Administrative Supplement to Study Mechanisms of Cancer Sensitivity and Resistance to Therapy Utilizing Samples and Information from Human Clinical Trials

Release date: May 31, 2016  
Application Receipt Date: July 12, 2016  
Anticipated Start Date: September 1, 2016

Purpose

The National Cancer Institute (NCI) announces the opportunity for supplemental funding to develop innovative strategies to understand and exploit mechanisms of tumor resistance to anticancer therapy. These administrative supplements to existing grants (see eligibility below) will support investigators studying mechanisms of intrinsic and acquired drug resistance, who wish to extend their research to human tumor tissue from patients on cancer clinical trials which may corroborate their hypotheses. The intent of this supplement is to translate preclinical discoveries regarding cancer sensitivity or resistance to specific targeted agents to clinical tumor biopsies and other human materials, or to patient-derived models (PDMs) which may predict clinical response of that tumor type to the agent. Therefore, each applicant for this supplement must demonstrate access to samples from a cancer clinical trial or to an adequate set of PDMs to demonstrate and extend their preclinical findings of cancer susceptibility to targeted therapy.

Intrinsic or acquired drug resistance is a recurrent theme in cancer therapies. Understanding and overcoming drug resistance mechanisms has become a focal point in precision cancer medicine. As the NCI/DCTD-supported trials networks become increasingly involved in strategies to identify tumors sensitive to targeted anticancer agents and to detect molecular alterations associated with the development of resistance, there is an urgent need to develop effective approaches and enhanced capacities for coordinated correlative studies involving analyses to discover the mechanisms of drug sensitivity and resistance.

Through the NCI NExT program, NCI/DCTD has formed collaborations with pharmaceutical companies and academic medical centers to develop over 60 anticancer agents, a list of which can be found at: ctep.cancer.gov/industryCollaborations2/agreements_agents.htm. One goal of this Administrative Supplement is to use sophisticated tools and models for the study of cancer drug resistance in order to identify new clinical development strategies. These strategies could then be advanced into early clinical trials in molecularly-defined disease subsets supported by NCI’s Early Clinical Trials program. Several networks and consortia participate in DCTD-sponsored early clinical trials including all NCI-supported Cancer Centers, NCI-Specialized Programs of Research Excellence (SPOREs), ETCTN Principal Investigators, and National Clinical Trials Network (NCTN) groups.

Eligibility Information

Supplemental funding will be available for active grants using the following grant mechanisms:

- P30 Cancer Center Support Grants (CCSG)
- P50 Specialized Program of Research Excellence (SPORE) Grants
- U10 Cooperative Clinical Research – Cooperative Agreements for the 5 US NCTN groups (both Operations and Statistical Grants)
- Adult Brain Tumor Consortium (ABTC)
- Pediatric Brain Tumor Consortium (PBTC)
- UM1 Research Project with Complex Structure Cooperative Agreement – Cooperative Agreements for the 11 US sites from NCI Experimental Therapeutics Clinical Trials Network (ETCTN).

**Number of Applications:**

Only one application per NCI award is allowed. Each application must include a cover letter from the grantee Principal Investigator (PI) or contact PI, with concurrence from the Authorized Organization Official (AOR).

Due to the limited time period for this supplement, the cancer clinical trial from which specimens will be obtained should be one which is close to completion or completed by the time of this award in September 2016, and from which a sufficient number of patient samples and clinical information have been obtained to derive robust corroboration of laboratory hypotheses. Other ways to satisfy the need for patient samples from clinical trials might be with existing *in vivo* or *in vitro* models, as long as the initiating cells are human and came from patients on clinical trials where the clinical annotation has been retained. For example, a set of pre-existing PDX models obtained from tumors of patients on a cancer trial would be an acceptable surrogate for studies on the actual tumor biopsies.

Another surrogate for sequential human tumor-derived materials from a clinical trial would be studies of drug resistance on an adequate set of cancer-derived conditionally-reprogrammed cell lines or organoid cultures, obtained from biopsies of a relevant human malignancy, and where clinical annotation regarding the patient’s response to systemic therapy was obtainable. Human cancer conditionally-reprogrammed cell lines and cancer organoid cultures hold great promise for studying tumor heterogeneity in drug response, can be established at relatively high efficiency, and hold the promise for large scale screening and fundamental cancer biology research. The supplement proposal should discuss the preclinical discovery and methods to be extended and corroborated with patient-derived tumor cell culture, and the additional mechanistic studies in resistance to targeted cancer therapy that might be performed with the conditionally-reprogrammed cancer cell lines and/or cancer organoid cultures.

The clinical trials from which tumor samples and other materials will be taken do not need to be CTEP sponsored, but must utilize targeted anticancer agents, alone or in combination with other targeted or cytotoxic agents. Trials that use investigational agents on the CTEP website will receive preference ([http://ctep.cancer.gov/protocolDevelopment/agents_drugs.htm](http://ctep.cancer.gov/protocolDevelopment/agents_drugs.htm)), but most targeted agents are eligible. Studies of resistance or sensitivity to agents targeting signaling pathways, including hormonal agents, are within the scope of this supplement. Trials involving agents targeting DNA repair or other factors in the DNA damage response, apoptosis, cell cycle regulation or epigenetic DNA modification are also within the scope of this supplement. Resistance to antibody therapy will be included in this supplement only if those antibodies block tumor growth or survival signaling pathways. Please note, however, that trials studying radioresistance, resistance to DNA damaging or other cytotoxic agents alone, or immunotherapeutic agents are outside the scope of this supplement.

The agent(s) tested in a clinical trial from which sequential samples are collected must be at level of evidence (LOE) 1 or 2 for efficacy in the clinical setting of the trial (LOE1: FDA approved agents; LOE2: Agent met a clinical endpoint [objective response, PFS, or OS] with evidence of target inhibition).
Applications utilizing resources from trials in which a high proportion of patients have biopsies both before and after therapeutic intervention, and/or at the time of progression on therapy may be preferred for funding by NCI reviewers, if those materials are sufficient for the proposed purpose of the study. For some trials, repetitive sampling for circulating tumor cells or plasma DNA may suffice, to study the development of malignant clones after targeted therapy. While not required, proposals for drug resistance studies in those tumors considered to have intrinsic drug resistance, such as pancreatic cancer, are encouraged in this initiative.

For some studies in Topic #2 (see below), investigating the mechanisms of synthetic lethality and cancer sensitivity to inhibitors of DNA repair and other DNA damage response (DDR) pathways, the loss of complementary DDR cellular pathways in cancer may lead to major responses to inhibitors of those pathways, with or without the addition of DNA damaging agents. In these cases, access to archival tumor materials from a cancer trial using these agents, and well annotated with clinical outcomes, may suffice for a response to this administrative supplement.

A letter of intent is not required. A full proposal of no more than 8 pages must be submitted by the request receipt date to the Investigational Drug Branch, Cancer Therapy Evaluation Program (CTEP), Division of Cancer Treatment and Diagnosis (DCTD), NCI, via the NCI CTEP Protocol Information Office (PIO). Funding is contingent upon NCI approval of the proposal, which will include both a scientific and budgetary evaluation.

**Supplement Goals and Background:**

To achieve the goals of this administrative supplement, studies should include corroboration of preclinical findings and hypotheses with information from clinical samples; determination of genetic and epigenetic alterations in tumor DNA with response to therapy, assessment when available of the pharmacodynamic impact of the drug on the target in the tumor and components of the tumor microenvironment, and interrogation of the mechanisms of action/resistance to specific agents.

The response to this supplement should be primarily responsive to either Topic 1 or Topic 2. These topics are used to organize issues in cancer drug resistance and sensitivity which the NCI wishes to address in this supplement. While some responses may address parts of both topics, investigators are free to choose to respond to only one of the two topics with no penalty in review.

**Topic 1:** To investigate mechanisms of intrinsic and acquired drug resistance in tumor biopsies, blood samples, or other biologic material from patients on trials with targeted anticancer agents.

The identification of drugable mutant kinases and the creation of small-molecule inhibitors designed to specifically target these mutant kinases have become important to the treatment of a number of human malignancies. Kinase inhibitors can induce dramatic responses in molecularly defined cancer cohorts. The success of the tyrosine kinase inhibitor (TKI) imatinib in BCR-ABL-positive chronic myelogenous leukemia and of kinase inhibitor and antibody therapy in HER2-amplified breast cancer, was followed by advances in the treatment of EGF receptor-mutant non-small cell lung cancer (NSCLC), ALK and ROS1-rearranged NSCLC, BRAF- and KIT-mutant melanoma and gastrointestinal stromal tumors. The development of resistance to these kinase inhibitors routinely limits the duration of their clinical benefit. Acquired resistance may be mediated by target gene modifications, activation of bypass tracks, which serve as compensatory signaling loops, or histologic transformation.
Other targeted therapeutics have also demonstrated efficacy in human cancers, and have also demonstrated evidence of the development of resistance to therapy. Ibrutinib, an inhibitor of Bruton’s tyrosine kinase and idelalisib, an inhibitor of PI3Kδ, do not require mutation of their target, but are highly active in B-cell malignancies. Palbociclib, an inhibitor of CDK4/6, has been FDA approved in combination with fulvestrant in ER-positive breast cancer. Ixazomib, a peptide binding PSMB5, joins bortezomib and carfilzomib as FDA-approved inhibitors of the proteosome. Lenalidomide interacts with the ubiquitin E3 ligase Cereblon and targets this enzyme to degrade IKZF1 and IKZF3. Studies of the development of resistance to any of these agents, using clinical materials from cancer clinical trials would be within the scope of this administrative supplement. Applicants are free to propose studies of other targeted agents, as long as these agents have LOE1 or LOE2 evidence of clinical efficacy and access to biospecimens or PDMs from trials utilizing that agent is demonstrated.

**Examples of potential proposals from eligible studies and trials could include, but are not limited to:**

1. **Early and sequential detection of genetic alterations in resistant tumor clones through less invasive means:** circulating DNA, circulating tumor cells, or other circulating soluble factors.
2. **Studies of paired or multiple biopsies or other acquisition of cancer material to examine alterations associated with adaptive or acquired resistance to inhibition of kinases or other components of critical cancer signaling pathways.** Target gene modification or activation of bypass tracks, which serve as compensatory signaling loops, can be considered.
3. **Analysis of drug resistance mechanisms through the use of patient derived xenograft tumors or cancer-derived conditionally-reprogrammed cell lines or cancer organoid cultures, developed from previously obtained clinical trial biopsies and with annotation to the original patient’s clinical response to targeted cancer therapy.**
4. **Examination of a putative mechanism of kinase inhibitor resistance in tumor biopsies following treatment, with correlation of expression/activity of that mechanism to clinical outcomes.** As an historic example, MET amplification could be examined in biopsy samples obtained from patients with tumors relapsing after erlotinib.
5. **Studies to understand drug resistance caused by epigenetic (non-mutation) mechanisms,** including epithelial-mesenchymal transition (EMT) and other changes in cell state, such as the acquisition of small cell histology in NSCLC patients developing resistance to EGFR-TKI.

**Topic 2:** To understand the genetic and cellular basis for increased sensitivity of cancers to treatment with agents targeting the DNA damage response, apoptosis and epigenetic pathways, and to corroborate these findings with the analysis of tumor specimens and clinical outcomes from cancer trials.

Cancer patients, on trials with targeted therapy, sometimes have dramatic and prolonged responses. The ability to sequence the tumor genome of such patients has sometimes led to the discovery of genetic alterations that may confer extreme dependence on the protein or pathway inhibited by the
targeted agent causing the response (e.g., TSC1 or mTOR kinase mutations confer sensitivity to everolimus). These findings are consistent with a concept of “synthetic lethality” in which a combination of mutations (or inhibition) of two genes leads to cell death, while knockdown of either gene alone continues viability. Tumors with specific DNA repair defects can be completely dependent on back-up DNA repair pathways for their survival. This dependence can be exploited therapeutically to induce synthetic lethality in tumor cells. For example, dysfunction of the breast-cancer susceptibility genes 1 and 2 (BRCA1 and BRCA2) dramatically sensitizes cells to poly(adenosine diphosphate [ADP]-ribose) polymerase (PARP) inhibitors because of an associated defect in homologous recombination (HR).

The DNA damage response (DDR) pathways evolved in response to the exposure of the genome to exogenous and endogenous genotoxins. Cells deploy a diverse repertoire of mechanisms to maintain genetic integrity. Disruption of the DDR is observed in many cancers and underlies the genomic instability that accompanies tumorigenesis and progression. Although DDR defects are causative and permissive of cancer development, they can provide a weakness that can be exploited therapeutically. Genotoxic drugs that cause DNA damage exceeding the repair capacity of DDR systems have been the mainstay of cancer therapy for over 30 years. Recent understanding of the DNA repair pathways involved in DDR has allowed the development of drugs that target individual proteins directly. These targets include the protein kinases involved in cell cycle DNA checkpoints that are induced by DNA damage and/or replicative stress (ATR, ATM, CHK1, WEE1), as well as individual enzymes involved in base excision repair (BER), non-homologous end joining (NHEJ), homologous recombination (HR), and telomere maintenance. Drugs inhibiting these specific targets can sometimes cause cytotoxicity in cancer cells which have lost complementary DDR pathways and are dependent on these remaining proteins, a form of synthetic lethality. Demonstration of these mechanisms in human tissue or models derived from patients treated with such therapy is an important goal of this supplement.

Epigenetic modification of tumor DNA can also modulate the sensitivity of cancer cells to other cytotoxic or targeted therapy. Temozolomide (TMZ)-based therapy is the standard of care for patients with glioblastoma multiforme (GBM), and resistance to this drug in GBM is modulated by the DNA repair protein O6-methylguanine-DNA methyltransferase (MGMT). Expression of MGMT is silenced by promoter methylation in approximately half of GBM tumors, and clinical studies have shown that elevated MGMT protein levels or lack of MGMT promoter methylation is associated with TMZ resistance in some, but not all, GBM tumors.

Recent next-generation sequencing studies of a large variety of cancers have brought into focus an important new theme regarding the recurrent mutations in epigenetic regulators, which are especially prevalent in the hematopoietic cancers. Studies of agents targeting epigenetic readers in cancer trials for tumors in which there is at least LOE2 evidence of activity are within the scope of this solicitation.

Tumor cells with certain genetic backgrounds have sensitivity to modulators of apoptosis and of the MDM2/p53 pathway. Venetoclax, a BH3 mimetic and inhibitor of BCL-2, is approved for the treatment of 17p deleted chronic lymphocytic leukemia. Patients with liposarcomas with MDM2 amplification and other patients with p53-wild type acute myelogenous leukemia have had objective responses to MDM2 inhibitors. Studies examining additional factors leading to sensitivity in clinical samples from these or similar trials would be responsive to this administrative supplement.

Studies of sensitivity to these drugs, or other agents with LOE1 or LOE2 clinical activity, that exploit genetic or epigenetic vulnerability of cancer cells are encouraged in the response to Topic 2 of this administrative supplement, as long as the investigator has access to adequate clinical materials of a completed or near completed cancer trial with the agent or of appropriate PDMs to conduct the proposed studies. While sequential biospecimens are preferred to examine pharmacodynamic effects
of drug on the target, a set of archival tumor materials to examine alterations of the tumor genome leading to sensitivity to the agent may be sufficient for topic 2 responses.

**Examples of potential proposals for eligible studies and trials could include:**

1. *Evaluation of samples from trials of inhibitors of the DNA damage response (DDR), with or without the addition of cytotoxic agents, to understand which genetic alterations in DDR genes render tumors dependent on compensatory DNA repair mechanisms.*
2. *Examination of biospecimens from clinical trials testing a hypothesis of synthetic lethality in cancer unrelated to DNA repair or the DNA damage response pathways.*
3. *Studies of agents targeting super enhancer regions or master regulatory nodes which are critical to a specific phenotype or cancer cell state, associated with a particular oncogenic driver or loss of regulatory genes.*
4. *Evaluation of samples from trials of inhibitors of MDM2, Bcl-2 or other apoptosis-enhancing agents in sensitive tumors such as chronic lymphocytic leukemia, to discover or confirm cellular factors associated with sensitivity to these agents.*

Investigators should establish collaborations to obtain samples from trials using targeted anticancer agents applicable to testable hypotheses of interest to your laboratory, and using assays fit for use with these samples. These trials do not need to be NCI sponsored or use agents within the CTEP portfolio, although such studies may receive preference in evaluation. Investigators are encouraged to collaborate with other NCI and non-NCI-supported clinical groups to obtain clinical samples and data.

**The types of projects may include:**

Projects which utilize specimens from NCI-supported clinical trials networks are encouraged, but trials funded by other mechanisms are acceptable. An expected outcome of the project should be a demonstration of the association of the result of the analysis of clinical samples with a clinical endpoint (e.g., survival, response, disease presence or absence). The objectives of the analysis may include readout of drug mechanism or identification or cross-validation of predictors of clinical outcomes.

**To qualify for this initiative, the applications should meet the following criteria:**

- The objectives of the proposed study should be achieved within a period of 1 year. However, NCI will consider a request for a one year extension.
- The proposed projects must fit within the scope of the parent award
- Applicants must demonstrate by a letter of support from one or more of the authorized trial organizations that they have access to the clinical samples and/or data necessary to propose studies under Topics 1 and 2 above. Proposals for studies on collections of PDX models, organoid cultures, conditionally-reprogrammed cancer cell lines or other PDMs must also have a letter of support regarding their use from the owners of those resources.
- Biospecimens from trials associated with this solicitation should already be collected by the time of the award in September 2016.
- Proposals should not be duplicative of studies already conducted or planned for the clinical trial in question or for which other funding is available.
• Specific criteria under topic 1 and 2 regarding eligible agents and types of clinical specimens must be adhered to.

**Investigators’ Team**

The projects proposed for this supplement require multi-disciplinary interaction to accomplish the design, execution and analysis of the drug sensitivity and resistance studies. Therefore, in addition to the PD/PI, the Investigators’ Team may include the following participants:

- **Clinical Investigator:** Member of the trial team, who can confirm collection of the biologic specimens, arrange for those samples to be sent to the laboratory sites, and provide clinical information for comparison with laboratory results.

- **Laboratory investigators:** Investigators are required to demonstrate expertise in the proposed laboratory assays, models or other experiments (e.g. molecular or clinical pathologist, molecular laboratory scientist)

- **Statistician/informatician/computational scientist:** Team members should be familiar with the methodology of bioassay studies. They should be capable of providing support for statistically valid design of studies and for selection and application of appropriate statistical analysis methods and computational and bioinformatics algorithms for assessment of the performance of the biomarker within the intended clinical context.

**Terms and Conditions of Funding and Allowable Costs:** The budget should justify all the direct and indirect costs. Up to $750,000 in total (direct plus indirect) costs will be available for each supplement. The award period will be for 1 year; however, NCI will consider a request for an unfunded extension of the project if needed.

(**Note: NCI expects to award up to 8 supplements**).

The budget should justify all the direct and indirect costs. Allowable costs include funding for the Project Leader of the study (maximum of 20% effort), funding for required expertise to complete this project, as well as supply costs. The purchase of large pieces of equipment through this supplement will not be permitted.

**Supplement Award Application Procedures**

1. **Cover letter:** Prospective applicants are asked to submit a letter of intent that includes the following information:
   i. Title and grant number of the parent grant
   ii. Names of other key personnel
   iii. Name of the contact person (Project Leader) of this project. Note: The PI on the supplement must be the same as the PI on the parent award.
   iv. Participating institution(s)
   v. Title of this funding opportunity

2. **Application**
   a. Standard PHS 398 (pgs 1-6)
i. Item 2: check yes and provide the title indicated in the cover letter, 1.b.

ii. Item 7A-8B, denote the direct and total costs for the project. Total costs may not exceed $750,000.

iii. The authorized organization representative must sign the face page.

iv. Include a detailed budget description.

Provide NIH biographical sketches for key members of the team not already provided in the parent grant.

b. **Summary of the Project.** On 8 pages or less describe:

**Specific Aims:** Describe the specific aims of the research project. Please indicate how the aims of the project fulfill Topics 1 or 2 of this Supplement.

i) **Background and Significance**
- Define the cancer problem to be addressed, including the assays and methods for detection and how they fit the intended clinical context in which they may be used.
- Provide the biologic rationale for the analysis and its potential implications to scientific understanding and/or development of exploiting cancer sensitivity or circumventing cancer resistance to therapy.

ii) **Preliminary Data**
- Describe the current state of analytical validation of the assay or method of detection in human specimens within the intended clinical context, including the current reagents and technologies and types, as well as the current availability of specimens that the assay will use (e.g., fresh frozen or formalin-fixed tissue, PDX tumor bank, PDMs, circulating tumor cells, serum or plasma).

iii) **Approach (describe applicable elements)**
- Plan for clinical use of the assay within one or more clinical trials.
- Provision of a statistical justification (e.g., power analysis) for the number of specimens needed.
- Plans for additional optimization of analytical performance to establish that the assay is fit-for-purpose. Some validation should have already been accomplished so that remaining optimization requirements are limited to more minor adjustments such as establishing or refining cut points for the assay.
- Plans to accrue specimens to perform the studies including identification of the clinical resource or trial that will provide specimens, documentation of appropriate availability and a letter of commitment to obtain specimens (i.e., indication that the repository holder identifies availability of specimens and that there is an appropriate process to obtain the specimens).
- Identification of potential pitfalls and alternative approaches to overcome obstacles.
- Discuss legal issues relating to the possibility of controlling intellectual property and plans for collaboration with commercial entities, if required.
- Demonstrate how the data will be analyzed and eventually made more broadly available to the research community using existing clinical and biomarker data from the treatment trial(s) described above or using other existing clinical and biomarker data from DCTD/CTEP-supported network trials. Also, describe how the data might be used to perform cross-trial and cross-site analyses.

iv) **Milestones and Timeline**
- A timeline including milestones is required.
Review Criteria: Applications will be administratively reviewed internally by NCI. Review of the applications will be based on: Responsiveness of the application to topic 1 or topic 2; Team and site organization; Scientific rationale, as well as feasibility and appropriateness of the research plan in the given clinical trial context; Availability of fit for purpose assays; Potential implications for scientific understanding or drug development; and Supportive letters of collaboration with one or more of the trial networks. The applicant needs to demonstrate access to the required tissue/blood samples for the study or demonstrate that the models being used were initiated using samples from clinical trials. The applicant must also demonstrate the ability to manage and analyze the data collected. Studies using NCI IND agents from NCI sponsored clinical trials may be prioritized; however studies that use other agents (as long as they meet LOE 1 or 2) are acceptable. Studies that use samples from clinical trials may be prioritized but samples in non-trial settings are permitted as long as they are well annotated clinically regarding treatment and response.

Review Process:
Drug resistance studies will be reviewed by NCI basic and translational research staff, statisticians and clinical experts regarding the tumor types from the trials being utilized. If samples for this supplement are acquired using NCI-supported clinical trials, it is expected that the applicant will include in the application a letter of commitment from the clinical trial leadership. If the samples come from DCTD-supported trials networks, the use of the samples will be “exempted” from the required DCTD/CTEP review process for network-funded trials. For example, NCTN samples will not have to undergo review by the Correlative Science Review Committee.

Budget
NCI will consider whether the budget and the requested period of support are fully justified and reasonable in relation to the proposed research. If NCI-supported trials permit specimen collection, shipping and/or biopsy costs in the parent grant for the trial, then these funds will be used and funding should not be requested in this supplement for these procedures. Only when funds are not available from the parent grant for the required specimen collection is the applicant permitted to include these costs in the supplement request.

Awards
Awards will be based on responsiveness to Topics 1 or 2 of this announcement and the availability of funds.

Reporting Requirements
Information on what has been accomplished via the administrative supplement during the funding period should be included in the progress report for the parent grant. Terms of award may also include milestones that will periodically be reviewed with the grantee by the NCI staff to provide assistance to the grantee, and to ensure progress toward achieving the aims of the study. A copy of the annual progress report for the administrative supplement should be sent to Dr. L. Austin Doyle (Telephone: 240-276-6565, Email: doylela@mail.nih.gov)
Contacts for Scientific Questions:

L. Austin Doyle, M.D.
Investigational Drug Branch
Cancer Therapy Evaluation Program (CTEP)
DCTD, NCI
(240) 276-6565 (Administrative Assistant)
Email: doylela@mail.nih.gov

Naoko Takebe, M.D., Ph.D.
Investigational Drug Branch
Cancer Therapy Evaluation Program (CTEP)
DCTD, NCI
(240)276-6565 (Administrative Assistant)
Email: takeben@mail.nih.gov

Beverly Teicher, M.D
Division of Cancer Treatment (DTP)
DCTD, NCI
(240)276-5972
Email: Beverly.teicher@nih.gov

Contact for Administrative Questions

Crystal Wolfrey
Chief Grants Management Officer
Director, Office of Grants Administration
National Cancer Institute, NIH
(240)276-6277
Email: wolfreyc@mail.nih.gov

Submission Instructions:

The grantee institution, on behalf of the PD/PI of the parent award, must submit the request for supplemental funds directly to NCI. Submit a signed scanned application, preferably via e-mail in an attached pdf file to the Protocol Information Office at pio@ctep.nci.nih.gov.