NCAB ad hoc Subcommittee on Experimental Therapeutics

NIH NATIONAL CANCER INSTITUTE

December 2, 2024

Challenge: Advancing New Therapeutics

Advancing new therapeutic strategies into commercial sector i.e. getting more drugs to patients and recruitment of partners and investors

Issue: Too many discoveries, not enough lead candidates in phase I

NCI extramural support (Division of Cancer Treatment & Diagnosis) for Translational Development

a. **Grant funding –** RPGs such as R01, P01, P50, supplements
   1. New initiatives take a long time to develop, publish, award, require dedicated funding from the Division/Institute,
   2. Limited RPG budget that can't cover expensive IND-enabling activities (GLP tox, GMP manufacturing)
   3. Study sections favor 'hypothesis-driven' research, not iterative drug development activities (dose range exploration, formulation optimization)

b. **NExT Program – NCI conducts the development activities on behalf of the PI/company**
   1. Competitive and limited capacity (currently ~20 development projects ongoing in DTP)
   2. Limited DCTD budget to conduct expensive IND-enabling activities
   3. Competitive entry to Clinical Trials network (ETCTN) not guaranteed

Academics: Supplemental funding to fill gaps

DCTD supplements to improve cGMP manufacturing for T-cell products targeting solid cancers

Site	MD Anderson Cancer Center (MDACC)	Memorial Sloan Kettering Cancer Center (MSKCC)	Moffitt Cancer Center
Focus	TILs	CAR T cells	TILs
Disease Target	pancreatic cancer (PDAC)	Chronic lymphocytic leukemia (CLL)	bladder cancer
Technology	Wave Bags	Miltenyi Clinimacs Prodigy	G-REX 100 MCS
Aims	• Develop more potent TILs using anti-4-1BB antibody in culture. • Streamline TIL manufacturing for multi-center trials. • Reducing the time & expertise for TIL expansion.	• Optimize manufacture of PSMA-specific CAR T cells, based on the 28z/4-1BBL design. • Validate full scale cGMP manufacturing process and validate shipping methods.	• Optimize antigen-specific TIL autologous products against solid tumor antigens. • Demonstrate preparation of TIL autologous products by cGMP for multi-center trials.
Outcomes	• 4-1BB agonistic antibody addition to culture enhanced total TIL #s (preferential CD8+ TIL expansion). • Validated receiving, cryopreservation & shipping.	• 5 Prodigy validation runs w/ apheresis from healthy/CLL donors. • 3/5 runs successful w/ high transduction efficiency.	• Increased TIL expansion in the pre-Rapid Expansion Phase (REP) culture by addition of anti 4-1BB • conversion to a closed system (G-REX 100 MCS)
Site Visit	October 1-2, 2018	October 1-2, 2018	October 1-2, 2018

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SBIR/STTR programs

a. **Traditional SBIR/STTR grants**
   Provides funding and Phase I to Phase II gate-keeping but not expertise and oversight

b. **SBIR Contracts:** Proposed contract topics must support R&D leading to the development of products, processes, or services that have commercial potential. All topics should focus on areas with strong underlying science and the potential to address unmet patient and/or research needs relevant to the broader cancer community.

Proposal: Partner with DTP to solicit translational projects to drive new therapies to clinical testing

Phase I: up to $400,000 for up to 12 months
Phase II: up to $2,250,000 for up to 2 years
Phase I, Fast Track and Direct to Phase II applications are accepted

a. Requires task updates, milestones, deliverables that must be reviewed and accepted by NCI Contract Officer Representative

NIH/NCI 472 - Antibody-Drug Conjugates as Radiopharmaceutical Theranostics for Cancer

NIH/NCI 468 - Synthetic Microbes (Excluding Oncolytic Viruses) for Immuno-Oncology Therapies - NCI (cancer.gov)

Request for Subcommittee: Translational Topics

- Antibody Drug Conjugate technology
- Therapeutic vaccines
  - mRNA
  - Peptide
- Other?

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