

BIOGRAPHICAL SKETCH

Provide Follow this format the following information for the key personnel and other significant contributors in the order listed on Form Page 2. for each person. **DO NOT EXCEED FOUR PAGES.**

NAME Eva Harris		POSITION TITLE	
eRA COMMONS USER NAME evaharris		Professor	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Harvard University, Cambridge, MA	B.A., mcl	1987	Biochemical Sciences
University of California, Berkeley, CA	Ph.D.	1993	Molecular & Cell Biology

PERSONAL STATEMENT:

Dr. Eva Harris is a Professor in the Division of Infectious Diseases and Vaccinology in the School of Public Health and Director of the Center for Global Public Health at the University of California, Berkeley. She has developed a multidisciplinary approach to study the molecular virology, pathogenesis, immunology, clinical aspects, epidemiology, and control of dengue, the most prevalent mosquito-borne viral disease in humans. Her work addresses viral and host factors that modulate disease severity and immune correlates of protection and pathogenesis using *in vitro* approaches, animal models, and research involving human populations. One major research focus is on studies of dengue in humans, focusing on antibody and B cell correlates of protection, host gene expression profiling, and viral evolution, fitness, and intrahost diversity. Another has been the development of a mouse model to study viral tropism and pathogenesis, investigate the immune response to dengue virus (DENV) infection, and generate a better model of disease. Her international work focuses on laboratory-based and epidemiological studies of dengue, chikungunya, and influenza in endemic Latin American countries, particularly in Nicaragua, where ongoing projects include clinical and biological studies of severe dengue, a pediatric cohort study of dengue, chikungunya and influenza transmission in Managua, and a recently concluded cluster randomized controlled trial of evidence-based, community-derived interventions for prevention of dengue via control of its mosquito vector. *This work has led to over 180 peer-reviewed articles, including 85 publications on DENV translation/replication and host-virus interactions, DENV evolution and fitness, diagnostic and prevention/control aspects of infectious diseases, as well as scientific capacity building in developing countries, that are not listed in the sections on contributions to science below.* She has been PI on ~36 grants, including 6 R series awards, a U19, and a Program Project (P01) from NIH. In 1997, Dr. Harris received a MacArthur "Genius" Award for her pioneering work over the previous ten years developing programs and working to build scientific capacity in developing countries to address public health and infectious disease issues. To continue and expand this work, in 1998 she founded a non-profit organization Sustainable Sciences Institute (SSI; www.sustainableciences.org), with offices in San Francisco, Nicaragua, and Egypt, and published a book on the subject with Oxford University Press. In 2001, Dr. Harris was named a Pew Scholar for her work on dengue pathogenesis. In 2002, she received a national recognition award from the Minister of Health of Nicaragua for her contribution to scientific development, and she was selected as a "Global Leader for Tomorrow" by the World Economic Forum. In 2012, she was elected Councilor of the American Society of Tropical Medicine and Hygiene and received a Global Citizen Award from the United Nations Association.

RESEARCH AND PROFESSIONAL EXPERIENCE:

1988-1993	Graduate Student, Dr. Jeremy Thorner, Dept of Molecular and Cell Biology, UC Berkeley, CA
1993-1996	Postdoctoral Fellow, Dr. Nina Agabian, Pgm. Molecular Pathogenesis, UC San Francisco, CA
1993-2001	Director, Applied Molecular Biology/Appropriate Technology Transfer Program, UCSF/UCB
1997-1999	Assistant Adjunct Professor, Program in Molecular Pathogenesis, UC San Francisco, CA
1998-present	President, Sustainable Sciences Institute, San Francisco, CA
1998-2005	Assistant Professor, Division of Infectious Diseases, School of Public Health, UC Berkeley, CA
2005-2008	Associate Professor, Division of Infectious Diseases, School of Public Health, UC Berkeley
2007-2008	Associate Dean for Research, School of Public Health, UC Berkeley
2008-present	Professor, Division of Infectious Diseases, School of Public Health, UC Berkeley
2007-present	Director, Center for Global Public Health, School of Public Health, UC Berkeley

HONORS AND AFFILIATIONS:

1988-1991	National Science Foundation Graduate Fellowship
1991-1993	Berkeley Graduate Fellowship, University of California, Berkeley

1997 *Doctor Honoris Causa*, Universidad Mayor de San Andrés, La Paz, Bolivia
 1998-present Visiting Professor, Universidad Autónoma de Guerrero, Acapulco, México
 1997-2002 MacArthur Fellowship, John D. and Catherine T. MacArthur Foundation
 1998-2001 King Sweesy and Robert Womack Chair in Medical Research and Public Health, UC Berkeley
 2001-2005 Pew Scholar, Pew Scholars Program in the Biomedical Sciences, Pew Charitable Trusts
 2002 Prytanean Alumnae Faculty Award, UC Berkeley Prytanean Faculty Association
 2002 Global Leader for Tomorrow, World Economic Forum
 2002 Award from Minister of Health, Nicaragua, recognizing support of scientific development
 2012 Global Citizen Award, United Nations Association, East Bay Chapter

PROFESSIONAL ACTIVITIES

1995 Invited Participant, IOM/NRC Meeting on Emerging Infectious Diseases, NAS
 1998 Invited Participant, NIAID/DMID Focus Group, National Institutes of Health
 1999, 2002 Reviewer, NIH Study Section for NIAID "Int'l Collaborations in Infectious Disease Research"
 1999 - 2005 Member, US National Committee for the IUBMB, National Academy of Sciences
 1999 - present Reviewer, *J Virol*, *J Infect Dis*, *J Immunol*, *Am J Trop Med Hyg*, *EID*, *Virus Res*, *J Med Virol*, *J Gen Virol*, *Virology*, *PLoS Med*, *PLoS Negl Trop Dis*, *PLoS Path*, *Nat Med*, *J Immunol Meth*
 2000,2,5,7,9 Temporary Advisor, World Health Organization and Pan American Health Organization
 2000 Reviewer, NIH Study Section for NIAID "Tropical Medicine Research Centers"
 2001 International Organizing Committee, WHO Conference "Harnessing Biotechnology for Health"
 2001 Frontiers of Science Symposium, National Academy of Sciences (Speaker)
 2002 Reviewer, NIH Study Section for NIAID "Int'l Collaborations in Infectious Disease Research"
 2002-2003 Consultant, Health Equity, Rockefeller Foundation
 2004 International Organizing Committee, WHO World Summit on Health Research
 2004 Reviewer, Ellison Medical Foundation, Global Infectious Diseases Program
 2005 – present Advisory Committee, President's Postdoctoral Fellowship Program, UC Office of the President
 2006 Reviewer, Virology A Study Section, NIAID, NIH
 2006-8 Program Committee, American Society for Virology
 2007-2011 Reviewer and Chair, ICP1 Study Section, NIH; Chair (2009), ICP2-B Study Section, NIH
 2007-present Associate Editor, *PLoS Neglected Tropical Diseases*
 2009 Invited Plenary, American Society for Virology Annual Meeting
 2010 Howard Hughes Medical Institute Holiday Lecture
 2011 Invited Speaker, NIH Wednesday Afternoon Lecture Series
 2012 Editor/Reviewer, Transformative R01 Study Section, NIH
 2012, 2014 Scientific Advisory Board, Pan American Dengue Research Network Meeting (Chair, 2014)
 2012-2014 Scientific Advisory Board, Novartis Institute of Tropical Diseases
 2012-present Council, American Society of Tropical Medicine and Hygiene
 2013-2015 Steering Committee, Models of Infectious Disease Agent Study (MIDAS), NIH
 2013-present Standing Member, Clinical Research and Field Studies (CRFS) Study Section, NIH
 2014-present Participant, Scientific Advisory Board, Sanofi Pasteur
 2014 Member (Ad hoc), NIAID Council, NIH
 2014-present Member, Scientific Advisory Board, SMART Infectious Diseases Program

CONTRIBUTIONS TO SCIENCE

1. Investigation of the human immune response to DENV infection

A long-standing interest of my group is to leverage our >25-year collaboration with the Nicaraguan Ministry of Health to investigate the human immune response to DENV infection and to identify correlates of protection and pathogenesis. To do so, we analyze the well-characterized serum and peripheral blood mononuclear cell (PBMC) samples from our two on-going long-term prospective studies of dengue in Managua, Nicaragua -- the community-based pediatric dengue cohort study (now in its 12th year) and the hospital-based study of pediatric dengue (now in its 17th year). The focus in my laboratory has been on the B cell and antibody response, with on-going collaborations to address gene expression profiling, immune cell phenotyping and T cell responses. Important findings, selected from ~25 publications, have included demonstration that the cross-reactive DENV-specific B cell response is higher against a prior heterotypic serotype than against the current infecting serotype in secondary DENV infections, the association of avidity and neutralizing antibody titer in human polyclonal sera, and convergent immune signatures in multiple dengue patients associated with specific CDR3 sequences. Most recently, we have established that anti-DENV neutralizing antibody titers correlate with reduced probability of symptomatic DENV infection in our cohort study and thus can serve as a correlate of

protection (submitted), which has important implications for studies of natural infections and vaccine trials. The consortia I have helped established in this arena have just been awarded an NIH P01 program grant, alongside the HIPC U19, to investigate innate and adaptive immune correlates of protection in natural infections and vaccines to continue and expand this work.

- a. Durbin, A., Vargas, M.J., Thumar, B., Hammond, S.N., Gordon, A., Rocha, C., Balmaseda, A., and **Harris, E.** (2008) Phenotyping of peripheral blood mononuclear cells during acute dengue illness demonstrates infection and increased activation of monocytes in severe cases compared to classic dengue fever. *Virology*. 376:429-35. PMC2546568
- b. Zompi, Z., Montoya, M., Pohl, M., Balmaseda, A., **Harris, E.** (2012) Dominant cross-reactive B cell response during secondary acute dengue virus infection in humans. *PLoS Negl Trop Dis*. 6:e1568. PMC3308930
- c. Popper, S.J., Gordon, A., Liu, M., Balmaseda, A., **Harris, E.**, and Relman D.A. (2012) Temporal dynamics of the transcriptional response to dengue virus infection in Nicaraguan children. *PLoS Negl. Trop. Dis*. 6: e1966. PMC3527342
- d. Loke, P., Hammond, S.N., Leung, J.M., Kim, C.C., Batra, S., Rocha, C., Balmaseda, A., and **Harris, E.** (2010) Gene expression patterns of DENV-1 infected children from Nicaragua reveal a distinct signature of increased metabolism. *PLoS Negl Trop Dis*. 4:e710. PMC2886038
- e. Parameswaran, P., Liu, Y., Roskin, K., Jackson, K., Dixit, V.P., Lee, J.-Y., Artiles, K., Zompi, S., Vargas, M.J., Simen, B.B., Hanczaruk, B., McGowan, K.R., Tariq, M.A., Pourmand, N., Koller, D., Balmaseda, A., Boyd, S.D.*, **Harris, E.***, Fire, A.Z.* (2013) Convergent antibody signatures in human dengue. *Cell Host Microbe* 13:691-700. *Co-corresponding authors. PMID: 23768493

2. Characterization of anti-DENV polyclonal and monoclonal antibodies

Through collaborative studies and a dozen publications, we have defined the characteristics of human polyclonal and monoclonal antibodies (MAbs), using our mouse model of protection and enhancement to complement *in vitro* assays. We demonstrated that MAbs act therapeutically *in vivo* by being both highly neutralizing and suppressing the enhancing potential of pre-existing antibodies. We contributed to generation of human MAbs (from children in our Nicaraguan studies) and characterization of the protective efficacy as well as enhancing ability of MAbs *in vivo*. We also analyzed antibody subsets in human polyclonal DENV-immune sera and showed that removal of serotype cross-reactive antibodies ablated enhancement of heterotypic virus infection *in vitro* and antibody-enhanced mortality *in vivo*. These studies blending *in vitro* and *in vivo* studies have shed light on the properties and mechanisms of antibodies that lead to neutralization/protection vs enhancement of DENV infection.

- a. Beltramello, M., Williams, K.L., Simmons, C.P., Macagno, A., Simonelli, L., Quyen, N.T.H., Sukupolvi-Petty, S., Navarro-Sanchez, E., de Silva, A.M., Rey, F.A., Varani, L., Whitehead, S.S., Diamond, M.S., **Harris, E.**, Lanzavecchia, A., Sallusto, F. (2010) Development of a broadly neutralizing cocktail of human monoclonal antibodies to dengue viruses that lacks infection-enhancing activity. *Cell Host Microbe*. 16:271-83. PMC3884547
- b. Williams, K.L., Sukupolvi-Petty, S., Beltramello, M., Johnson, S., Sallusto, F., Lanzavecchia, A., Diamond, M.S., **Harris, E.** (2013) Therapeutic efficacy of antibodies lacking Fcγ receptor binding against lethal dengue virus infection is due to neutralizing potency and blocking of enhancing antibodies. *PLoS Pathog*. 9:e1003157. PMC3573116
- c. de Alwis, R., Williams, K.L., Schmid, M.A., Patel, B., Lai, C.-Y., Smith, S.A., Crowe, J.E., Wang³, W.-K., **Harris, E.***, de Silva, A.M.* (2014) Dengue viruses are enhanced by distinct populations of serotype cross-reactive antibodies in human immune sera. *PLoS Pathog*. 10(10):e1004386. *co-corresponding authors PMC4183589
- d. Smith, S.A., de Alwis, R., Kose, N., **Harris, E.**, Ibarra, K.D., Kahle, K.M., Pfaff, J.M., Xiang, X., Doranz, B.J., de Silva, A., Austin, K., Sukupolvi-Petty, S., Diamond, M.S., and Crowe, J.E., Jr. (2013) The potent and broadly neutralizing human dengue virus-specific monoclonal antibody 1C19 reveals a unique cross-reactive epitope focused on the BC loop of envelope protein domain II. *mBio*. 4(6):e00873-13. PMC3870244
- e. Fibriansah, G., Ibarra, K.D., Ng, T.-S., Smith, S.A., Tan, J.L., Lim, X.-N., Kostyuchenko, V.A., Wang, J., de Silva, A.M., **Harris, E.**, Crowe, J.E., Jr., and Lok, S.-M. (2015) CryoEM structure of an antibody that neutralizes dengue virus type 2 by locking E protein dimers. *Science*. 349:88-91.

3. Development and use of mouse models of DENV infection, disease, and immune response

Another major research area (~20 publications) has been the generation of a mouse model of DENV infection and disease that we use for mechanistic studies of dengue pathogenesis and immune response, which we then correlate with human DENV infection, disease, and immune responses in our studies in Nicaragua (see below). These parallel studies have focused on virus tropism, immune response, and viral structure/function. Major findings have included the first *in vivo* demonstration of lethal antibody-dependent enhancement of

DENV infection, characterization of waves of DENV infection of resident followed by recruited immune cells in an intradermal model of infection, and, most relevant to the current application, the discovery of a direct role for DENV NS1 protein alone in inducing vascular leak *in vivo*.

- a. Shresta, S., Sharar, K.L., Prigozhin, D.M., Beatty, P.R., and **Harris, E.** (2006) Murine model for dengue lethal disease with increased vascular permeability. *J. Virol.* 80: 10208-10217. PMC1617308
- b. Balsitis, S.*, Williams, K.L.*, Lachica, R., Flores, D., Kyle, J.L., Mehlhop, E., Johnson, S., Diamond, M., Beatty, P.R., and **Harris, E.** (2010) Lethal antibody enhancement of dengue disease in mice is prevented by Fc modification. *PLoS Path.* 6 :e1000790. PMC2820409
- c. Zompi, S., Santich, B.H., Beatty, P.R., and **Harris, E.** Protection from secondary dengue virus infection in a mouse model reveals the role of serotype cross-reactive B and T cells. (2012) *J. Immunol.* 188:404-16. PMC3244532
- d. Schmid, M.A. and **Harris, E.** (2014) Monocyte recruitment to the dermis and differentiation to dendritic cells increases the targets for dengue virus replication. *PLoS Pathog.* 10(12):e1004541. PMC4256458
- e. Beatty, P.R., Guardo, H.P., Killingbeck, S., Glasner, D., Hopkins, K., and **Harris, E.** (2015) Dengue virus non-structural protein 1 (NS1) triggers vascular leak that can be inhibited by anti-NS1 antibodies. *Sci Transl Med* 7:304ra141.

4. Epidemiology of dengue and chikungunya

I have been active over the last 20 years in directing studies on the epidemiology of dengue in Nicaragua, based on our 17-year hospital study of dengue, our 12-year cohort study, and other studies in communities, health centers and hospitals in Nicaragua. These studies have led to >20 papers, documenting trends in transmission of dengue, the effect of viral genetics, prior host immunity, and interval between infections on the outcome of DENV infection, the expansion factor needed to calculate the true burden of disease, and a cluster-randomized controlled trial to show the effectiveness of evidenced-based community participation in mosquito control for the prevention of dengue, among others. Since 2014, we have initiated a series of similar projects on chikungunya, including studies of incidence, clinical attack rate, seroprevalence, etc.

- a. **Harris, E.**, Pérez, L., Videa, E., Sandoval, E., Tellez, Y., Pérez, M.A., Cuadra, R., Rocha, J., Idiaquez, W., Alonso, R.E., Delgado, M.A., Acevedo, F., Campo, L.A., Gonzalez, A., Amador, J.J., and Balmaseda, A. (2000) Clinical, epidemiologic, and virologic features of dengue in the 1998 epidemic in Nicaragua. *Am. J. Trop. Med. Hyg.* 63:5-11.
- b. Balmaseda, A., Standish, K., Mercado, J.C., Matute, J.C., Tellez, Y., Saborío, S., Hammond, S.N., Nuñez, A., Henn, M.R., Holmes, E.C., Gordon, A., Coloma, J., Kuan, G., and **Harris, E.** (2010) Trends in patterns of dengue transmission in a pediatric cohort study in Nicaragua. *J. Infect. Dis.* 201:5-14.
- c. OhAinle, M., Balmaseda, A., Macalalad, A.R., Tellez, Y., Zody, M.C., Saborío, S., Nuñez, A., Lennon, N.J., Birren, B.W., Gordon, A., Henn, M.R., **Harris, E.** (2011) Dynamics of dengue disease severity determined by the interplay between viral genetics and serotype-specific immunity. *Science Transl Med.* 3:114ra128.
- d. Montoya, M.,* Gresh, L.,* Mercado, J.C., Williams, K.L., Vargas, M.J., Gutierrez, G., Kuan, G., Gordon, A., Balmaseda, A., **Harris, E.** (2013) Symptomatic versus inapparent outcome in repeat dengue virus infections is influenced by the time interval between infections and study year. *PLoS Negl Trop Dis.* 7:e2357. PMC3738476
- e. Andersson, N., Nava-Aguilera, E., Arostegui, J., Morales-Perez, A., Suazo-Laguna, H., Legorreta-Soberanis, J., Hernandez-Alvarez, C., Fernandez-Salas, I., Balmaseda, A., Cortés-Guzmán, A.J., Coloma, J., Ledogar, R.J., and **Harris, E.** (2015) Camino Verde (Green Way) to Dengue Prevention: a pragmatic cluster-randomised controlled trial of evidence-based community mobilisation in Nicaragua and Mexico. *BMJ* 351:h3267.

5. Clinical research and laboratory diagnostics

Another area of research, resulting in over 40 papers, is clinical research and the development and application of diagnostic assays for dengue and other infectious diseases. This includes work on the classification of dengue severity, which led to the inclusion of Nicaragua in the multi-center WHO/TDR study that formed the basis for the new dengue guidelines; validation and implementation of ultrasound as a prognostic indicator of vascular leak; development of new serological and molecular biological assays for diagnosis and typing of DENV, characterization of clinical features and biomarkers of DENV infection and disease, and the like.

- a. Balmaseda, A., Hammond, S.N., Perez, L., Tellez, Y., Saborío, S.I., Mercado, J.C., Perez, M.A., Silva, S., Rocha, C., and **Harris, E.** (2006) Serotype-specific differences in clinical manifestations of dengue. *Am. J. Trop. Med. Hyg.* 74:449-456.
- b. Aviles, W., Ortega, O., Kuan, G., Coloma, J., and **Harris, E.** (2007) Integration of information technologies in clinical studies in Nicaragua. *PLoS Medicine.* 4:1578-1583. PMC2039765
- c. Narvaez, F.,* Gutierrez, G.,* Perez, M.A., Elizondo, D., Nuñez, A., Balmaseda, A., and **Harris, E.** (2011) Evaluation of the Traditional and revised WHO classifications of dengue disease severity. *PLoS Negl Trop*

Dis. 5:e1397. PMC3210746

- d. Balmaseda, A., Saborio, S., Tellez, Y., Mercado, J.C., Pérez, L., Hammond, S.N., Rocha, C., Kuan, G., **Harris, E.** (2008) Evaluation of immunological markers in serum, filter-paper bloodspots, and saliva for dengue diagnosis and epidemiological studies. *J. Clin. Virol.* 43:287-91. PMID: 18783984
- e. Biswas, H., Ortega, O., Gordon, A., Standish, K., Balmaseda, A., Kuan, G., **Harris, E.** (2012) Early clinical features of dengue virus infection in Nicaraguan children: A longitudinal analysis. *PLoS Negl Trop Dis.* 6:e1562. PMC3295819

6. Dengue virus evolution and fitness

A series of studies have addressed DENV evolution and fitness, stemming from sequence and phylogenetic analysis of the circulating serotypes, genotypes and clades in our studies in Nicaragua. Importantly, we have combined these with functional studies of the viruses in question. In one large study of DENV-2 clade replacement temporally associated with an increase in disease severity, we found that it was the complex interaction of viral genetics and population dynamics of serotype-specific immunity that *together* contributed to risk of severe dengue disease. We also showed via *in vitro* analyses of viral isolates from the different clades (NI-1 vs. NI-2B) and analysis of patient viremia a more fit virus likely emerged in later epidemic seasons. We then analyzed the replicative ability of the two clades in mosquito cell lines and *Ae. aegypti* mosquitoes reared from eggs collected in Managua and showed that clade NI-2B holds a replicative advantage over clade NI-1 early in infection.

- a. OhAinle, M., Balmaseda, A., Macalalad, A.R., Tellez, Y., Zody, M.C., Saborio, S., Nuñez, A., Lennon, N.J., Birren, B.W., Gordon, A., Henn, M.R., **Harris, E.** (2011) Dynamics of dengue disease severity determined by the interplay between viral genetics and serotype-specific immunity. *Science Transl Med.* 3:114ra128.
- b. Parameswaran, P., Charlebois, P., Tellez, Y., Nunez, A., Ryan, E.M., Malboeuf, C.M., Levin, J.Z., Lennon, N., Balmaseda, A., **Harris, E.***, and Henn, M.R.* (2012) Genome-wide patterns of intrahuman dengue virus diversity reveal associations with phylogenetic clade and interhost diversity. *J. Virol.* 86(16):8546. PMC3421746 *Co-corresponding authors.
- c. Quiner, C.A., Parameswaran, P., Ciota, A.T., Ehrbar, D.J., Dodson, B.L., Schlesinger, S., Kramer, L.D., and **Harris, E.** (2014) Increased replicative fitness of a dengue virus 2 clade in native mosquitoes: Potential contribution to a clade replacement event in Nicaragua. *J. Virol.* 88(22):13125-34. PMC4249086
- d. Manokaran, G., Finol, E., Wang, C., Gunaratne, J., Bahl, J., Ong, E.Z., Tan², H.C., Sessions, O.M., Ward, A.M., Gubler, D.J., **Harris, E.**, Garcia-Blanco, M.A., and Ooi, E.E.. (2015) Subgenomic RNA of dengue-2 virus binds tripartite motif 25 protein to inhibit interferon expression providing a mechanism for epidemiological fitness. *Science.* Jul 2. pii: aab3369. [Epub ahead of print]

7. Dengue virus translation/replication and host-virus interactions.

My laboratory performed a series of investigations to define viral and host determinants that modulate DENV translation and replication. This led to the discovery of a non-canonical mechanism of DENV translation that could provide a survival advantage under certain infection conditions and to the identification of novel *cis* sequence and structural elements that control viral RNA translation and replication. We also further defined the molecular requirements for 5'-3' circularization of the viral genome for both translation and replication of the DENV RNA and identified *trans* cellular factors involved in regulation of these processes. Finally, we characterized the host response to DENV infection in relation to modulation of the unfolded protein response and the rearrangement and expansion of the endoplasmic reticulum. This body of work comprises ~25 publications; these studies involved molecular genetic, biochemical, structural, and confocal microscopy studies similar to those proposed in this application. Currently, NS1 mutagenesis and protein expression systems have been established alongside a series of *in vitro* assay platforms to dissect the mechanisms of NS1-induced endothelial permeability, as described in Preliminary Results.

- a. Edgil, D., Polacek, C., and **Harris, E.** (2006) Dengue virus utilizes a novel strategy for translation initiation when cap-dependent translation is inhibited. *J. Virol.* 80:2976-2986. PMC1395423
- b. Clyde, K. and **Harris, E.** (2006) RNA secondary structure in the coding region of dengue virus type 2 directs translation start codon selection and is required for viral replication. *J. Virol.* 80:2170-2182. PMC1395379
- c. Paranjape, S. and **Harris, E.** (2007) Y box-binding protein-1 binds to the dengue virus 3' untranslated region and mediates anti-viral effects. *J. Biol. Chem.* 282:30497-30508.
- d. Peña, J. and **Harris, E.** (2011) Dengue virus modulates the unfolded protein response in a time-dependent manner. *J. Biol. Chem.* 286:14226-14236. PMC3077624
- e. Friebe, P. and **Harris, E.** (2011) The 5' and 3' downstream AUG region elements are required for mosquito-borne flavivirus RNA replication. *J. Virol.* 85:1900-5. PMC3028882

Complete List of Published Work in MyBibliography: <http://www.ncbi.nlm.nih.gov/sites/myncbi/12Sg-8tp-CpQN/bibliography/40921741/public/?sort=date&direction=ascending>.

D. Research Support (Selected active on-going grants)

P01 AI106695 (Harris Program Director, PI Project 1, Core C); NIAID/NIH 7/1/15-6/30/20; 1.2 acad, 0.6 sum m
Protective immunity following dengue virus natural infections and vaccination

The main goal of this Program Project is to bring together a consortium of leading experts in B and T cell immunology together with dengue field sites and vaccine developers to improve understanding of the human B and T cell response to DENV natural infection and vaccination and identify adaptive immune correlates of protection from disease.

U19 AI118610 (Harris Co-Program Director; PI Project 1); NIAID/NIH 7/1/15-6/30/20; 0.26 acad, 1.15 sum m
Dengue Human Immunology Project Consortium (DHIPC); Project 1 Immune profiling of natural dengue virus infections

The main goal of this program is to develop molecular signatures that define immune response and correlate with the outcome of dengue virus infection and vaccination. We will use “omics” technology platforms including immune profiling, genomics, RNAi, and proteomics to study well-characterized human cohorts of DENV infected children in dengue endemic areas (Project 1), live attenuated DENV vaccinations in humans and human challenge studies (Project 2), and infection of human cells from healthy donors (Project 3).

(Harris PI); BMGF/ICSS 4/1/13-10/31/16; 0.3 acad m

Fighting Infections through Research, Science and Technology (FIRST)

The main goal of this program is the dengue portfolio for the FIRST tool development phase, including developing immune assays for vaccine evaluation, antibody landscape analysis, and low-cost dengue diagnostics.

U19 AI109761 (Harris Subcontract PI; Lipkin PD); NIAID/NIH 3/1/15-2/18/19; 0.6 sum m

Diagnostic/prognostic indicators of severe dengue disease and protection in mice and humans

The main goal of this project is to investigate novel approaches to defining host signatures associated with and/or predictive of severe dengue disease or, conversely, protection vs. severe disease.

U19 AI118626 (Harris Subcontract PI; Sette PD); NIH/NIAID 6/15/15-5/31/20; 0.57 acad m

Human immune signatures of Dengue virus and Mycobacterium tuberculosis exposure

The goal of this subcontract is to help supervise the collection, separation, coding & shipping of human PBMCs from Nicaraguan blood donors for analysis at LIAI to determine dengue virus-specific signatures in T cells.

U01 AI088654-01 (Harris Co-PI); NIAID/NIH 8/15/10-7/31/15; NCE to 7/31/16; 0.3 acad m

Epidemiology, transmission, and phylogenetics of influenza in a tropical country

The major goal of this ICIDR program is to characterize influenza in a tropical developing country by conducting two related studies in Managua, Nicaragua: a prospective cohort study of the epidemiologic and phylogenetic features of influenza in children and a study of the household transmission of influenza.

R01 AI099631 (Harris Co-Investigator; Balmaseda PI); NIAID/NIH 6/28/12-5/31/17; 0.45 acad m

Characterization of 3rd & 4th dengue virus infections in a pediatric cohort study; Chikungunya suppl.

The main goals of this project are to examine the epidemiological, clinical and immunological characteristics of 3rd & 4th dengue virus infections in a long-term pediatric cohort study in Nicaragua. A supplement was awarded study the introduction of chikungunya virus (CHIKV) in our pediatric cohort study population (8/18/14-5/31/16).

R21/R33 AI100186 (Harris PI subcontract, Beaty PI); NIAID/NIH 6/1/12-5/31/17; 0.38 acad m

Metabolomics-based discovery of small molecule biomarkers for noninvasive dengue diagnosis & prognosis

The main goal of this project is to identify small molecule biomarkers (SMBs) in serum, saliva, and urine of dengue patients for both prognosis and diagnosis of dengue virus infections and validate the top candidates in clinical studies in Nicaragua.