BIOGRAPHICAL SKETCH

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NAME: PELLETT, PHILIP

eRA COMMONS USER NAME (agency login): philip_e_pellett

POSITION TITLE: Professor

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

INSTITUTION AND LOCATION	DEGREE	Completion Date	FIELD OF STUDY
Ohio University, Athens, Ohio	BS	05/1980	Chemistry (Honors Tutorial College)
University of Chicago, Chicago, Illinois	PHD	12/1985	Virology

A. Personal Statement

I have led a diverse range of scientific projects and programs, including large-scale epidemiology studies, studies of virus genome structure and genetic content, diagnostic assay development (including patented, FDA-approved products), antiviral development and evaluation, virus immunobiology, and molecular aspects of the cell-virus interaction. I have deliberately distributed my research efforts along the spectrum from basic to applied. Success in these areas has required the ability to learn new and often distantly related subjects, the ability to develop productive collaborations with experts in areas that complement my own, and to guide complex long-term projects to fruition. My laboratory has employed a wide range of methods, with recent studies involving the use of siRNAs, Illumina human gene arrays, miRNA profiling, proteomics, bioinformatics, recombineering of human cytomegalovirus genomes, and quantitative three-dimensional confocal microscopy.

Recent work in my laboratory has focused on human cytomegalovirus (HCMV) pUL103, a virion tegument protein that has homologs in all other members of the Herpesviridae. Published data from our and other laboratories has demonstrated roles for pUL103 along the pathway to secondary envelopment, and observations that the HSV homolog of UL103 (HSV UL7) can be present in nuclei suggests additional functions. We found that pUL103 is important for biogenesis of the HCMV cytoplasmic virion assembly complex. Work from my laboratory demonstrated that the assembly complex is built on a framework consisting of a highly remodeled cellular protein secretory apparatus. We are working to define the roles played by pUL103 in HCMV biology, and to define pUL103 domains and residues important for these activities. Such activities will be evaluated in the context of closely and more distantly related herpesviruses. The results of this work will illuminate aspects of virus replication that will be relevant across the Herpesviridae, and will provide targets and assays that can be exploited for development of novel antiviral compounds that can be used to reduce the societal burden of this important pathogen.

1. Das S, Ortiz DA, Gurczynski SJ, Khan F, Pellett PE. Identification of human cytomegalovirus genes important for biogenesis of the cytoplasmic virion assembly complex. J Virol. 2014 Aug;88(16):9086-99. PubMed PMID: 24899189; PubMed Central PMCID: PMC4136295.
2. Gurczynski SJ, Das S, Pellett PE. Deletion of the human cytomegalovirus US17 gene increases the ratio of genomes per infectious unit and alters regulation of immune and endoplasmic reticulum stress response genes at early and late times after infection. J Virol. 2014 Feb;88(4):2168-82. PubMed PMID: 24335296; PubMed Central PMCID: PMC3911563.
3. Das S, Pellett PE. Spatial relationships between markers for secretory and endosomal machinery in human cytomegalovirus-infected cells versus those in uninfected cells. J Virol. 2011 Jun;85(12):5864-79. PubMed PMID: 21471245; PubMed Central PMCID: PMC3126327.
4. Das S, Vasanji A, Pellett PE. Three-dimensional structure of the human cytomegalovirus cytoplasmic virion assembly complex includes a reoriented secretory apparatus. J Virol. 2007 Nov;81(21):11861-9. PubMed PMID: 17715239; PubMed Central PMCID: PMC2168812.

B. Positions and Honors

Positions and Employment

1986 - 2003	Chief, Herpesvirus Section, Centers for Disease Control and Prevention, Atlanta, GA
1990 - 2003	Adjunct Professor, Emory University, Microbiology and Immunology, Atlanta, GA
1993 - 2002	Adjunct Assistant Professor of Biology, Georgia State University, Atlanta, GA
1994 - 2000	Editor, Archives of Virology
1995 - 2001	Member, Task Force on Herpes Simplex Virus Resistance
2000 -	Editorial Boards:, Clinical & Vaccine Immunology (2009-present), Journal of Virology (2005-present), Virology (2000-present), Virus Research (2014-present)
2003 - 2007	Director of Translational and Basic Herpesvirus Research, Cleveland Clinic, Cleveland, OH
2004 - 2007	Professor, Case Western Reserve University, Departments of Molecular Medicine and Molecular Biology & Microbiology, Cleveland, OH
2005 - 2007	Graduate Program Director, Molecular Virology Program, Case Western Reserve University, Cleveland, OH
2007 -	Professor, Wayne State University School of Medicine, Detroit, MI
2015 -	Editor, Journal of Medical Virology
2015 -	Interim Chair of Immunology and Microbiology, Wayne State University School of Medicine

Other Experience and Professional Memberships

	Editorial Boards:, Clinical & Vaccine Immunology (2009-present), Journal of Virology (2005-present), Virology (2000-present), Virus Research (2014-present)
1993 -	Member (Chair, 2006-2012), Herpesvirus Study Group of the Vertebrate Virus Subcommittee of International Committee for Taxonomy of Viruses
1995 -	Conceived and organized the first conference; on the Organizing Committees the subsequent conferences; co-organizer of the 2015 meeting, International Conference on HHV-6 and 7
2013 -	Co-organizer (with Steve Triezenberg); International Organizing Committee most years since 1995, International Herpesvirus Workshop
2014 -	Organizing Committee (co-chair with Mary Caserta), NIH workshop on Roseoloviruses: clinical impact, interventions, and research needs

Honors

	Journal covers: Virology 269(1), 2000, J. Virol. 80(15), 2006, and Virus Research 157(2), 2011
	James H. Nakano citations for outstanding scientific papers published in 2001 and 2006 (New England J. Med. 455:637-643 and 355:1331-1338)., National Center for Infectious Diseases
	Spotlight Articles: 81:11861; 82:9065; 88:9086, Journal of Virology
2006	Charles C. Shepard Award for the Best Assessment and Epidemiology paper published in 2006 (Hladik et al., New England J. Med. 355:1331-1338, 2006), Centers for Disease Control and Prevention
2006	Paper cited as one of the top 100 G protein papers of 2006 (Das et al. J. Virol. 80:1191-1203,2006), ionchannels.org/newsletters/gproteins-2006-lit.html
2008	Journal Highlights (Microbe 3:530 for J. Virol. 82:9065-9074), ASM Microbe
2015	Dharam H. Ablashi Lifetime Achievement Award, HHV-6 Foundation
2015	Top 25 Peer Reviewer, Journal of Virology

C. Contribution to Science

1. HCMV remodeling of the endosecretory system

   Prior to our work, the HCMV cVAC was described as a place where viral proteins congregate to form virions, and from which cellular proteins are occluded. Our work demonstrated that the cVAC is the product of a virally-regulated remodeling process that results in a major reorientation of the endosecretory system, and significant shits in the identity of its component organelles. Based on the structure and spatial arrangements of endosecretory machinery within the cVAC, we proposed a model in which the cVAC structure and composition provide a mechanism for regulating the order of assembly of the tegument prior

to secondary envelopment. This model has proven useful to other investigators and has become the standard framework for current descriptions of activities in and around the cVAC. The illustration of our model (Fig. 6 in paper "b" below) has been adopted and adapted by numerous investigators. Our work in this area has thus had tangible influence on the thoughts and work of others in the field.

a. Das S, Pellett PE. Members of the HCMV US12 family of predicted heptaspanning membrane proteins have unique intracellular distributions, including association with the cytoplasmic virion assembly complex. Virology. 2007 May 10;361(2):263-73. PubMed PMID: 17188320.

b. Das S, Vasanji A, Pellett PE. Three-dimensional structure of the human cytomegalovirus cytoplasmic virion assembly complex includes a reoriented secretory apparatus. J Virol. 2007 Nov;81(21):11861-9. PubMed PMID: 17715239; PubMed Central PMCID: PMC2168812.

c. Das S, Pellett PE. Spatial relationships between markers for secretory and endosomal machinery in human cytomegalovirus-infected cells versus those in uninfected cells. J Virol. 2011 Jun;85(12):5864-79. PubMed PMID: 21471245; PubMed Central PMCID: PMC3126327.

d. Das S, Ortiz DA, Gurczynski SJ, Khan F, Pellett PE. Identification of human cytomegalovirus genes important for biogenesis of the cytoplasmic virion assembly complex. J Virol. 2014 Aug;88(16):9086-99. PubMed PMID: 24899189; PubMed Central PMCID: PMC4136295.

2. Herpesvirus genetic content and relationships among herpesviruses

I have a long-standing interest in herpesvirus genetic content and the relationships among herpesviruses. The list below includes examples from each of the past four decades. My dissertation work involved determination of the nucleotide sequences of the HSV-1 genes for glycoprotein B and the alpha trans-inducing factor (UL46 or VP16). As part of this, I published the first inter-subfamily comparison of a conserved herpesvirus protein (paper "a" below). The genomic architecture common to Roseoloviruses was deduced in my laboratory, and we determined the complete genomic sequence of HHV-6B (now part of NCBI's RefSeq collection). These interests led to my membership on the *Herpesvirales* Study Group of the International Committee for Taxonomy of Viruses, a group I chaired for the allowable two terms. Under my leadership, we updated the definition of herpesvirus species, and laid the foundation for a more informative formal nomenclature system for herpesviruses.

This connects to the current submission, in that we are proposing studies of a conserved herpesvirus tegument protein, and we intend to explore the generality of our observations.

a. Pellett PE, Biggin MD, Barrell B, Roizman B. Epstein-Barr virus genome may encode a protein showing significant amino acid and predicted secondary structure homology with glycoprotein B of herpes simplex virus 1. J Virol. 1985 Dec;56(3):807-13. PubMed PMID: 2999435; PubMed Central PMCID: PMC252651.

b. Dominguez G, Dambaugh TR, Stamey FR, Dewhurst S, Inoue N, Pellett PE. Human herpesvirus 6B genome sequence: coding content and comparison with human herpesvirus 6A. J Virol. 1999 Oct;73(10):8040-52. PubMed PMID: 10482553; PubMed Central PMCID: PMC112820.

c. Baines JD, Pellett PE. Genetic comparison of human alphaherpesvirus genomes. Arvin A, Campadelli-Fiume G, Mocarski E, Moore PS, Roizman B, Whitley R, Yamanishi K, editors. Cambridge: Cambridge University Press; 2007. Chapter c05asz-h9w-ae2-gh5

d. Pellett PE, Davison AJ, Eberle R, Ehlers B, Hayward GS, Lacoste V, Minson AC, Nicholas J, Roizman B, Studdert MJ, Wang F. Virus taxonomy: Ninth report of the International Committee on Taxonomy of Viruses. King E,, editor. Oxford: Elsevier; 2011. Order Herpesvirales; p.99-107.

3. Functions of herpesvirus proteins

From the earliest days, my study of genetic content of herpesviruses has been driven by my interest in the nuts and bolts of how viruses work, something that obviously connects to protein structure and function. The four examples provided below include examples from each of the past four decades. This and other published work includes experiments driven by assessment and consideration of protein structure and function, as well as robustly quantitative bioinformatics analysis of cellular gene expression during infection. As illustrated in paper "d" below and in the Das and Ortiz et al. paper listed in the endosecretory section, my laboratory has become adept at genetic manipulation of HCMV BACs, including use of regulated protein stability, and we are experienced at evaluating a wide variety of meaningful end points.

a. Pellett PE, McKnight JL, Jenkins FJ, Roizman B. Nucleotide sequence and predicted amino acid sequence of a protein encoded in a small herpes simplex virus DNA fragment capable of trans-inducing alpha genes. Proc Natl Acad Sci U S A. 1985 Sep;82(17):5870-4. PubMed PMID: 2994050; PubMed Central PMCID: PMC390655.

b. Inoue N, Pellett PE. Human herpesvirus 6B origin-binding protein: DNA-binding domain and consensus binding sequence. J Virol. 1995 Aug;69(8):4619-27. PubMed PMID: 7609026; PubMed Central PMCID: PMC189261.

c. Lesniewski M, Das S, Skomorovska-Prokvolit Y, Wang FZ, Pellett PE. Primate cytomegalovirus US12 gene family: a distinct and diverse clade of seven-transmembrane proteins. Virology. 2006 Oct 25;354(2):286-98. PubMed PMID: 16904149.

d. Gurczynski SJ, Das S, Pellett PE. Deletion of the human cytomegalovirus US17 gene increases the ratio of genomes per infectious unit and alters regulation of immune and endoplasmic reticulum stress response genes at early and late times after infection. J Virol. 2014 Feb;88(4):2168-82. PubMed PMID: 24335296; PubMed Central PMCID: PMC3911563.

4. Herpesvirus biology in human populations

I have led numerous high-profile projects that involved complex international collaborations. My studies of the human biology of herpesviruses have included development and validation of a wide array of diagnostic assays for detection and measurement of viruses and responses to them (including patented reagents that underlie commercial FDA-licensed tests), studies of virus prevalence and transmission in various populations, roles of herpesviruses in disease, development of novel antivirals and evaluation of antiviral resistance, and biological properties of latent vs. lytic infections in humans.

a. Cannon MJ, Dollard SC, Smith DK, Klein RS, Schuman P, Rich JD, Vlahov D, Pellett PE. Blood-borne and sexual transmission of human herpesvirus 8 in women with or at risk for human immunodeficiency virus infection. N Engl J Med. 2001 Mar 1;344(9):637-43. PubMed PMID: 11228278.

b. Martró E, Cannon MJ, Dollard SC, Spira TJ, Laney AS, Ou CY, Pellett PE. Evidence for both lytic replication and tightly regulated human herpesvirus 8 latency in circulating mononuclear cells, with virus loads frequently below common thresholds of detection. J Virol. 2004 Nov;78(21):11707-14. PubMed PMID: 15479812; PubMed Central PMCID: PMC523251.

c. Hladik W, Dollard SC, Mermin J, Fowlkes AL, Downing R, Amin MM, Banage F, Nzaro E, Kataaha P, Dondero TJ, Pellett PE, Lackritz EM. Transmission of human herpesvirus 8 by blood transfusion. N Engl J Med. 2006 Sep 28;355(13):1331-8. PubMed PMID: 17005950.

d. Pellett PE, Ablashi DV, Ambros PF, Agut H, Caserta MT, Descamps V, Flamand L, Gautheret-Dejean A, Hall CB, Kamble RT, Kuehl U, Lassner D, Lautenschlager I, Loomis KS, Luppi M, Lusso P, Medveczky PG, Montoya JG, Mori Y, Ogata M, Pritchett JC, Rogez S, Seto E, Ward KN, Yoshikawa T, Razonable RR. Chromosomally integrated human herpesvirus 6: questions and answers. Rev Med Virol. 2012 May;22(3):144-55. PubMed PMID: 22052666; PubMed Central PMCID: PMC3498727.

5. Creation of authoritative reference material and opportunities for professional development

I have been invited to write reviews, commentaries, editorials, and chapters that now span multiple editions of widely used reference books, on diverse subjects that span basic molecular biology, cell biology, immunobiology, diagnostics, epidemiology, and evidence-based clinical practice guidelines. I have been invited to provide numerous continuing education presentations for physicians and clinical laboratorians. These activities have necessitated understanding a broad range of literature related to viruses in general and herpesviruses in particular.

Another aspect of my community leadership has come in the form of meeting organization. I convened and led the first of what became a series of HHV-6 satellite meetings at the 1989 International Herpesvirus Workshop. This led me to conceive and organize the first International Conference on HHV-6 in 1995; I co-organized the 9th conference in the series, which was held in Boston in November 2015. I co-organized the 2013 International Herpesvirus Workshop and co-chaired the organizing committee of a meeting about Roseoloviruses that was held at NIH in 2014. All of these meetings were designed to maximize exposure to outstanding multi-disciplinary science, and more importantly, to maximize opportunities for developing personal relationships of the sort that enhance scientific quality and productivity, as well as creation of

opportunities for younger scientists to present data and to have active and responsible roles in meeting development and organization.

a. Braun DK, Dominguez G, Pellett PE. Human herpesvirus 6. Clin Microbiol Rev. 1997 Jul;10(3):521-67. PubMed PMID: 9227865; PubMed Central PMCID: PMC172933.

b. Pellett PE, Roizman B. Fields Virology. 6th (also 4th and 5th) ed. Knipe EE, editor. Philadelphia: Lippincott, Williams, & Wilkins; 2013. Chapter 59, The family Herpesviridae: a brief introduction; p.1802-1822.

c. Pellett PE, Tipples G. Manual of Clinical Microbiology. 11th (also 8th, 9th, and 10th) ed. Jorgensen et al., editor. Washington DC: ASM Press; 2015. Chapter 102, Human herpesviruses 6, 7, and 8; p.1754-1768.

d. Pellett PE. Indictment by Association: Once Is Not Enough. J Infect Dis. 2015 Aug 15;212(4):509-12. PubMed PMID: 25632040; PubMed Central PMCID: PMC4512607.

Complete List of Published Work in My Bibliography: http://1.usa.gov/1PJQoGo