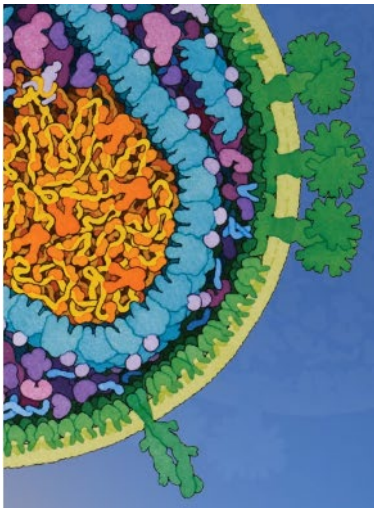

SCIENCE SPOTLIGHT™

Predictive Models of ART Responses Among Acutely Infected Individuals

Robert Paul

University of Missouri, St. Louis
St. Louis, Missouri, USA

Disclosure: ***Nothing to disclose***

Disclaimer: The views expressed are those of the authors and should not be construed to represent the positions of the U.S. Army, the Department of Defense or the Henry M. Jackson Foundation for the Advancement of Military Medicine, Inc.
The investigators have adhered to the policies for protection of human subjects as prescribed in AR 70–25

CROI 2021

Introduction

Background:

- Fewer than 50% of people with acute HIV (AHI) achieve milestones that correspond to a favorable clinical phenotype (Table 1) after 96 weeks of anti-retroviral therapy (ART) initiated during acute infection.
- Risk factors and disease mechanisms underlying phenotype differences remain unknown.

Table 1. Favorable Clinical Phenotype

- No serious clinical events
  - No deaths
  - No AIDS-defining illness
  - No grade 4 adverse events
- Undetectable viral load after 6 months of ART
- Latest CD4 > 500 cells/mm^3
- Latest CD4/CD8 ratio > 1

Ananworanich et al., 2018

INHCC International NeuroHIV Cure Consortium

Methods

Participants:

- 412 Thai adults enrolled in RV254/SEARCH 010. Participants were mostly male (97%), Fiebig stages I-III (86%), with a CD4 T cell count >350 at baseline and undetectable viral status by week 24.

Assessments:

- Multi-dimensional assessments (e.g., viral, immune, neuro, psychosocial) at week 0 and at structured follow-up visits through week 144.
- Individuals were classified into favorable vs. unfavorable clinical phenotypes at weeks 96 and 144 using previously established criteria (Ananworanich et al., 2018).

Analytic Approach:

- The frequency of phenotype designation was defined at weeks 96 and 144 post ART.
- Ensemble machine learning was used to identify features that differentiated individuals according to phenotype designation.
- Multivariate group-based trajectory analyses were employed to identify clusters of participants with distinct risk profiles from week 0 through week 144.

INHCC International NeuroHIV Cure Consortium

Results

- 41% of the sample met criteria for a favorable clinical phenotype at week 144 (Fig. 1)
- CD4/CD8 T-cell ratio was the strongest classifier of phenotype designation (Fig. 2).

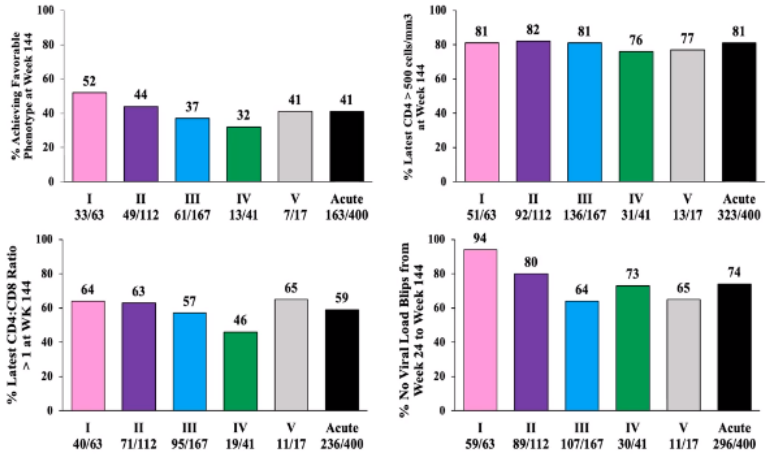

Figure 1. Frequency of phenotype designation by Fiebig stage.

INHCC International NeuroHIV Cure Consortium

Results and Conclusions

- Trajectory analysis revealed 5 distinct patterns of CD4/CD8 T-cell ratio from week 0 through week 144.
- Two subgroups (49% of the sample) exhibited early and chronic CD4/CD8 T-cell ratio inversion, owing to elevated CD8 T cell-counts with (group 4) or without (group 1) a strong CD4 T-cell response to ART.
- Baseline depressive symptoms, later Fiebig stage at ART onset, and levels of IL-7, IL-23, CD27, Tim-3, and RANTES differentiated the trajectory subgroups with based on CD4/CD8 T-cell inversion and clinical phenotype designation at week 144.

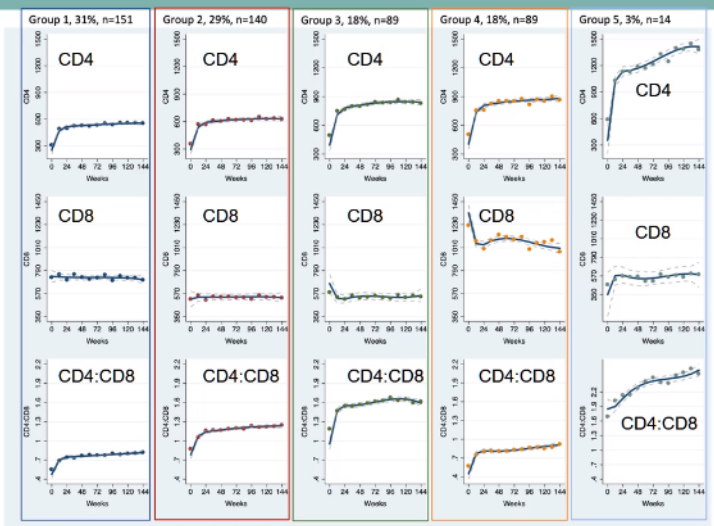

Figure 3. Five CD4/CD8 T-cell trajectory groups. Top row = CD4 T-cell count, Middle row = CD8 T-cell count, Bottom row = CD4/CD8 T-cell ratio. Each column represents a unique latent class. Columns 2 and 4 depict the groups with chronic CD/CD8 T-cell inversion.

INHCC International NeuroHIV Cure Consortium

Thai Red Cross
Nittaya Phanuphak
Praphan Phanuphak
Eugene Kroon
Carlo Sacdalan
Somchai Sriplienchan
Nipat Teeratakulpisarn
Nitiya Chomchey
Ponpen Tantivitayakul
Phillip Chan
Jintana Intasan
Ratchapong Kanaprach
Udom Likhitwonnawut
RV254 Clinical Teams

AFRIMS
Denise Hsu
Alexandra Schuetz
COL Mark Fukuda
Suchai Kitsiripornchai
Siriwat Akapirat
Rapee Trichavaroj
Bessara Nantapinit
Pornsuk Visudhiphan
Clinical Operations Group

Chulalongkorn University
Supranee Buranapraditkun
Sunee Sirivichayakul
Rungsun Rerknimitr
Netsiri Dumrongpisutikul
Phandee Wattanaboonyongcharoen
Sopark Manasnayakorn

Gates MRI
Jintanat Ananworanich

MHRP/WRAIR
Nelson Michael
Julie Ake
Merlin Robb
Morgane Rolland
Suteeraporn Pinyakorn
Thembi Mdluli
Adam Yates
Leilani Francisco
Donn Colby
Sodsai Tovanabutra
Linda Jagodzinski
Trevor Crowell
Mark de Souza
Diane Bolton
Shelly Krebs
Bonnie Slike
Sheila Peel
Leigh Ann Eller
Rasmi Thomas
Michael Eller
Ellen Turk
Oratai Butterworth
Corinne McCullough
Lisa Reilly
Jamie Livengood

U Montréal
Nicolas Chomont

Yale
Serena Spudich

NIH
John Mascola
Barney Graham
Carl Dieffenbach
Sarah Read
Peter Kim
Carl Swazedel
Leia Novak
Richard Koup
Julie Ledgerwood
Adrian McDermott
Robert Bailer
Nicole Doria-Rose
Randall Tressler
Bijal Patel
Irini Sereti
Daniel Douek
Eli Bortiz
Frank Maldarelli
Lawrence Fox

Leidos-NCI Frederick
Jeff Lifson
Claire Deleage
Robert Gorelick
Brandie Fullmer

U Missouri
Robert Paul

U Hawaii
Napapon Sailasuta

OHSU
Lydie Trautmann
Hiroshi Takata
Julie Mitchell
Jacob Estes

Weill Cornell
Lishomwa Ndhlovu

U Pittsburgh
John Mellors
Sharon Riddler

BIDMC
Dan Barouch
Summer Zheng

Ragon Institute
Galit Alter
Boris Juelg

Janssen
Hanneke Schuitemaker
Maria Pau
Frank Tomaka
Michal Sarnecki
Daniel Stieh

UNC
Gail Henderson

RTI International
Holly Peay

U Minnesota
Timothy Schacker

Drexel
Elias Haddad

Case Western
Rafick Sékaly
Slim Fourati

UCSF
Victor Valcour

Duke University
Guido Ferrari

U Melbourne
Sharon Lewin

Canada Natl. Lab
Adam Burgener

Ghent
Linos Vandekerckhove

U Manitoba
Lyle McKinnon

U Gothenburg
Henrik Zetterberg

Los Alamos
Bette Korber
William Fischer
Alan Perelson

Johns Hopkins
Robert Siliciano
Joel Blankson

UCSD
Doug Richman

INM RAS
Gennady Bocharov

U Nebraska
Courtney Fletcher

Emory
Eric Hunter

IrsiCaixa
Javier Martinez-Picado

Fred Hutchinson
Josh Schiffer

IHV
Hongshuo Song

Acknowledgements

RV254 & substudy participants

WRAIR Walter Reed Army Institute of Research
สภากาชาดไทย The Thai Red Cross Society
MHRP U.S. MILITARY HIV RESEARCH PROGRAM
hjf
NIMH National Institute of Mental Health
National Institutes of Health
IHRI
INHCC International NeuroHIV Cure Consortium