

BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Jacobs, Bertram L.	Primary Investigator

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
Rutgers University	BS	1974	Biology
U. California, Berkeley	PhD	1975-81	Biochemistry
U. California, Santa Barbara	Post-doc	1981-85	Molecular/Cellular Biology

A. Positions and Honors:

8/74-8/75	Research Assistant, Cornell University Medical College
9/75-1/81	NIH Pre-Doctoral Fellow, Dept. of Biochemistry, University of California, Berkeley
1/81-8/85	Lecturer /Post-Doctoral Research Associate, Dept. of Bio. Sciences, Section of Biochemistry and Molecular Biology, University of California, Santa Barbara
8/85-3/90	Assistant Professor, Department of Microbiology, Arizona State University
6/91-1/92	Visiting Associate Research Professor, Molecular Mechanisms of Carcinogenesis Laboratory, NCI, Frederick Cancer Research Facility
8/90-8/96	Associate Professor, Department of Microbiology, Arizona State University
8/96-7/00	Director, Graduate Program in Molecular and Cellular Biology, Arizona State University
7/00-6/01	Distinguished Visiting Professor, Centro Nacional Biotecnologia, Madrid, Spain Aventis Pasteur, Toronto, Canada Department of Microbiology and Molecular Genetics, University of Florida
8/96-present	Professor, Dept. of Microbiology, Graduate Program in Molecular and Cellular Biology, ASU
5/02	Invited Presenter, NIH Orthopoxvirus Research Group Meeting
6/02	Member, NIH Rapid Response to Bioterrorism Study Section
7/02	Scientific Advisor, HHS/DoD/ISTC Smallpox Audit Team, VECTOR, Koltsovo, Novosibirsk, Russia
9/02	Chair, Pathogenesis Workshop, 14 th International Poxvirus and Iridovirus Workshop
10/02	Ad hoc Member, NIH Experimental Virology Study Section
12/02	Member, NIH Poxvirus Proteomics Review Panel
2/03	Keynote Speaker, Annual Meeting Arizona/Nevada Branch ASM
4/03	Keynote Speaker, U. of Illinois Annual Conference on New and Re-emerging Infectious Diseases
7/03	Ad-hoc member, Virology Study Section, NIH
7/03	Invited Speaker, NIH Poxvirus Bioterrorism Research Meeting
9/03	Chair, Poxvirus Proteomics Review Panel, NIH
10/03	Ad-hoc member, Experimental Virology Study Section, NIH
10/03	Member, Atopic Dermatitis and Vaccinia Immunization Network Review Panel
2/04	Ad-hoc member, Virology Study Section, NIH
2/04	Member VATID Review Panel, NIH
10/04-	Member, Virology A Study Section, NIH

B. Selected peer-reviewed publications

- Jacobs BL, Miyamoto NG, Samuel CE. Mechanism of interferon action: studies on the activation of protein phosphorylation and the inhibition of translation in cell-free systems. *J Interferon Res.* 1988; 8:617-31.
- Imani F, Jacobs BL. Inhibitory activity for the interferon-induced protein kinase is associated with the reovirus serotype 1 sigma 3 protein. *Proc Natl Acad Sci U S A.* 1988;85:7887-91.
- Jacobs BL, Imani F. Histone proteins inhibit activation of the interferon-induced protein kinase by binding to double-stranded RNA. *J Interferon Res.* 1988;8:821-30.
- Jacobs BL, Ferguson RE. The Lang strain of reovirus serotype 1 and the Dearing strain of reovirus serotype 3 differ in

- their sensitivities to beta interferon. *J Virol.* 1991;65:5102-4.
5. Watson JC, Chang HW, Jacobs BL. Characterization of a vaccinia virus-encoded double-stranded RNA-binding protein that may be involved in inhibition of the dsRNA-dependent protein kinase. *Virology.* 1991;185:206-16.
 6. Langland JO, Jacobs BL. Cytosolic double-stranded RNA-dependent protein kinase is likely a dimer of partially phosphorylated Mr = 66,000 subunits. *J Biol Chem.* 1992;267:10729-36.
 7. Chang HW, Watson JC, Jacobs BL. The E3L gene of vaccinia virus encodes an inhibitor of the interferon-induced, double-stranded RNA-dependent protein kinase. *Proc Natl Acad Sci U S A.* 1992;89:4825-9.
 8. Davies MV, Chang HW, Jacobs BL, Kaufman RJ. The E3L and K3L vaccinia virus gene products stimulate translation through inhibition of the dsRNA-dependent protein kinase by different mechanisms. *J Virol.* 1993;67:1688-92.
 9. Chang HW, Jacobs BL. Identification of a conserved motif that is necessary for binding of the vaccinia virus E3L gene products to double-stranded RNA. *Virology.* 1993;194:537-47.
 10. Park H, Davies MV, Langland JO, et al. TAR RNA-binding protein is an inhibitor of the interferon-induced protein kinase PKR. *Proc Natl Acad Sci U S A.* 1994;91:4713-7.
 11. Langland JO, Pettiford S, Jiang B, Jacobs BL. Products of the porcine group C rotavirus NSP3 gene bind specifically to double-stranded RNA and inhibit activation of the interferon-induced protein kinase PKR. *J Virol.* 1994;68:3821-9.
 12. Beattie E, Denzler KL, Tartaglia J, Perkus ME, Paoletti E, Jacobs BL. Reversal of the interferon-sensitive phenotype of a vaccinia virus lacking E3L by expression of the reovirus S4 gene. *J Virol.* 1995;69:499-505.
 13. Langland JO, Pettiford SM, Jacobs BL. Nucleic acid affinity chromatography: preparation and characterization of double-stranded RNA agarose. *Protein Expr Purif.* 1995;6:25-32.
 14. Chang HW, Uribe LH, Jacobs BL. Rescue of vaccinia virus lacking the E3L gene by mutants of E3L. *J Virol.* 1995;69:6605-8.
 15. Beattie E, Kauffman EB, Martinez H, et al. Host-range restriction of vaccinia virus E3L-specific deletion mutants. *Virus Genes.* 1996;12:89-94.
 16. Shors T, Jacobs BL. Complementation of deletion of the vaccinia virus E3L gene by the Escherichia coli RNase III gene. *Virology.* 1997;227:77-87.
 17. Kibler KV, Shors T, Perkins KB, et al. Double-stranded RNA is a trigger for apoptosis in vaccinia virus-infected cells. *J Virol.* 1997;71:1992-2003.
 18. Shors T, Kibler KV, Perkins KB, Seidler-Wulff R, Banaszak MP, Jacobs BL. Complementation of vaccinia virus deleted of the E3L gene by mutants of E3L. *Virology.* 1997;239:269-76.
 19. Rager KJ, Langland JO, Jacobs BL, Proud D, Marsh DG, Imani F. Activation of antiviral protein kinase leads to immunoglobulin E class switching in human B cells. *J Virol.* 1998;72:1171-6.
 20. Shors ST, Beattie E, Paoletti E, Tartaglia J, Jacobs BL. Role of the vaccinia virus E3L and K3L gene products in rescue of VSV and EMCV from the effects of IFN-alpha. *J Interferon Cytokine Res.* 1998;18:721-9.
 21. Langland JO, Kao PN, Jacobs BL. Nuclear factor-90 of activated T-cells: A double-stranded RNA-binding protein and substrate for the double-stranded RNA-dependent protein kinase, PKR. *Biochemistry.* 1999;38:6361-8.
 22. Tan SL, Nakao H, He Y, et al. NS5A, a nonstructural protein of hepatitis C virus, binds growth factor receptor-bound protein 2 adaptor protein in a Src homology 3 domain/ligand-dependent manner and perturbs mitogenic signaling. *Proc Natl Acad Sci U S A.* 1999;96:5533-8.
 23. Brandt TA, Jacobs BL. Both carboxy- and amino-terminal domains of the vaccinia virus interferon resistance gene, E3L, are required for pathogenesis in a mouse model. *J Virol.* 2001;75:850-6.
 24. He Y, Tan SL, Tareen SU, et al. Regulation of mRNA translation and cellular signaling by hepatitis C virus nonstructural protein NS5A. *J Virol.* 2001;75:5090-8.
 25. He, Y., H. Nakao, S. L. Tan, S. J. Polyak, P. Neddermann, S. Vijaysri, B. L. Jacobs and M. G. Katze (2002). "Subversion of cell signaling pathways by hepatitis C virus nonstructural 5A protein via interaction with Grb2 and P85 phosphatidylinositol 3-kinase." *J Virol* **76**(18): 9207-17.
 26. Langland, J. and B. Jacobs (2002). "The Role of the PKR-Inhibitory Genes, E3L and K3L, in Determining Vaccinia Virus Host Range." *Virology* **299**(1): 133.
 27. Xiang, Y., R. C. Condit, S. Vijaysri, B. Jacobs, B. R. Williams and R. H. Silverman (2002). "Blockade of interferon induction and action by the E3L double-stranded RNA binding proteins of vaccinia virus." *J Virol* **76**(10): 5251-9.
 28. Kim, Y. G., M. Muralinath, T. Brandt, M. Percy, K. Hauns, K. Lowenhaupt, B. L. Jacobs, and A. Rich. 2003. A role for Z-DNA binding in vaccinia virus pathogenesis. *Proc Natl Acad Sci U S A* 100:6974-9.
 29. Langland, J. O., P. Kao, and B. L. Jacobs. 2003. Regulation of IL-2 gene expression and nuclear factor-90 translocation in vaccinia virus-infected cells. *J Interferon Cytokine Res* 23:489-500.

30. Vijaysri, S., L. Talasela, A. A. Mercer, C. J. McInnes, B. L. Jacobs, and J. O. Langland. 2003. The Orf virus E3L homologue is able to complement deletion of the vaccinia virus E3L gene in vitro but not in vivo. *Virology* 314:305-14.
31. Auch, C. J., R. N. Saha, F. G. Sheikh, X. Liu, B. L. Jacobs, and K. Pahan. 2004. Role of protein kinase R in double-stranded RNA-induced expression of nitric oxide synthase in human astroglia. *FEBS Lett* 563:223-8.
32. Kibler, K. V., A. Miyazato, V. S. Yedavalli, A. I. Dayton, B. L. Jacobs, G. Dapolito, S. J. Kim, and K. T. Jeang. 2004. Polyarginine Inhibits gp160 Processing by Furin and Suppresses Productive Human Immunodeficiency Virus Type 1 Infection. *J Biol Chem* 279:49055-63.
33. Langland, J. O., and B. L. Jacobs. 2004. Inhibition of PKR by vaccinia virus: role of the N- and C-terminal domains of E3L. *Virology* 324:419-29.

Research Projects Completed During the Last 3 Years:

1 R21 AI52347-01 (Jacobs)	09/01/02 – 08/31/03	33%
NIH/NIAID	\$289,850 /Total Costs	

“Role of the E3L gene in poxvirus pathogenesis”

The Aims of this proposal are to correlated the biochemical functions of the vaccinia virus E3L gene with the biological functions, both in cells in culture and in a mouse model for pathogenesis.

Jacobs, PI	07/01/99-06/30/02	10%
Arizona Disease Control Research Commission	\$100,000	

“Specific Induction of dsRNA-mediated suicide in lung cancer cells”

The major goals of this grant are to develop methods for specifically inducing the synthesis of dsRNA in lung cancer cells.

Rich, Alex, PI	10/01-10/02	5%
NIH, Sub-contract to end-of year-extension	\$42,353	

The goal of this award is to investigate the role of Z-DNA protein interactions in pathogenesis of vaccinia virus.

1 R21 AI52787-01 (Jacobs)	09/01/02 – 08/31/04	17%
NIH/NIAID	\$449,125/Total Costs	

“Mucosal Vaccination With A Vaccinia Virus-Based Vector”

The Aims of this proposal are to prepare strains of vaccinia virus that express HIV proteins to test as mucosal vaccines in mice.

1 R21 AI53457-01 (Jacobs)	09/01/02 – 08/31/04	17%
NIH/NIAID	\$439,142/Total Costs	

“An Improved Vaccine for Protection Against Smallpox”

The Aims of this proposal are to prepare mutants of vaccinia virus with reduced pathogenesis in a virus background appropriate for use in humans.

Dana Foundation (Jacobs/ Rich, co-PIs)	01/01/01 – 12/31/05	5%
“Pathogenic Mechanisms in Poxviruses”	\$500,000/Total Costs	

The Aim of this project is to determine the role of Z-DNA-binding in vaccinia virus pathogenesis.

Ongoing Research Projects:

1 R01 AI066501-01	03/15/05 – 08/31/06	10%
HHS-NIH-NIAID	642,266.00	

Development of a Post-Exposure Vaccine for Smallpox

The major goal of this project is to develop optimize post-exposure prophylaxis for treatment of smallpox. There is no overlap with the current proposal.

Wallace Foundation (Jacobs) 01/01/03 – 12/31/06 5%
“Development of Viruses to Treat Chemotherapy-resistant Cancer” \$300,000/Total Costs
The Aim of this project is to identify mutants of vaccinia virus that preferentially replicate in cancer cells.

1 R01 AI052347-01A1 (Jacobs) 07/01/03 – 12/21/07 11%
NIH/NIAID \$177,423/Yr 1 Total Costs
“Role of the E3L gene in poxvirus pathogenesis”
The Aims of this proposal are to correlate the biochemical functions of the vaccinia virus E3L gene with the biological functions, both in cells in culture and in a mouse model for pathogenesis.

1 U01 AI057303-01 (Jacobs) 09/01/03 – 08/31/08 23%
NIH/NIAID \$923,733/Yr1 Requested Total Costs
“Development of a Safer Smallpox Vaccine.”
The Aims of this proposal are to design, construct and evaluate a treatable smallpox vaccine. There is no overlap with the current proposal.

5U01AI066326 (Jacobs) 07/01/05 – 06/30/09 18.25%
HHS-NIH-CSR 2,424,175.00
Disabling Vaccinia IFN γ : A New Smallpox Vaccine

The Bill and Melinda Gates Foundation (Jacobs Co-PI) 08/01/06 – 07/31/11
Poxvirus T Cell Discovery Consortium 877,550.00