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Update on NCI/NIH Programs for the Cancer Immunotherapy Community

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SITC Annual Meeting Nov. 5, 2011

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Topics

- Clinical research funding: R01 & R21 PAs at NCI and NHLBI
- P01s, SPORES, Bench to Bedside
- STRAP and CITN; available IT agents in NCI/BRB
- NeXT, CADP programs and NIH/OBBR
- Provocative Questions and budget picture

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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

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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
  - Mesencyhmal stem cells to enhance engraftment
- Due Dates: Oct. 5, 2011 and Oct 5, 2012
- Contact: Dr. John Thomas
  - Division of Blood Diseases
  - ThomasJ@nhlbi.nih.gov; 301-435-9065

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Cancer Biomarkers PA in NCI

- New PA: "Validation of Molecular Diagnostics to Predict Patient Outcomes Using Specimens from Multi-Site Cancer Trials"
- R01 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)

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P01s: 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

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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

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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

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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

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4 of Top 5 Ranked Agents at NCI Conference Now Available to CITN with Trials in Development

#	AGENT	Source	Category
1	*IL-15*	NCI/BRB	T cell growth factor
2	*Anti-PD1*	Curetech	T cell checkpoint inhibitor
3	IL-12		Vaccine adjuvant
4	*Anti-CD40* and/or CD40L	Pfizer	APC stimulator
5	*IL-7*	Cytheris	T-cell growth factor
6	CpG		Vaccine adjuvant
7	1-methyl tryptophan (1-MT)		IDO inhibitor
8	Anti-4-1BB		T-cell stimulator
9	Anti-TGFβ		Signaling inhibitor
10	Anti-IL-10		Suppression inhibitor
11	Flt3L		DC growth factor
12	Anti-GITR		T cell stimulator

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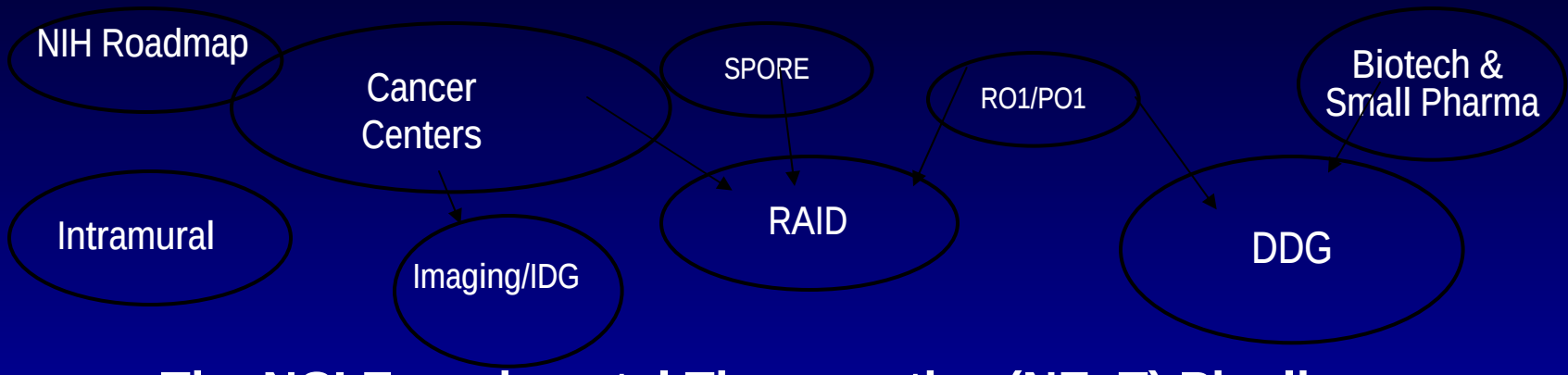
IT Rgts for Pre-clinical Studies from NCI/BRB

- 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

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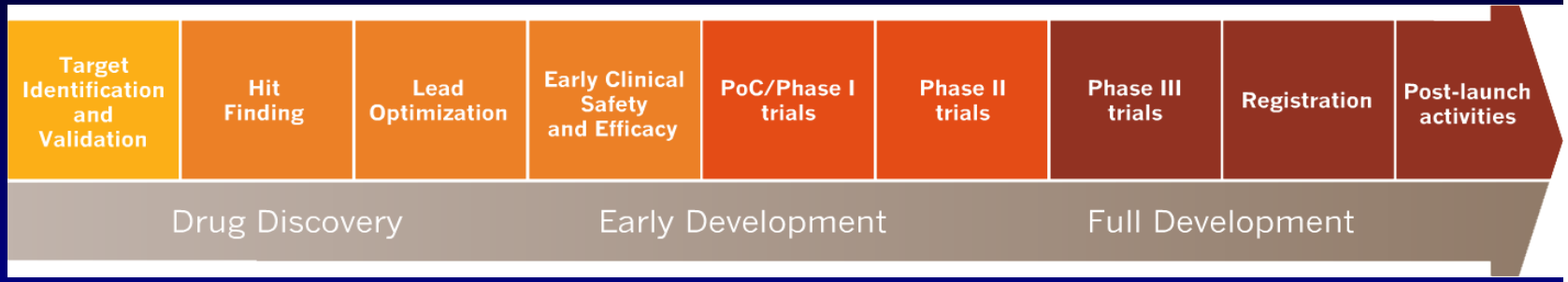
NExT Pipeline: Phase and Agreement Types



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

Associated Agreement

Slide Graphic courtesy of Barbara Mrockowski

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Access to NExT

Who: Researchers in academia, government and industry, nationally and internationally

http://next.cancer.gov/

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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)

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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
- http://biospecimens.cancer.gov/

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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
  - http://provocativequestions.nci.nih.gov/rfa
- NCI Budget: Continuing Resolution Nov 18th
  - Slight decreases in funding expected for FY12
  - Pay structure for FY12 grants unknown at this time