

FOA webinar September 20, 2021

Acquired Resistance to Therapy Network “ARTNet”

U54/U24 Program Pre-Application Webinar

RFA-CA-21-052 <https://grants.nih.gov/grants/guide/rfa-files/RFA-CA-21-052.html>

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ARTNet Programmatic Goals

- Build upon the Moonshot's Drug Resistance & Sensitivity Network (DRSN, [RFA-CA-17-009](#)) with an emphasis on the mechanistic basis of acquired resistance to cancer therapies and disease recurrence;
- Balance basic, pre-clinical, and translational research using an iterative team science structure that will enable hypothesis testing on the biological basis of acquired resistance in clinically relevant model systems;
- Provide evidence along the shared tumor-TME continuum to inform new strategies that can be better translated into future clinical trials;
- Support Centers that will collectively represent a range of treatment modalities and cancer types in pursuit of addressing compelling questions and significant barriers in acquired therapy resistance research.

RFA CA-21-052 “Acquired Resistance to Therapy (ARTNet) Centers”

Funding Mechanism: U54 Research Center – Cooperative Agreement

Anticipated Number of Awards: up to 5

Overall Research Focus: Each proposed ARTNet 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 acquired resistance to cancer therapy.

Acquired Resistance: Adaptive changes that result in resistance evoked by response to treatment.

Research Team: Interdisciplinary. MPI strongly encouraged. Foreign components are allowed.

Center Organizational Structure:

- Projects: Each ARTNet Center *must* have a minimum of *three* synergistic and complementary research projects.
 - Two basic/mechanistic projects and one preclinical/translational project; or
 - One basic/mechanistic project and two preclinical/translational projects.
- Cores:
 - One Administrative Core
 - One to Three Shared Resource Cores

RFA CA-21-053 “ARTNet U24 Coordinating & Data Management Center (CDMC)”

Funding Mechanism: U24 Resource-Related Research Project – Cooperative Agreement

Anticipated Number of Awards: 1

Overall Purpose: To facilitate and support the overall ARTNet coordination and advance multidisciplinary team science.

- Integrate, manage, and coordinate network-level activities of the ARTNet;
- Facilitate collaborations with closely aligned NCI-sponsored programs and resources;
- Coordinate network-specific cross-cutting interest groups.

Key Requirements:

- Network coordination and collaboration;
- Data management and analytical support;
- Basic, translational, and clinical expertise.

Research Team: Multidisciplinary. Foreign components are not allowed.

ARTNet Network: Awarded Centers will form a Network with joint activities (ARTNet Steering Comm. governance, trans-network collaborative pilot projects, trans-network working groups).

RFA CA-21-052 / -053 “Key Dates”

Application Due Date: November 1, 2021

- Single receipt date
- Not eligible for continuous submission extensions
- Late applications will not be accepted

Letter of Intent Due Date: October 1, 2021

- Not required, but encouraged
- Aids SRO in setting up review panel

Review: February/March 2022

- RFA review by NCI Special Emphasis Panel
- Optimally equal representation from cancer biology, radiation oncology, medical oncology in accord with applications received

Award: May 2022 Council

RFA CA-21-052 / -053 “Budget Information”

RFA Allocation: \$6.6M/yr (U54s); \$1.0M/yr (U24)

Application Direct Cost Limit: \$850K/yr (U54s); \$600K/yr (U24)

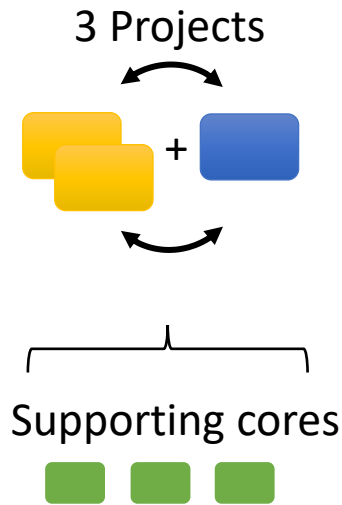
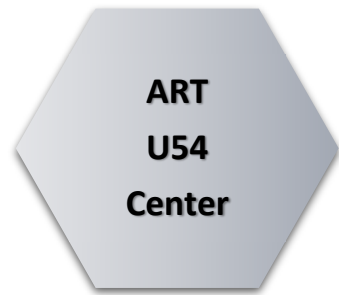
Restricted Fund (U54s ONLY): 15% of the direct costs in years 02 – 05

- Supports trans-network pilot projects
- Each Center will establish their own prioritization process, final ranking by NCI

Leveraging Value-added Partnerships:

- Although not required, integration of a proposed ARTNet Center with existing infrastructures or leveraging support to combine with the NCI award is encouraged.

ARTNet U54 Center Organization:



Required Structure: 3 Projects


- Minimum of 2 **Basic - Mechanistic** Projects and 1 **Pre-Clinical - Translational** Project;
- OR
- Minimum of 2 **Pre-Clinical - Translational** Projects and 1 **Basic - Mechanistic** Project;
- Relevant Cores (e.g., models, -omics, biospecimen; Admin core is required);

†label as such

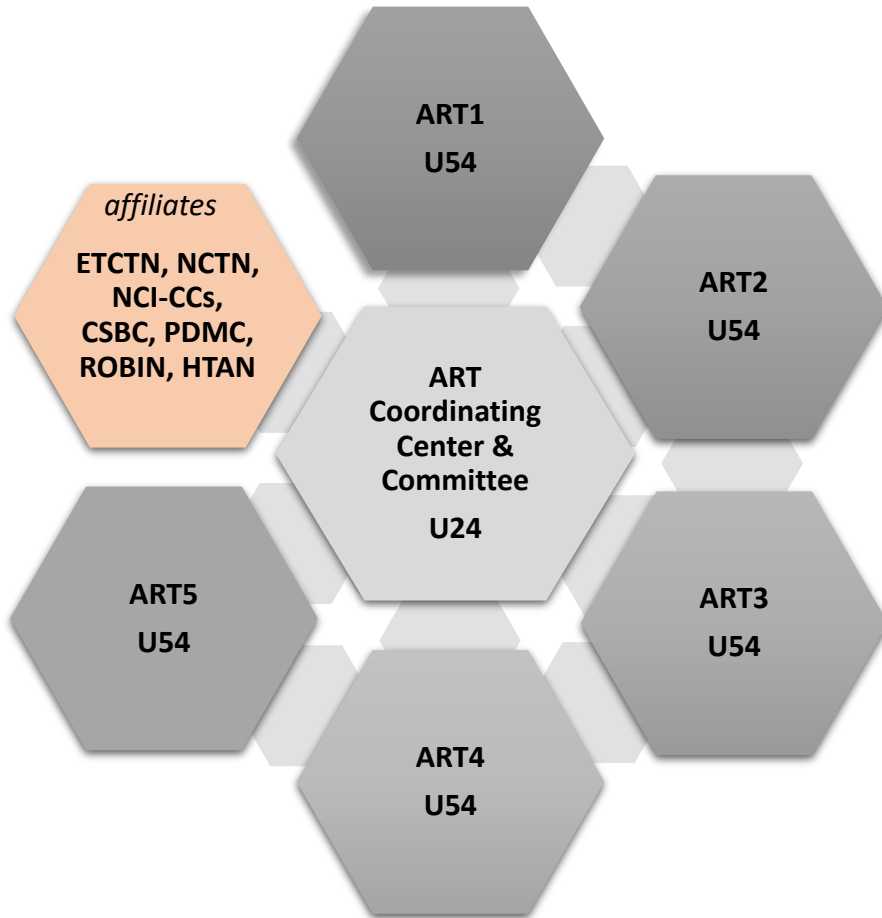
Thematic Focus:

- Center is **defined by a central hypothesis** related to the **mechanistic basis of acquired resistance**;

Special Review Criteria:

- Rationale and significance for chosen cancer and treatment types;
- Degree of innovation in predicting and thwarting acquired resistance; and,
- Level of iteration (= ) between basic, preclinical, and translational components;

ARTNet Structure and Networking:



Structure:

≤ 5 U54 Research Centers

1 U24 Coordinating and Data Management Center

Networking and Collaboration:

Restricted funds (~15%) for collaborative pilot projects

Sharing of tools, reagents, therapeutics, tissues, and resources (facilitated by the coordinating center, Steering Comm. charter)

Working groups to address common goals and challenges

- Identify collaborative projects to support the basic-translational pipeline, including treatment development
- Enhance and amplify the pre-clinical and pre-analytical basic understanding of resistance and sensitivity

Opportunities to interact with other basic and clinical research networks

RFA CA-21-052, 053 “General Pointers”

Read the RFA carefully

- In 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:** To what extent does”
 - “**Specific to this FOA:** How well does...”

Each component is equally important

- Strive for balance and integration within a Center, so-called Center-ness;
- Center design should ideally show synergistic potential between projects to address the overarching theme;
- Special Emphasis Panel reviewers will have broad interdisciplinary representation.

RFA CA-21-052 “Non-Responsiveness”

Applications with one or more of the following attributes will be deemed non-responsive and will not be reviewed:

- Applications that do not propose a combination of two (2) basic/mechanistic projects and one (1) preclinical/translation project structure (and vice versa); – *refer to RFA Part 2/Section IC (Areas of Scientific Priority and Interest) for examples;*
- Applications that do not include cores that directly support acquired resistance research and the needs for iterative basic/mechanistic and preclinical/translational aspects of all projects;
- Applications that do not test an overarching acquired resistance hypothesis; and
- Studies that focus solely on intrinsic mutations in cancer cells or fail to triangulate immune-oncology studies with additional non-immune stromal elements.

RFA CA-21-052 / -053 “PHS 398 Research Plan: 12 Page Limit/Project”

Significance:

- Does the U54 Center adequately address basic/mechanistic AND preclinical/translational challenges in acquired resistance in the project(s) across the tumor-tumor microenvironment continuum;
- Is there a central/overarching 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 ARTNet site, and the overall theme of ARTNet site as a whole; and
- Will the Shared Resource Cores have the capabilities of supporting the proposed basic and translational projects within the U54 Center?

Approach:

- Rationale for the tumor-TME targets, pathways, etc that will be studied;
- Strength and complementarity of multidisciplinary team design and approaches to iteratively bridge basic and translational research across the tumor-TME continuum in each U54 site

RFA CA-21-052 / -053 “PHS 398 Research Plan: 12 Page Limit/Project”

Approach (continued):

- Does the U54 involve hypothesis-driven approaches that bridge basic/mechanistic and preclinical/translational research to address unresolved acquired resistance challenges within the tumor-microenvironment continuum?
- How well matched are the Core Capabilities to the needs of the overall Site? Are they essential to the goals of bridging the basic/mechanistic and preclinical/translational aspects of the U54 Center?

Environment

- How well does the scientific environment at the participating site(s) stimulate trans-disciplinary research collaborations; and the iterative flow between basic/mechanistic and preclinical/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 within and outside the institution, especially with other members of the ARTNet?

RFA CA-21-052 / -053 “Review Information”

- Applications will be evaluated for scientific and technical merit by an appropriate ad-hoc Special Emphasis Panel convened by the NCI, using the *stated review criteria*.
- As part of the scientific peer review, all applications:
 - May undergo a selection process in which only those applications deemed to have the highest scientific and technical merit will be discussed and assigned an overall impact score – *applications will not be percentiled*.
 - Will receive a written critique.