• Trends and priorities in funding

• IT agents available from NCI

• Changes in the Early Clinical Trials program
Trend in RPGs funded by NCI

Research Project Grants: Number of Awards
Fiscal Years 2002-2012

*Includes Small Business Innovation Research and Small Business Technology Transfer Awards

[Bar chart showing the number of awards from 2002 to 2012 for competing and non-competing grants]
1R01-Equivalent grants  Competing applications, awards, and success rates
Funding of RPGs
by Mechanism (number of grants funded)
### Change in NCI Funding FY11 – FY13 (dollars, millions)

<table>
<thead>
<tr>
<th></th>
<th>FY11</th>
<th>FY12</th>
<th>FY13</th>
<th>% Change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appropriation</td>
<td>5,103</td>
<td>5,082</td>
<td>5,069</td>
<td>-0.3</td>
</tr>
<tr>
<td>Final</td>
<td>5,050</td>
<td>5,066</td>
<td>4,78</td>
<td>-5.1</td>
</tr>
</tbody>
</table>
### Number of RPGs Awarded FY11-FY13 (not including SBIR/STIR)

<table>
<thead>
<tr>
<th>Research Projects</th>
<th>FY11</th>
<th>FY12</th>
<th>FY13</th>
</tr>
</thead>
<tbody>
<tr>
<td>Competing</td>
<td>1,103</td>
<td>1,094</td>
<td>1,095</td>
</tr>
<tr>
<td>Non-competing</td>
<td>3,769</td>
<td>3,710</td>
<td>3,562</td>
</tr>
<tr>
<td>Total</td>
<td>4,872</td>
<td>4,804</td>
<td>4,657</td>
</tr>
</tbody>
</table>
NCI Director: Maintain Priorities
Investigator-initiated Grants High

- **FY13 fundable range** - 9% (few are not paid at or below)
- **10-15% range** (or higher if well justified): can be paid by “exception”
- **Rationale:** Grants just above “best of the best” need to be prioritized to fill gap in NCI grants portfolio and/or have especially novel and/or promising approach - broad range of applications considered

- **Process:**
  - PD prepares justification for funding
  - Rank-ordered in Programs and then Divisions
  - Final decisions at Senior Leadership meeting (Division leaders with NCI director)
Success Rates: FY12
For each Percentiled R01 application

[Diagram showing success rates across percentiles with bars and line graph]
Result of Budget Cuts to RPGs

Reduce costs while keeping numbers steady:

- Award T5s at 94% of committed
- Discontinue inflation allowance for T5s (lowers cost of non-competing by 1% of FY12)
- Fund T1s at -17% or -13% (if below $200K)
- Fund T2s at current level
- Review of grants at NCAB for highly funded investigators (over $1 million in DCs)
Cuts to Programs other than RPGs

- Cut Cancer Centers by 6.5%
- Cut R and D contracts by 8.5%
- Cut Intramural program budget
- Cut DCTD SPORE program budget
Maintain Priorities (continued)

- Center for Cancer Genomics:
  - Lou Staudt heads
- Reorganization clinical trials
  - OEWG implementation
  - NCTN (RFA-CA-12-010) and ET-CTN (RFA-CA-13-006)
- Frederick National Laboratory for Cancer Research
- Center for Global Health
- Recent initiatives:
  - Provocative questions: LOIs due December 16, 2013
  - Collaborative Research with NIH Clinical Center (PAR-13-358): X02 pre-application for new U01 due November 20, 2013 (PAR-13-357)
  - Omnibus R21 (PAR-12-145)
• Continuing Resolution (FY13 budget) until January 15th

• President Obama proposal:
  – 1.5% increase to NIH over FY12 & cancel sequestration
  – if no compromise in Congress: ??

• RPG funding:
  – “Fundable range” remains at 9% for R01s and R21s
  – award non-competing (T5s) at 90% of committed (possible revision to committed if/when final budget allows)
## Cancer Immunotherapy Trials Network (CITN)
### Agents Currently under Study

<table>
<thead>
<tr>
<th>Rank</th>
<th>Agent</th>
<th>Category</th>
<th>Source</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>IL-15</td>
<td>T cell growth factor</td>
<td>NCI/BRB</td>
<td>Patient Enrollment ongoing!</td>
</tr>
<tr>
<td>1a</td>
<td>IL-15/ IL15Rα</td>
<td>T cell growth factor</td>
<td>Altor</td>
<td>Protocol approved; trial to open 12/13</td>
</tr>
<tr>
<td>3</td>
<td>Anti-PD1/PDL1</td>
<td>T cell checkpoint inhibitor</td>
<td>Merck</td>
<td>2 LOIs submitted to CTEP for review</td>
</tr>
<tr>
<td>4</td>
<td>Anti-CD40</td>
<td>APC stimulator</td>
<td>New source: Roche</td>
<td>Study opened for accrual but on hold due to agent supply constraint</td>
</tr>
<tr>
<td>5</td>
<td>IL-7</td>
<td>T cell growth factor</td>
<td>New source: Cognate BioServices</td>
<td>2 trials: 1 combination trial activated &amp; CITN to join NCI/CCR trial; both on hold due to agent supply constraint</td>
</tr>
<tr>
<td>7</td>
<td>1-MT or alternate</td>
<td>IDO inhibitor</td>
<td>Incyte</td>
<td>2 trials: 1 protocol in melanoma activated; 1 protocol for ovarian Ca in revision</td>
</tr>
<tr>
<td>11</td>
<td>Flt3-L</td>
<td>DC growth factor</td>
<td>Celldex</td>
<td>LOI approved; protocol submitted to CTEP</td>
</tr>
</tbody>
</table>
Clinical Grade Agents Developed in Biological Resources Branch/NCI

- rhIL-15
  - Availability good and BRB will supplement current lots
- ch14.18 anti-GD$_2$ monoclonal antibody
  - Available for future studies
  - Now also supplied by United Therapeutics
- rhIL-4 (small amounts available)
- rhIL-7
  - Potential alternative/replacement IL-7 for new company product

- Contact Dr. Steve Creekmore (creekmores@mail.nih.gov)
- Submit NeXT application! (http://next.cancer.gov)
Agents for Pre-clinical Studies
NCI Biological Resources Branch

- Cytokines: IL-15, IL-7, IL-4 and IL-12
- Vaccine adjuvant: MPL (monophosphoryl Lipid A)
- Chemokines: Adv-CCL21
- Anti-ganglioside antibodies:
  - Anti-GD$_2$ (ch.14.18, hu14.18-IL2, 1A7 anti-idiotype)
  - Anti-GD$_3$ (R24)

For current development status and information on how to obtain one of these agents, please contact:

Dr. Karen Muszynski (muszynskik@mail.nih.gov)
Immunomodulatory Agents in NCI/CTEP

- **Anti-CTLA4 (ipilimumab)**
  - 17 active or soon to be activated protocols
  - 9 in hem malignancies; 8 in solid tumors

- **IL-15**
  - Drug Master File with FDA
  - Not accepting LOIs now until data from Phase I studies received

- **IL-12**: 2 LOIs approved

- **Anti-PD1**
  - CRADA with Merck and BMS
  - Solicitation in December, 2013 for studies

- **Pomalidomide**

- **NY-ESO vaccine**

- **ID0 inhibitors**: I-MT and INCB02436 (IND in process)
## NCI Early Clinical Trials Program: Scientific Changes

<table>
<thead>
<tr>
<th>Scientific Elements</th>
<th>Current Program</th>
<th>Proposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Molecular Characterization of Tumor</td>
<td>Occasional</td>
<td>Expected</td>
</tr>
<tr>
<td>Team Science</td>
<td>Infrequent</td>
<td>Required</td>
</tr>
<tr>
<td>Tackle critical unanswered questions:</td>
<td>Often, optional</td>
<td>Expected</td>
</tr>
<tr>
<td>• Disease-based</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Biomarker-based</td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Drug combinations</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## NCI Early Clinical Trials Program: Operational Changes

<table>
<thead>
<tr>
<th>Operational Elements</th>
<th>Current Program</th>
<th>Proposed</th>
</tr>
</thead>
<tbody>
<tr>
<td>Organization</td>
<td>In Silos (14 sites)</td>
<td>Integrated Network</td>
</tr>
<tr>
<td>Centralized Support</td>
<td>Limited: •Safety •Auditing</td>
<td>Comprehensive: •Safety •Auditing •Data capture/monitoring •Central Institutional Review Board •Registration/Roster/Regulatory •Project management •Pharmacokinetics</td>
</tr>
<tr>
<td>Timeline-LOI approval</td>
<td>~21 months</td>
<td>~15 months</td>
</tr>
<tr>
<td>Set-aside for Molecular Characterization and Sample Acquisition</td>
<td>Limited</td>
<td>• Fewer sites, fewer trials, more extensive characterization • Single pipeline from pre-clinical to clinical development</td>
</tr>
</tbody>
</table>