Minority PDTCs RFA Working Group

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Goals/Output:

1.) Development of new PDX models and methods for standardized preclinical testing of single agents and/or combinations

2.) Completion of response studies testing agents in the newly established (and existing) PDXs

3.) Prioritization and rationale for use of NCI-IND agents in combination in ETCTN human clinical trials

NCI PDMR: NCI Patient-Derived Model Repository
ETCTN: NCI Experimental Therapeutics Clinical Trials Network
NCI-IND: NCI Investigational New Drugs
Goals/Output:

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2.) Completion of response studies testing agents in the newly established (and existing) PDXs

3.) Prioritization and rationale for use of NCI-IND agents in combination in ETCTN human clinical trials

4.) Increased diverse representation of racial/ethnic minority populations in the PDXNet

5.) Advancements in cancer health disparity research
Why are Minority PDTCs needed?

- Racial/ethnic diversity in public/private/academic repositories is historically low.

![Racial/Ethnic Representation Chart]

- Evidence supports that therapeutic outcome disparities exist among racial/ethnic minority populations
  - ARID5B SNPs contribute to racial dierptites in treatment outcomes for pediatric ALL
  - Differences in drug metabolizing enzymes (e.g. cytochrome P450, DPYD, and NUDT15) exist among population groups
  - Differences in response to anthracycline-based therapies amongst population groups

TCGA: The Cancer Genome Atlas
PDMR: NCI Patient Derived Models Repository
PLCO: Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial

NH: Native Hawaiians; PI: Pacific Islanders; AN: Alaska Natives; AI: American Indians
Minority PDTCs: Potential Outcomes

- **PDXNet Expansion**
  - Diversity of models
  - Number of Models
  - Research Goals
  - Investigator Expertise
  - Strengthened links and infrastructure within communities

- **ETCTN studies better equipped to focus upon minority populations**

- **Facilitate extramural cancer health disparities research**
  - Improved access to models
  - PDXNet preclinical data
Minority PDTCs: Requirements

- A minimum of **60%** of the PDX collections *to be developed* must be derived from minority populations.

- Require **at least 2** Full Research projects
  - Both projects must test multiple agent combinations in PDX models
  - One project must propose a health disparity research question using large scale PDX models comparing at least two populations (with a focus on therapeutic outcome disparities).

- Four required cores
  - Administrative core
  - PDX core
  - Bioinformatics core
  - Pilot projects and Trans-Network Activities Core

- Expected that research projects will employ **large scale** PDX collections (>100 models per project)
Evaluation of RFA

- Development of diverse PDX models.

- Demonstration of increased awareness/knowledge of biospecimen research among minority populations, as well as access to minority patient populations.

- Integration of the M-PDTCs into the overall PDXNet.

- Demonstrated commitment to sharing models and data.

- New data generated using targeted therapeutic agents to address CHDs

- Influence on ETCTN studies

- New data supporting if therapeutic outcome disparities exist among minority populations.
Minority PDT Cs: Potential Applicant Pool

- Administrative Supplements to Generate Cancer Models to Advance Cancer Health Disparity Research (NOT-CA-16-033), FY 2016
  - 29 applications received (15 proposed PDX models), **12 awards** (7 developing PDX models)

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th># of PDX Models</th>
<th>Population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute Lymphoblastic Leukemia</td>
<td>80</td>
<td>Hispanic and Non Hispanic</td>
</tr>
<tr>
<td>Acute Lymphoblastic Leukemia</td>
<td>12</td>
<td>African American and Hispanic</td>
</tr>
<tr>
<td>Colon</td>
<td>12</td>
<td>Hispanic, White, and African American</td>
</tr>
<tr>
<td>Liver</td>
<td>4</td>
<td>African American</td>
</tr>
<tr>
<td>Pancreatic</td>
<td>35</td>
<td>African American</td>
</tr>
<tr>
<td>Prostate</td>
<td>10</td>
<td>African American</td>
</tr>
<tr>
<td>Multiple Myeloma</td>
<td>2</td>
<td>African American</td>
</tr>
<tr>
<td>Colon**</td>
<td>30</td>
<td>African American, White</td>
</tr>
</tbody>
</table>

**Awarded in FY 2015

- Admin Supplements to Support Collaborative Research Efforts to Enhance Preclinical Drug Development and Preclinical Clinical Trials Utilizing PDX Models (DCTD)
  - 65 applications received, **17 awards**

- U54 RFA: PDX Development and Trial Centers (RFA-CA-17-003), FY 2017
Minority PDTCs: Budget Request

$3M total costs per year

- **M-PDTC (U54)**
  - Up to (2) U54 Cooperative Agreement PDTCs will be awarded.
  - Each U54 award would be $1.25M TC per year ($800K DC).
  - Total request for 2 U54 awards is $2.5M TC per year

- **Administrative Supplement for the U24**
  - Funds are requested to accommodate 2 additional PDTCs being added to the PDCCC site (U24).
  - The supplemental funds requested are $250K TC/award/year
  - Total request for the U24 supplement is $500K TC per year

- **Total Request for the full project period (5 years) is $15M.**