement to facilitate integration across the TBEL Program

Application Type: Type 1 (new applications) and Multi-PI. No resubmissions are allowed.

Budget: Application Budgets are Limited to $1.0 M/ year (DC). Applicants must budget for travel to meetings and post-award trans-network collaborative projects using restricted funds (15% of budget) initiated in years 2-5 of the program.

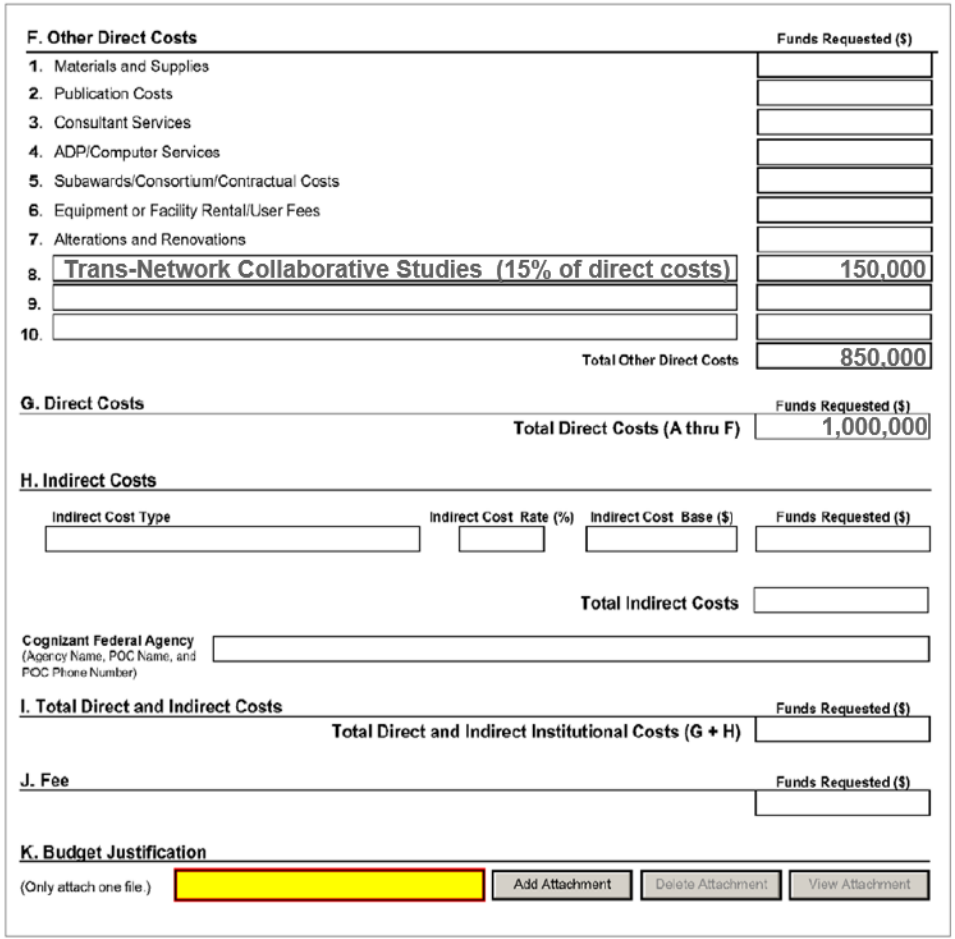
Minimum Levels of Effort: Contact PI: 2.4 CM effort; Project Leads: 1.8 CM (multiple leads 1.2 CM each); Resource Core Lead(s): 0.6 CM

Project Period: Up to 5 years.

Note on Eligible Applicants: Foreign (non-U.S.) institutions are not eligible; non-domestic (non-U.S.) components of U.S. Organizations are not eligible; foreign components are allowed.

Anticipated Number of Awards: Up to five U54 awards.
Contingent upon submission of a sufficient number of meritorious applications.

Collaborative Project Funds (15%) Included in Annual Budget in Years 2-5



F. Other Direct Costs

		Funds Requested ($)
1.	Materials and Supplies	
2.	Publication Costs	
3.	Consultant Services	
4.	ADP/Computer Services	
5.	Subawards/Consortium/Contractual Costs	
6.	Equipment or Facility Rental/User Fees	
7.	Alterations and Renovations	
8.	Trans-Network Collaborative Studies (15% of direct costs)	150,000
9.		
10.		
	Total Other Direct Costs	850,000

G. Direct Costs

Funds Requested ($)

Total Direct Costs (A thru F) 1,000,000

H. Indirect Costs

Indirect Cost Type	Indirect Cost Rate (%)	Indirect Cost Base ($)	Funds Requested ($)

Total Indirect Costs

Cognizant Federal Agency (Agency Name, POC Name, and POC Phone Number)

I. Total Direct and Indirect Costs

Funds Requested ($)

Total Direct and Indirect Institutional Costs (G + H)

J. Fee

Funds Requested ($)

K. Budget Justification

(Only attach one file.) Add Attachment | Delete Attachment | View Attachment

- Collaborative project funds will support within-scope collaborative projects with other TBEL sites or outside investigators (years 2-5)
- These funds should be listed in the budget in the Other Expenses category under the heading "Collaborative Funds“.

RFA-CA-21-055: TBEL Coordinating and Data Management Center (U24 Clinical Trial Not Allowed)

Purpose of this Funding Opportunity Announcement

This FOA solicits applications for the TBEL Coordinating and Data Management Center (CDMC) from investigators with expertise in data management, data science, protocol development, biostatistics, and information technology, and in coordinating and providing logistical support for meetings and conferences.

- Today's presentation provides only a high-level overview of the CDMC FOA. Applicants must consult RFA-CA-21-055 for detailed information on the scope of the FOA, the application procedures and requirements, and the application review criteria.

CDMC Scope: Areas of Responsibilities

The CDMC will serve as the scientific and organizational hub for the entire TBEL program. Its responsibilities will be to:

1. Coordinate program-wide meetings and conferences, and cross-network collaborative activities;
2. Provide statistical and computational analysis support; and
3. Serve as a program data hub for data capture, curation and management, and for protocol development.

1. Network Coordination and Outreach

- Provide logistical and administrative support for TBEL meetings (Steering Committee, Workshops, Working Groups, other as needed) and conference calls.
- Produce and maintain documents, including Manual of Operations, and maintain the TBEL central filing system.
- Employ various electronic channels of communication to promote and disseminate information among TBEL investigators and the broader scientific community.

2. Provide statistical and computational analysis support

- Provide study design, statistical analysis, and computational support for TBEL post-award collaborative studies supported by set-aside (U54) funds.
- Work closely with TBEL investigators to support data analysis and utilize visualization tools. Utilize data analytics (statistics, Artificial Intelligence, Machine Learning, Deep Learning, bioinformatics tools, etc.) to improve the understanding of early lesion biology and progression.
- Additional consultations and support on statistics and modeling will be made available through the NCI's Division of Cancer Prevention's Biometry Research Group.

3. Serve as a program data hub for data capture, curation and management, and for protocol development

- Coordinate the collection, curation, and dissemination of all data and metadata, data analysis and visualization tools, and computational models.
- Lead the development of CDEs as needed, data and metadata standards, clinical and epidemiological data requirements, and data processing pipelines.
- Implement state-of-the-art system for study protocol development and monitoring, data management, and specimen tracking, selection and distribution as needed.
- Guide and lead a Network-wide effort to prepare and make data and resources broadly available through the Cancer Research Data Commons (e.g., dbGaP), and/or other public repositories as appropriate and as directed by the TBEL Steering Committee.

Research Strategy (up to 30 pages)

- **Investigators' Leadership and Experience**
  - Describe the training and demonstrated experiences of the PD(s)/PI(s) and their collaborators in the areas of program management, statistical, mathematical, and computational biology
  - Describe any unique skills that the investigators' team will contribute to the overall objectives of the TBEL program
- **Plans for the Required Areas of Responsibility**
  - Describe any theoretical and applied research management and program coordination plans
  - Describe any methods and approaches to address the anticipated overall TBEL program needs, including study design approaches, and methods/plans for the analysis, harmonization, and stewardship of the generated data

Mechanisms of Support & Funding
(RFA-CA-21-055)

Mechanism of support: U24 – Resource-Related Research Project – Cooperative Agreement
Used to accommodate substantive programmatic involvement to facilitate coordination and integration across the TBEL Program.

Application Type: All submissions will be Type 1 (new applications). No resubmissions are allowed.

Budget: Application budgets are limited to $500 K/year (DC). The contact PD/PI must commit a minimum of 1.8 CM/year and all other PDs/PIs (if multiple) must commit a minimum of 1.2 CM/year throughout the life of the U24 award. Applicants must also budget for the PD(s)/PI(s) and an additional senior investigator to travel to biannual TBEL face-to-face Steering Committee meetings.

Project Period: Up to 5 years.

Note on Eligible Applicants: Foreign (non-U.S.) institutions **are not** eligible; non-domestic (non-U.S.) components of U.S. Organizations **are not** eligible; foreign components **are not** allowed.

Anticipated Number of Awards: One U24 award.

ERRATUM

Section IV. Application and Submission Information

PHS 398 Research Plan

Research Strategy: *Section 2.* Plans for the Required Areas of Responsibility

(a) Consortium Coordination:

The sentence “There will be **one** face-to-face Steering Committee Meeting per year and monthly teleconferences;” should read as “There will be **two** face-to-face Steering Committee Meetings per year and monthly teleconferences;”

Additional Information Relevant to both FOAs (RFA-CA-21-054 & RFA-CA-21-055)

Data Sharing and Consortium Integration

New awardees are expected to adhere to TBEL data use and sharing policies:

- Deposition of data, protocols and SOPs with the TBEL Coordinating & Data Management Center (CDMC)
- Standard NIH Public Access, Data Sharing and Unique Resource Sharing policies

New awardees are also expected to participate in TBEL Working Groups, monthly Steering Committee Teleconferences and bi-annual Face-to-Face Meetings

- The PD/PI (or MPI) is required to serve as a voting member of the TBEL Steering Committee

Letter of Intent (LOI)

Highly encouraged, but not required. Not binding and does not enter into review.

Standard elements:

- Descriptive title of proposed activity
- Name(s), address(es), telephone number(s) of the PD(s)/PI(s)
- Names of other key personnel
- Participating Institution(s)
- Number and title of funding opportunity (RFA-CA-21-054 or -055)

Additional recommended information:

- Provide a brief summary of the Research Project.
- Include relevant expertise and Keywords

Email LOI to:
U54 RFA-CA-21-054 – Elisa Woodhouse: woodhousee@mail.nih.gov
U24 RFA-CA-21-055 – Christos Patriotis: patriotisc@mail.nih.gov

Key Dates

LOI Due Date	Application due Date	Review Date	Earliest Anticipated Start Date
October 3, 2021	November 2, 2021	February 2022	July 2022

* No late applications will be accepted for the two TBEL FOAs

Agency Contacts

Scientific/Research Contacts:

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THANK YOU!

QUESTIONS?

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