BIOGRAPHICAL SKETCH

Provide the following information for the key personnel and other significant contributors in the order listed on Form Page 2.
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NAME	POSITION TITLE
Steven Lewis Wechsler, Ph.D.	Professor
eRA COMMONS USER NAME swechsler	

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
City College of New York, New York	BS	1970	Biology
Univ.of North Carolina, Chapel Hill, NC	Ph.D.	1975	Molecular Genetics
Harvard Med.School Boston,MA(w/Dr. BN Fields)	Post Doc	1975-1980	Virology

NOTE: The Biographical Sketch may not exceed four pages. Follow the formats and instructions on the attached sample.

A. **Positions and Honors.** List in chronological order previous positions, concluding with your present position. List any honors. Include present membership on any Federal Government public advisory committee.

PROFESSIONAL EXPERIENCE:

1980-1986 Assistant Member: Dept.Mol.Virology, Gamble Institute Med.Res.
1986-2002 Assoc Dir-Ophthal Res and Director-Virology Labs, Cedars-Sinai Medical Center, L.A., CA.
2002-present Professor and Dir Virol Res, The Eye Institute, University of California Irvine, Irvine, CA
2007-present Professor, Dept of Microbiology & Molecular Genetics, University of California, Irvine, CA
2007-present Professor, Center for Virology Research, University of California, Irvine, CA

OTHER EXPERIENCE AND PROFESSIONAL MEMBERSHIPS:

1990-present: Ad Hoc Reviewer: J.of Virol., Virology, J.Gen.Virol., Infect. & Immun., IOVS
1992-2002: Vice Chair IACUC (Institutional Animal Care and Use Committee) Cedars-Sinai Medical Center.
2002-2006: Member IACUC (Institutional Animal Care and Use Committee) UCI

B. **Selected peer-reviewed publications (in chronological order).** Do not include publications submitted or in preparation. For publicly available citations, URLs or PMC submission identification numbers may accompany the full reference. (selected from over 100 publications)

1. **Wechsler SL** and Fields BN (1978). Differences between the intracellular polypeptides of measles and subacute sclerosing panencephalitis virus. Nature. 272:458-460.
2. Rock DL, Nesburn AB, Ghiasi H, Ong J, Lewis TL, Lokensgard JR and **Wechsler SL** (1987) Detection of latency-related viral RNAs in trigeminal ganglia of rabbits latently infected with herpes simplex virus type 1. J Virol. 61:3820-3826.
3. **Wechsler SL**, Nesburn AB, Watson R, Slanina SM and Ghiasi H (1988) Fine mapping of the latency-related gene of herpes simplex virus type 1: alternative splicing produces distinct latency-related RNAs containing open reading frames. J Virol. 62:4051-4058.
4. Perng GC, Dunkel EC, Geary PA, Slanina SM, Ghiasi H, Kaiwar R, Nesburn AB and **Wechsler SL** (1994) The latency-associated transcript gene of herpes simplex virus type 1 (HSV-1) is required for efficient in vivo spontaneous reactivation of HSV-1 from latency. J Virol. 68:8045-8055.
5. Perng GC, Slanina SM, Ghiasi H, Nesburn AB and **Wechsler SL** (1996) A 371-nucleotide region between the herpes simplex virus type 1 (HSV-1) LAT promoter and the 2-kilobase LAT is not essential for efficient spontaneous reactivation of latent HSV-1. J Virol. 70:2014-2018.
6. Perng GC, Ghiasi H, Slanina SM, Nesburn AB and **Wechsler SL** (1996) The spontaneous reactivation function of the herpes simplex virus type 1 LAT gene resides completely within the first 1.5 kilobases of the 8.3- kilobase primary transcript. J Virol. 70:976-984.

7. Perng GC, Chokephaibulkit K, Thompson RL, Sawtell NM, Slanina SM, Ghiasi H, Nesburn AB and **Wechsler SL** (1996) The region of the herpes simplex virus type 1 LAT gene that is colinear with the ICP34.5 gene is not involved in spontaneous reactivation. J Virol. 70:282-291.
8. Drolet BS, Perng GC, Cohen J, Slanina SM, Yukht A, Nesburn AB and **Wechsler SL** (1998) The region of the herpes simplex virus type 1 LAT gene involved in spontaneous reactivation does not encode a functional protein. Virology. 242:221-232.
9. Loutsch JM, Perng GC, Hill JM, Zheng X, Marquart ME, Block TM, Ghiasi H, Nesburn AB and **Wechsler, SL** (1999) Identical 371-base-pair deletion mutations in the LAT genes of herpes simplex virus type 1 McKrae and 17syn+ result in different in vivo reactivation phenotypes. J Virol. 73:767-771.
10. Perng, GC Slanina SM, Yukht A, Drolet BS, Keleher W Jr, Ghiasi H, Nesburn AB and **Wechsler SL** (1999) A herpes simplex virus type 1 latency-associated transcript mutant with increased virulence and reduced spontaneous reactivation. J Virol. 73:920-929.
11. Perng GC, Slanina SM, Yukht A, Ghiasi H, Nesburn AB and **Wechsler SL** (1999) Herpes simplex virus type 1 serum neutralizing antibody titers increase during latency in rabbits latently infected with latency-associated transcript (LAT)-positive but not LAT-negative viruses. J Virol. 73:9669-9672.
12. Drolet BS, Perng GC, Villosis RJ, Slanina SM, Nesburn AB and **Wechsler SL** (1999) Expression of the first 811 nucleotides of the herpes simplex virus type 1 latency-associated transcript (LAT) partially restores wild-type spontaneous reactivation to a LAT-null mutant. Virology. 253:96-106.
13. Perng GC, Slanina SM, Yukht A, Ghiasi H, Nesburn AB and **Wechsler SL** (2000) The latency-associated transcript gene enhances establishment of herpes simplex virus type 1 latency in rabbits. J Virol. 74:1885-1891.
14. Perng GC, Jones C, Ciacci-Zanella J, Stone M, Henderson G, Yukht A, Slanina SM, Hofman FM, Ghiasi H, Nesburn AB and **Wechsler SL** (2000) Virus-Induced Neuronal Apoptosis Blocked by the Herpes Simplex Virus Latency-Associated Transcript. Science. 287:1500-1503.
15. Inman M, Perng GC, Henderson G, Ghiasi H, Nesburn AB, **Wechsler SL**, and Jones C (2001) Region of herpes simplex virus type 1 latency associated transcript sufficient for wild type spontaneous reactivation promotes cell survival in tissue culture. J.Virol. 75:3636-3646.
16. Perng GC, Slanina SM, Ghiasi H, Nesburn AB, **Wechsler SL** (2001) The effect of LAT (latency associated transcript) on the herpes simplex virus type 1 (HSV-1) latency-reactivation phenotype is mouse strain dependent. J.g.Virol. 82:1117-1122.
17. Samoto K, Perng GC, Ehtesham M, Liu Y, **Wechsler SL**, Nesburn AB, Black KL, and Yu JS (2001) A herpes simplex virus type 1 mutant deleted for γ34.5 and LAT kills glioma cells in vitro and is inhibited for in vivo reactivation. Cancer Gene Therapy. 8:269-277.
18. Perng GC, Esmaili D, Slanina SM, Yukht A, Ghiasi H, Osorio N, Mott KR, Maguen B, Jin L, Nesburn AB, and **Wechsler SL** (2001) Three HSV-1 LAT mutants with distinct asymmetric effects on virulence in mice compared to rabbits. J.Virol. 75:9018-9028.
19. Ghiasi H, Osorio Y, Perng GC, Nesburn AB, and **Wechsler SL** (2001) Recombinant Herpes Simplex Virus Type 1 Expressing Murine Interleukin-4 Is Less Virulent than Wild-Type Virus in Mice. J Virol 75:9029-9036.
20. Samoto K, Ehtesham M, Perng GC, Hashizume K, **Wechsler SL**, Nesburn AB, Black KL, and Yu JS (2002) A herpes simplex virus type 1 mutant with gamma 34.5 and LAT deletions effectively oncolyses human U87 glioblastomas in nude mice. Neurosurgery 50:599-605.
21. Perng GC, Maguen B, Jin L, Mott KR, Osorio N, Slanina SM, Yukht A, Ghiasi H, Nesburn AB, Inman M, Henderson G, Jones C, and **Wechsler SL** (2002) A gene capable of blocking apoptosis can substitute for the herpes simplex virus type 1 latency-associated transcript gene and restore wild-type reactivation levels. J Virol 76:1224-1235.
22. Henderson G, Peng W, Jin L, Perng GC, Nesburn AB, **Wechsler SL**, and Jones C (2002) Suppression of caspase 8 and caspase 9 induced apoptosis by the herpes simplex virus (HSV-1) encoded latency associated transcript (LAT). J Neurovirol 8:103-111.
23. Perng GC, Maguen B, Jin L, Mott KR, Kurylo J, Benmohamed L, Yukht A, Osorio N, Nesburn AB, Henderson G, Inman M, Jones C, and **Wechsler SL** (2002) A novel herpes simplex virus type 1 transcript (AL-RNA) antisense to the 5' end of the latency-associated transcript produces a protein in infected rabbits. J.Virol. 76:8003-8010.
24. Perng GC, Mott KR, Osorio N, Yukht A, Salina S, Nguyen QH, Nesburn AB, and **Wechsler SL** (2002) Herpes simplex virus type 1 mutants containing the KOS strain ICP34.5 gene in place of the McKrae

ICP34.5 gene have McKrae-like spontaneous reactivation but non-McKrae-like virulence. J Gen Virol 83:2933-2942.

25. Jin L, Peng W, Perng GC, Brick DJ, Nesburn AB, Jones C, and **Wechsler SL** (2003) Identification of Herpes Simplex Virus Type 1 Latency-Associated Transcript Sequences That both Inhibit Apoptosis and Enhance the Spontaneous Reactivation Phenotype. J. Virol. 11:6556-6561.
26. BenMohamed L, Bertrand G, McNamara CD, Gras-Masse H, Hammer J, **Wechsler SL**, and Nesburn AB (2003) Identification of Novel Immunodominant CD4+ Th1-Type T-Cell Peptide Epitopes from Herpes Simplex Virus Glycoprotein D That Confer Protective Immunity J. Virol. 77: 9463-9473.
27. Mott KR, Osorio N, Jin L, Brick D, Naito J, Cooper J, Henderson G, Inman M, Jones C, **Wechsler SL**, and Perng, GC (2003) The BHV-1 LR ORF-2 is critical for this gene's ability to restore the high wild type reactivation phenotype to an HSV-1 LAT null mutant. J. gen. Virol. 84: 2975-2985.
28. Jin L, Perng GC, Brick DJ, Naito J, Nesburn AB, Jones C, and **Wechsler SL** (2004) Methods for detecting the HSV-1 LAT anti-apoptosis activity in virus infected tissue culture cells. J.Virol.Methods. 118: 9-13.
29. Peng W, Jin L, Henderson G, Perng GC, Brick DJ, Nesburn AB, **Wechsler SL**, and Jones C (2004) Mapping herpes simplex virus type 1 latency associated transcript sequences that protect from apoptosis mediated by a plasmid expressing caspase-8. J. NeuroVirol. 10:260-265.
30. Drolet BS, Mott KR, Lippa AM, **Wechsler SL**, and Perng GC (2004) Glycoprotein C of Herpes Simplex Virus Type 1 Is Required to Cause Keratitis at Low Infectious Doses In Intact Rabbit Corneas. Current Eye Res. 29:181-189.
31. Barsam CA, Brick DJ, Jones C, **Wechsler SL**, and Perng GC (2005) A viral model for corneal scarring and neovascularization following ocular infection of rabbits with a HSV-1 mutant. Cornea. 24:460-466.
32. Peng W, Henderson G, Inman M, BenMohamed L, Perng GC, **Wechsler SL**, and Jones C (2005) The locus encompassing the latency associated transcript of herpes simplex virus type 1 interferes with and delays interferon expression in productively infected neuroblastoma cells and trigeminal ganglia of acutely infected mice. J. Virol. 79:6162-6171.
33. Jin L, Perng GC, Mott KR, Osorio N, Naito J, Brick DJ, Carpenter D, Jones C, and **Wechsler SL** (2005) A herpes simplex virus type 1 mutant expressing a baculovirus inhibitor of apoptosis gene (cpIAP) in place of LAT (Latency Associated Transcript) has a wild type reactivation phenotype in the mouse. J. Virol. 79:12286-12295.
34. Chan D, Cohen J, Naito J, Mott KR, Osorio N, Jin L, Fraser NW, Jones C, **Wechsler SL**, and Perng GC (2006) A mutant deleted for most of the herpes simplex virus type 1 (HSV-1) UOL gene does not affect the spontaneous reactivation phenotype in rabbits. J. Neurovirol. 12:5-16.
35. Morishige N, Naito J, Osorio N, Wahlert A, Jones C, Everett RD, Jester JV, **Wechsler SL**, and Perng GC (2006) HSV-1 ICP0 localizes in the stromal layer of infected rabbit corneas and predominantly resides in the cytoplasm and or perinuclear region of rabbit keratocytes. J.gen.Virology 87:2817-2825.
36. Nesburn AB, Bettahi I, Zhang X, Zhu X, Chamberlain W, Afifi RE, **Wechsler SL**, and BenMohamed L (2006) Topical/mucosal delivery of sub-unit vaccines that stimulate the ocular mucosal immune system. Ocul Surf 4:178-187.
37. Solbrig MV, Adrian R, **Wechsler SL**, and Koob GF (2007) Activators of potassium M currents have anticonvulsant actions in two rat models of encephalitis. Eur J Pharmacol. 555:23-29.
38. Jin L, Perng GC, Carpenter D, Mott KR, Osorio N, Naito J, Brick DJ, Jones C, and **Wechsler SL** (2007) Reactivation Phenotype in Rabbits of a Herpes Simplex Virus Type 1 (HSV-1) Mutant Containing an Unrelated Anti-Apoptosis Gene in Place of LAT. J. Neurovirol. 13:78-84.
39. Nesburn AB, Bettahi I, Dasgupta G, Chentoufi AA, Zhang X, You S, Morishige N, Wahlert AJ, Brown DJ, Jester JV, **Wechsler SL**, and BenMohamed L (2007) Functional Foxp3+ CD4+ CD25(Bright+) "natural" regulatory T cells are abundant in rabbit conjunctiva and suppress virus-specific CD4+ and CD8+ effector T cells during ocular herpes infection. J Virol 81:7647-7661.
40. Carpenter D, Hsiang C, Brown DJ, Jin L, Osorio N, Benmohamed L, Jones C, and **Wechsler SL** (2007) Stable cell lines expressing high levels of the herpes simplex virus type 1 latency associated transcript are refractory to caspase 3 activation and DNA laddering following cold shock induced apoptosis. Virology. 369:12-18.
41. Bettahi I, Nesburn AB, Yoon S, Mohebbi A, Suey V, Vanderberg A, Wechsler SL, and BenMohamed L (2007) Protective Immunity Against Ocular Herpes Infection and Disease Induced by Highly Immunogenic Self-Adjuvanting Glycoprotein D Lipopeptide Vaccines. Invest. Ophthalmol. Vis. Sci. 48:4643-4653.

42. Carpenter D, Henderson G, Hsiang C, Osorio N, BenMohamed L, Jones C, and Wechsler SL (2008) Introducing point mutations into the ATGs of the putative open reading frames of the HSV-1 gene encoding the latency associated transcript (LAT) reduces its anti-apoptosis activity. Microbial Pathogenesis. 44:98-102.
43. Peng W, Vitvitskaia O, Carpenter D, Wechsler SL, Jones C (2008) Identification of two small RNAs within the first 1.5-kb of the herpes simplex virus type 1 (HSV-1) encoded latency-associated transcript (LAT). J. Neurovirol. 14:41-52. PMID: 18300074.
44. Chentoufi AA, Zhang X; Lamberth K, Dasgupta G, Bettahi I, Nguyen A, Wu M, Zhu X, Mohebbi A, Buus S, Wechsler SL, Nesburn AB, and BenMohamed L (2008) Human Leukocyte Antigen (HLA)-A*0201-Restricted CD8+ Cytotoxic T-Lymphocyte Epitopes Identified from Herpes Simplex Virus Glycoprotein D. J.Immunol. J.Immunol. 180:426-437. PMID: 18097044
45. Jin L, Carpenter D, Moerdyk-Schauwecker M, Vanarsdall AL, Osorio N, Hsiang C, Jones C and **Wechsler SL** (2008) Cellular FLIP can substitute for the herpes simplex virus type 1 LAT gene to support a wild type virus reactivation phenotype in mice. J. Neurovirol. In press.

C. **Research Support.** List selected ongoing or completed (during the last three years) research projects (federal and non-federal support). Begin with the projects that are most relevant to the research proposed in this application. Briefly indicate the overall goals of the projects and your role (e.g. PI, Co-Investigator, Consultant) in the research project. Do not list award amounts or percent effort in projects.

Ongoing Research Support

PI: Corneal HSV-1: LAT's anti-apoptosis activity and latency
NIH: RO1 (EY13191-01) Period: June 1, 2005 to May 31, 2009
Major Goals: Understanding how LAT's ability to block apoptosis accounts for LAT's ability to enhance spontaneous reactivation.

PI: Corneal HSV-1: Immunopathologic Mechanisms of HSK
NIH: RO1 (EY018171) Period: Jan 1, 2008 to Dec 31, 2010
Major Goals: Understanding the molecular and immunological mechanisms by which HSV-1 causes recurrent herpetic stromal keratitis (HSK), the leading cause of infectious corneal blindness in the US. Particular emphasis is given to *in vivo* and *ex vivo* confocal microscopy as well as experimental manipulations using our newly developed CJLAT (HSV-1 mutant)-rabbit model in which recurrent HSK develops in >70% of eyes.

Co-investigator: Ocular mucosal immunity induced by HSV-1 lipopeptides.
NIH: RO1 (EY14900-01) Period: Sept 30, 2003 to Sept 29 2008
Major Goals: Discover useful glycoprotein epitopes of HSV-1 and develop novel immunogenic approaches to HSV vaccines. Particular emphasis is given to lipopeptide-based vaccines, which have recently gained considerable interest and represent a promising novel approach.

Co-investigator: Ocular mucosal immunity
NIH: RO1 (EY15225-01) Period: August 1, 2004 to June 30, 2008.
Major Goals: Characterize the ocular mucosal immune system in rabbits.

PI: Ocular HSV-1: latency and pathogenesis.
Research to Prevent Blindness: Senior Scientific Investigator Award. Period: 1-1-05 (open ended).
Major Goals: This is a one time small amount of unrestricted funds for supplies to help support new or ongoing ocular herpes studies. Terminates when the funds are expended.

Completed Research:
PI: Corneal HSV-1: A novel virulence/reactivation gene
NIH: RO1 (EY12823-02) Period: May 1, 2000 to April 30, 2006
Major Goals: Initial characterization of the newly discovered HSV-1 AL gene.

PI: Ocular HSV-1: Preventing recurrent corneal disease
NIH: RO3 (EY15100-01) Period: Dec 1, 2004 to Nov 30, 2007
Major Goals: Determine if a novel, noninvasive, treatment with high intensity magnetic ion impulses can decrease spontaneous reactivation in rabbits latently infected with HSV-1.