Update on NCI/NIH Programs for the Cancer Immunotherapy Community

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SITC Annual Meeting Nov. 5, 2011
Topics

- Clinical research funding: R01 & R21 PAs at NCI and NHLBI
- PO1s, SPORES, Bench to Bedside
- STRAP and CITN; available IT agents in NCI/BRB
- NeXT, CADP programs and NIH/OBRR
- Provocative Questions and budget picture
Clinical Research Funding: R21 vs R01

- Expired/expiring NCI R21 PAs
  - "Quick-trials" R21: PA expired and not reissued
  - PA-09-198: Biomarkers for Early Detection of Hematopoietic Malignancies (Expiring May 2012)
  - PA-08-267: Exploratory Studies in Cancer Detection & Diagnosis (Expiring Sept. 2012)

- Options
  - Short-term 3 yr R01 application, include clinical trial
    - use "pilot"," limited"," initial"," preliminary" trial in abstract, summary, etc.
    - Request CONC (Clinical Oncology) study section
  - NCI omnibus/parent R21 PA: watch for upcoming NCI announcement for specifics
  - 2 new PAs from NCI & NHLBI for trials and biomarkers
Early-Phase Clinical Trials for Blood Cell Therapies

- NHLBI PAR-11-204 R01 mechanism
- Areas of research adjunct to hematologic stem cell transplant
- Specific areas of research stated in RFA:
  - Prevent post-transplant relapse using CAR T cells
  - Other adoptive T cell therapies (virus-specific)
  - Treat GvHD or increase immune reconstitution with Tregs
  - Mesenchymal stem cells to enhance engraftment
- Contact: Dr. John Thomas
  - Division of Blood Diseases
  - ThomasJ@nhlbi.nih.gov; 301-435-9065
Cancer Biomarkers PA in NCI

- New PA: “Validation of Molecular Diagnostics to Predict Patient Outcomes Using Specimens from Multi-Site Cancer Trials”
- RO1 and R21
- Purpose: to transition candidate biomarkers from initial observations into a marker suitable for use for determining prognosis or predicting response to therapies
- Late 2011 release; Winter 2012 first submission (standard receipt dates apply)
- Contact: M. Thurin (DCTD/CDP) or Min Song (DCTD/CTEP)
PO1s: Program Project Grants

- Multi-disciplinary program having a strong central theme with clear integration; often multi-institutional.
- Minimum of 3 projects (no more than 6).
- Program Overview section: Section on Program Integration and Management key.
- Encourage advance communication with appropriate program official (Consult); budget.
- LOI required 6 weeks in advance of submission, including resubmissions.
- Review: NCI/DEA SEPs new each round.
- Funding: no payline; case-by-case pay.
- [http://deainfo.nci.nih.gov/funding.htm#grants](http://deainfo.nci.nih.gov/funding.htm#grants)
SPORE Grant (P50)

- Organ/disease-based research with focus on translation: All projects need human endpoint within 5 yrs.
- Projects do not have to interact (as in P01): emphasis on new and diverse approaches
- Team Science approach (must have clinical/applied and basic PI for each project)
- Inter-SPORE or other collaborations to accelerate translational research required; interactions with Cancer Center projects and cores stated in application
- Flexibility to terminate projects and/or add promising projects within funding period without peer review
- Requires a human Biospecimen Core; share specimens with community
- Contact: Dr. Toby Hecht (hechtt@mail.nih.gov)  
http://trp.cancer.gov
Bench-to-Bedside Program

- Program to promote new partnerships between basic science and clinical investigators
- Extended in 2006 to foster collaborations between extramural scientists and NCI intramural investigators
- Both intramural and extramural investigators can initiate applications
- Two year awards at $135K/year
- Active clinical protocol in time of award or within 3-4 yrs

See: www.cc.nih.gov/ccc/btb
STRAP and the CITN

**STRAP** (Special Translational Research Acceleration Project)
- Pilot phase supported two proposals in IRM pathway in 2010 (R. Brentjens, MSKCC and A. Raubitschek, City of Hope)
- Solicitations for new proposals not anticipated for 2012

**CITN** (Cancer Immunotherapy Trials Network)
- PI, Mac Cheever, FHCRC; includes 27 Member sites and NCI intramural as subcontract sites to FHCRC
- Purpose: To select, design and implement early phase trials using high priority immunotherapy agents with known biologic function
- Working groups to design first clinical trials: IL-15, IL-7, anti-CD40 and anti-PD1
- 2 LOIs (anti-CD40, IL-15) submitted to CTEP
- Concept submission process and other information: http://citninfo.org/index.html
4 of Top 5 Ranked Agents at NCI Conference
Now Available to CITN with Trials in Development

<table>
<thead>
<tr>
<th>#</th>
<th>AGENT</th>
<th>Source</th>
<th>Category</th>
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<tbody>
<tr>
<td>1</td>
<td>IL-15</td>
<td>NCI/BRB</td>
<td>T cell growth factor</td>
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<tr>
<td>2</td>
<td>Anti-PD1</td>
<td>Curetech</td>
<td>T cell checkpoint inhibitor</td>
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<tr>
<td>3</td>
<td>IL-12</td>
<td></td>
<td>Vaccine adjuvant</td>
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<tr>
<td>4</td>
<td>Anti-CD40 and/or CD40L</td>
<td>Pfizer</td>
<td>APC stimulator</td>
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<tr>
<td>5</td>
<td>IL-7</td>
<td>Cytheris</td>
<td>T-cell growth factor</td>
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<tr>
<td>6</td>
<td>CpG</td>
<td></td>
<td>Vaccine adjuvant</td>
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<tr>
<td>7</td>
<td>1-methyl tryptophan (1-MT)</td>
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<td>IDO inhibitor</td>
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<tr>
<td>8</td>
<td>Anti-4-1BB</td>
<td></td>
<td>T-cell stimulator</td>
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<td>9</td>
<td>Anti-TGFβ</td>
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<td>Signaling inhibitor</td>
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<td>Anti-IL-10</td>
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<td>Suppression inhibitor</td>
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<td>11</td>
<td>Flt3L</td>
<td></td>
<td>DC growth factor</td>
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<tr>
<td>12</td>
<td>Anti-GITR</td>
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<td>T cell stimulator</td>
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IT Rgts for Pre-clinical Studies from NCI/BRB

- Cytokines: IL-15, IL-7, IL-12
- Vaccine adjuvant: MPL (monophosphoryl Lipid A)
- Ligands: CD40L (Celldex)
- Chemokines: Adv-CCL21
- Anti-ganglioside antibodies: Anti-GD2 (ch.14.18, hu14.18-IL2, 1A7) and Anti-GD3 (R24, stock)
- Other antibodies and cytokines from BRB pre-clinical repository: http://web.ncifcrf.gov/research/brb/default.aspx

- Contact Karen Muszynski in BRB for NCI 2007 prioritized agents and anti-GD2 Abs
- Order Stock Reagents through BRB website
Transformation of the NCI Therapeutics Pipeline

The NCI Experimental Therapeutics (NExT) Pipeline: Target discovery through early stage clinical trials

Harmonize Activities into Single Pipeline
# NExT Pipeline: Phase and Agreement Types

<table>
<thead>
<tr>
<th>Drug Discovery</th>
<th>Early Development</th>
<th>Full Development</th>
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<tr>
<td>Target Identification and Validation</td>
<td>Hit Finding</td>
<td>Lead Optimization</td>
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<tr>
<td>Early Clinical Safety and Efficacy</td>
<td>PoC/Phase I trials</td>
<td>Phase II trials</td>
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<tr>
<td>Phase III trials</td>
<td>Registration</td>
<td>Post-launch activities</td>
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### Associated Agreement

- Chemical Biology Consortium target discovery through lead compound
- Formerly RAID and DDG – “Mid-phase projects
- CTEP – Sponsored Clinical Trials
- CBC Consortium Agreement
- “NExT MTA”, CDA’s, MTA’s
- CTA’s, CRADA’s and CSA’s subject to CTEP IP Option

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Slide Graphic courtesy of Barbara Mrockowski
Who: Researchers in academia, government, and industry, nationally and internationally

http://next.cancer.gov/
Clinical Assay Development Program (CADP) in NCI/CDP

- **Purpose:** Provide services to facilitate moving potential clinical assay to validated biomarker
- **Come in** after assay in hand but before development
- Test assay performance using retrospective samples
- Assay optimization: controls, analytical parameters, lot acceptance criteria
- Platform migration for suitability for clinical assay application
- Statistical support to assist in assay clinical validation
- Integral vs. integrated biomarkers preferred
- Link to Phase III vs. Phase II trial preferred
- **Contact:** Dr. M. Thurin (thurinm@mail.nih.gov)
OBBR
Office of Biorepositories and Biospecimen Research

- OBBR Best Practices guidelines: updated in 2010
- Biospecimen Research Database: search for articles on handling biospecimens and assays
- caHUB: coordinate specimen collection efforts within NIH and with external partners using well-defined SOPs; currently no central biobank
Provocative Questions RFA and NCI Budget Picture

- Provocative Questions RFA is designed to use R01/R21 mechanisms for novel, mission-driven science
  - Due date for first 24 questions: Nov. 14th
  - Workshops being established second round of PQs

- NCI Budget: Continuing Resolution Nov 18th
  - Slight decreases in funding expected for FY12
  - Pay structure for FY12 grants unknown at this time