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NCI Update to SITC

November, 2013

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National Cancer Institute/NIH

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
National Institutes of Health

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Outline

- Trends and priorities in funding
- IT agents available from NCI
- Changes in the Early Clinical Trials program

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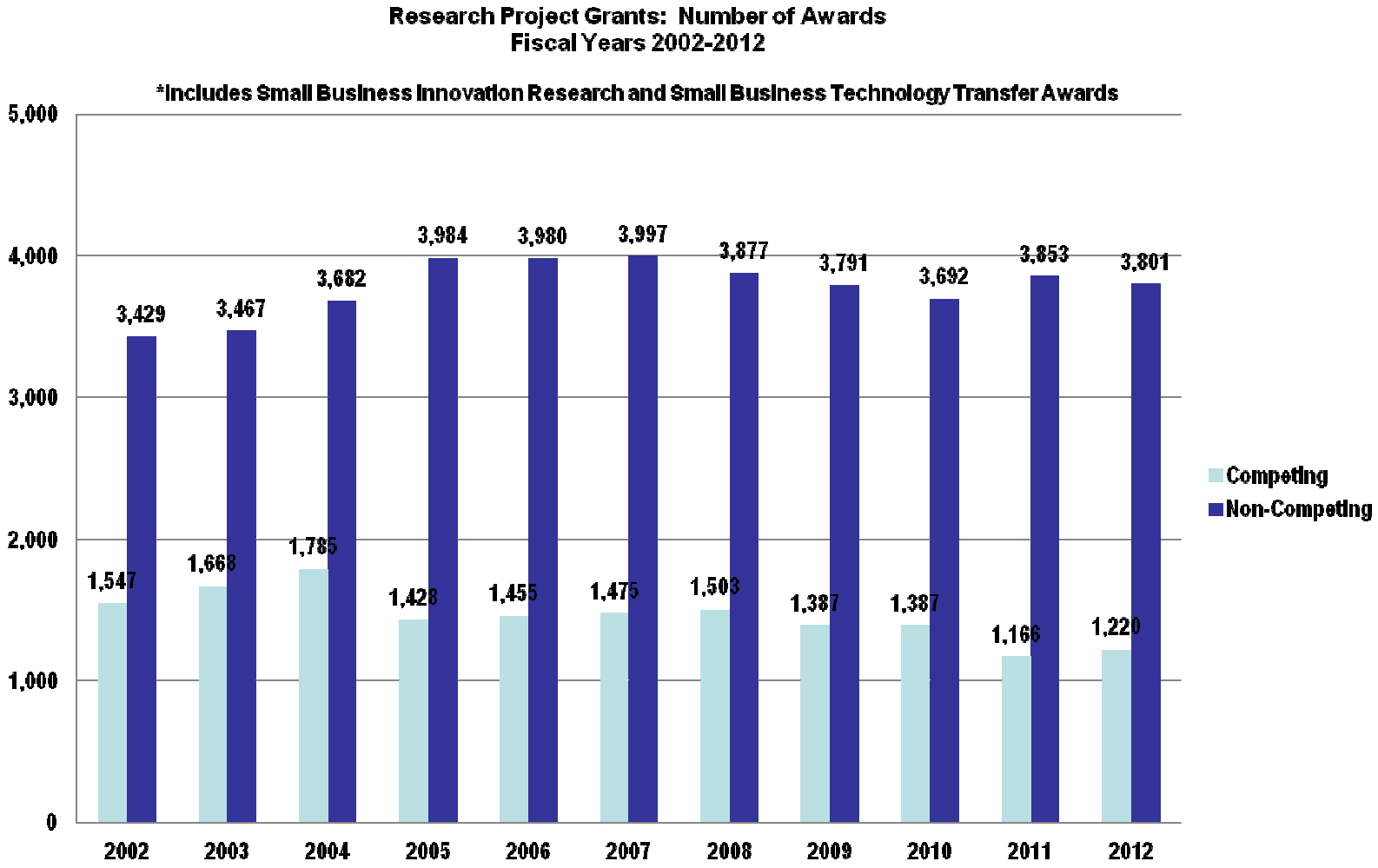
Trend in RPGs funded by NCI



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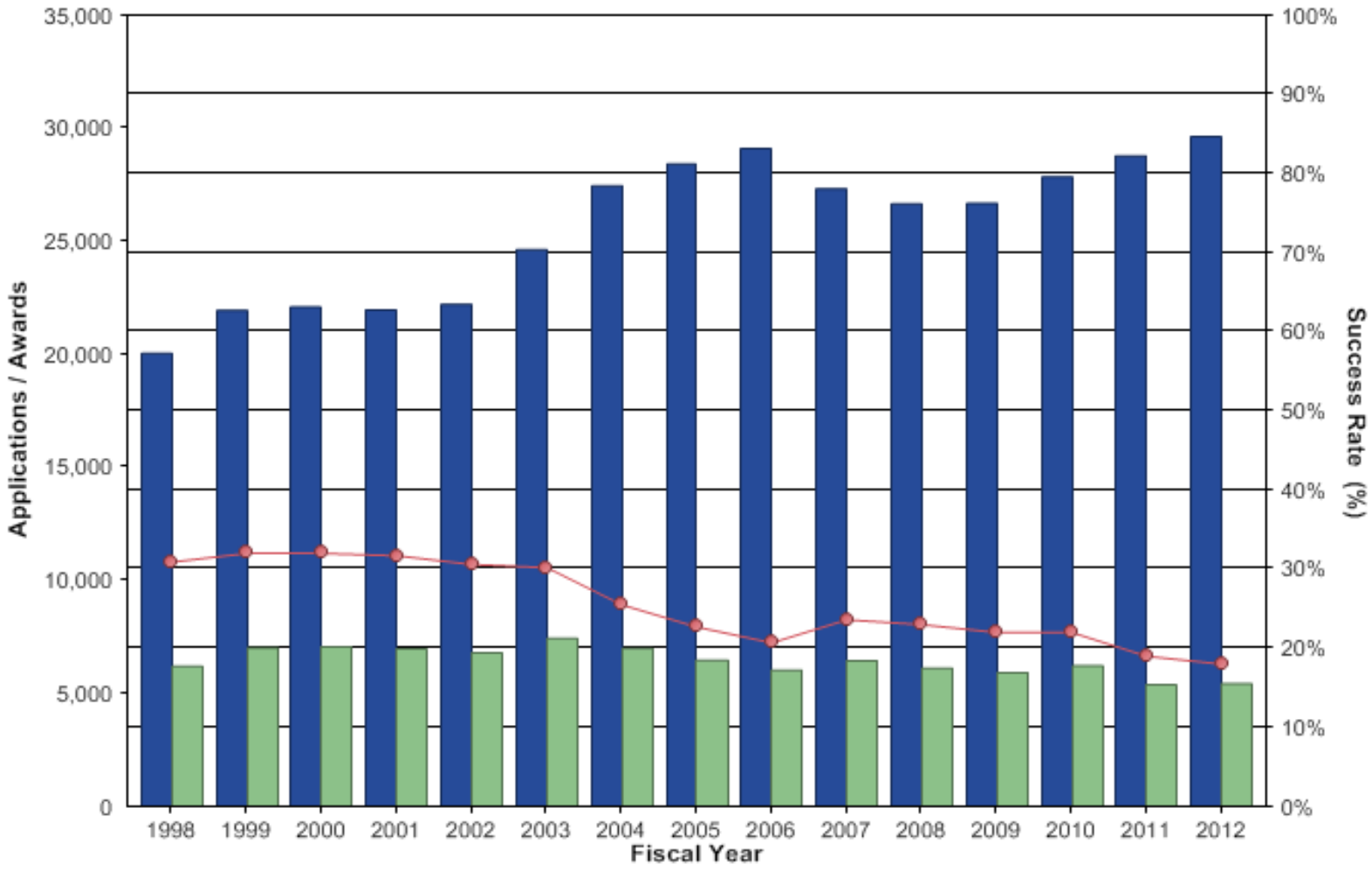
1R01-Equivalent grants Competing

applications, awards, and success rates



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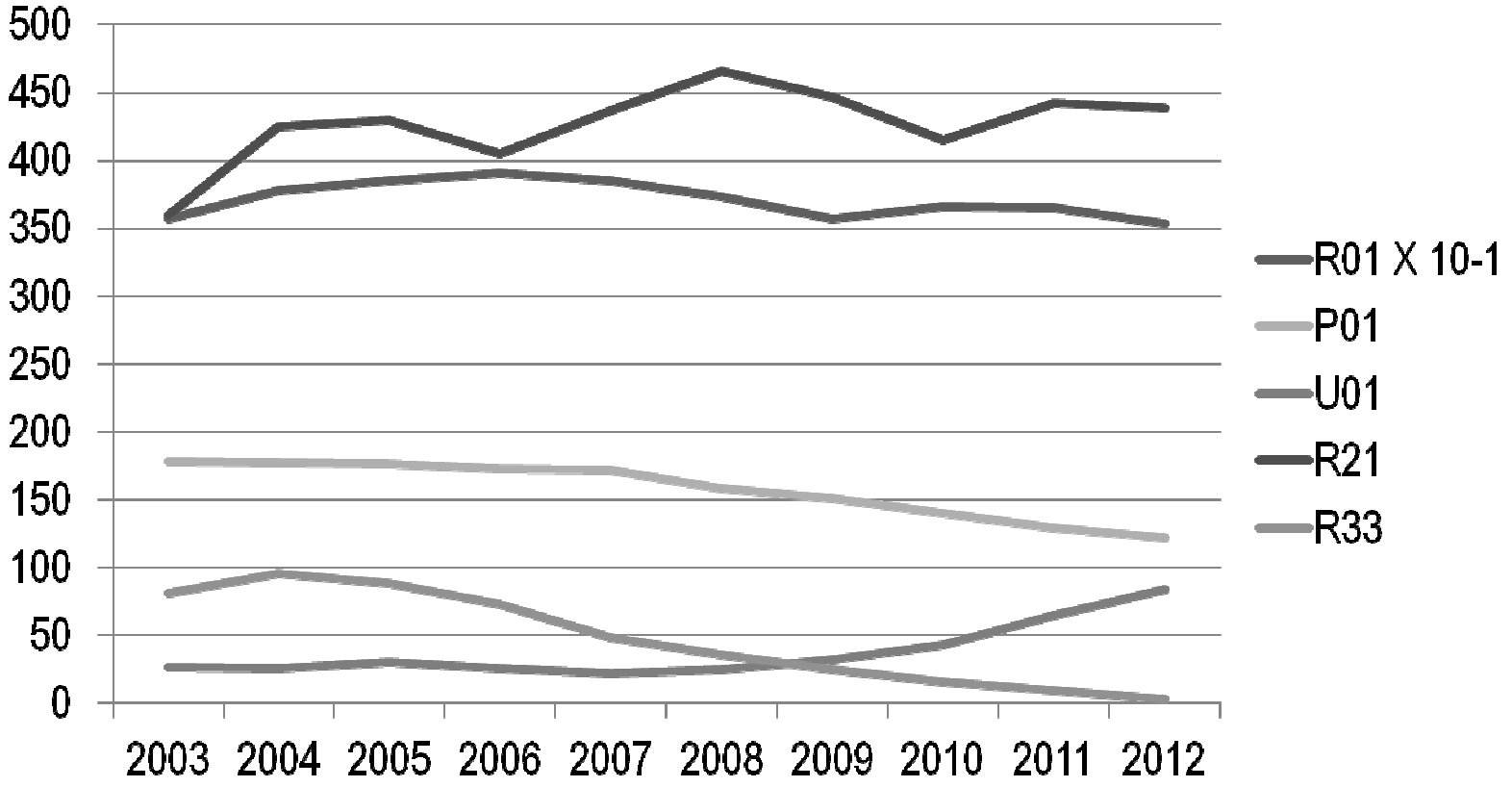
Funding of RPGs

by Mechanism (number of grants funded)



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Change in NCI Funding FY11 – FY13 (dollars, millions)

	FY11	FY12	FY13	% Change
Appropriation	5,103	5,082	5,069	- 0.3
Final	5,050	5,066	4,78	- 5.1

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Number of RPGs Awarded FY11-FY13
(not including SBIR/STIR)

Research Projects	FY11	FY12	FY13
Competing	**1,103**	**1,094**	**1,095**
Non-competing	3,769	3,710	3,562
Total	4,872	4,804	4,657

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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)

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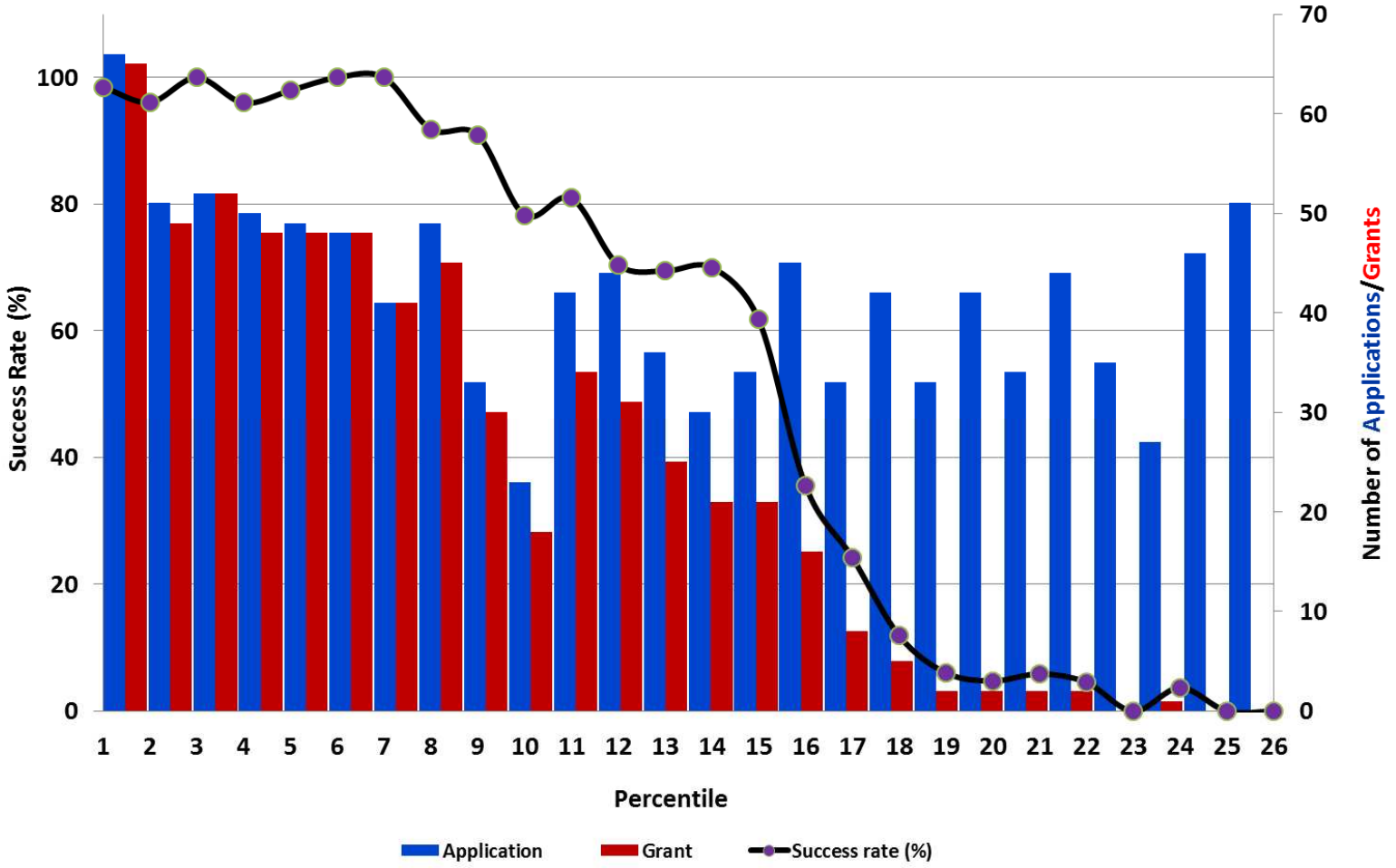
Success Rates: FY12
For each Percentiled R01 application



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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)**

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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

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Maintain Priorities (continued)

- Center for Cancer Genomics:
  - http://www.cancer.gov/aboutnci/budget_planning_leg/plan-2013/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
  - http://ncifrederick.cancer.gov
- Center for Global Health
  - http://www.cancer.gov/aboutnci/globalhealth
- Recent initiatives:
  - Provocative questions: LOIs due December 16, 2013 http://provocativequestions.nci.nih.gov/
  - 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)

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FY14 NCI Budget

- 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)

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Cancer Immunotherapy Trials Network (CITN)

Agents Currently under Study

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

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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)

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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)

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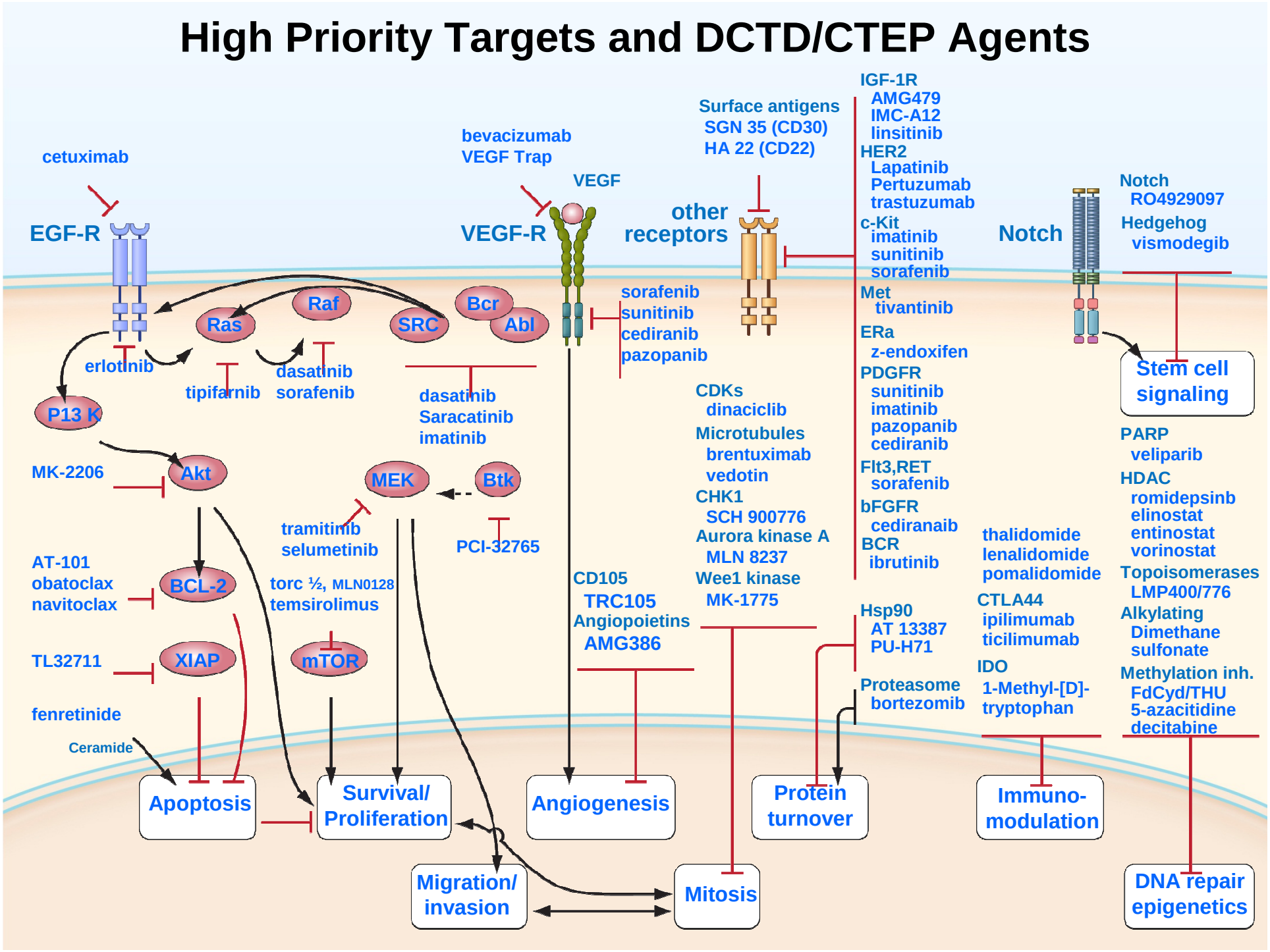
Immunomodulatory Agents in NCI/CTEP

- **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)

High Priority Targets and DCTD/CTEP Agents



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NCI Early Clinical Trials Program: Scientific Changes

Scientific Elements	Current Program	Proposed
Molecular Characterization of Tumor	Occasional	Expected
Team Science	Infrequent	Required
Tackle critical unanswered questions: •Disease-based •Biomarker-based •Drug combinations	Often, optional	Expected

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NCI Early Clinical Trials Program: Operational Changes

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

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Integration of NCI-Sponsored Experimental Therapeutics Programs: NCI Team Science-Project Development