Request for Application (RFA)

U24 Cooperative Agreement for Biospecimen Banks to Support NCI Clinical Trials Network (NCTN)

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Biospecimens are collected on NCTN Trial protocols (U10 grants) and used for integral and integrated marker studies/assays (prognosis/prediction)

Specimens that remain in excess after clinical trial requirements have been met become “legacy” specimens and are distributed to investigators following a defined NCTN access process and approval of the study by expert review

NCTN Biospecimens
- Validation studies of predictive/prognostic markers
- Assay development/validation
- Discovery
Cooperative Group Banks (CGB) History

- Current 9 Cooperative Group Banks:
  ACOSOG, CALGB, NCCTG, NSABP, RTOG, GOG, ECOG, SWOG, COG

- Banks are an integral part of the NCTN (supported by U10 grants)

- Unique resource: collect, store and provide researchers with well-annotated specimens and clinical data from phase III and large phase II NCI Cooperative Group Clinical trials

- NCI Cooperative Group Banking RFA (Cancer Diagnosis Program):
  9 U24 grant supplements (4/1/2010-3/31/2012)
  9 U24 Cooperative Agreement Grants (4/1/2012-3/31/2015)
  Supplements for common IT Navigator development (9/2012-present)

- Present U24 CA RFA supports a harmonized NCTN banking network for reorganized 4 Adult and 1 Pediatric NCTN Groups:
  ALLIANCE, NRG, ECOG-ACRIN, SWOG, COG
### Specimen Activities in 9 Cooperative Group Banks (2008-2012)

<table>
<thead>
<tr>
<th>Specimen Type</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Solid Tumor</strong></td>
<td></td>
</tr>
<tr>
<td>Specimens Collected</td>
<td>400,866</td>
</tr>
<tr>
<td>Specimens Distributed</td>
<td>277,063</td>
</tr>
<tr>
<td><strong>Serum</strong></td>
<td></td>
</tr>
<tr>
<td>Specimens Collected</td>
<td>129,148</td>
</tr>
<tr>
<td>Specimens Distributed</td>
<td>45,823</td>
</tr>
<tr>
<td><strong>Intra/Inter Group Investigators Supported</strong></td>
<td>418</td>
</tr>
<tr>
<td><strong>External Investigators Supported</strong></td>
<td>93</td>
</tr>
<tr>
<td><strong>Leukemia</strong></td>
<td></td>
</tr>
<tr>
<td>Specimens Collected</td>
<td>93,805</td>
</tr>
<tr>
<td>Specimens Distributed</td>
<td>37,501</td>
</tr>
<tr>
<td><strong>Intra/Inter Group Investigators Supported</strong></td>
<td>109</td>
</tr>
<tr>
<td><strong>External Investigators Supported</strong></td>
<td>54</td>
</tr>
</tbody>
</table>
**Scientific Impact (2008-2012)**

- High-dose daunorubicin selectively benefits AML patients with mutations in DNMT3A, NPM1 or MLL translocations (Patel JP, *et al.*, *NEJM*; 2012)


- Relative paucity of recurrent somatic mutations in pediatric neuroblastomas challenges current therapeutic strategies that rely on frequently altered oncogenic drivers (Pugh TJ, *et al.*, *Nature Genet*, 2013)

- HPV associated oropharyngeal cancers are a different clinical entity compared to smoking related head and neck cancers (Ang KK, *et al.*, *NEJM*, 2010; & Fakhry C, *et al.*, *JNCI*, 2008)

- Identification of new recurrent mutations, such as ID3, in Burkitt’s & DLBCL opens possibility of better clinical trial design in patients with targetable mutations (Love C, *et al.*, *Nature Genet.*, 2012)
U24 Banking RFA Goals

- Consolidate current CGBs into a harmonized NCTN biospecimen banking network for 4 Adult and 1 Pediatric NCTN Groups
- Support banking infrastructure for prospective collection and storage of specimens on ongoing and new NCI trials
- Build a system for cataloging and retrieving of “legacy specimens” and specimen-associated data
- Support NCTN Biospecimen IT Navigator system, a central inventory database of specimens available for research with an integrated search engine to access specimens for the research community
- Support a bank to collect, store, and distribute biospecimens from early phase trials performed by CTEP’s Experimental Therapeutics-Clinical Trials Network (ET-CTN)
- Streamline access to biospecimens:
  - Create a centralized Front Door specimen application process to support access to the NCTN Banks (CDP)
  - Create Central Correlative Science Review Committee to review NCTN biospecimen proposals (CTEP)
NCTN IT-Navigator Goals

1. Consolidate inventory of biospecimens
2. Connect biospecimens and clinical data
3. Provide biospecimen access to research community
‘Front Door (FD)’ NCTN Biospecimen Request Process

*Investigator with a correlative science study idea is requesting NCTN bank biospecimens

Bank evaluates request for specimen availability

STAT/Data Center evaluates request for data availability and statistical considerations

Investigator / FD Concierge queries for specimens

Investigator / FD Concierge submits LOI / Request

Investigator develops full study design

Investigator’s team performs clinical correlative study analysis

Bank(s) distribute specimens to investigator

Publications

FD Concierge

Study review by NCTN Central Corr. Science Committee

Approve

Investigator finalizes regulatory documentation

IRB MTA DSA

Fully Designed Study

Investigator's team performs clinical correlative study analysis

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New U24 Banking RFA

- Consolidated NCTN biospecimen banking network
- One U24 banking grant for each new NCTN Group (5 awards)
- Grant PIs - specialists in biospecimen banking
- ALL solid tumor & leukemia banking infrastructure & operations with common SOPs
- NCTN Biospecimen IT Navigator: common inventory; specimen-data link; access for researchers; monitoring
- Centralized Front Door process: access to “legacy” specimens; application tracking, timekeeping
- One bank to collect, store & distribute biospecimens from ET-CTN trials
U24 Banking RFA Budget

- Portfolio analysis: no similar resource at the NCI

- 5 awards to support 5 NCTN Biospecimen Banks

- Total cost for 5 banks per year: $11.75M
  - Banking Operations/Infrastructure: $9.68M
  - Banking IT + IT Navigator Maintenance: $1.32M
  - Banking Early Phase Clinical Trial Specimens: $0.75M (restricted funds)

- Total cost for 5 banks over 5 years: $58.75M