

**Norris Research Program
October 2009**

I. INTRODUCTION

Major research areas

Primary HIV/SIV infection
West Nile virus (WNV)
HTLV Immunology
Transfusion Immunology

Major BSRI collaborations

M. Busch, T-H. Lee – Microchimerism
M. Busch, L. Tobler – WNV
M. Busch, L. Tobler, R. Endres – Antileukocyte antibodies
E. Murphy – HTLV immunology

Major non-BSRI collaborations

Steven Deeks, Doug Nixon (UCSF) – HIV pathogenesis
Barton Haynes (Duke), Persephone Borrow (Jenner Institute/Oxford) – Immune responses of acute HIV
Norm Letvin, Dan Barouch, Joern Schmitz (Harvard) – Cytokine responses in SIV
Rosemary Sparrow (Australian Red Cross), Philip Spinella (University of Connecticut) – RBC storage effects

Staff

John Heitman, Research Associate
Dale Hirschhorn, Sr. Research Associate
Rachael Jackman, PhD, Postdoctoral Fellow
Sheila Keating, PhD, Staff Scientist
Marion Lanteri, PhD, Staff Scientist
Jacqueline Law, Research Associate
Mila Lebedeva, Research Associate

II. PROGRAM SUMMARY/ PROGRESS REPORT/PLANS

Primary HIV infection

Early HIV infection has formed one of the key research areas for the Norris lab, most recently focusing on defining the cytokine profile associated with acute HIV infection. We originally worked with plasma donor panels to track cytokine measurements spanning time points prior to infection through the acute period of viremia and seroconversion. Initial studies performed using high-sensitivity ELISA kits revealed early elevations in IL-10, TNF- α , and IFN- γ in primary HIV (1). Since the initial publication, high-sensitivity multiplex cytokine testing has become available on the Luminex platform using bead-coupled reagents collected using flow-cell technology. These assays have exponentially expanded the amount of data that can be collected from a single plasma or serum sample. As part of the Center for HIV/AIDS Vaccine Immunology (CHAVI), we generated a much more comprehensive picture of the evolution of cytokine responses in early HIV infection (Fig. 1). The HIV positive plasma donors have been compared to those with HBV and HCV infection, revealing that HIV causes a robust cytokine response that is much higher in breadth and magnitude than other chronic viral infections (2).

The CHAVI project has transitioned to study of cytokine responses in acute SIV infection, allowing greater manipulation of the immune system while measuring the effects on cytokine production. The initial findings from the CHAVI studies have also formed the basis for a research project with the Women's Interagency Health Study (WIHS). The advantage of studying a retrospective cohort with banked samples is that endpoints have been defined for many subjects for whom early samples are available.

The goal of the WIHS study is to identify predictors of disease progression that act independently of viral load.

Effector CD4+ T cells and HIV

There are two projects related to effector CD4+ T cells. The first, performed by Dr. Rachel Owen, is to quantify the frequency of *ex vivo* HIV-specific CD4+ T cells and correlate the frequency with the ability of these cells to kill cells expressing HIV proteins. These experiments will be performed in patients with and without control of HIV replication, with the hypothesis being that CD4+ CTL activity will be associated with control of HIV replication. The initial screening phase of the experiment has been completed in collaboration with Drs. Steven Deeks at UCSF, identifying a panel of rare individuals with high frequency HIV-specific CD4+ T cell responses. Dr. Owen's data suggest that HIV-specific CD4+ T cells undergo increased rates of apoptosis upon stimulation after long-term storage, and these findings formed the basis for her first publication (3).

The second CD4+ CTL project, performed by Dr. Moraima Pagan, focuses on how HIV escapes from CD4+ T cell responses. In early work we showed that HIV-specific CD4+ T cells can lyse HIV-infected target CD4+ T

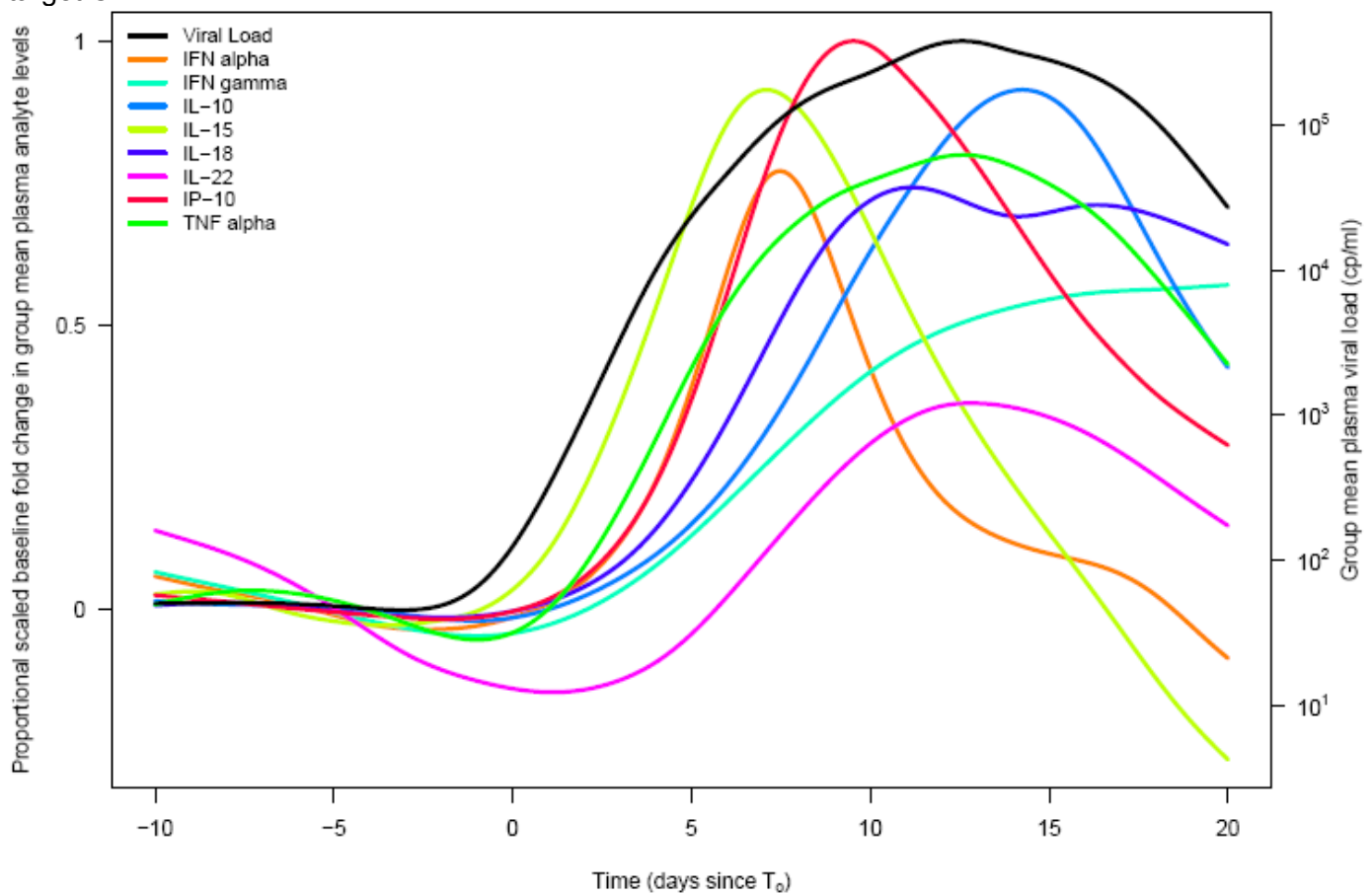


Figure 1. Scaled proportional group mean fold change relative to baseline over time in plasma levels of selected analytes in subjects acutely infected with HIV.

The proportional fold change relative to baseline in plasma levels of selected analytes (see key) and the viral load over time in the entire group of HIV-infected subjects is shown. The peak heights for different analytes are scaled according to the percentage of HIV-infected subjects studied who exhibited an elevation in plasma levels of the analyte concerned. Time is plotted in days relative to T_0 .

cells and can suppress viral replication in an MHC-restricted and cell contact dependent manner (4). To test whether this suppression will result in viral escape, both X4- and R5-tropic HIV will be replicated in the presence of HIV-specific CD4+ T cell clones. Dr. Pagan has demonstrated that a number of HIV-

specific clones can drive the evolution of HIV, with mutations arising within the T cell epitopes recognized by a series of HIV-specific CD4+ T cell clones. Furthermore, she has demonstrated that the mutated HIV sequence codes for peptides not recognized by the effector CD4+ T cells.

West Nile virus (WNV)

Dr. Marion Lanteri's project has been to define the immune response associated with acute WNV infection. Overlapping pools of peptides spanning the whole WNV proteome have been used to determine which areas of the virus are recognized by T cells in infected subjects. In addition, the phenotype and HLA restriction of responding T cells has been characterized for those subjects with high-level responses (5). Finally, the frequency of regulatory T cell responses have been measured longitudinally through the acute period of infection (Fig. 3A). We have shown that the Treg cell markers are consistent with classic Tregs and that cells sorted based on these markers will suppress proliferation of target cells (data not shown). The frequency of these responses rises significantly by one month after infection. By separating subjects based on whether or not they developed symptoms of WNV infection, it can be seen that symptomatic subjects have lower levels of Tregs early in infection (Fig 3B). Most remarkably, Treg levels at one year, when Treg frequencies had returned to normal control levels, were still significantly lower in patients who had suffered symptomatic WNV infection. These results imply that "Treg tone" may predict how people will respond to acute viral infection (6).

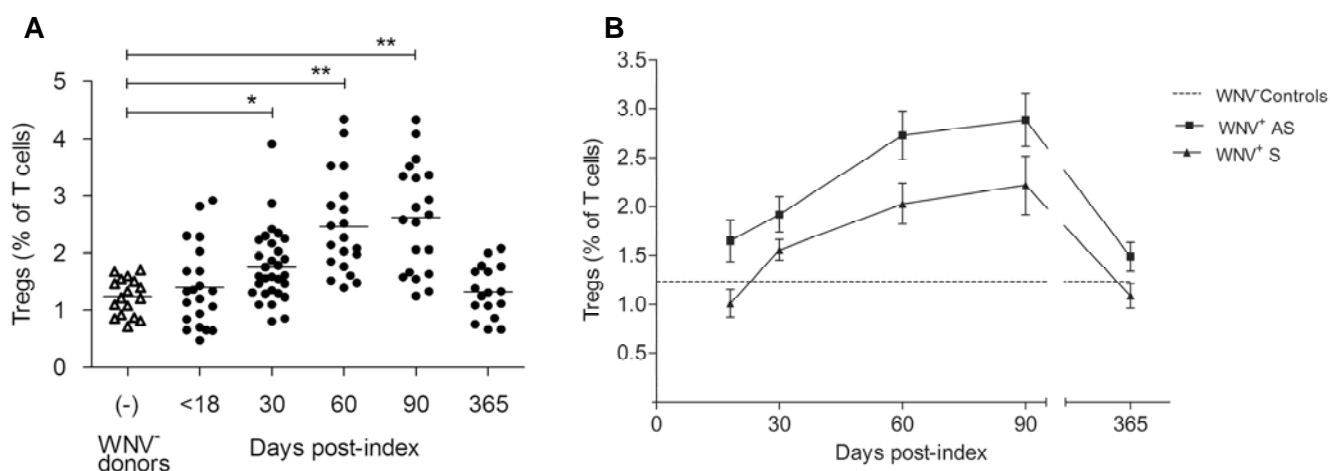


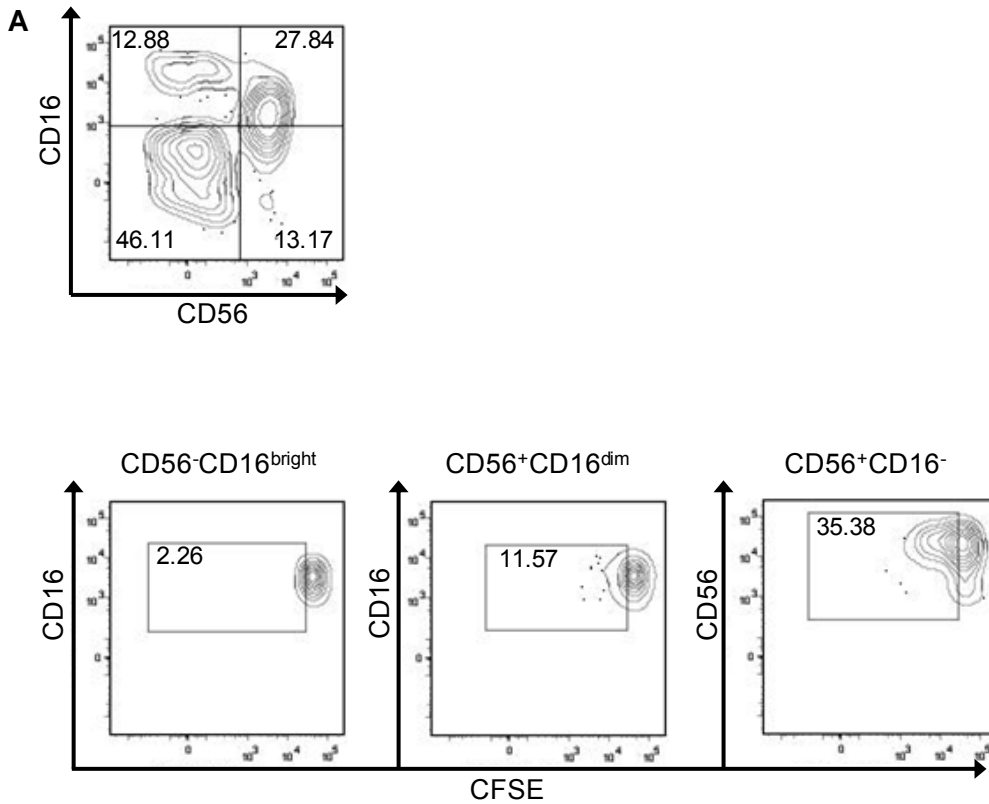
Figure 3. Longitudinal Treg frequency in symptomatic vs. asymptomatic subjects.

A. Average Treg frequencies of 29 WNV infected subjects peaked at 3 months. Treg were measured as percent of viable lymphocytes, excluding EMA, CD14, CD16, CD19 positive cells. Treg were defined as CD4+CD25+CTLA4+CD127-. Control WNV negative subject samples were run in parallel with each assay.

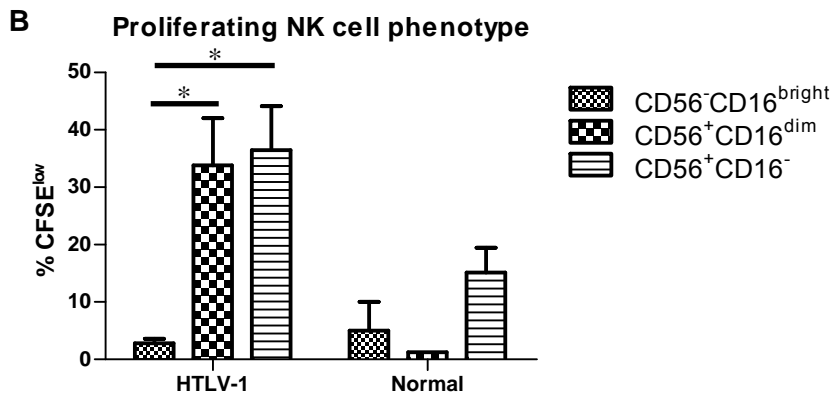
B. Treg levels were statistically significantly higher using the generalized estimating equation for asymptomatic patients (AS) compared to symptomatic (S) patients.

HTLV Immunology

The goal of this project is to correlate lymphocyte activation with outcome in a cohort of subjects prospectively followed for over ten years. Spontaneous lymphocyte proliferation is a feature of HTLV infection. Using banked frozen specimens, we will measure spontaneous lymphocyte proliferation in subjects who have developed complications of HTLV infection such as HTLV-associated myelopathy or T cell leukemia. Upon examination of the cohort we made the novel finding that not only T cells, but also NK cells spontaneously proliferate to high levels in about half of HTLV-1 infected subjects (7). Future work will focus on the mechanisms responsible for NK cell spontaneous proliferation and how this relates to HTLV pathogenesis.



Phenotype of proliferating NK cells after seven days' culture *ex vivo*. (A) NK cells were first identified as viable CD3⁺ lymphocytes based on FSC/SSC, aqua amine-reactive dye, and anti-CD3 staining. The NK cells were then gated into three subsets based on CD56 and CD16 expression (upper panel) and CFSE dilution was measured within each subset (lower panel). (B) For each of the three defined NK cell phenotypes, proliferating cells were measured in HTLV-1 infected and normal control subjects. A minimum of 30,000 live lymphocytes was collected for each subject, and cell subsets with at least 50 gated events were included for analysis of proliferation (%CFSE^{low}). Error bars represent standard error; * p<0.05



Anti-HLA antibody prevalence in blood donors

As part of the Core Immunology laboratory the Norris lab measured the presence of anti-HLA antibodies in 9,000 blood donor specimens. Anti-HLA antibodies may be implicated in the pathogenesis of transfusion-related acute lung injury (TRALI). The project required assay optimization, data review, and creation of an expert review panel to interpret the complicated anti-HLA antibody results. While mainly a core lab function, a methods manuscript was published (8), and multiple blood bank related manuscripts detailing the prevalence of anti-HLA antibodies in various donor populations and the implications for the safety and availability of the blood supply will result from the work (9).

Transfusion-associated microchimerism

Microchimerism is defined as the persistence of a minor population of allogeneic cells within a host recipient. This can occur after events such as pregnancy, with persistence of fetal cells in the maternal circulation, and overt chimerism occurs after bone marrow transplant. Microchimerism has also been shown to occur in transfusion recipients who receive blood in the post-trauma phase, and prolonged persistence of chimeric cells can occur without ongoing exogenous immunosuppression (10). It is remarkable that the transient immunosuppression associated with trauma will allow persistence of

allogeneic cells for up to at least one year post-transfusion. The Norris lab is exploring how allogeneic donor cells persist in trauma patients who develop microchimerism post-transfusion. The studies will focus on immune function at and shortly after the time of transfusion, as well as on longitudinal samples obtained from subjects who have persistent microchimerism and those who clear the allogeneic cells. We hypothesize that those subjects who develop microchimerism will have more profoundly disrupted immune systems at the time of trauma and will be better matched to the donors implicated in microchimerism than to those donors whose cells do not persist. Many of the techniques to be used in the microchimerism studies, such as multiplex cytokine testing and Treg quantification, have been developed in prior studies of immune responses to viral infections. The microchimerism studies will hopefully provide significant advances in our understanding of immune tolerance.

III. GRANTS, CONTRACTS, AND AWARDS

R01HL095470-01 (Norris) 9/18/09-7/31/13 3.0 calendar
NIH/NHLBI

Properties of stored RBCs: minimization of immune and vascular reactivity

The purpose of this research proposal is to discover changes that occur in stored RBC units and test methods of reversing or preventing these changes.

Role: PI

U01-AI-034993-15 (Minkoff) 9/30/09 – 9/29/11 1.2 calendar
NIH / NIAID

Women's Interagency HIV Study (WIHS) IV

Administrative Supplement to fund testing of soluble and cellular markers of inflammation, immune activation, and markers of microbial translocation using a consensus protocol developed jointly by the MACS and WIHS.

Role: Project PI

U01-AI-034993-15 (Cohen) 1/1/08 – 12/30/12 1.4 calendar
NIH / NIAID

Women's Interagency HIV Study (WIHS) IV, Chicago Consortium

The WIHS cohort provides longitudinal assessment of women with and without HIV spanning over ten years with specimen collection and examination every six months. As a member of the Pathogenesis working group the Norris lab will assess soluble markers of inflammation (cytokines and chemokines) in key comparison groups, such as those who progress to AIDS and long-term nonprogressors.

Role: Project PI

U01-AI-067854 (Haynes) 7/14/05 – 6/30/12 1.8 calendar
NIH / NIAID

Center for HIV/AIDS Vaccine Immunology (CHAVI)

The major goals of this project are to characterize the evolution of the innate and early T cell immune responses from the earliest point of HIV infection by studying HIV-infected paid plasma donors.

Role: Project PI

1RC2HL101632 (Busch) 9/30/09-9/29/11 1.2 calendar
NIH/NHLBI

Viral/immune parameters of Dengue and WNV in donors: blood safety implications

The goals of this grant are to establish the infectivity of low-level WNV viremic units in the early convalescent stage of infection not detected by current NAT screening, to implement sensitive NAT screening in Puerto Rico under an FDA IND, and to launch follow-up studies of DENV+ donors. In addition, we will establish an NHLBI repository of extensively characterized, longitudinal specimens from Dengue and WNV infected donors to advance research into the pathogenesis of these important agents.

Role: Co-Investigator

R01-HL-083388-01A1 (Busch) 9/1/06 – 7/31/11 2.3 calendar
NIH / NHLBI

Mechanisms and clinical effects of microchimerism in transfused trauma patients

The objectives of the study are to demonstrate the clinical effects of persisting donor white blood cells in transfusion recipients, the immune mechanisms responsible for donor cell persistence, and whether or not donor cells actually engraft in transfusion recipients in the post-trauma setting. The Norris lab will focus on mechanisms of immune tolerance associated with microchimerism.

Role: Co-Investigator

N01 HB-057181 (Busch)

3/15/05 – 8/31/10

0.6 calendar

NIH / NHLBI

Retrovirus Epidemiology Donor Study (REDS) - II Central Laboratory

BSRI will establish and maintain a central laboratory for all REDS specimen testing. Specific projects include testing for anti-HLA antibodies in blood donors and determining the presence of influenza viremia in donor populations.

Role: Co-Investigator

P30 AI027763 (Volberding)

9/15/07 – 8/31/12

0.3 calendar

NIH/NIAID

UCSF-GIVI Center for AIDS Research

The primary aim of this center grant is to nurture and sustain innovative multidisciplinary HIV research at the intersections of the basic, clinical, behavioral, and epidemiologic scientific disciplines. Funding is salary support for Dr. Norris as Associate Director, Center for AIDS Research.

R01 HL095140-01 (Kaplan)

9/25/08 – 6/30/13

0.6 calendar

NIH/NHLBI

Inflammatory and Immune Mechanisms of Atherosclerosis in HIV-Infected Women

The present study will assess the association of circulating levels of IGF-I, and two major IGF binding proteins (IGFBP-1, IGFBP-3) with functional limitation, disability, performance-based tests of physical function, brain morphologic changes, and survival/longevity among older adults. The Norris Lab will quantify soluble markers of inflammation in HIV infected patients at risk for cardiovascular disease.

Role: Co-Investigator

R01 HL095130-01 (Hsue)

9/25/08 – 6/30/13

.036 calendar

NIH/NHLBI

Inflammation, Viral Replication, and Atherosclerosis in Treated HIV Infection

We propose to determine 1. the influence of traditional and novel markers of inflammation on endothelial function and IMT progression; 2. if "intensification" with raltegravir in subjects on long-term antiretroviral therapy with clinically undetectable HIV RNA levels will improve endothelial function, and to determine if this effect is mediated by alterations in inflammatory markers, lipoproteins and/or thrombotic factors; and 3. the potentially beneficial aspects of CCR5 inhibition on inflammation and endothelial function as measured by brachial artery reactivity.

Role: Co-Investigator

P50HL081027-04 (Toy)

4/1/08 – 8/31/10

0.3 calendar

NIH/NHLBI

Transfusion and Lung Injury

Assist PD/PI with data analysis for HLA antibody testing and manuscript preparation for on-going TRALI-SCCOR study.

Role: Co-Investigator

5423 (Norris)

01/01/09 – 12/31/09

0.0 calendar

BSI / BSRI

Immunology Research Program

This funding supports Norris lab staff, supplies, and sundry expenses for multiple research projects.

Role: PI

Pending

(Kwok) 9/1/09-8/31/14 0.3 calendar
 NIH/NIAID
 Identifying epitopes recognized by influenza and flavivirus responsive CD4+ T cells following vaccination or natural infection
 Goals include the mapping of CD4+ T cell epitopes and studying the phenotype of CD4+ cells identified using newly developed class II tetramers.
 Role: Co-Investigator

(Spinella) 1/1/10-12/31/12 0.3 calendar
 DOD
 RBC Storage Age Effect on Inflammation, Immune Function, Coagulation and Microchimerism and their Correlation with Outcomes in Critically Ill Patients
 Role: Co-Investigator

(Goodrich) 9/1/09-7/31/14 1.2 calendar
 DOD
 A Transportable Pathogen Reduction System for Treatment of Whole Blood
 To measure immune modulation in subjects receiving Mirasol treated RBC units.
 Role: Co-Investigator

R01-HL-062235 (Murphy) 4/01/10 – 3/31/15 1.2 calendar
 NIH / NHLBI
 Pathophysiology of HTLV-I and HTLV-II Infection (HOST)
 The major goals of this renewal application are to characterize the natural history of HTLV-I and –II infection in a longitudinal cohort of asymptomatic subjects identified through blood donation screening.
 Role: Co-Investigator

Completed Research Support.

R01-HL-062235 (Murphy) 04/05/05-03/31/09
 NIH/NHLBI
 Pathophysiology of HTLV-I and HTLV-II Infection (HOST)
 The major goals of the study are to characterize the natural history of HTLV-I and –II infection in a longitudinal cohort of asymptomatic subjects identified through blood donation screening. The goals for the Norris lab are to determine the immunologic consequences of long-term HTLV-I/II infection in a prospective cohort.
 Role: Co-Investigator

Navigant Biotechnologies (Norris) 12/01/07-11/30/08
 Pathogen reduction and platelet refractoriness
 The sponsored research agreement with Navigant will define the mechanism by which pathogen reduction methods abrogate antigen presenting capacity of treated mononuclear cells. Cell surface markers and cell-cell interactions will be characterized.
 Role: PI

New Investigator Award (Norris) 01/01/04-12/31/06
 Blood Systems Foundation
 Immunology
 The major goals of this project were to determine the relationship between HIV-specific cytolytic CD4+ T cells and control of HIV replication, and to expand T cell immunology studies to examine West Nile virus immunity and the immunology surrounding the development of microchimerism.
 Role: PI

U01 AI-41531 (Levy)

08/01/04-06/30/07

NIH

Immunologic and Virologic Features of Early HIV Infection

The major goals of this study are to characterize the natural history and pathogenesis of primary HIV infection. Specific projects include developing a staging system to determine the timing of primary HIV infection and to determine the protective role T cells might play in early HIV infection.

Role: Co-Investigator

R01 C1000214-01 (Busch)

09/30/04-09/29/07

CDC

Natural History and Pathogenesis of WNV in Viremic Donors

The major goals of this study are to characterize the natural history and pathogenesis of West Nile virus infection in blood donors. The role of T cell immune responses in protection from and manifestations of disease will be clarified.

Role: Co-Investigator

Unsuccessful applications:

CFAR 'Outside-the-Box' AIDS Vaccine Discovery Awards, Letter of Intent

07/01/09-06/30/10

Vaccine design to boost HIV-specific CD4+ T cell responses

Role: PI

Bill & Melinda Gates Foundation, Grand Challenges Exploration grant

Vaccine design to boost HIV-specific CD4+ T cell responses

Role: PI

1RC1HL100429-01 (Norris)

09/30/09-09/29/11

NIH/NHLBI

Ensuring safe blood; does pathogen reduction also reduce allo-immunization?

Role: PI

1RC2HL101730-01

09/30/09-09/29/11

NIH/NHLBI

A pedigreed RECESS trial repository; mechanisms of RBC storage age effects

Role: PI

R21

12/01/09-11/30/11

NIH

Liver fibrosis and immunologic correlations in HIV and Hepatitis C coinfection

Role: Co-Investigator

IV. OTHER SIGNIFICANT ACTIVITIES

Associate Director, UCSF-GIVI Center for AIDS Research

Associate Director, Blood Systems Research Institute

Mentor, UCSF-GIVI CFAR Mentoring Program

Infectious Diseases Consult Attending, SFGH

Radiation Safety Officer, BCP

BSRI Lab Meeting – Organized and maintained ongoing BSRI-wide weekly scientific lab meeting and journal club

BSRI Retreat – Led organization of annual BSRI scientific retreat and monthly happy hours.

Reviewer for professional programs/publications

Editorial board: *Virulence*

Regular reviewer: *AIDS* (1)

Ad hoc referee: *Journal of Virology* (1), *Vaccine* (1), *Journal of Infectious Diseases* (2), *Journal of Clinical Immunology* (1).

Grant review:

Chair, UCSF Resource Allocation Program, Basic HIV/AIDS, Infectious Diseases, Global Health Review Committee

NIH Special Emphasis Panel: RFA # AI-08-013 “Immune Mechanisms of Virus Control (U01/U19)”

US Army Medical Research and Materiel Command, WNV vaccine grant review

Department of Defense Congressionally Directed Medical Research Programs, WNV vaccine grant review

NIH Special Emphasis Panel: PAR-09-134 “HIV Vaccine Research and Design Program (HIVRAD)”

Abstract review:

5th IAS Conference on HIV Pathogenesis, Treatment and Prevention

V. ABSTRACTS, PUBLICATIONS, AND PRESENTATIONS

Publications

1. Stacey AR*, **Norris PJ***, Qin L, Haygreen EA, Taylor E, Heitman J, Lebedeva M, DeCamp A, Li D, Grove D, Self SG, Borrow P. Induction of a striking systemic cytokine cascade prior to peak viremia in acute HIV-1 infection, in contrast to more modest and delayed responses in acute hepatitis B and C virus infections. *J Virol* 83(8):3719-3733 (2009).
*These authors contributed equally to this work.
2. Triulzi DJ, Kleinman S, Kakaiya RM, Busch MP, **Norris PJ**, Steele WR, Glynn SA, Hillyer CD, Carey P, Gottschall JL, Murphy EL, Rios J, Ness PM, Wright DJ, Carrick D, Schreiber GB. The Effect of Previous Pregnancy and Transfusion on HLA Alloimmunization in Blood Donors: Implications for a Transfusion Related Acute Lung Injury (TRALI) Risk Reduction Strategy. *Transfusion* 49(9):1825-35 (2009).
3. Jackman RP, Heitman JW, Marschner S, Goodrich RP, **Norris PJ**. Understanding loss of donor white blood cell immunogenicity following pathogen reduction: mechanisms of action in UV illumination and riboflavin treatment. *Transfusion* August 2009 (Epub ahead of print).
4. Lanteri MC, O'Brien KM, Cameron MJ, Purtha WE, Lund JM, Owen RE, Heitman JW, Custer B, Hirschorn DF, Tobler LH, Kiely N, Prince HE, Ndhlovu LC, Nixon DF, Kamel HT, Kelvin DJ, Busch MP, Rudensky AY, Diamond MS, **Norris PJ**. Regulatory T cells control the development of symptomatic West Nile virus infection. *J Clin Invest* (in press).
5. **Norris PJ**, Hirschorn DF, DeVita DA, Lee TH, Murphy EL. Human T cell leukemia virus type 1 infection drives spontaneous proliferation of natural killer cells. *Virulence* (in press).
6. Ndhlovu LC, Leal FE, Eccles-James IG, Jha AR, Lanteri MC, **Norris PJ**, Wachter DJ, Andersson J, Tasken K, Torheim EA, Aandahl EM, Kallas EG, Nixon DF. A novel human CD4⁺ T cell inducer subset with potent immunostimulatory properties. *Eur J Immunol* (in press).
7. Beal AM, Anikeeva N, Varma R, Cameron TO, **Norris PJ**, Dustin ML, Sykulev Y. Granule delivery by CTL follows the pattern of proximal signaling foci. *Immunity* (in press).
8. Law JP, Hirschorn DF, Owen RE, Biswas HH, **Norris PJ**, Lanteri MC. The importance of Foxp3 antibody and fixation/permeabilization buffer combinations in identifying CD4⁺CD25⁺Foxp3⁺ regulatory T cells. *Cytometry Part A* (in press).

9. Khurana S, **Norris PJ**, Busch MP, Haynes BF, Park S, Mlisana K, Salim AK, Hecht FM, Mulenga J, Chomba E, Hunter E, Allen S, Nemo G, Rodrigueez-Chavez IR, WIHS, MACS, Golding H. HIV-SELECTEST EIA and rapid test: Ability to detect seroconversion following HIV-1 infection J Clin Micro (in press).

Submitted manuscripts

Owen RE, Heitman JW, Hirschhorn DF, Lanteri MC, Biswas HH, Martin JN, Krone MR, Deeks SG, **Norris PJ** and the NIAID Center for HIV/AIDS Vaccine Immunology. HIV⁺ elite controllers have low levels of HIV-specific T cell activation yet maintain strong, polyfunctional T cell responses (submitted).

Hunt PW, Martinson JA, Sinclair E, Hatano H, Emu B, **Norris PJ**, Busch MP, Martin JN, Brooks C, McCune JM, Landay AL, Deeks SG. Low Treg Frequencies May Augment HIV-specific Immune Responses but Drive Generalized Immune Activation in HIV-infected Elite Controllers (submitted).

Ronquillo RE, Desai SN, **Norris PJ**, Golub E, Greenblatt RM, Gange SJ, Landay AL. Elevated Caspase-3 Expression and CD8+ T Cell Activation in Elite Suppressors (submitted).

Kakaiya RM, Triulzi DJ, Wright DF, Steele WR, Kleinman SH, Busch MP, **Norris PJ**, Hillyer CD, Gottschall JL, Rios JA, Carey P, Glynn SA. Prevalence of HLA antibodies in remotely transfused volunteer blood donors (submitted).

Endres RO, Kleinman SH, Carrick DM, Steele W, Wright D, **Norris PJ**, Triulzi D, Kakaiya R, Busch MP. Identification of specificities of antibodies against human leukocyte antigens in blood donors (submitted).

Presentations

Abstracts

Hatano H, Delwart E, **Norris PJ**, Lee TH, Dunn-Williams J, Hunt P, Hoh R, Martin JN, Busch MP, Deeks SG. Evidence of persistent low-level viremia in long-term HAART-suppressed individuals. Conference on Retroviruses and Opportunistic Infections, Montreal, Canada, February 2009.

Lopez-Verges S, Milush JM, Pandey S, **Norris PJ**, Nixon D, Lanier LL. CD57 defines a functionally unique subset of NK cells in humans. American Association of Immunologists Annual Meeting, Seattle, WA, May 2009.

Garrett PE, **Norris PJ**, Perry K, Delwart E, Weiblen B, Manak M, Busch MP, Schumacher RT. 20 years of research and development experience with HIV, HCV and HBV seroconversion panels. 25th Annual Clinical Virology Symposium, Daytona Beach, FL, April 2009.

Norris PJ, Hirschhorn DF, Devita D, Lee T-H, Murphy EL. HTLV-I induced spontaneous lymphocyte proliferation is not limited to CD8+ T cells. 14th International Conference on Human Retrovirology: HTLV and Related Retroviruses. Salvador, Brazil, July, 2009.

Huston L, Stacey A, Dibben O, del Pugar S, Dragun J, **Norris P**, Forns X, Borrow P. The systemic cytokine response activated following liver transplantation in patients chronically infected with hepatitis C virus (HCV) mirrors that observed in primary acute HCV infection. European Congress of Immunology, Berlin, Germany, September 2009.

Keating S, Heitman J, Zahn R, Borrow P, Barouch D, Letvin N, Schmitz J, **Norris PJ**. Early Immune Responses in SIV infection. HIV Acute Infection Meeting, Boston, MA, September 2009.

Jackman RP, Heitman JW, Munz MM, Biswas HH, Svoboda K, Rivers RM, Geffer N, Busch MP, Utter MP, **Norris PJ**. Immune response to trauma and transfusion. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

Jackman RP, Heitman JW, Marschner S, Goodrich RP, **Norris PJ**. Understanding Loss of Donor White Blood Cell Immunogenicity Following Pathogen Reduction: Mechanisms of Action in UV Illumination and Riboflavin Treatment. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

Norris PJ, Carrick DM, Kleinman S, Pandey S, Lee JH, Vorhaben R, Roback J, Chance S, Lebedeva M, Busch MP. Comparison of Assays to Detect HLA Antibodies. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

Manish G, **Norris PJ**, Toy P. Prevalence of HLA antibody positive screen in blood components implicated in TRALI. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

Carrick D, Endres B, Kleinman S, Sun Y, Wright D, **Norris PJ**, Steele W, Busch MP. Association of the strength of signal on a Luminex HLA screening assay with breadth of specific HLA antigen reactivity supports the use of high cutoffs for donor TRALI screening. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

Endres RO, Kleinman S, Carrick D, Steele W, Sun Y, **Norris PJ**, Busch MP. Specificities of HLA antibodies in blood donors: baseline data for a TRALI lookback study. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

Gottschall J, Kleinman S, Triulzi D, Kakaiya R, Busch MP, Carrick D, **Norris PJ**, Carey P, Hillyer C, Curtis, B. HNA Antibodies in Blood donors. American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA, October 2009.

National/International

March 2009: Advances in WNV Research (NIH sponsored conference), Washington, DC
The role of regulatory T cells in WNV infection

March 2009: One Lambda Advanced HLA Technical Program, Rancho Mirage, CA
Transfusion Related Acute Lung Injury (TRALI)

May 2009: ABC 2009 Technical/Lab Directors Workshop, Chicago, IL
TRALI risk reduction strategies

October 2009: American Association of Blood Banks, 61st Annual Meeting. New Orleans, LA
Assessment for influenza A virus in blood donors

Local/Regional

January 2009: Symposium on HIV/AIDS, Episcopal Church of Our Saviour, Mill Valley, CA
HIV Therapy

February 2009: UCSF/GIVI Center for AIDS Research External Advisory Committee, San Francisco, CA
Cytokine perturbations in early HIV infection

March 2009: CaridianBCT site visit, Lakewood, CO
Mirasol Pathogen Reduction: Understanding loss of white blood cell immunogenicity

References

1. Norris, P. J., B. L. Pappalardo, B. Custer, G. Spotts, F. M. Hecht, and M. P. Busch. 2006. Elevations in IL-10, TNF-alpha, and IFN-gamma from the earliest point of HIV Type 1 infection. *AIDS Res Hum Retroviruses* 22:757-762.
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