
BIOGRAPHICAL SKETCH

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NAME Kenneth M. Kaye	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME (credential, e.g., agency login) kenkaye			
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 (if applicable)	MM/YY	FIELD OF STUDY
Harvard College, Cambridge, MA	AB	1982	Biology
Harvard Medical School, Boston, MA	MD	1986	Medicine

Please refer to the application instructions in order to complete sections A, B, C, and D of the Biographical Sketch.

A. Personal Statement

My laboratory focuses on the investigation of Kaposi's sarcoma herpesvirus (KSHV) and its persistence in cells. KSHV latently infects tumor cells and is maintained as an extrachromosomal, circular episome (plasmid). The KSHV latency-associated nuclear antigen (LANA) maintains the KSHV genome in latently infected cells. We have broad experience and expertise with KSHV and with LANA. We have performed a detailed analysis of LANA and its function for more than 15 years. Among our discoveries are the episome maintenance function of LANA (Science 1999;284:641), identification of LANA's DNA binding sequence (J. Virology 2001;75:3250), identifying LANA's binding partner on mitotic chromosomes (Science 2006;311:856), and identifying LANA's recruitment of the DNA polymerase clamp loader as a key step for viral replication and persistence (PNAS 2014;111:11,816). In summary, my laboratory has a record of productive and in depth investigation and experience in viral oncology research involving KSHV and LANA, which have well-prepared us to perform the proposed project.

B. Positions and Honors

Post-Graduate Medical Education

1986-1989 Internal Medicine Residency, Massachusetts General Hospital, Boston, MA
1989-1991 Fellowship in Infectious Diseases, Combined Program at Brigham and Women's Hospital, Beth Israel Hospital and Dana Farber Cancer Institute, Boston, MA

Awards and Honors

1978-1982 John Harvard Scholarship
1978-1982 Dean's List
1982 Phi Beta Kappa
1982 summa cum laude
1985 Soma Weiss Research Assembly oral presentation selectee
1986 Honors in Microbiology and Molecular Genetics
1991 The Edward H. Kass Award for Clinical Excellence- Massachusetts Infectious Diseases Society
2006 American Society for Clinical Investigation

Academic Appointments

1991-1995 Instructor in Medicine, Harvard Medical School

1991- Associate Physician, Brigham and Women's Hospital
1995-2006 Assistant Professor of Medicine, Harvard Medical School
1999- Harvard University Program in Virology
2000- Harvard/Partners Center for AIDS Research
2000- Dana Farber/Harvard Cancer Center
2007- Associate Professor of Medicine, Harvard Medical School

Other Professional Positions

1991-1992 Howard Hughes Medical Institute Postdoctoral Research Fellowship for Physicians
1992-1997 Physician Scientist Award, NIH
1999-2004 Member, Steering Committee on Virology Preliminary Qualifying Examination
1999-2004 Member, Committee on Virology Admissions
2001-2004 Chairman, Committee on Virology Admissions
2002 Ad Hoc Member of NIH AIDS and Related Research 4 Study Section
2003-2007 Member, NIH AIDS-associated Opportunistic Infections and Cancer Study Section
2007 Member, Special Emphasis Panel for P01s Multidisciplinary Research on Oral manifestations Associated With HIV/AIDS
2010 Member, NIH Special Emphasis Panel Study Section for HIV Associated Diseases
2011 Member, NIH Special Emphasis Panel Study Section for Lasker Clinical Research Scholars Program
2012 Ad Hoc Member, NIH AIDS-associated Opportunistic Infections and Cancer Study Section
2013 Member, NCI Program Project Meeting Study Section
2013 Member, NIAID Special Emphasis U19 Meeting Study Section
2013 Ad Hoc Member, NIH Virology B Study Section
2014 Member, NCI Special Emphasis U54 Meeting Study Section
2014 Ad Hoc Member, NIDCR Special Grants Review Committee DSR1

C. Selected Publications (15 selected from a total of 95)

1. Ballestas ME, Chatis PA, Kaye KM. Efficient persistence of extrachromosomal KSHV DNA mediated by latency-associated nuclear antigen. *Science* 1999; 284:641-644.
2. Ballestas ME, Kaye KM. Kaposi's sarcoma-associated herpesvirus latency-associated nuclear antigen 1 mediates episome persistence through cis-acting terminal repeat (TR) sequence and specifically binds TR DNA. *J Virol.* 2001;75:3250-3258. PMID: PMC114118
3. Barbera A, Ballestas ME, Kaye KM. The Kaposi's sarcoma-associated herpesvirus latency-associated nuclear antigen 1 N-terminus is essential for chromosome association, DNA replication, and episome persistence. *J Virol.* 2004;78:294-301. PMID: PMC303411
4. Barbera AJ, Chodaparambil JV, Kelley-Clarke B, Joukov V, Walter JC, Luger K, Kaye KM. The nucleosomal surface as a docking station for Kaposi's sarcoma herpesvirus LANA. *Science* 2006;311:856-861.
5. Chodaparambil JV, Barbera AJ, Lu X, Kaye KM, Hansen JC, Luger K. A charged and contoured surface on the nucleosome regulates chromatin compaction. *Nature Structural and Molecular Biology* 2007;14:1105-1107. PMID: PMC2366819
6. DeLeon Vazquez E, Kaye KM. Rapid and quantitative assessment of KSHV LANA-mediated DNA replication. *Arch Virol.* 2011;156:1323-1333. PMID: PMC3145832
7. DeLeon Vazquez E, Kaye KM. The internal Kaposi's sarcoma-associated herpesvirus LANA regions exert a critical role on episome persistence. *J Virol.* 2011;85:7622-7633. PMID: PMC3147901
8. Ballestas ME, Kaye KM. The latency-associated nuclear antigen, a multifunctional protein central to Kaposi's sarcoma-associated herpesvirus latency. *Future Microbiology* 2011;6:1399-1413.

9. Habison AC, Beauchemin C, Simas JP, Usherwood EJ, Kaye KM. Murine gammaherpesvirus 68 LANA acts on terminal repeat DNA to mediate episome persistence. *J Virol.* 2012;86:11863-76. PMID: PMC3486315
10. Dheekollu J, Chen H-S, Kaye KM, Lieberman PM. *Timeless*-dependent DNA replication-coupled recombination promote KSHV episome maintenance and terminal repeat stability. *J Virol.* 2013;87:3699.
11. Rodrigues L, Popov N, Kaye KM, Simas JP. Stabilization of Myc through heterotypic poly-ubiquitination by mLANA is critical for gamma-herpesvirus lymphoproliferation. *Plos Pathogens.* 2013;9:e1003554.
12. DeLeon Vazquez E, Carey VJ, Kaye KM. Identification of KSHV LANA regions important for episome segregation, replication, and persistence. *J Virol.* 2013;87:12270-83.
13. Correia B, Cerqueira SA, Beauchemin C, de Miranda MP, Li S, Ponnusamy R, Rodrigues L, Schneider TR, Carrondo MA*, Kaye KM*, Simas JP*, McVey CE*. Crystal structure of the gamma-2 herpesvirus LANA DNA binding domain identifies charged surface residues which impact viral latency. *Plos Pathogens* 2013;9:e1003673. (*Corresponding authors.)
14. Beauchemin C, Moerke NJ, Faloon P, Kaye KM. Assay development and high throughput screening for inhibitors of Kaposi's sarcoma associated herpesvirus N-terminal LANA binding to nucleosomes. *J Biomolec Screening* 2014;19:947.
15. Sun Q, Tsurimoto T, Juillard J, Li L, Li S, DeLeon Vazquez E, Chen S, Kaye KM. KSHV LANA recruits the DNA polymerase clamp loader to mediate efficient replication and virus persistence. *Proc. Natl Acad. Sci, USA* 2014;111:11,816-21.

D. Research Support

Ongoing Research Support

7/1/99-12/31/19 NIH/R01 (CA82036) Role: PI
 Genetic and Biochemical Studies of the KSHV LANA Gene
 This work investigates KSHV LANA mediated episome maintenance.

1/1/12-12/31/14 Harvard Medical School-Portugal Program in Translational Research
 Role: PI (Project 1)
 Pathogenesis of Kaposi's sarcoma herpesvirus LANA (PI Simas)
 This work investigates Murine gammaherpesvirus 68.

4/1/15-3/31/20 NIH/R01 (DE025208) Role: PI
 KSHV latent infection replication
 This work investigates KSHV DNA replication during latent infection.

Overlap

There is no overlap between projects.

Recently Completed Support

3/1/10-2/28/13 (NCE 2/28/14) DoD/PRMRP (PR093491) Role: PI
 Tumor virus lymphoma (blood cancer)