BIOGRAPHICAL SKETCH

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NAME: **Rinaldo, Charles R.**

eRA COMMONS USER NAME (credential, e.g., agency login): **rinaldo**

POSITION TITLE: **Chairman and Professor**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Syracuse University, Syracuse, NY	AB	1969	Bacteriology
University of Utah, Salt Lake City, UT (J.C. Overall, advisor)	PhD	1973	Microbiology
Massachusetts General Hospital, Harvard Medical School, Boston, MA (M.S. Hirsch, mentor)	Post-Doc Fellow	1974-78	Viral Immunology

A. Personal Statement

I head the Pittsburgh site of the Multicenter AIDS Cohort Study, a natural history study of HIV (therapy, aging, chronic diseases, viral coinfections, human genetics and immunopathogenesis) that I established in 1983, which is now one of 13 Clinical Research Sites of the MACS-Women's Interagency HIV Study Combined Cohort Study (MACS-WIHS CCS). My MACS-WIHS CCS research laboratory focuses on innate and adaptive immunity in immunopathogenesis of HIV and human herpesvirus 8 (KSHV) infections, and dendritic cell (DC)-based immunotherapies for curing HIV infection. I also lead an Immunology Specialty Laboratory (Pitt ISL) in the AIDS Clinical Trials Group (ACTG) that focuses primarily on cell-mediated immunity, immunoregulation and immune activation for clinical protocols of the ACTG HIV Reservoirs and Viral Eradication Transformative Science Group and End-Organ Disease/Inflammation Transformative Science Group. My clinical specialty is diagnostic virology, particularly herpesviruses and influenza viruses, and new analyses of the human virome.

B. Positions and Honors

Positions and Employment

1974-1978 Research Fellow, Harvard Medical School, Mass. Gen. Hospital, Boston, MA
1978-pres. Assistant Director, Clinical Microbiology Lab, University of Pittsburgh Medical Center
1978-1984 Assistant Professor, Department of Pathology, University of Pittsburgh School of Medicine, and Department of Microbiology, University of Pittsburgh Graduate School of Public Health (GSPH), Pittsburgh, PA
1985-1991 Associate Professor, Department of Pathology, University of Pittsburgh, School of Medicine, and Department of Infectious Diseases and Microbiology (IDM), University of Pittsburgh, GSPH
1992-pres. Professor, Department of Pathology, University of Pittsburgh School of Medicine, and Department of IDM, University of Pittsburgh GSPH
1997-pres. Chairman, Department of IDM, University of Pittsburgh GSPH

Other Experience (selected)

1997-2000 Member, NIH-NIAID AIDS Research Advisory Committee, NIH
1997-2004 Member, AARR2/AIP Study Section, NIH
2002-2007 Member, ACTG Immunology Research, Experimental Therapeutics Research Advisory, Translational Research and Drug Development Committees, NIH

2004-2010 Chair, Basic Science Track, Ontario HIV Treatment Network Scientific Review Committee
2007-2011 Section Editor, *Journal of Immunology*
2011-2014 Member, ACTG HIV Reservoirs and Viral Eradication Transformative Science Working Group
2015-present Member, Editorial Board, *AIDS*

Selected Honors

1974-77 USPHS-NIH Postdoctoral Research Fellow, National Cancer Institute, NIH
1977 Junior Investigator, Charles A. King Trust
1999 Special Award for AIDS Research, Pennsylvania Public Health Association
2004-2014 MERIT award, NIH-NIAID
2007, 2009 Honoree, Outstanding Faculty, University of Pittsburgh Annual Honors Convocation

B. Contributions to Science

1. **CMV infection and immunosuppression:** Primary CMV infection is detectable in blood neutrophils and can cause a profound but self-limiting immunosuppression in normal adults with primary, symptomatic CMV infection; Importance: Was an integral factor referenced in original CDC report on AIDS, June, 1981; Specific role: My postdoctoral fellowship project with Dr. M. S. Hirsch; Selected References:
    a. **Rinaldo CR Jr**, Black PH, Hirsch MS. Interaction of cytomegalovirus with leukocytes from patients with mononucleosis due to cytomegalovirus. J Infect Dis. 1977;136:667-678.
    b. **Rinaldo CR Jr**, Richter BS, Black PH, Callery R, Chess L, Hirsch MS. Replication of herpes simplex virus and cytomegalovirus in human leukocytes. J Immunol. 1978;120:130-136.
    c. Levin MJ, **Rinaldo CR Jr**, Leary PL, Zaia JA, Hirsch MS. Immune response to herpesvirus antigens in adults with acute cytomegaloviral mononucleosis. J Infect Dis. 1979;140:851-857.
    d. **Rinaldo CR Jr**, Carney WP, Richter BS, Black PH, Hirsch MS. Mechanisms of immunosuppression in cytomegaloviral mononucleosis. J Infect Dis. 1980;141:488-495.

2. **HIV-1 load as predictor of AIDS:** First reports to demonstrate that HIV-1 RNA levels in blood in the first year of infection can predict risk for development of AIDS 10 years later; Importance: Viral load testing became the standard of care in management and prognosis of HIV infection; Specific role: PI and immunologist in the Pitt MACS investigative team led by J. Mellors; Selected References:
    a. Mellors JW, Kingsley LA, **Rinaldo CR Jr**, Todd JA, Hoo BS, Kokka RP, Gupta P. Quantitation of HIV- 1 RNA in plasma predicts outcome after seroconversion. Ann Intern Med. 1995;122:573-579.
    b. Mellors JW, **Rinaldo CR Jr**, Gupta P, White RM, Todd JA, Kingsley LA. Prognosis in HIV-1 infection predicted by the quantity of virus in plasma. Science. 1996;272:1167-1170.
    c. Mellors JW, Muñoz A, Giorgi JV, Margolick JB, Tassoni CJ, Gupta P, Kingsley LA, Todd JA, Saah AJ, Detels R, Phair JP, **Rinaldo CR Jr**. Plasma viral load and CD4+ lymphocytes as prognostic markers of HIV-1 infection. Ann Intern Med. 1997;126:946-954.
    d. Mellors, JW, Margolick, JB, Phair, JP, **Rinaldo, CR**, Detels, R, Jacobson, LP, and Munoz, A. Prognostic value of HIV-1 RNA, CD4 cell count, and CD4 Cell count slope for progression to AIDS and death in untreated HIV-1 infection. JAMA 2007; 297:2349-2350.

3. **Myeloid DC are key to activating latent HIV-1 and inducing anti-HIV-1 T cell immunity:** First comprehensive report in 1997 showing that programmed DC expressing HIV-1 antigens are potent antigen-presenting cells (APC); First evidence that DC maintain a strong APC function for induction of cytokines in memory $CD8^+$ T cells during chronic HIV-1 infection and on ART, but these T cells are poor CTLs; Evidence that DC can prime naïve T cells to HIV-1 during ART to produce cytokines and kill HIV-1 infected cells; Recent discovery that immune checkpoint PD-1 on CD8 T cells has dual, contradictory roles in anti-HIV-1 T cell immunity; Recent study showing DC loaded with CMV or HIV-1 peptides can activate latent HIV-1 and CTL that kill these infected cells. Importance: DC are being used in immunotherapeutic "kick and kill" approaches in attempts to cure HIV-1 infection; Specific role: Senior co-leader of the project with Dr. Mailliard in my laboratory team; Selected Recent References:
    a. Macatangay BJ, Riddler SA, Wheeler ND, Spindler J, Lawani M, Hong F, Buffo MJ, Whiteside TL, Kearney MF, Mellors JW, **Rinaldo, CR**. Therapeutic vaccination with dendritic cells loaded with autologous HIV-1-infected apoptotic cells. J Infect Dis 2016;213:1400-1409. PMCID: PMC4813736

b. Smith KN, Mailliard RB, Piazza PA, Fischer W, Korber BT, Fecek RJ, Ratner D, Gupta P, Mullins JI, **Rinaldo CR.** Effective cytotoxic T lymphocyte targeting of persistent HIV-1 during antiretroviral therapy requires priming of naive $CD8^+$ T cells. MBio 2016;7(3). PMCID: PMC4895106
c. Garcia-Bates TM, Palma ML, Shen C, Gambotto A, Macatangay BJC, Ferris RL, **Rinaldo CR,** Mailliard RB. Contrasting roles of the PD-1 signaling pathway in dendritic cell-mediated induction and regulation of HIV-1-specific effector T cell functions. J Virol. 2018 Dec 12. PMID: 30541848.
d. Kristoff J, Palma ML, Garcia-Bates TM, Shen C, Sluis-Cremer N, Gupta P, **Rinaldo CR,** Mailliard RB. Type 1-programmed dendritic cells drive antigen-specific latency reversal and immune elimination of persistent HIV-1. EBioMed 2019 Apr 2. pii: S2352-3964(19)30222-1. PMID: 30952614

4. **T cell control and DC/B cell targeting by HHV-8:** Importance: First reports of $CD8^+$ T cell responses to HHV-8 (KSHV) during primary infection, HHV-8 targeting of APC via DC-SIGN, and HHV-8 targeting B cell subsets for lytic infection and poly-cytokine responses in relation to increased risk for KS; Specific role: Senior co-leader of the project with Dr. Rappocciolo in my laboratory team; Selected References:
   a. Rappocciolo, G., Jenkins, F.J., Hensler, H.R., Piazza, P., Jais, M., Borowski, L., Watkins, S.C., and **Rinaldo, C.R., Jr**. DC-SIGN is a receptor for human herpesvirus 8 on dendritic cells and macrophages. J. Immunol. 2006; 176(3):1741-1749.
   b. Rappocciolo G, Hensler HR, Jais M, Reinhart TA, Pegu A, Jenkins FJ, **Rinaldo CR**. Human herpesvirus 8 infects and replicates in primary cultures of activated B lymphocytes through DC-SIGN. J Virol. 2008;82(10):4793-4806. PMCID: PMC2346758
   c. Knowlton ER, Rappocciolo G, Piazza P, Lepone LM, Nadgir SV, Bullotta A, Berendam SJ, Li J, Reinhart TA, Jenkins FJ, **Rinaldo CR**. Human herpesvirus 8 induces polyfunctional B lymphocytes that drive Kaposi's sarcoma. mBio 2014;5:e01277-14. PMCID: PMC4173773
   d. Rappocciolo, G., Jais M., Piazza, P.A., DeLucia, D.C., Jenkins, F.J., **Rinaldo, C.R.** Human herpesvirus 8 infects and replicates in Langerhans cells and interstitial dermal dendritic cells and impairs their function. J Virol. 91:e000909-17, 2017. PMCID: PMC5625489

5. **HIV-1 *trans* infection in nonprogressors:** Recent discovery that HIV-1 *trans* infection mediated by APC is greatly restricted in nonprogressors due to a genetically linked alteration in APC cholesterol metabolism; Importance: Novel genetic basis for the innate ability of the host to control HIV-1 disease progression that opens new approaches for controlling of HIV-1 infection, and could have broader, non-HIV-1 clinical implications; Specific role: Senior investigator in the project with Dr. Rappocciolo in my laboratory team; Selected References:
   a. Rappocciolo G, Piazza P, Fuller CL, Reinhart TA, Watkins SC, Rowe DT, Jais M, Gupta P, **Rinaldo CR**. DC-SIGN on B lymphocytes is required for transmission of HIV-1 to T lymphocytes. PLoS Pathog. 2006;2(7):e70. PMCID: PMC1500807
   b. Rappocciolo G, Jais M, Piazza P, Reinhart TA, Berendam SJ, Garcia-Exposito L, Gupta P, **Rinaldo CR**. Alterations in cholesterol metabolism restrict HIV-1 *trans* infection in nonprogressors. mBio 2014;5:e01031-13. PMCID: PMC4010827
   c. DeLucia DC, **Rinaldo CR**, Rappocciolo G. Inefficient HIV-1 *trans* infection of CD4+ T cells by macrophages from HIV-1 nonprogressors is associated with altered membrane cholesterol and DC-SIGN. J Virol. 2018: 92(13). pii: e00092-18 PMCID: PMC6002718
   d. Rappocciolo G, Sluis-Cremer N, **Rinaldo CR.** Efficient HIV-1 trans infection of CD4+ T cells occurs in the presence of antiretroviral therapy. Open Forum Infect Dis. 2019 May 24;6(7):ofz253 PMID: 31304185.

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/myncbi/browse/collection/40699585/?sort=date&direction=ascending

C. Additional Information: Research Support

Ongoing Research Support

U01-AI35041 (MPI: Rinaldo/Martinson/Kingsley) 04/01/1993 – 04/30/2020
NIH/NIAID/NCI/NIDA
University of Pittsburgh Multicenter AIDS Cohort Study (MACS)

Over 2,000 men who have sex with men in the Pittsburgh area have been studied since 1984 to define the natural history of HIV infection, effects of ART and risk for development of AIDS as part of the national Multicenter AIDS Cohort Study. Volunteers are studied every six months for clinical signs and symptoms, T cell phenotyping and HIV-1 load, viral immunopathogenesis, antiviral drug effects, comorbidities, and various chronic conditions of aging. Study will focus on the addition of new testing to the MACS protocol as follows: a) electrocardiograms (ECGs), both 12-lead ECG done at the study visit and a cardiac monitor worn for two weeks for the detection of intermittent heart arrhythmias, and b) pulmonary function tests (PFT). The Pitt MACS will serve as the central reading center for the pulmonary research data, and will conduct two studies of laboratory-measured biomarkers that contribute to vascular and pulmonary disease, using stored plasma or serum.
Role: PI

U01HL146208 (MPI: Rinaldo/Martinson) 04/01/2019-03/31/2026
NHLBI/NIAID/NCI/NIDA
University of Pittsburgh MACS/WIHS CCS
A continuation of U01AI35041 with focus on the epidemiologic, clinical, virologic, immunologic, and behavioral relationships of HIV infection to chronic comorbidities in men and women that represent the current HIV epidemic in the United States.
Role: PI

U01-AI068636 (Kuritzkes) 06/29/2006 – 12/31/2020
NIH/NIAID
The Adult AIDS Clinical Trials Group - Brigham & Women's Hospital (BWH): Prime Award No 7UM1AI068636- 07 Principal Investigator: Daniel R. Kuritzkes, MD; Pittsburgh ACTG Immunology Specialty Laboratory; Principal Investigator in Pittsburgh: Charles Rinaldo. The Pitt Immunology Specialty Laboratory provides immunologic testing for the AIDS Clinical Trials Group.
Role: PI Pittsburgh site

R01-AI118403 (MPI: Rappocciolo/Rinaldo) 01/01/2015 – 12/31/2019
NIH/NIAID
Cholesterol-dependent control of HIV progression by antigen presenting cells
The proposed research should reveal novel information on how antigen presenting cells in a low percentage of people control HIV disease progression without drug therapy. This could lead to new approaches in preventing and curing HIV infection.
Role: PI

U01-CK000337 (Zimmer) 09/01/2015 – 08/31/2020
JHU/CDC
Monitoring cause-specific school absenteeism for estimating community wide influenza
Surveillance, Monitoring Absenteeism & Respiratory Transmission in Schools (SMART2) will lead to improved understanding of how diseases such as influenza spread between school children and the community. This research will provide useful data for dealing with seasonal and pandemic (like H1N1) flu.
Role: Co-I

UM1-AI126603 (Barouch) 07/14/2016 – 06/30/2021
NIH/NIAID
I4C Collaboratory: Combined Immunologic Approaches to Cure HIV-1
The goal of this collaboratory that is part of the NIH Martin Delaney Collaboratory:Towards an HIV-1 Cure program is to develop novel combined immunologic approaches to cure HIV-1 through a highly collaborative and multifaceted research program. We are assessing the efficacy of highly advanced, dendritic cell-based therapeutic vaccines, broadly neutralizing antibodies, and latency reversing agents to contribute to a functional cure in both preclinical and clinical studies.
Role: Co-I

R01-MD010680 (Stall) 10/01/2015 – 09/30/2020

NIH/NIMHD
Understanding patterns of healthy aging among MSM
This study will use a theory-based approach to follow aging MSM in six waves of an ongoing cohort study to document how resiliencies moderate the effects of health risks to better explain patterns of health and illness among aging MSM.

Role: Co-I

R35DE026631 (D'Souza) 09/20/2016 – 06/30/2020
NIH/NIDRC
Impacting the oral HPV continuum: prevention, screening, and early detection (subaward)
Exploring HIV, antiretroviral therapy, gender, drug use, and sexual behavior in oral HPV infection.
Role: Co-I

Completed Research Support (last 3 years)

U01-AI105870 (Riddler) 03/01/2014 – 02/28/2018
NIH/NIAID
Dipyridamole as a Modulator of HIV-1 Inflammation by Adenosine Regulation
Increased risk for chronic diseases of aging in HIV-1-infected individuals despite effective antiretroviral therapy has been associated with persistent immune activation and systemic inflammation. This project will identify a specific regulatory pathway involved in HIV-1-associated inflammation by testing a drug intervention that will target it. Identification of this pathway and a therapeutic strategy to reduce its inflammation could be a major advance in controlling chronic HIV-1 infection.
Role: Co-I

R01-AI118403S1 (MPI: Rinaldo/Rappocciolo) 01/01/2015 – 12/31/2016
NIH/NIAID
Cholesterol-dependent control of HIV progression by antigen presenting cells – supplemental funds
These supplemental funds will allow us to use RNA-seq to generate a more complete dataset of whole transcriptome expression data in our NP and PR samples. This will enhance and expand our utilization of resources in order to generate significant data that will be used to strengthen the data results for the parent project and for future extramural applications.
Role: PI

R01-DE021395 (D'Souza) 08/20/2010 – 06/30/2018
NIH/NIDRC; Effect of HIV and Immunosuppression on Oral HPV Persistence in the HAART Era (subaward) Exploring HIV, antiretroviral therapy, gender, drug use, and sexual behavior in oral HPV infection.
Role: Co-I