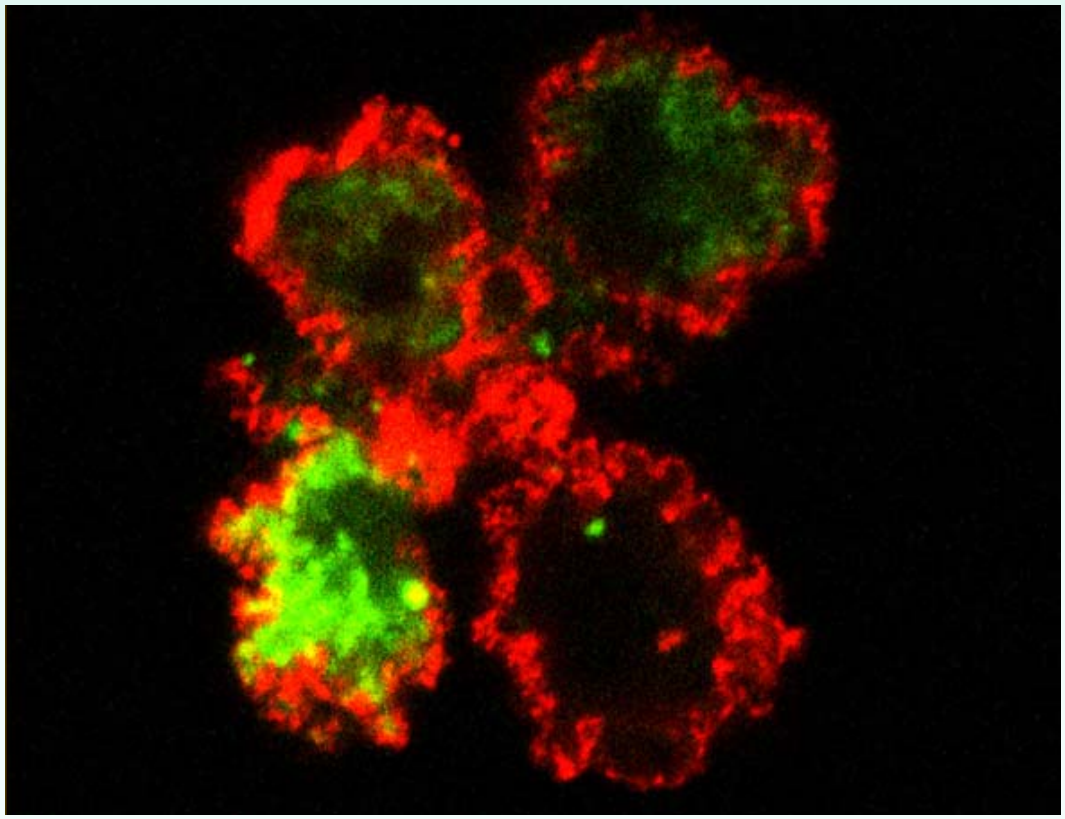
Cancer Immunotherapy Trials Network

iSBTc 25th Annual Meeting (Oct 4, 2010)



CITN: Vision

- To provide a highly collaborative structure to efficiently develop innovative, intelligent & biologically dictated immunotherapy regimens

Overall Strategy

- To design, develop & conduct important trials not otherwise possible
  - Best peer reviewed concepts
  - Optimal trial design, monitoring & trial sites provided by the CITN
  - Use of the best agents not generally available
    - Provided with the assistance of the NCI and/or industry.

Overall Strategy

- Tactics:
  - To be determined by Member Site PIs, External Advisory Board
    - With the PI & Co-Investigators

- My View:
  - To develop regimens that prospectively & predictably greatly increase the number of T cells specific for known and defined antigens
  - To develop “off the shelf” regimens that can be used by multiple investigators in multiple circumstances to serve as the backbone for further immunotherapy agent development
  - To focus on agents, antigens and regimens that have received consensus prioritization in previous workshops

Priority Agents

(from NCI Immunotherapy Agent Workshop)
(**Bold** agents - prioritized by the Immune Response Modifier Prioritization Working Group)

- T cell growth factors
  - **IL-7, IL-15**
- Dendritic cell activators
  - **Anti-CD40,** CD40L
- Dendritic cell growth factors
  - **Flt3L**
- Vaccine adjuvants
  - **IL-12 CpG MPL,** Poly I:C, Resiquimod, 852A
- T cell stimulators
  - **4-1-BB,** Anti-GITR, Anti-OX40
- T cell attracting chemokines
  - **CCL21**
- Inhibitors of T cell checkpoint blockade
  - **Anti-PD1 & PD1 Ligand,** Anti-B7-H4, Anti-LAG-3, LIGHT
- Inhibitors
  - IDO immunosuppression (**1-methyl tryptophan**)
  - Signaling (**Anti-TGF-b)**
  - Inhibition (**Anti-IL 10** & anti-IL 10R)

CITN: Basic Tenets

- Hybrid clinical trials model
  - Academic hypothesis-driven, peer-reviewed
  - Pharmaceutical-like efficiencies
- Proactively seek & initiate the best trials
  - Open submission of trials from any investigator
  - Selection by panel of successful immunologists & immunotherapists
    - Selection based on best science & likelihood of success in cancer therapy
- Design optimal trials using the best agents available
  - Will develop selected trials into “best” trials possible using combined Network skills & best agents available
  - To work with CTEP, industry & academic investigators to bring best agents together

CITN: Basic Tenets

- Provide key personnel and services for optimal trials
  - Protocol specialists, regulatory affairs, contracting, forms developer, statistician, etc.
- Set up and accrue trials rapidly
  - To provide experienced, preselected & precontracted trial sites
- Provide optimal immune response data
  - Centralized laboratory for validated immune response data
- Provide quality monitoring to assure quality outcome data
- Provide adequate, on-time funding
- Rapidly disseminate results

CITN: Organization

- COSC
  - (Central Operations & Statistical Center)
  - Based at the Fred Hutchinson Cancer Research Center (FHCRC)
  - To provide leadership & organizational resources
    - Infrastructure
    - Protocol coordination
    - Statistical support
- Up to 25 member institutions
  - To select & refine trials
  - To accrue patients

CITN: Leadership

- Mac Cheever – PI
  - Responsible for the Central Operations & Statistical Center (COSC)
    - Background – Principles of T cell therapy, cancer antigen discovery, industry cancer vaccine & therapeutic antibody product development, consensus prioritization of immunotherapy agents, antigenic targets, and regimens
- Dr. Mary L. “Nora” Disis - Co-Investigator
  - Responsible for immune monitoring
    - Background – Development, conduct and evaluation of phase I and II cancer vaccine and T cell therapy trials, development and application of novel techniques in immune monitoring.
    - PI of the University of Washington Clinical Translational Science Award (CTSA) Institute for Translational Health Science
- Kim Margolin - Co-Investigator
  - Shared responsible for organization & trial development
    - Background - Organizing, conducting and participating in multi-institutional trials as a leader of the Cytokine Working Group.
    - Expertise related to the FDA approval of immunotherapy agents as a past member of the Oncologic Drugs Advisory Committee (ODAC)

CITN: Leadership

- John Thompson
  - Consultant – Phase I/II protocol design
    - Director FHCRC/UW Phase I program
- Francesco Marincola
  - Consultant - Immune monitoring
    - Chief of the Infectious Disease and Immunogenetics Section in the Department of Transfusion Medicine at the Clinical Center of the NIH in Bethesda.
- Anna Karolina Palucka
  - Consultant - Analysis of blood transcriptional profiles and biomarker signatures
    - Investigator, Baylor Institute for Immunology Research

FHCRC – Extensive Experience Leading Coordinating Centers

- WHI - Clinical Coordinating Center for the Women's Health Initiative
- EDRN - Early Detection Research Network - Data Management and Coordination Center
- SWOG - Southwest Oncology Group Statistical Center
- HVTN - HIV Vaccine Trials Network
- Center for Human Embryonic Stem Cell Research,
- TREC - Center for Ecogenetics/Environmental Health, the Transdisciplinary Research on Energetics and Cancer Coordinating Center,
- CARET - Carotene and Retinol Efficacy Trial (CARET) Coordinating Center,
- Northwest Genome Engineering Consortium,
- Center for Evaluation of Biomarkers for Breast Cancer.

- Standard processes and procedures for monitoring financial and regulatory aspect of Networks in place

CITN: Management in association with the HVTN (HIV Vaccine Trials Network)

- PI: Larry Corey – Director of FHCRC
- NIH NIAID funded multi-institutional multinational consortium
  - 28 trial sites in 17 countries on 4 continents
  - Conducted 44 vaccine trials
    - 17 first-in-human
    - 2 phase IIB large-scale “proof of concept” trials
    - Enrolled 8700 people
    - 10 trials to be initiated within the next 10 months
- To provide expertise in running early phase clinical trials with immunogens without having to establish a parallel infrastructure.
- HVTN personnel
  - 6 staff physicians for protocol design and safety monitoring
  - 6 PhD scientists for GLP immune monitoring assay
  - Statistical Center & Regulatory specialists

CITN: Trial Selection Process

- Peer-review process
  - Top scientists from the field
  - Assurance that all applicants are given thorough and fair consideration
- Open call for proposals
  - Year round
  - Investigator driven
  - Reviewed by Network personal and Site PIs
  - Emphasis on merit, significance, investigator experience and scientific merit
- Successful applicants submit a more detailed “Full Application”
  - Full applications to be developed by PI with assistance from Network
- Network to provide detailed conditions for acceptance including recommended changes
  - Protocol
  - Study design
  - Adjuvant & agents
  - Immunologic studies
  - Ethics processes
  - Etc

Trial Management: Comprehensive Support to be Provided to PI – From COSC & Member Site PIs

- Agents for “best trial possible” not otherwise possible
- Expertise and support for:
  - Protocol design
  - Regulatory approval
  - Collaborators/clinical site identification
  - Mechanistic study design
  - Site training
  - Patient recruitment
  - Protocol monitoring
  - Data acquisition
  - Immune response assays and marker studies and data analysis
  - Data analysis
  - Correlative studies

What can we expect?

How big is it?

- CITN - Projected 15 trials over 5 years
  - $17M total cost (direct & indirect)

  < $1M/ trial
- Immune Tolerance Network (ITN)
  - Initiated with $140M direct costs over 7 years from NIAID
  - Renewal at $213M over 7 years
  - Receives considerable funding from non-NIH sources
    - 10% Industry
    - 10% Foundations
- HIV Vaccine Trials Network (HVTN)
  - Received >$250M over 9 years from NIAID
  - Key components supplemented by Gates Foundation
  - Some industry support

Prioritization is Mandatory!

Leveraged Support is Possible

- Funding from multiple sources will be facilitated by other organization desire for Network functions not readily available elsewhere:
  - “Best” trials possible based on biology
  - Immunologic & immunotherapy expertise
  - Efficient & cost effective trials
- Sources of leveraged funding
  - NCI – e.g., correlative studies / NExT / intramural collaboration
  - Industry
  - Non-governmental funding agencies & foundations
    - Disease focused organizations
  - Advocates & individual donations

Member Site Selection

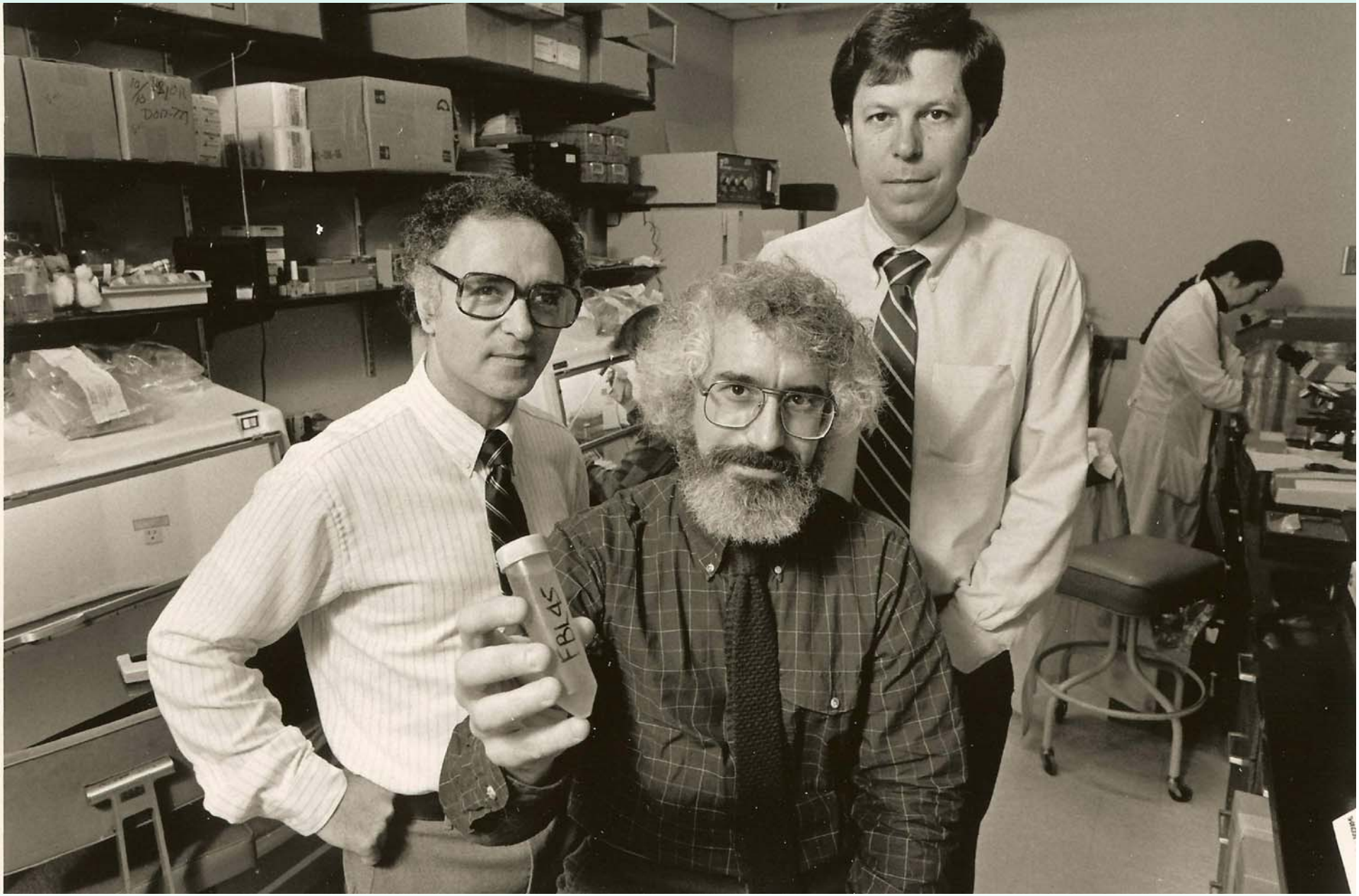
- To be chosen based on
  - Past experience in leading or participating in Phase I and II immunotherapy trials
  - Capacity to contribute to the scientific leadership of the CITN

- Application due November 15, 2010
- LOI should be received by October 15, 2010

- CTEP web site for details

http://ctep.info.nih.gov/

T Cell Therapy: The Early Years



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