Weill Cornell Medicine

Faculty Management of Complex, Federally Funded, Clinical Research Projects

Douglas F. Nixon, MD, PhD
Professor of Immunology in Medicine
Principal Investigator

Robert L. Furler, PhD
Assistant Professor of Immunology in Medicine
UM1 Program Manager

Timothy Wilkin, MD
Associate Professor of Medicine
Co-Investigator

October 8, 2019
RAPID Meeting

Weill Cornell Medicine

NIH UM1 Grant Overview

BELIEVE

IN THE CURE

MARTIN DELANEY COLLABORATORY

Bench to bed Enhanced Lymphocyte Infusions to Engineer Viral Eradication

Bench to Bed Enhanced Lymphocyte Infusions to Engineer Viral Eradication

Goal: To enhance and improve immune responses to HIV, targeting antibodies, innate and adaptive cells as therapies; combine with other agents; and to target to sites where latent virus resides: Enhanced immunotherapy to HIV

Why should you BELIEVE?

Questions: Can we make an individual's immune system work better? Could an improved immune system eradicate the virus?

Progress: Our first clinical safety trial started enrolling in Spring 2019. We will expand an individual's white blood cells that attack parts of HIV that do not mutate.

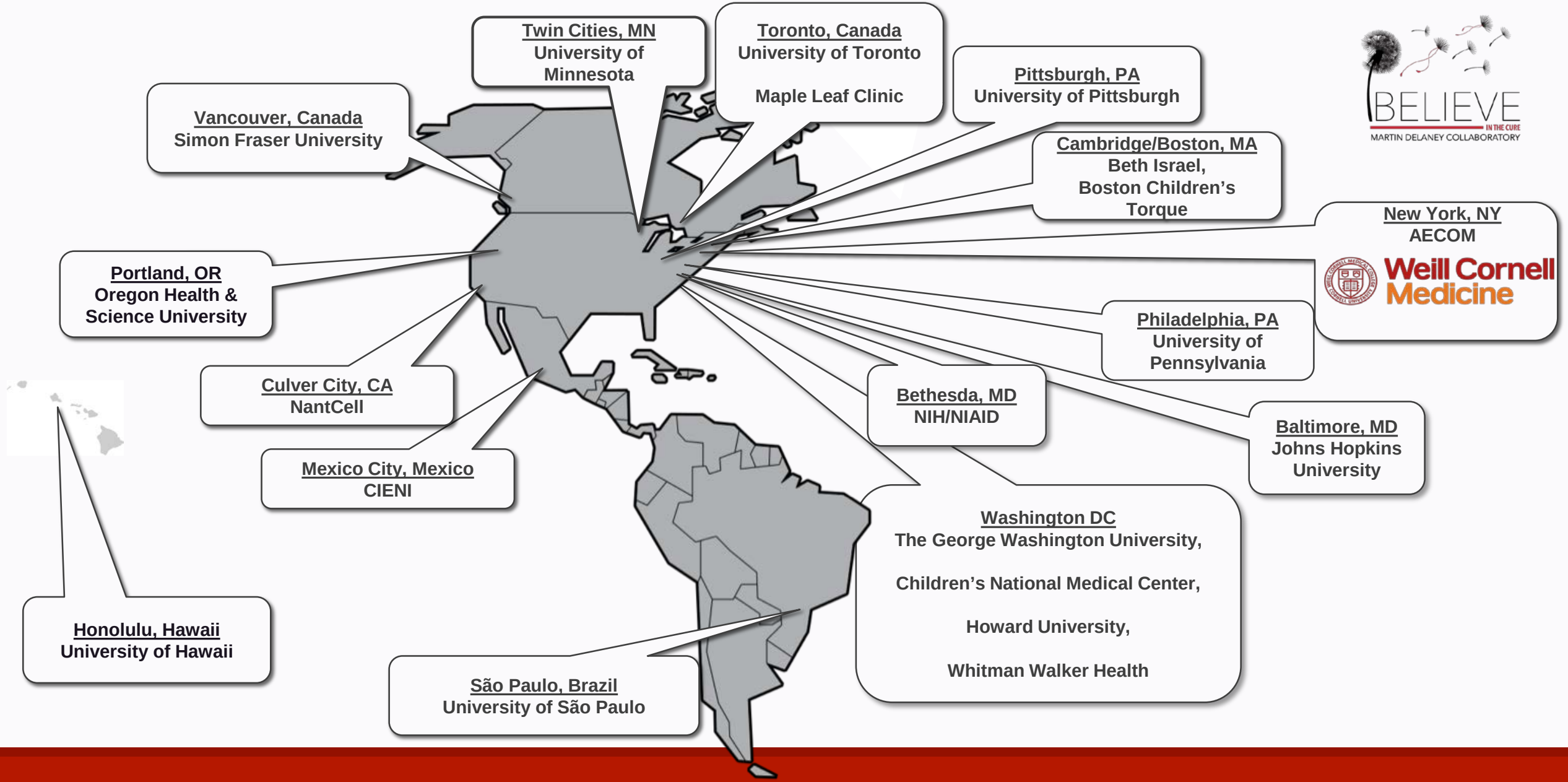
Meaning: This personalized medicine uses an individual's own immune cells to fight HIV. Generalized approaches are also underway.

Bench to Bed Enhanced Lymphocyte Infusions to Engineer Viral Eradication

NIAID UM1 Martin Delaney Collaboratory (AI126617; 7/14/2016-6/30/2021)

NIAID Program & Medical Officers: Eric Refsland, (Lillian Kuo), Tony Conley & Larry Fox

PI: Douglas Nixon (and soon R. Brad Jones as co-PI)
Program Manager: Robert Furler
Investigators: Edward Berger, Catherine Bollard, Alberto Bosque, Mark Brockman, Zabrina Brumme, Amanda Castel, Elizabeth Connick, C. Russell Cruz, Harris Goldstein, Alan Greenberg, David Hardy, Brad Jones, Esper Kallas, Princy Kumar, Rebecca Lynch, Manya Magnus, Sergei Nekhai, Ulrik Nielsen, Douglas Nixon, Una O'Doherty, Mario Ostrowski, Deborah Persaud, Gustavo Reyes-Teran, Gary Simon, Pam Skinner, Thomas Smithgall, James Whitney, Jeffrey Safrit & Peter Rhodes

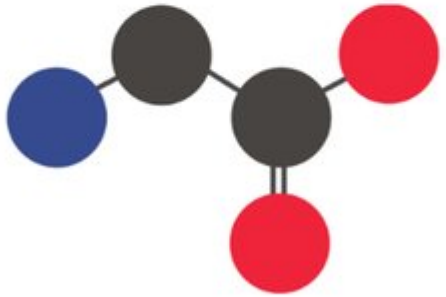

Twin Cities, MN
University of Minnesota
Toronto, Canada
University of Toronto
Maple Leaf Clinic
Pittsburgh, PA
University of Pittsburgh
Vancouver, Canada
Simon Fraser University
Cambridge/Boston, MA
Beth Israel,
Boston Children's
Torque
New York, NY
AECOM
Weill Cornell Medicine
Portland, OR
Oregon Health & Science University
Philadelphia, PA
University of Pennsylvania
Culver City, CA
NantCell
Bethesda, MD
NIH/NIAID
Baltimore, MD
Johns Hopkins University
Mexico City, Mexico
CIENI
Washington DC
The George Washington University,
Children's National Medical Center,
Howard University,
Whitman Walker Health
Honolulu, Hawaii
University of Hawaii
São Paulo, Brazil
University of São Paulo

Pediatrics

Industry Partners

NantCell™

Altor BioScience



torque

Community Engagement & CAB

International Collaborators

Centro de Investigación en Enfermedades Infecciosas
CIENI

USP
Universidade de São Paulo

SFU
SIMON FRASER UNIVERSITY

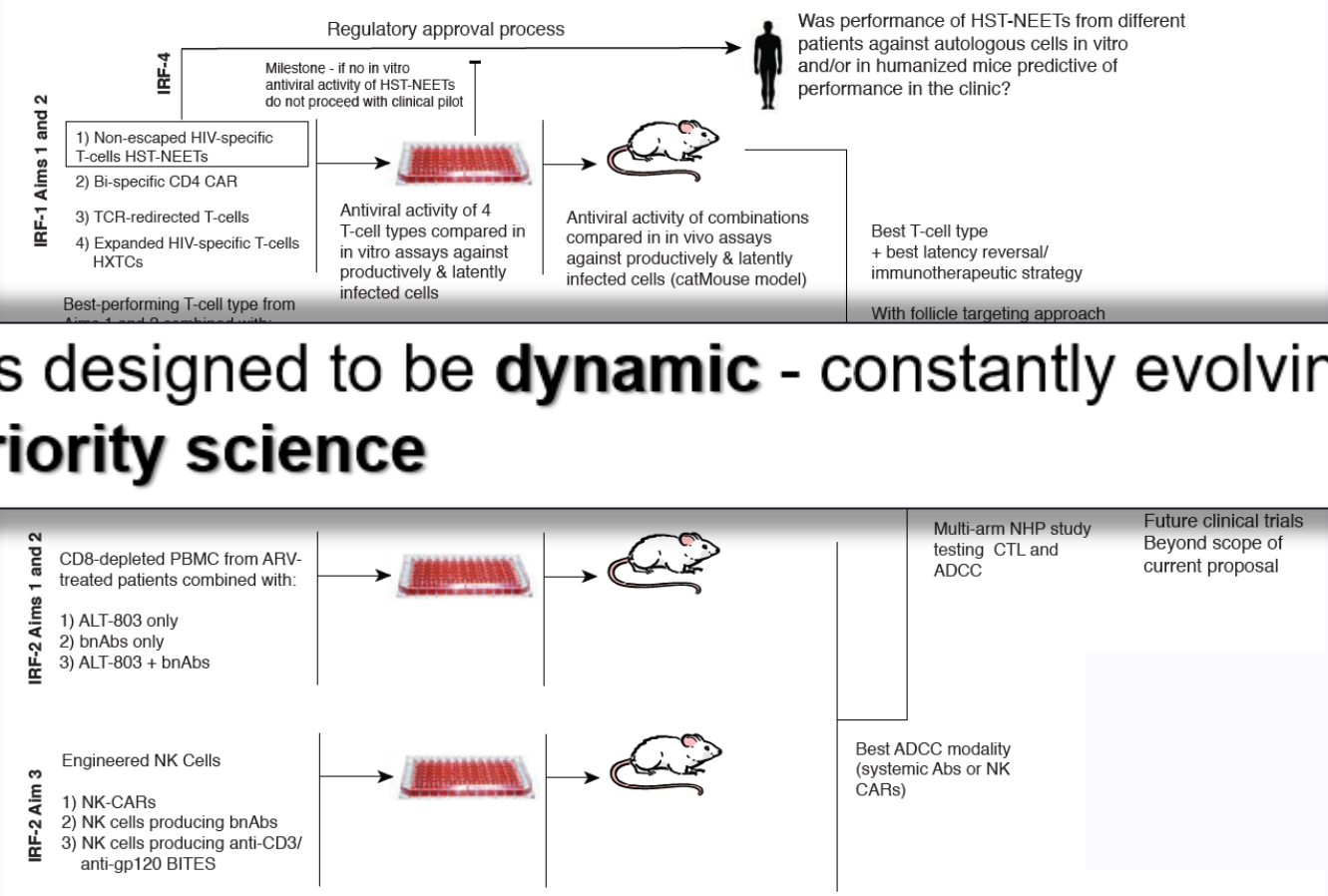
UNIVERSITY OF TORONTO

MAPLE LEAF CLINIC

Who We Are

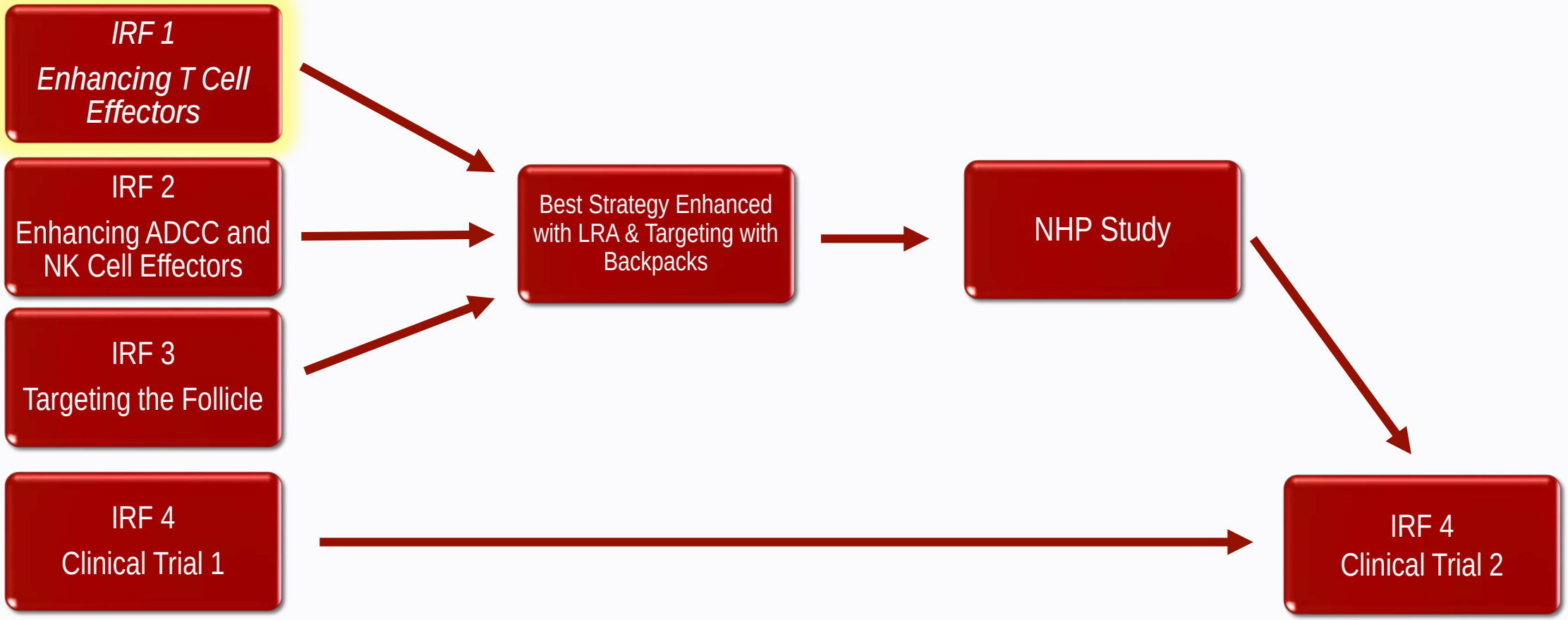
KICKOFF MEETING- OCTOBER 2016

Scientific Strategy



The UM1 is designed to be **dynamic** - constantly evolving to address the **highest priority science**

Enhanced Targeted Immunotherapy



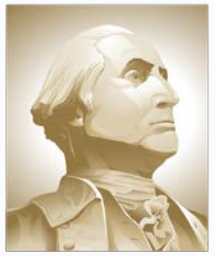
Enhanced Targeted Immunotherapy

- IRF 1
  Enhancing T Cell Effectors
- IRF 2
  Enhancing ADCC and NK Cell Effectors
- IRF 3
  Targeting the Follicle
- IRF 4
  Clinical Trial 1

JONES

NIXON

Weill Cornell Medicine



THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

IRF 1

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

Weill Cornell Medicine

Penn

SFU
SIMON FRASER UNIVERSITY

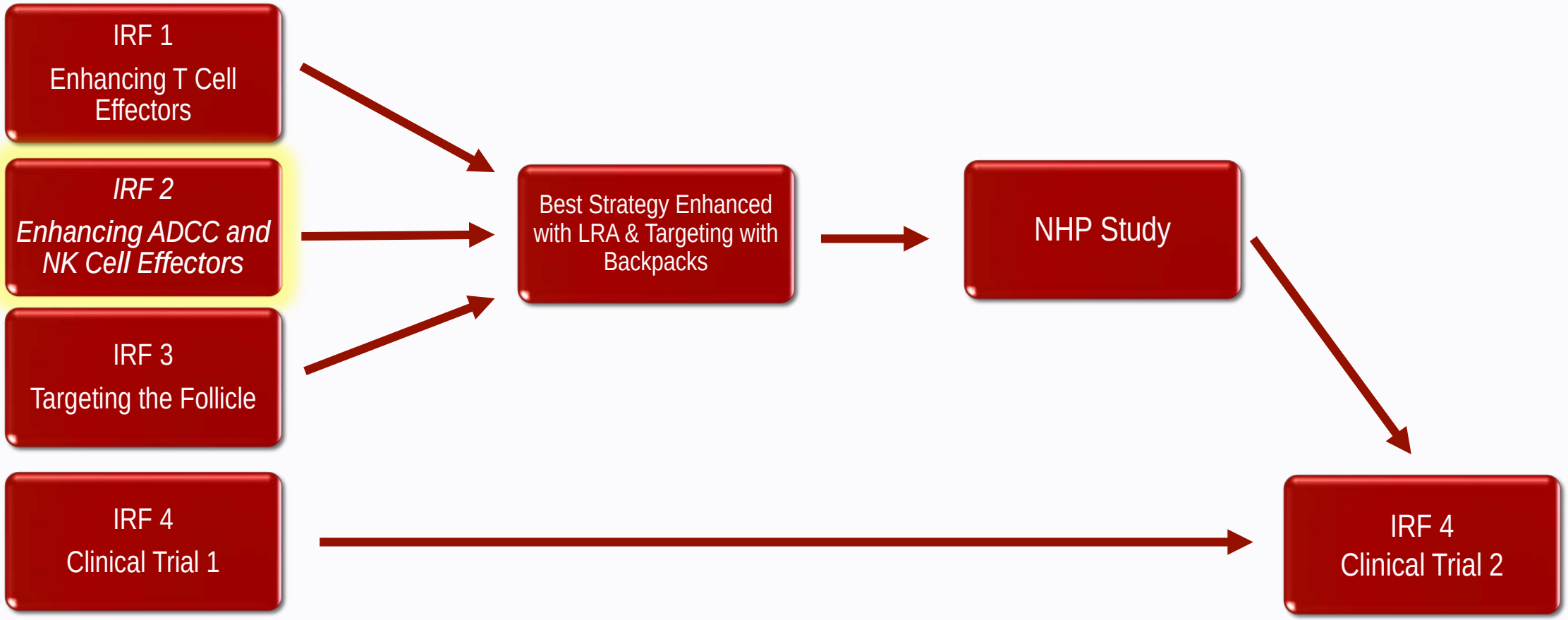
1867
HOWARD UNIVERSITY

UNIVERSITY OF TORONTO

University of Pittsburgh

BELIEVE
IN THE CURE
MARTIN DELANEY COLLABORATORY

Enhanced Targeted Immunotherapy

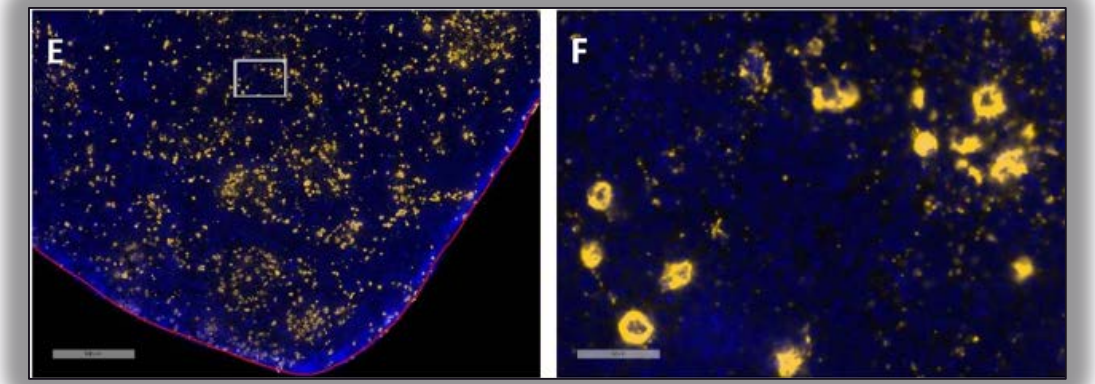


Enhanced Targeted Immunotherapy

- **IRF 1**
  Enhancing T Cell Effectors
- **IRF 2**
  Enhancing ADCC and NK Cell Effectors
- **IRF 3**
  Targeting the Follicle
- **IRF 4**
  Clinical Trial 1

GOLDSTEIN

Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY



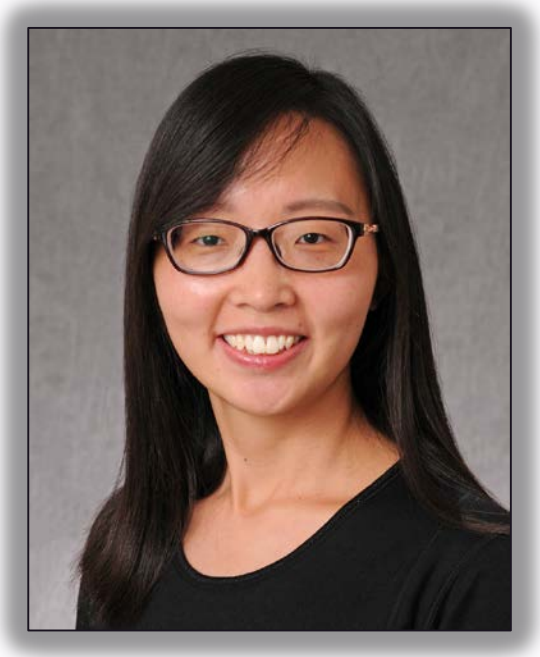
IRF 2

Albert Einstein College of Medicine
OF YESHIVA UNIVERSITY

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

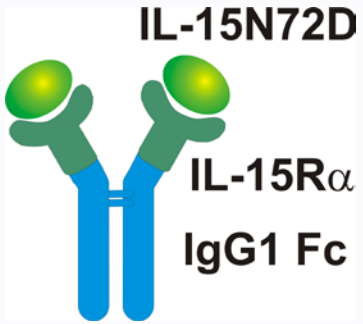
Weill Cornell Medicine

BELIEVE IN THE CURE
MARTIN DELANEY COLLABORATORY



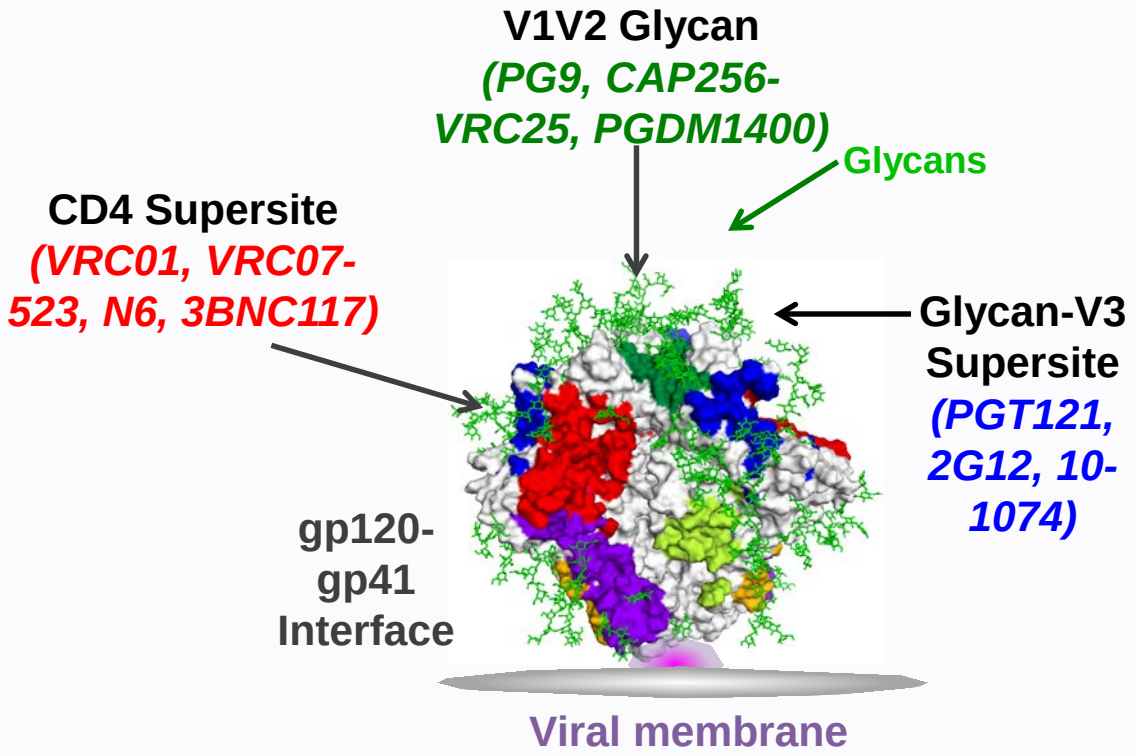
ACTG Clinical Trial & NHP Study Development
N-803 + bnAbs

Enhancing ADCC and NK Cell Effectors

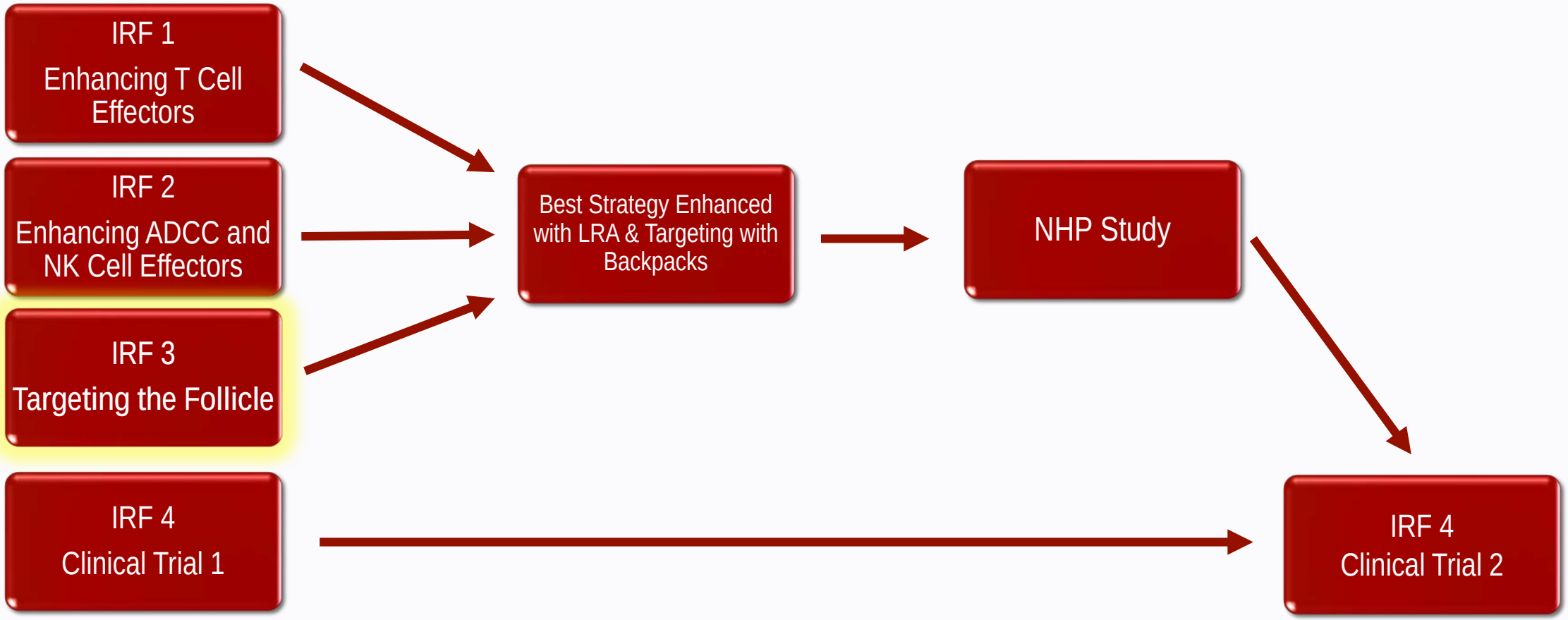


N-803

+



Enhanced Targeted Immunotherapy



Enhanced Targeted Immunotherapy

- **IRF 1**
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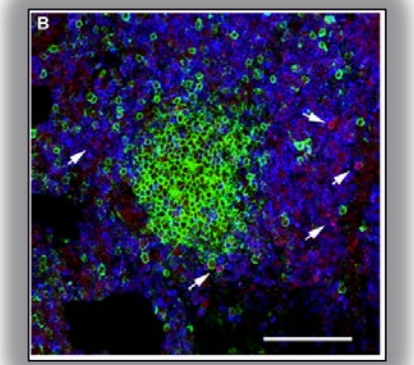
  Enhancing ADCC and NK Cell Effectors
- **IRF 3**
  Targeting the Follicle
- **IRF 4**
  Clinical Trial 1

SKINNER



UNIVERSITY OF MINNESOTA

IRF 3

National Institute of Allergy and Infectious Diseases

HARVARD UNIVERSITY

OREGON HEALTH & SCIENCE UNIVERSITY

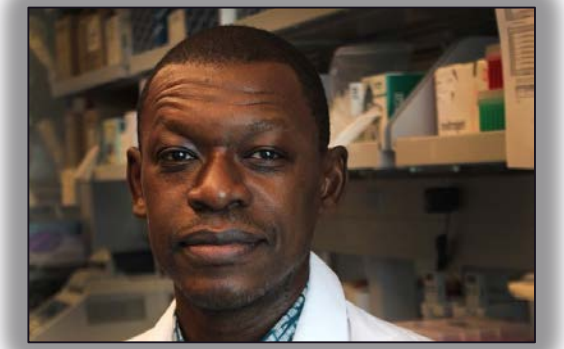
BELIEVE IN THE CURE
MARTIN DELANEY COLLABORATORY

UNIVERSITY OF MINNESOTA

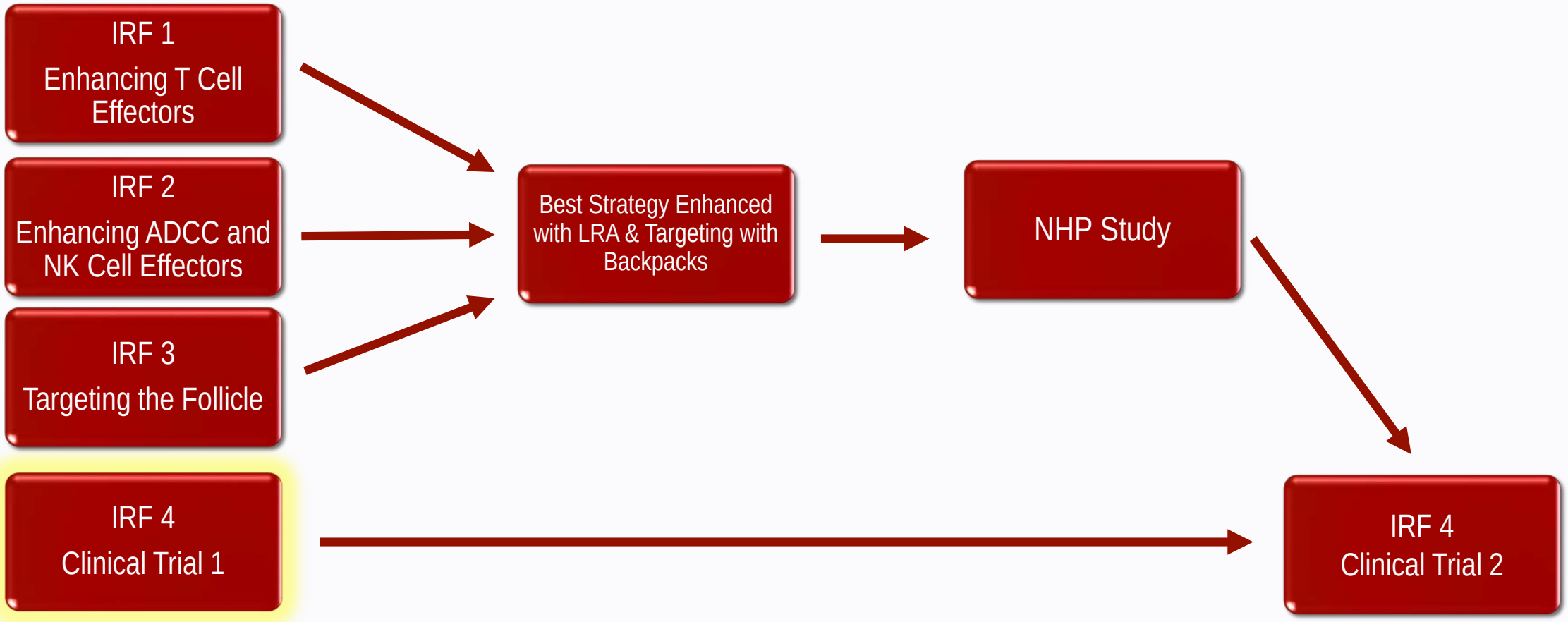
Beth Israel Deaconess Medical Center

Seattle Children's
HOSPITAL · RESEARCH · FOUNDATION

UNIVERSITY of HAWAI'I MĀNOA



Enhanced Targeted Cell Therapy



Enhanced Targeted Immunotherapy

- IRF 1
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- IRF 3
  Targeting the Follicle
- IRF 4
  Clinical Trial 1

Children's National

THE GEORGE WASHINGTON UNIVERSITY
WASHINGTON, DC

IRF 4 & RAGPACS

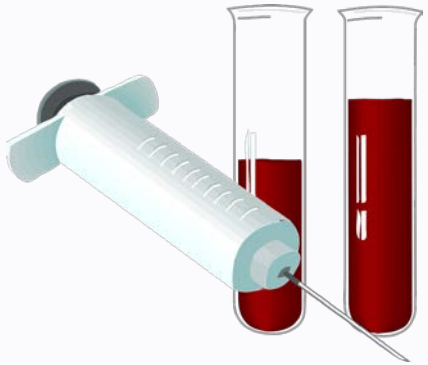
Children's National

Whitman-Walker Health

The George Washington University
Washington, DC

BELIEVE IN THE CURE
MARTIN DELANEY COLLABORATORY

Selection & expansion of white blood cells with conserved HIV peptides



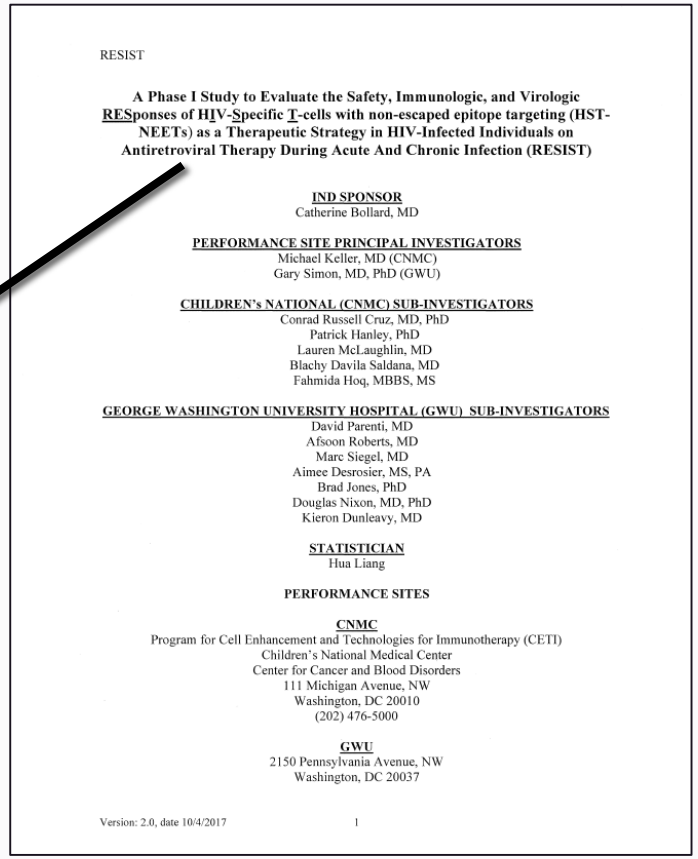
Blood Draw

Infusion of Cell Therapy Product

Phase I Safety Trial for HST-NEETs

Spring 2019 Enrollment

A Phase I Study to Evaluate the Safety, Immunologic, and Virologic Responses of HIV-Specific T-cells with non-escaped epitope targeting (HST-NEETs) as a Therapeutic Strategy in HIV-Infected Individuals on Antiretroviral Therapy During Acute and Chronic Infection



RESIST

A Phase I Study to Evaluate the Safety, Immunologic, and Virologic RESponses of HIV-Specific T-cells with non-escaped epitope targeting (HST-NEETs) as a Therapeutic Strategy in HIV-Infected Individuals on Antiretroviral Therapy During Acute And Chronic Infection (RESIST)

IND SPONSOR
Catherine Bollard, MD

PERFORMANCE SITE PRINCIPAL INVESTIGATORS
Michael Keller, MD (CNMC)
Gary Simon, MD, PhD (GWU)

CHILDREN's NATIONAL (CNMC) SUB-INVESTIGATORS
Conrad Russell Cruz, MD, PhD
Patrick Hanley, PhD
Lauren McLaughlin, MD
Blachy Davila Saldana, MD
Fahmida Hoq, MBBS, MS

GEORGE WASHINGTON UNIVERSITY HOSPITAL (GWU) SUB-INVESTIGATORS
David Parenti, MD
Afsoon Roberts, MD
Marc Siegel, MD
Aimee Desrosier, MS, PA
Brad Jones, PhD
Douglas Nixon, MD, PhD
Kieron Dunleavy, MD

STATISTICIAN
Hua Liang

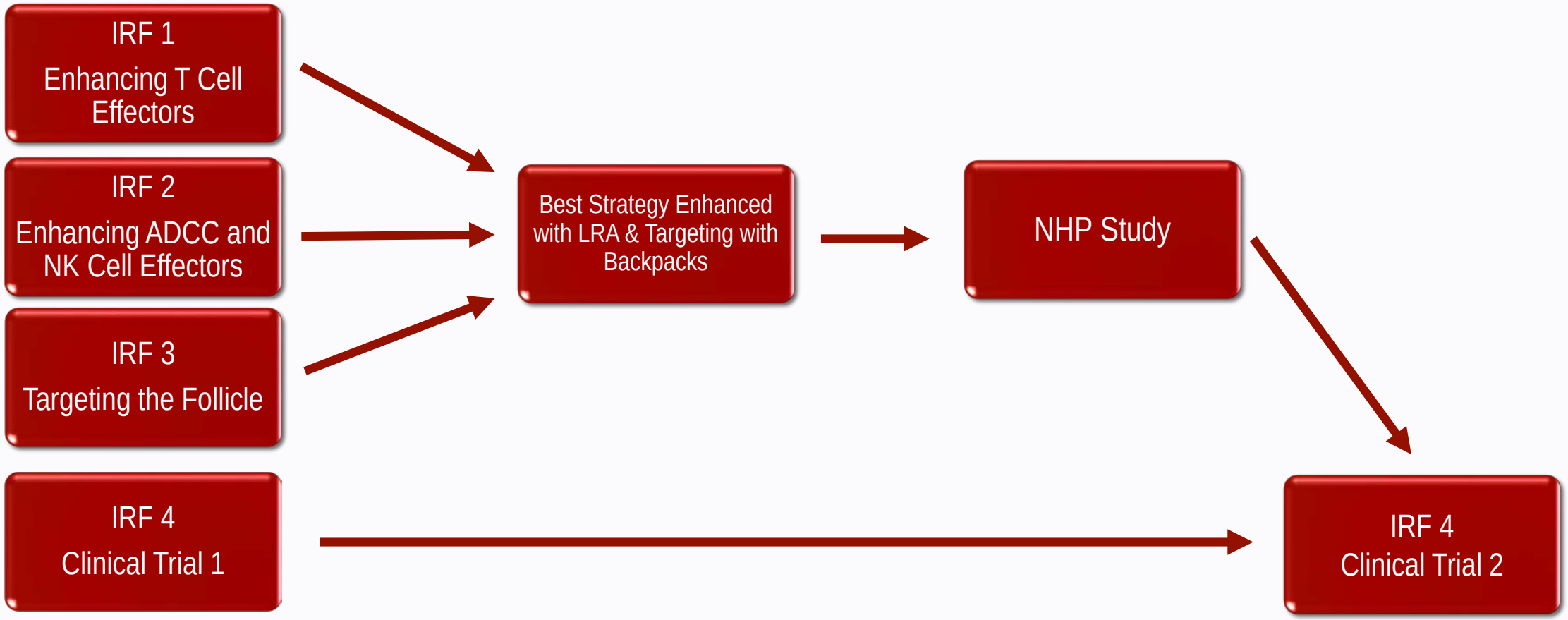
PERFORMANCE SITES

CNMC
Program for Cell Enhancement and Technologies for Immunotherapy (CETI)
Children's National Medical Center
Center for Cancer and Blood Disorders
111 Michigan Avenue, NW
Washington, DC 20010
(202) 476-5000

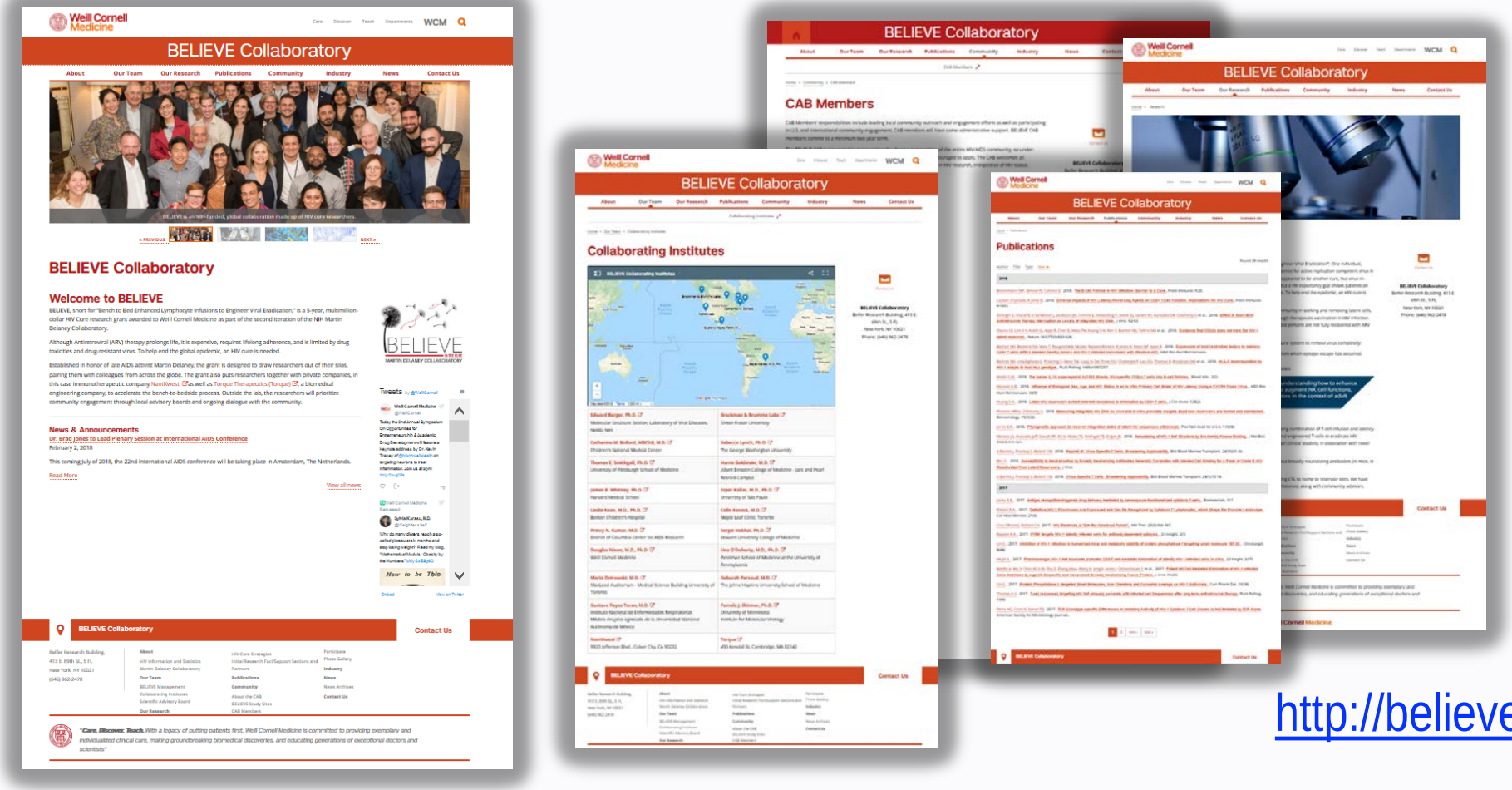
GWU
2150 Pennsylvania Avenue, NW
Washington, DC 20037

Version: 2.0, date 10/4/2017 1

Enhanced Targeted Cell Therapy



Website



http://believe.weill.cornell.edu

BELIEVE

IN THE CURE

MARTIN DELANEY COLLABORATORY

NIH

National Institute of Allergy and Infectious Diseases

NIMH National Institute of Mental Health

National Institute of Neurological Disorders and Stroke

NIH National Institute on Drug Abuse

The Science of Drug Abuse & Addiction

Weill Cornell Medicine

Planning for complex submissions

*How far out do you start thinking about the submission?
-(Recompetition)

*How far out do you begin preparing the submission?

*How do you engage collaborators within the college, and at other institutions?

*How can research administration work with you to make your application as successful as possible.

*Scientific Editing

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Resources

*What resources do you look to for support?

*How do you use them?

*Cores?
*CTSC services?

*Data Management Services (ITS)?

*Do you use any services provided by our Ithaca Campus?

*Do you use any Qatar resources?

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Staffing

*Do you have a non-academic staffing model?

*How do you know how many administrative staff, coordinators, etc. you will need to hire for a complex project?

*Administrative space & clarification for administrative duties between grant admin & institutional admin

*Institutional large grant committee (PIs + Program Managers)

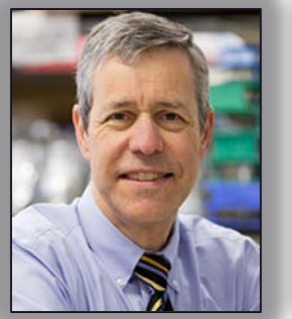
Leadership & Management

Executive Committee

NIXON

JONES

BOLLARD



GOLDSTEIN

SKINNER

WHITNEY

REFSLAND

Management & Operations

FURLER

MACHADO

WCM Division of Infectious Diseases

BELIEVE
IN THE CURE
MARTIN DELANEY COLLABORATORY

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What are some best practices for the administrative and strategic management of complex projects?

*How often do you meet with collaborators?

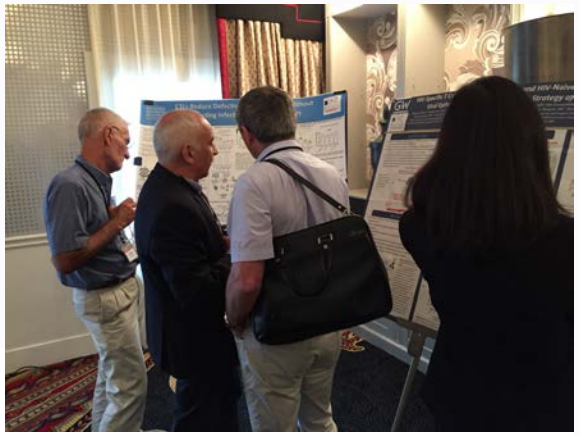
*Do you meet via conference calls or in person?

*What do you discuss in the meetings?

Communication

MEETINGS

- Monthly Executive Committee Meetings
- Monthly Scientific Working Group Meetings
  - IRF 1 Enhancing T Cells
  - IRF 2 Enhancing NK Cells
  - IRF 3 Localization
  - IIRF 4 Clinical Trials
  - CAR T Optimization Working Group
  - Nef Inhibitor Working Group
- Monthly Community Advisory Board Meetings
- Monthly NIH Individual Management Team
- Quarterly Steering Committee Meetings
- Quarterly Collaboratory Meetings
- Annual Meeting
- Individual Site Visits



GoToMeeting

*How do you decide if a collaborator is meeting expectations?

*What do you do if they aren’t meeting expectations?

*How to mitigate conflict?

*How do you develop meaningful relationships with collaborators?

*How do you leverage collaborators to build a successful scientific and administrative proposal?

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Using Grant Mechanism to Promote Career Growth for Members

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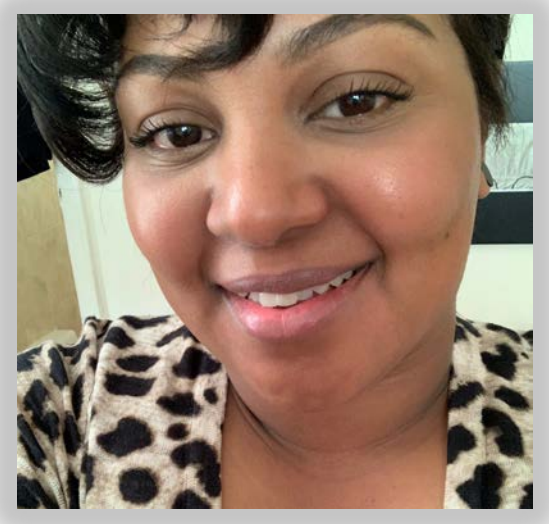
How have departmental and central research administration personnel contributed to your success?

Financial Management and Compliance Oversight



- **Mariela Flambury, Assistant Director of Research Business Management**
- **Omarys Herasme, Grant Portfolio Manager, Research Business Management**
- **Stephen Hunt, Associate Director, Research Operations**

Weill Cornell Medicine

Scientific Impact

BELIEVE
IN THE CURE
MARTIN DELANEY COLLABORATORY

Publications from Years 1 & 2

The B-Cell Follicle in HIV Infection: Barrier to a Cure

PLOS | PATHOGENS

RESEARCH ARTICLE

T-cell responses targeting HIV Nef uniquely correlate with infected cell frequencies after long-term antiretroviral therapy

Allison S. Thomas, Kimberley L. Jones, Rajesh T. Gandhi, Deborah K. McMahon, Joshua C. Cyktor, Dora Chan, Szu-Han Huang, Ronald Truong, Alberto Bosque, Amanda B. Macedo, Colin Kovacs, Erika Benko, Joseph J. Eron, Ronald J. Bosch, Christina M. Lalama, Samuel Simmons, Bruce D. Walker, John W. Mellors, R. Brad Jones

Biomaterials 117 (2017) 44–53

Contents lists available at ScienceDirect

Biomaterials

journal homepage: www.elsevier.com/

Antigen recognition-triggered drug delivery mec
nanocapsule-functionalized cytotoxic T-cells

R. Brad Jones, Stephanie Mueller, Sudha Kumari, Andrew M. Tager, Todd M. Allen, Bruce D. Walker

JCI insight

RESEARCH ARTICLE

Pharmacologic HIV-1 Nef blockade promotes CD8 T cell–mediated elimination of latently HIV-1–infected cells in vitro

Shariq Mujib, Aamir Saiyed, Saleh Fadel, Ardalan Bozorgzad, Nasra Aidarus, Feng Yun Yue, Erika Benko, Colin Kovacs, Lori A. Emert-Sedlak, Thomas E. Smithgall, and Mario A. Ostrowski

Journal of Virology

T-Cell Receptor (TCR) Clonotype-Specific Differences in Inhibitory Activity of HIV-1 Cytotoxic T-Cell Clones Is Not Mediated by TCR Alone

Nina C. Flerin, Huabiao Chen, Tynisha D. Glover, Pedro A. Lamo, Jian Hua Zheng, Justin W. Fang, Zaza M. Ndhlovu, Evan W. Newell, Mark M. Davis, Bruce D. Walker, Harris Goldstein

Biology of Blood and Marrow Transplantation

ASBMT

Educational Reviews

Reprint of: Virus-Specific T Cells: Broadening Applicability

A. John Barrett, Susan Prockop, Catherine M. Bollard

Biology of Blood and Marrow Transplantation

ASBMT

Educational Reviews

Virus-Specific T Cells: Broadening Applicability

A. John Barrett, Susan Prockop, Catherine M. Bollard

Published in final edited form as:

Curr Pharm Des. 2017 ; 23(28): 4122–4132. doi:10.2174/1381612823666170704123620.

Protein Phosphatase-1 –targeted Small Molecules, Iron Chelators and Curcumin Analogs as HIV-1 Antivirals

Xionghao Lin, Tatyana Ammosova, Namita Kumari, and Sergei Nekhai

Center for Sickle Cell Disease, Howard University, Washington DC 20059

Department of Medicine, Howard University, Washington DC 20059

Yakut Science Center for Complex Medical Problems, Yakutsk, Russia 677019

frontiers in Immunology

ORIGINAL RESEARCH

Simian Immunodeficiency Virus (SIV)-Specific Chimeric Antigen Receptor-T Cells Engineered to Target B Cell Follicles and Suppress SIV Replication

Kumudhini Preethi Haran, Agnes Hajduczki, Mary S. Pampusch, Gwantwa Mwakalundwa, Diego A. Vargas-Inchaustegui, Eva G. Rakasz, Elizabeth Connick, Edward A. Berger and Pamela J. Skinner

Cell Host & Microbe

Defective HIV-1 Proviruses Are Expressed and Can Be Recognized by Cytotoxic T Lymphocytes, which Shape the Proviral Landscape

Graphical Abstract

Authors

Ross A. Pollack, R. Brad Jones, Mihaela Pertea, ..., Erika Benko, Robert F. Siliciano, Ya-Chi Ho

Correspondence

yho10@jhmi.edu

In Brief

Defective HIV-1 proviruses (HIV-1def) are considered clinically irrelevant. Pollack and Jones et al. find that HIV-1def can be transcribed, spliced, and translated. Cells

CELLULAR RESPONSE TO INFECTION

Journal of Virology

o NK Cell-Mediated Elimination of HIV-1-Infected Cells Mobilized by a gp120-Bispecific and Hexavalent Broadly Neutralizing Fusion Protein

Ariola Bardhi, Yanling Wu, Weizao Chen, Zhongyu Zhu, Jian Hua Zheng, Jennifer Jones, Christina Ochsenbauer, Dimitris S. Dimitrov, Tianlei Ying, Harris Goldstein

frontiers in Immunology

The B-Cell Follicle in HIV Infection: Barrier to a Cure

Matthew P. Bronnimann, Pamela J. Skinner and Elizabeth Connick

REGULAR ARTICLE

blood advances

The human IL-15 superagonist ALT-8
into B-cell follicles

Gabriela M. Webb, Shengbin Li, Gwantwa Mwakalundwa, Joy M. Alfred W. Legasse, Theodore Hobbs, Lauren D. Martin, Byung S. Douglas F. Nixon, R. Brad Jones, Elizabeth Connick, Pamela J. Sk

Journal of Virology

CELLULAR RESPONSE TO INFECTION

Potent *In Vivo* NK Cell-Mediated Elimination of HIV-1-Infected Cells Mobilized by a gp120-Bispecific and Hexavalent Broadly Neutralizing Fusion Protein

Ariola Bardhi, Yanling Wu, Weizao Chen, Wei Li, Zhongyu Zhu, Jian Hua Zheng, Hing Wong, Emily Jeng, Jennifer Jones, Christina Ochsenbauer, John C. Kappes, Dimiter S. Dimitrov, Tianlei Ying, Harris Goldstein

Journal of Virology

Monitoring Integration over Time Supports a Role for Cytotoxic T Lymphocytes and Ongoing Replication as De Size

Marilia Rita Pinzone, Erin Graf, Lindsay Lynch, Brigit McLaughlin, Frederick M. H. Wei-Ting Hwang, Giuseppe Nunnari, Una O'Doherty

RESEARCH ARTICLE

Latent HIV reservoirs exhibit inherent resista
to elimination by CD8+ T cells

Szu-Han Huang, Yanqin Ren, Allison S. Thomas, Dora Chan, Stefanie Mueller, Adam R. Ward, Shab
Catherine M. Bollard, Conrad Russell Cruz, Sara Karandish, Ronald Truong, Amanda B. Macedo, Alberto Bosque,
Colin Kovacs, Erika Benko, Alicja Piechocka-Trocha, Hing Wong, Emily Jeng, Douglas F. Nixon, Ya-Chi Ho,
Robert F. Siliciano, Bruce D. Walker, and R. Brad Jones

JCI insight

RESEARCH ARTICLE

IFITM1 targets HIV-1 latently infected cells for antibody-dependent cytolysis

Rui André Saraiva Raposo, Miguel de Mulder Rougvie, Dominic Paquin-Proulx, Phillip M. Brailey, Vinicius D. Cabido, Paul M. Zdinak, Allison S. Thomas, Szu-han Huang, Greta A. Beckerle, Richard B. Jones, and Douglas F. Nixon

Retrovirology

REVIEW

Open Access

Measuring integrated HIV DNA ex vivo and in vitro provides insights about how reservoirs are formed and maintained

Marilia Rita Pinzone and Una O'Doherty

Pinzone and O'Doherty *Retrovirology* (2018) 15:22
https://doi.org/10.1186/s12977-018-0396-3

Retrovirology

REVIEW

Open Access

Measuring integrated HIV DNA ex vivo and in vitro provides insights about how reservoirs are formed and maintained

Marilia Rita Pinzone and Una O'Doherty*

JVI Accepted Manuscript Posted Online 28 March 2018

J. Virol. doi:10.1128/JVI.00285-18

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Accepted Manuscript Posted Online

EFFECT OF SHORT-TERM ART INTERRUPTION ON LEVELS OF INTEGRATED HIV DNA

Zachary Strongin, Radwa Sharaf, D. Jake VanDolzen, Jeffrey M. Jacobsen, Elizabeth Connick, Paul Volberding, Daniel J. Skiest, Rajesh T. Gandhi, Daniel R. Kuritzkes, Una O'Doherty, Jonathan Z. Li

SCIENCE TRANSLATIONAL MEDICINE | RESEARCH ARTICLE

SIV

TLR7 agonists induce transient viremia and reduce the viral reservoir in SIV-infected rhesus macaques on antiretroviral therapy

So-Yon Lim, Christa E. Osuna, Peter T. Hraber, Joe Hesselgesser, Jeffrey M. Gerold, Tiffany L. Barnes, Srisowmya Sanisetty, Michael S. Seaman, Mark G. Lewis, Romas Geleziunas, Michael D. Miller, Tomas Ciblar, William A. Lee, Alison L. Hill, James B. Whitney

www.impactjournals.com/oncotarget/ Oncotarget, 2017, Vol. 8, (No. 44), pp: 76749-76769

Research Paper

Inhibition of HIV-1 infection in humanized mice and metabolic stability of protein phosphatase-1-targeting small molecule 1E7-03

Xionghao Lin, Namita Kumari, Catherine DeMarino, Yasemin Saygideğer Kont, Tatiana Ammosova, Amol Kulkarni, Marina Jerebtsova, Guelaguetza Vazquez-Meves, Andrey Ivanov, Dmytro Kovalskyy, Aykut Üren, Fatah Kashanchi and Sergei Nekhai

frontiers in Immunology

Virus-Specific T Cells for the Immunocompromised Patient

Amy Houghtelin and Catherine M. Bollard

Remodeling of HIV-1 Nef Structure by Src-Family Kinase Binding

Jamie A. Moroco, John Jeff Alvarado, Ryan P. Staudt, Haibin Shi, Thomas E. Wales, Thomas E. Smithgall and John R. Engen

Year 3 Publications

*What is the impact of your science?

*How has it progressed over time?

*How has your program management developed over time?

*Key factors that have contributed to your success?

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Key lessons learned throughout your careers about successfully applying for and managing Complex, Federally Funded, Clinical Research Programs?

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