

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

NIH UM1 Grant Overview





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



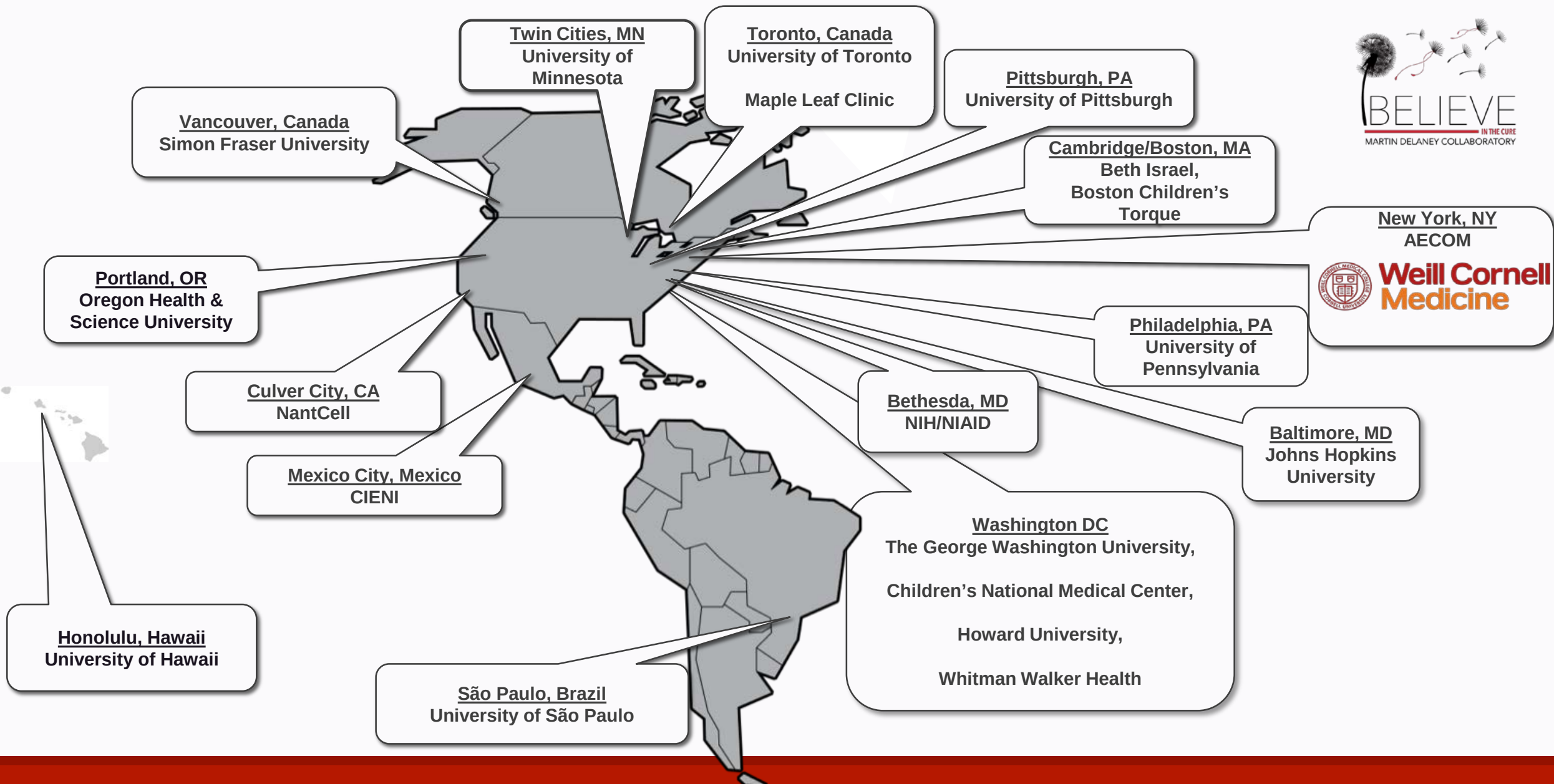
NIAID UM1 Martin Delaney Collaboratory (AI126617; 7/14/2016-6/30/2021)

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



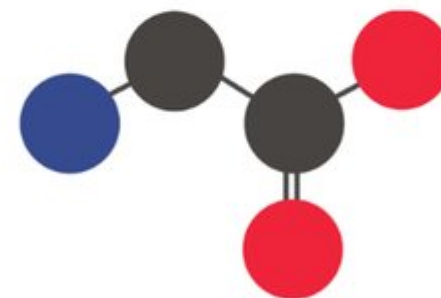
Pediatrics



Industry Partners



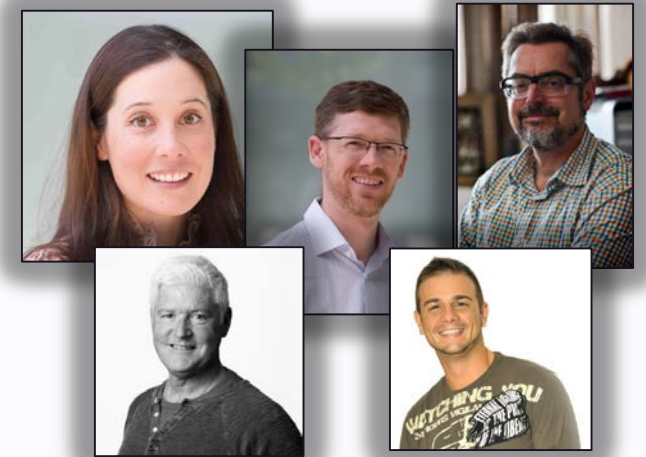
Altor BioScience



Community Engagement & CAB



International Collaborators

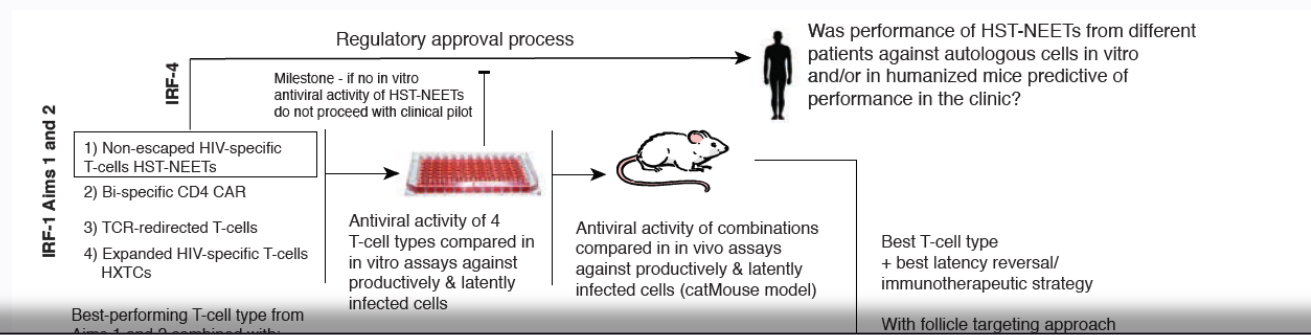


Who We Are

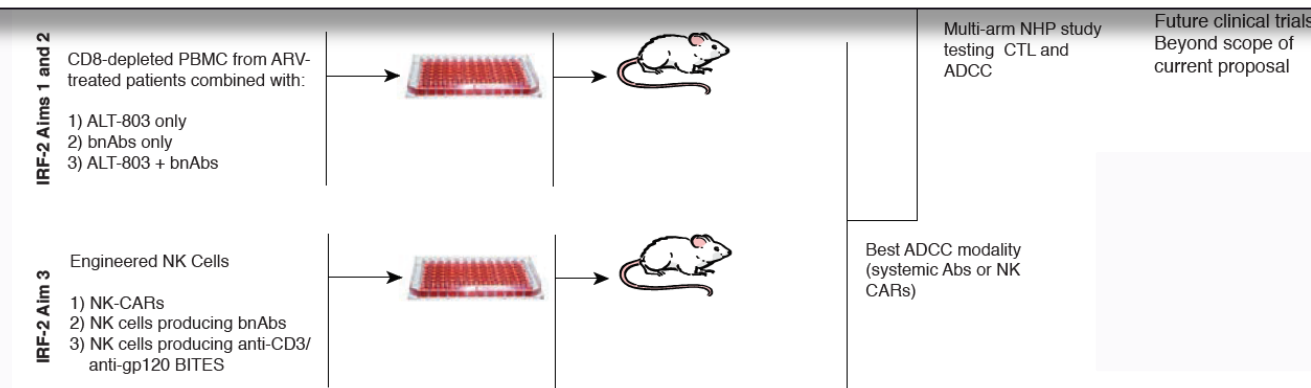


KICKOFF MEETING- OCTOBER 2016

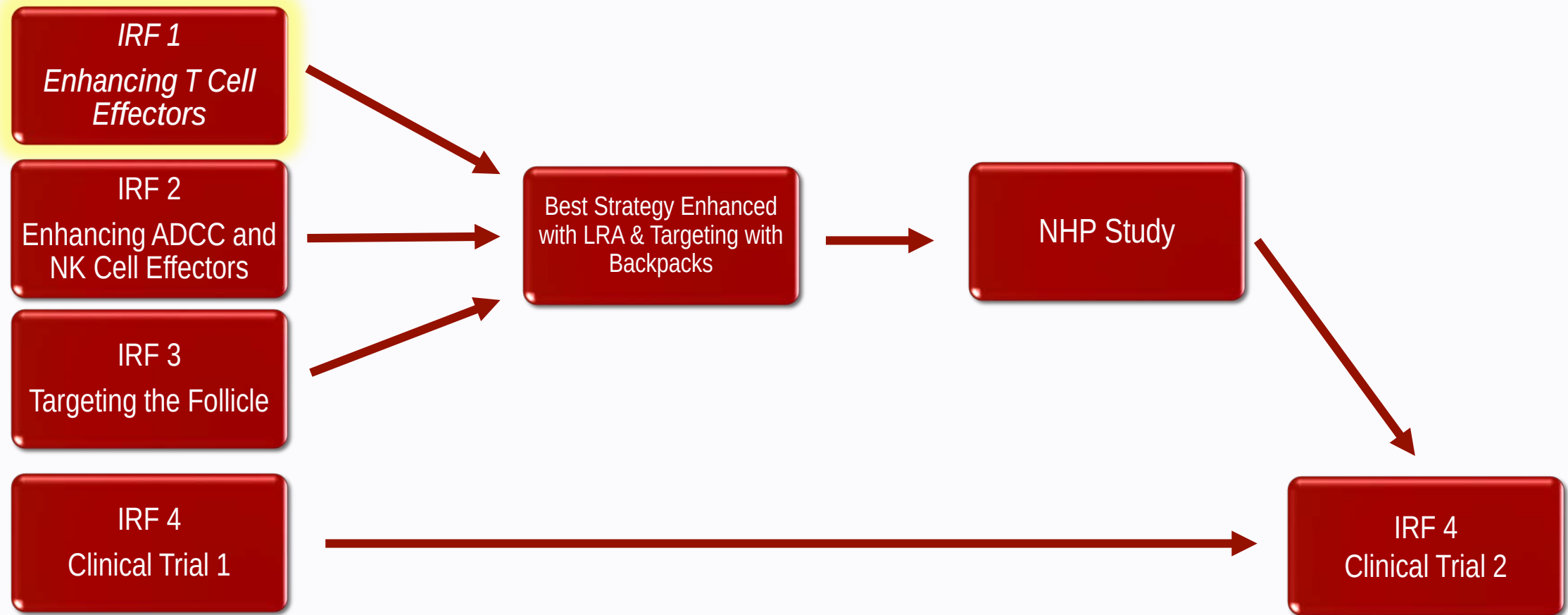
Scientific Strategy



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



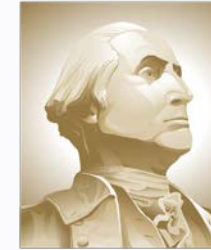
JONES



NIXON

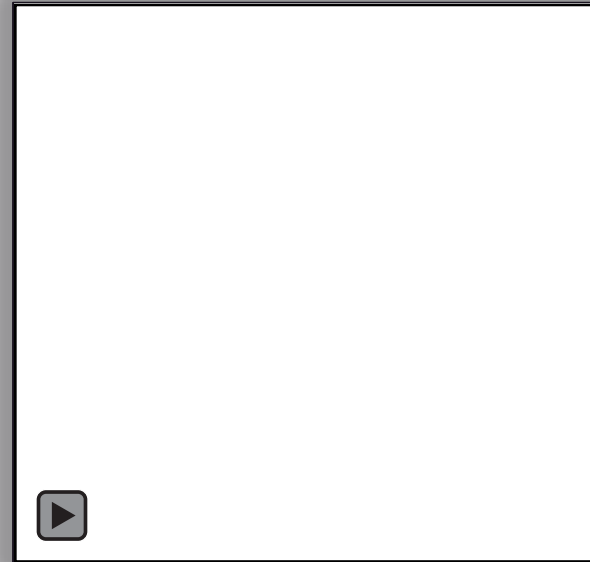


Weill Cornell
Medicine



**THE GEORGE
WASHINGTON
UNIVERSITY**

WASHINGTON, DC



IRF 1



SIMON FRASER
UNIVERSITY

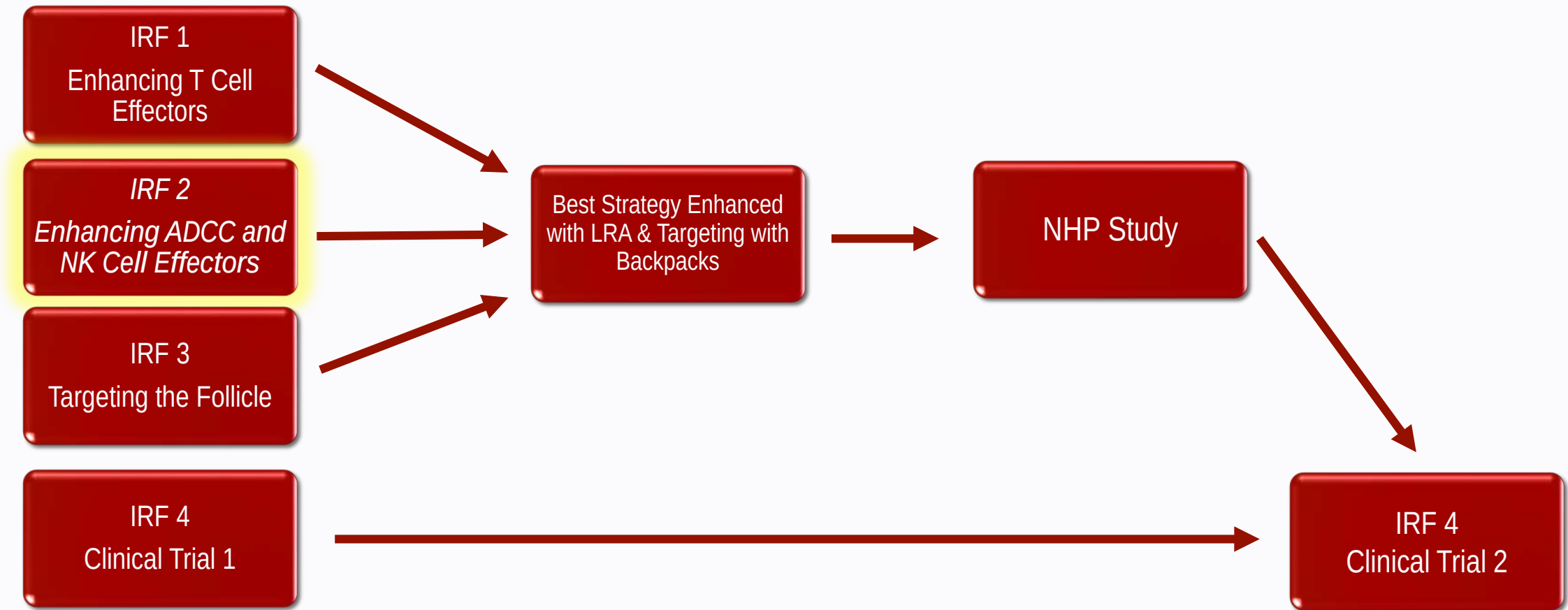


University of Pittsburgh



BELIEVE 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

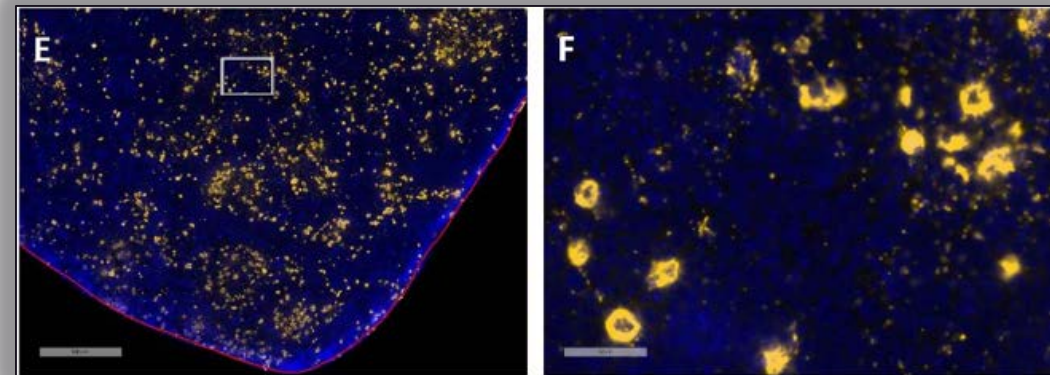
Targeting the Follicle

IRF 4

Clinical Trial 1



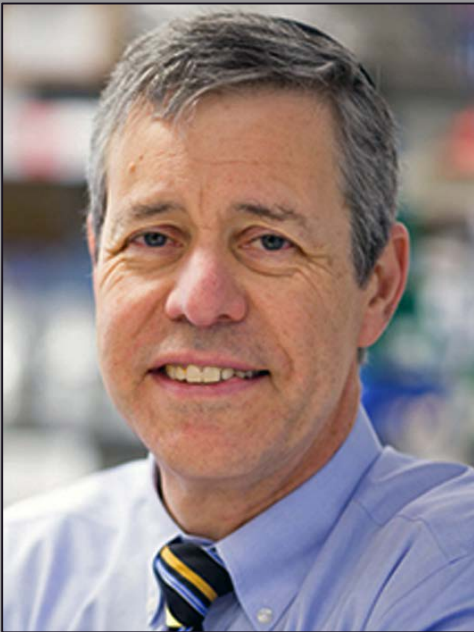
GOLDSTEIN



IRF 2



Weill Cornell
Medicine

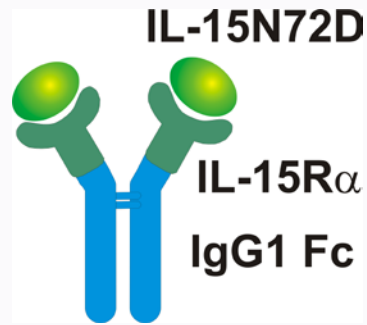


BELIEVE MARTIN DELANEY COLLABORATORY

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



Enhancing ADCC
and NK Cell
Effectors



N-803

+

CD4 Supersite
(VRC01, VRC07-
523, N6, 3BNC117)

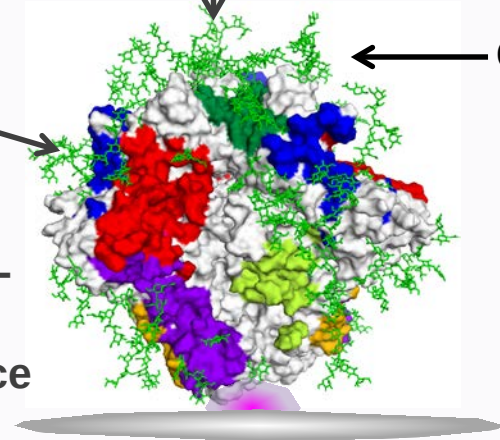
V1V2 Glycan
(PG9, CAP256-
VRC25, PGDM1400)

Glycans

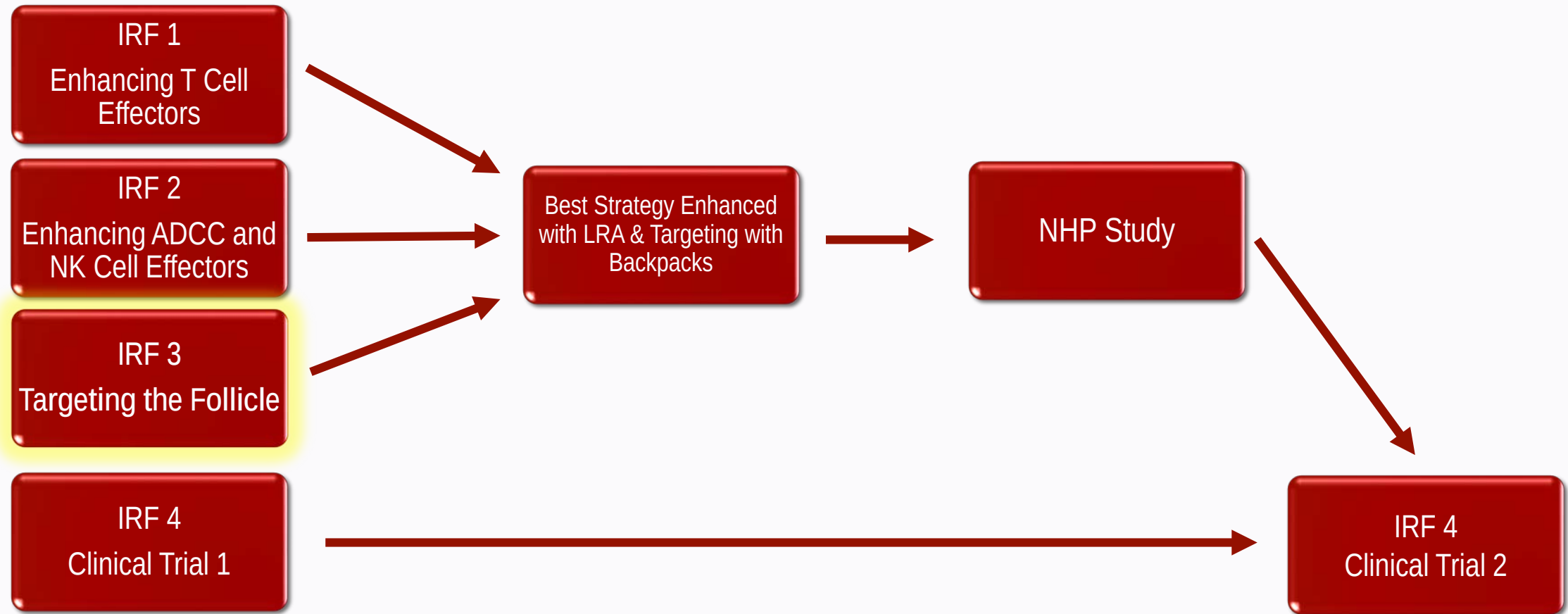
Glycan-V3
Supersite
(PGT121,
2G12, 10-
1074)

gp120-
gp41
Interface

Viral membrane



Enhanced Targeted Immunotherapy



Enhanced Targeted Immunotherapy

IRF 1

Enhancing T Cell
Effectors

IRF 2

Enhancing ADCC and
NK Cell Effectors

IRF 3

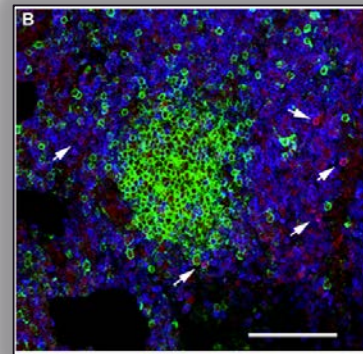
Targeting the Follicle

IRF 4

Clinical Trial 1



SKINNER



UNIVERSITY OF MINNESOTA

IRF 3

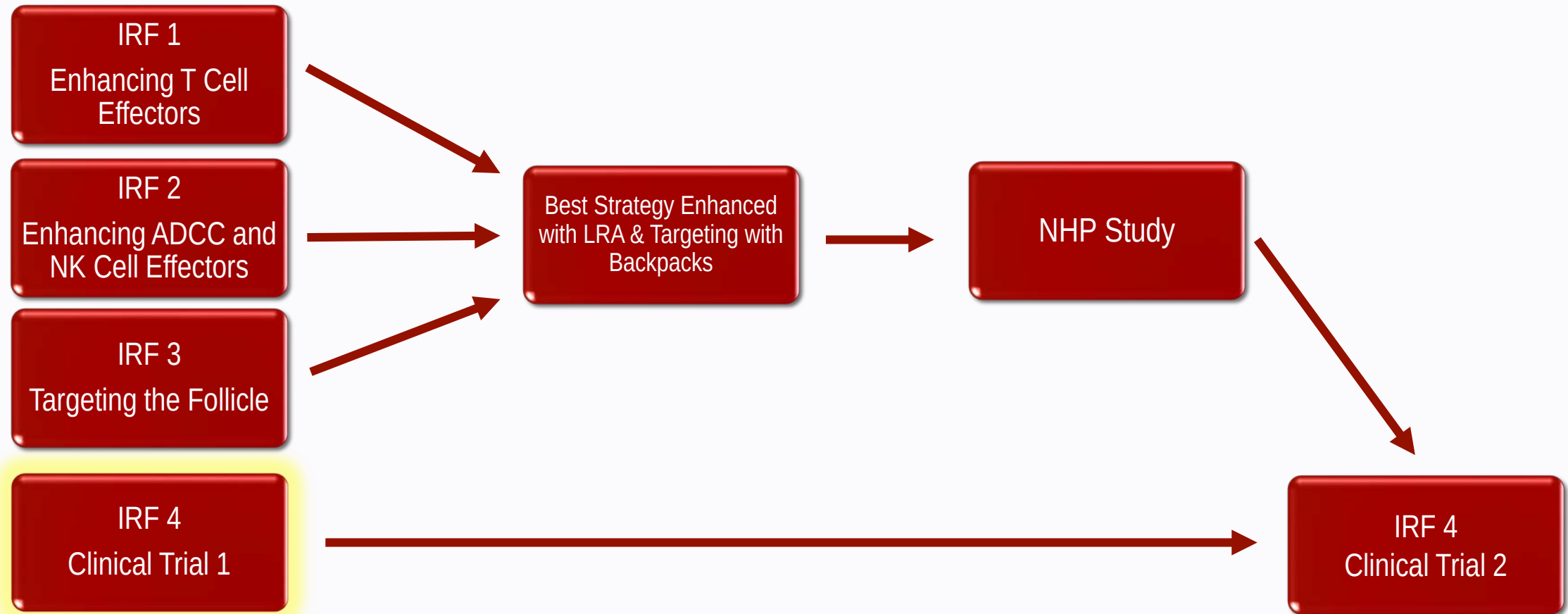


HARVARD
UNIVERSITY



BELIEVE MARTIN DELANEY COLLABORATORY

Enhanced Targeted Cell Therapy



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



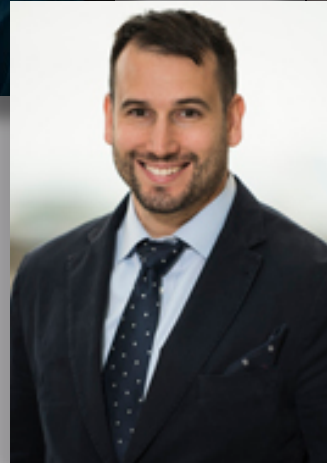
Children's National™



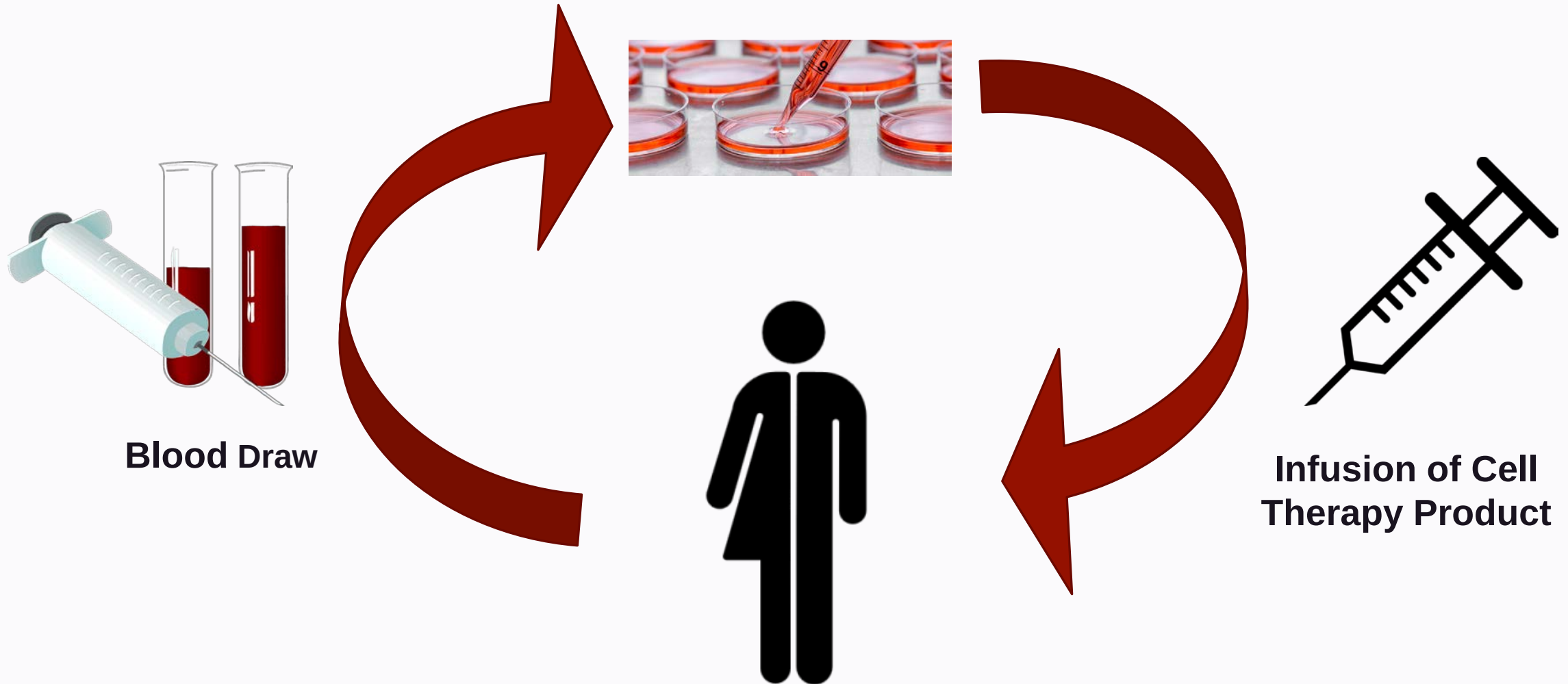
**THE GEORGE
WASHINGTON
UNIVERSITY**

WASHINGTON, DC

IRF 4 & RAGPACS



Selection & expansion of white blood cells with conserved HIV peptides



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

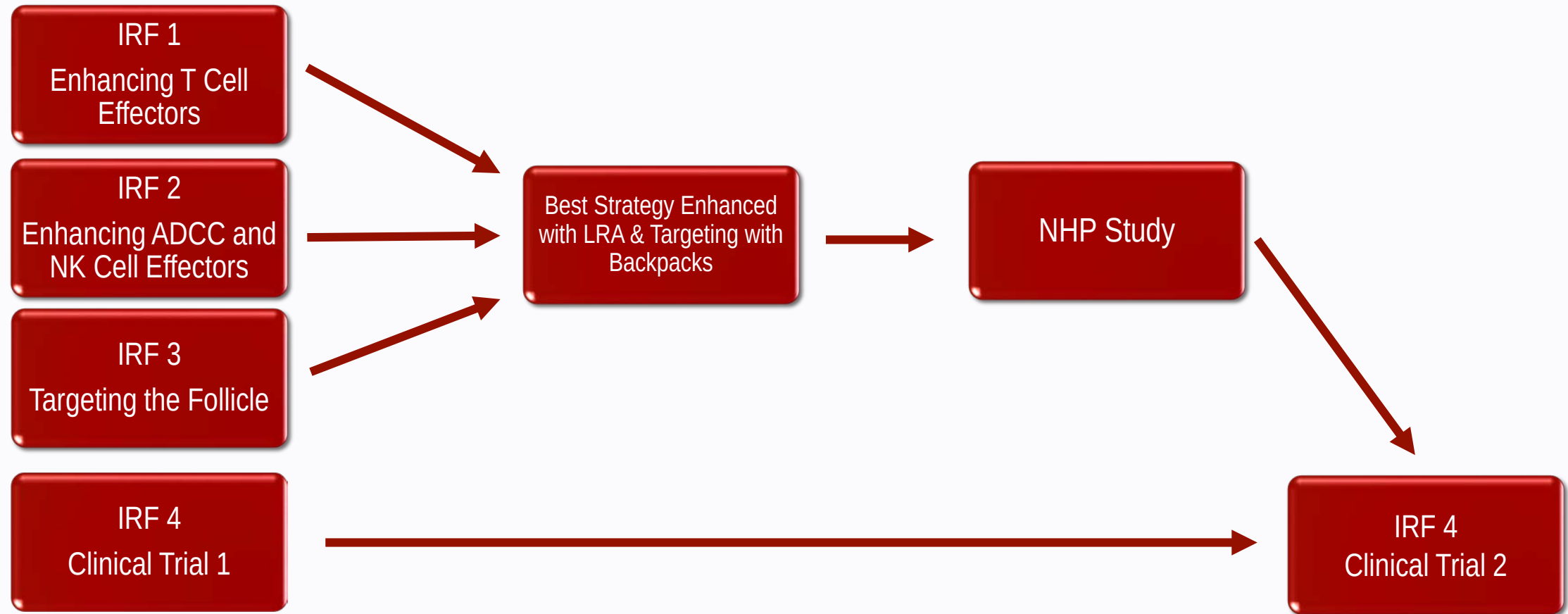
PERFORMANCE SITES

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

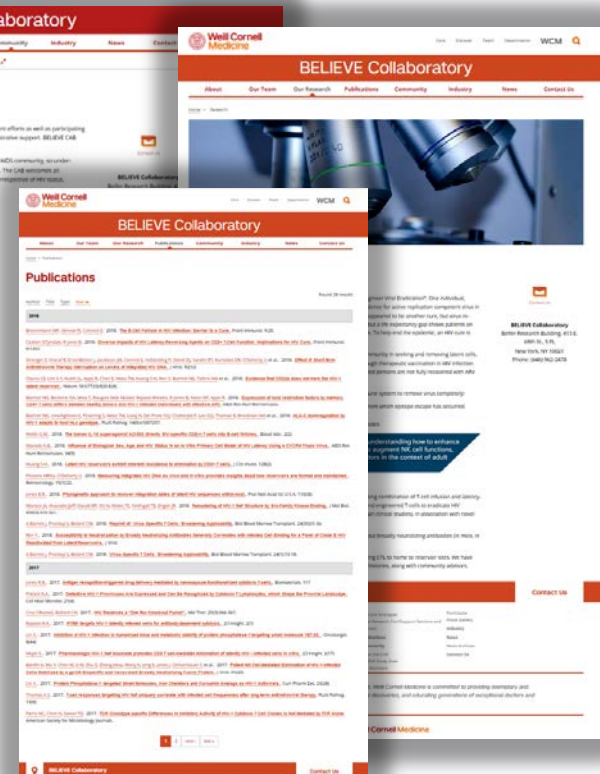
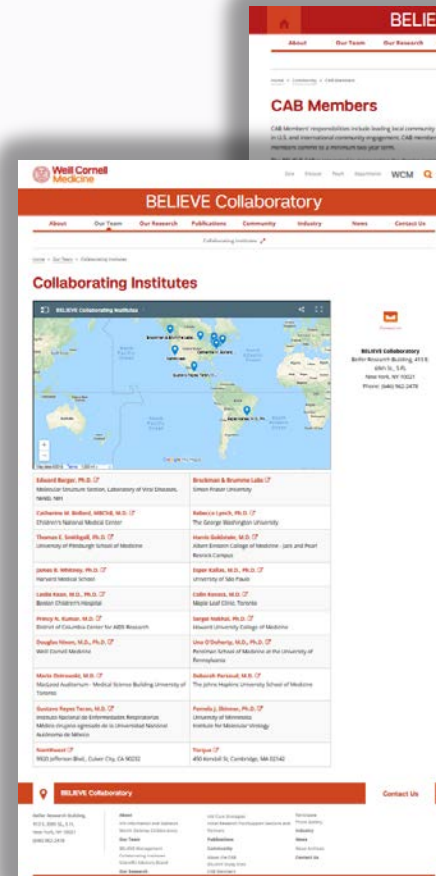
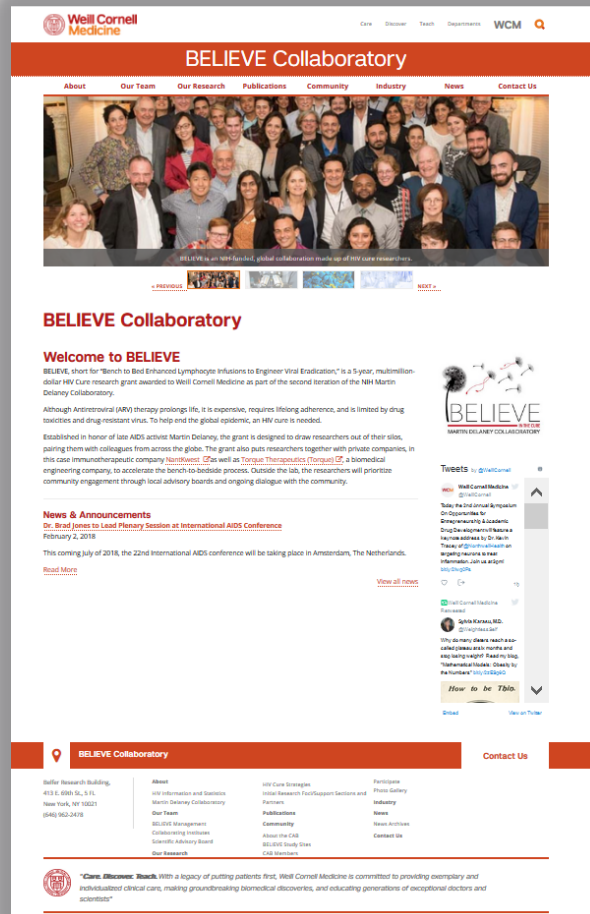
GWU
2150 Pennsylvania Avenue, NW
Washington, DC 20037

Version: 2.0, date 10/4/2017 1

Enhanced Targeted Cell Therapy



Website



<http://believe.weill.cornell.edu>



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

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?

**Weill Cornell
Medicine**

Staffing



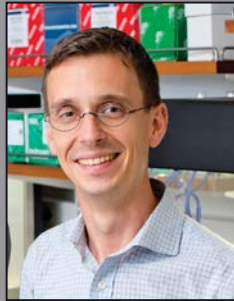
- *Do you have a non-academic staffing model?
- *How do you know how many administrative staff, coordinators, etc. you will need to hire for a complex project?
- *Administrative space & clarification for administrative duties between grant admin & institutional admin
- *Institutional large grant committee (PIs + Program Managers)

Leadership & Management

Executive Committee



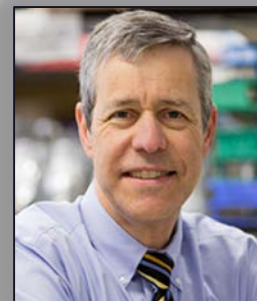
NIXON



JONES



BOLLARD



GOLDSTEIN



SKINNER



WHITNEY



REFSLAND

Management & Operations



FURLER



MACHADO



WCM Division of Infectious
Diseases



**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



*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?

Using Grant Mechanism to Promote Career Growth for Members



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



Financial Management and Compliance Oversight

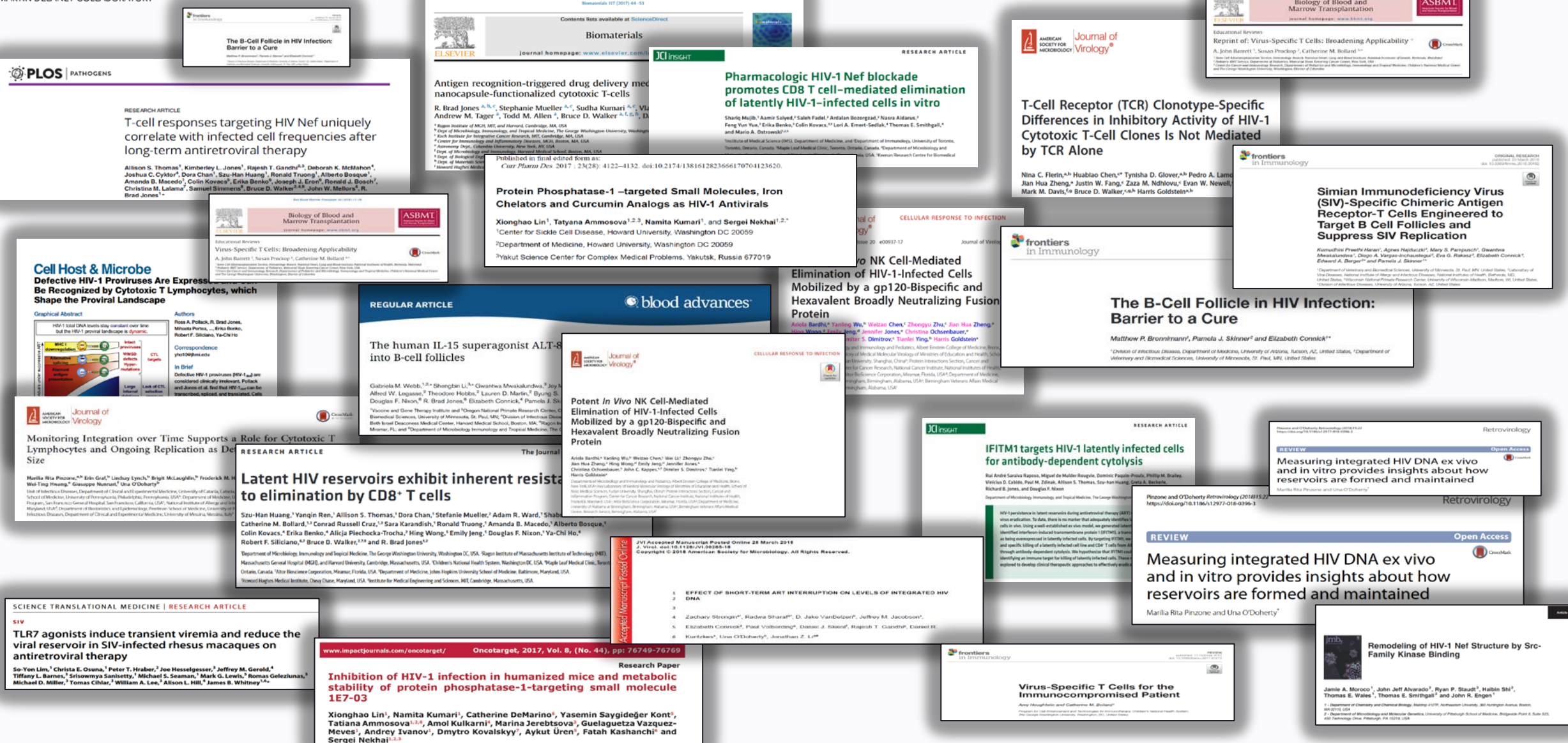


- **Mariela Flambury, Assistant Director of Research Business Management**
- **Omarys Herasme, Grant Portfolio Manager, Research Business Management**
- **Stephen Hunt, Associate Director, Research Operations**

Scientific Impact



Publications from Years 1 & 2



Year 3 Publications

SCIENCE TRANSLATIONS



ARTICLE

<http://dx.doi.org/10.1371/journal.plos.0100000>

Pr

rh

Jam

Po-Ting Liu¹, Peter Abbink¹, Erica N. Borducci¹, Alison Hill³, Mark G. Lewis⁴, Romas Geleziunas⁵, Merlin L. Robb⁶, Nelson L. Michael⁷ & Dan H. Barouch^{1,2}

Rui A



seeding in
viral therapy

Elsa Chen¹, Gyeol Yoon¹,

*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?

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





Weill Cornell Medicine