

BIOGRAPHICAL SKETCH

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NAME Jeremy M. Boss	POSITION TITLE Professor and Chair		
eRA COMMONS USER NAME (credential, e.g., agency login) jmboss5973			
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
State University of New York, Albany, Albany, NY	BS	1977	Biological Sciences
State University of New York, Albany, Albany, NY	MS	1979	Molecular Biology
State University of New York, Albany, Albany, NY	PhD	1982	Molecular Biology
Harvard University, Cambridge, MA	Postdoc	82-86	Immunology

A. Personal Statement

I was initially trained as a molecular biologist/geneticist, studying the mechanisms of gene regulation in *Saccharomyces cerevisiae*. My postdoctoral studies with Dr. Jack Strominger focused on understanding the molecular bases for antigen presentation with the cloning of major histocompatibility complex (MHC) class II genes. Towards the end of my time in his lab, I began to examine the mechanisms by which these MHC-II genes were regulated. Since then, my lab has explored the regulation of this system and the function of chromatin and epigenetics on immune system gene expression and function. In addition to the MHC-II regulation program, we have collaborated with Dr. Rafi Ahmed to explore the regulation of Programmed death-1 (PD-1). Under chronic infection settings, PD-1 expression can lead to an exhausted T cell phenotype in which the antigen specific CD8 T cells cannot mount a response to their cognate antigen. We have found that PD-1 is regulated by a host of competing transcription factors and epigenetic mechanism, several of which will be explored in this proposal. Recently, we have begun to explore the role of global epigenetic mechanisms and outcomes on T and B cell immune responses. Our recent study on antigen-specific CD8 T cell DNA methylation dynamics, highlights the potential for epigenetic mechanisms to control transcription factor access and function. Using these genomic skills as a base, we have collaborated with Dr. Inaki Sanz to explore the epigenetic components associated with systemic lupus erythematosus and found that there are clear epigenetic components associated with a number of immune response genes that may be responsible for susceptibility of autoimmune B cells to prolonging disease. Following the finding by Hamza et al., of a polymorphism in the MHC that correlated with Parkinson's Disease, we developed a series of projects with Dr. Malu Tansey's group studying the role of MHC-II expression and immune cell function as it relates to Parkinson's Disease development and progression. In all of our studies, we use cellular immunology technologies, whole genome approaches, bioinformatics, animal model systems, and state-of-the-art molecular biology approaches to dissect the mechanisms that control adaptive immunity.

I have been an advocate for career development and training. To this end, I have published a book on academic careers entitled "Academic Scientists at Work" and published a dozen articles on career development on *Science's* Next Wave, career site. I have trained more than 17 PhD students and 16 postdoctoral fellows. Currently, I am the director of a T32 training grant in genetics and molecular biology and offer our students career sessions to help them navigate the mysteries of becoming a scientist.

B. Positions and Honors**Positions and Employment**

1977-1982. Graduate Student in the laboratory of Dr. Richard S. Zitomer, SUNY Albany

1982-1986. Postdoctoral Fellow in the laboratory of Dr. Jack L. Strominger, Harvard University.

1986-1992. Assistant Professor, Department of Microbiology & Immunology, Emory University School of Medicine.

1990-1994. Director of Graduate Studies, Graduate Program in Genetics and Molecular Biology at Emory.

1992-1997. Associate Professor, Department of Microbiology and Immunology, Emory University School of Medicine.

1994-2001; 2004-2008. Director, Graduate Program in Genetics and Molecular Biology at Emory.

1997-present. Professor, Dept. of Microbiology & Immunology, Emory University School of Medicine.

2009-present. Chairman, Department of Microbiology & Immunology, Emory University School of Medicine.

Other Experience and Professional Memberships

- Member, American Cancer Society Study Section for Personnel - 1994-1996
- Member, American Cancer Society Study Section for Cancer Immunology - 1996-1998; Ad hoc member in 1/2000, 5/2008.
- Ad hoc reviewer, for NIH study sections: CMIA, June/July '07; ALY special project review April '04, Nov. '04; NIDDK Special Prog. Proj. Rev., 2003, 2004; NBRR, Instrumentation review panel, July '99; NINDS, Program Project (NSDB), June '97; Allergy and Immunology Study Section, Oct. '95 and June '01; NIAID - DMID Special Study Section "Design and construction of vaccines for *Plasmodium falciparum* malaria" Mar. '93; NIAID - Special Study Section for "Program Projects on new methods of immune intervention" Mar. '92.
- Member, NIH BRT-A and BRT-B study sections for NIGMS – 2001-2005. Ad hoc in 2006, 2008, 2011.
- Associate Editor, *The Journal of Immunology* – 2001 - 2002.
- Deputy Editor, *The Journal of Immunology* – 2003 - 2008.
- Editor-in-Chief, *The Journal of Immunology* – 2008 – 2013 and *Ex officio* member of Council, *American Association of Immunologists*.
- Councilor, *Association of Medical School Microbiology & Immunology Chairs* – 2012-2015.

Honors:

1982 Distinguished Doctoral Dissertation Award, State University of New York at Albany

1983 Damon Runyon Cancer Fund Postdoctoral Fellowship

1983 NIH Postdoctoral Fellowship Award

2008 Outstanding Faculty Service Award, Graduate Program in Genetics & Molecular Biology

2013 Elected Member, Henry Kunkel Society

C. Selected Publications (from ~115) that are related to this application

1. **Boss, J.M.**, and Strominger, J.L. (1984) Cloning and sequence analysis of a DC-3b gene. *Proc. Natl. Acad. Sci. USA* 81: 5199-5203.
2. Collins, T., Korman, A., Wake, C., **Boss, J.M.**, Kappes, D., Fiers, W., Ault, K., Gimbrone Jr., M., Strominger, J.L., and Pober, J. (1984) Immune interferon activates multiple class II major histocompatibility complex genes and the associated invariant chain gene in human endothelial cells and dermal fibroblasts. *Proc. Natl. Acad. Sci. USA* 81: 4917-4921.
3. Spies, T., Sorrentino, R., **Boss J.M.**, Okada, K., and Strominger, J.L. (1985) Structural organization of the DR region of the human major histocompatibility complex. *Proc. Natl. Acad. Sci. USA* 82: 5165-5169.
4. Collins, T., Ginsburg, D., **Boss, J.M.**, Orkin, S.H., and Pober, J.S. (1985) Cultured human endothelial cells express platelet-derived growth factor B chain: cDNA cloning and structural analysis. *Nature* 316: 748-750.
5. Dialynas, D.P., Murre, C., Quertarmous, T., **Boss, J.M.**, Seidman, J.G., and Strominger, J.L. (1985) Cloning and characterization of complementary DNA encoding an aberrantly rearranged human T cell gamma chain. *Proc. Natl. Acad. Sci. USA* 83: 2619-2623.
6. **Boss, J.M.**, and Strominger, J.L. (1986) Regulation of a transfected human class II MHC gene in human fibroblasts. *Proc. Natl. Acad. Sci. USA*. 83: 9139-9143.
7. Sloan, J.H. and **Boss, J.M.** (1988) Conserved upstream sequences of the human MHC gene, DQb, direct B cell specific expression: comparison to a class II negative B cell line. *Proc. Natl. Acad. Sci. USA*. 85: 8186-8190.
8. Riley, J.L. and **Boss, J.M.** (1993). Class II Major Histocompatibility Complex Transcriptional Mutants are Defective in Higher Order Complex Formation. *Journal of Immunology* 151: 6942-6953.
9. Chin, K.-C., Mao, C., Skinner, C., Riley, J.L., Wright, K.L., Moreno, C.S., Stark, G.R., **Boss, J.M.**, Ting, J.P.-Y. (1994) Molecular analysis of G1B and G3A IFN γ mutants reveals that defects in CIITA or RFX result in defective class II MHC and Ii gene induction. *Immunity* 1: 687-698.
10. Riley, J.L., Westerheide, S., Brown, J., Price, J., and **Boss, J.M.** 1995. Activation of class II MHC genes requires both the X box region and the class II transactivator CIITA. *Immunity* 2:533-543.

11. Ping, D., Jones, P.L., and **Boss, J.M.** 1996. TNF regulates the in vivo occupancy of both distal and proximal regulatory regions of the MCP-1/JE gene. *Immunity* 4: 455-469.
12. Moreno, C.S., Beresford, G., Louis-Plence, P., Morris, A.C., Rogers, E.M., and **Boss, J.M.** 1999. CREB regulates MHC class II expression. *Immunity* 10:143-151.
13. Nagarajan, U., Louis-Plence, P., DeSandoro, A., Nilsen, R., Bushey, A., and **Boss, J.M.** 1999. RFX-B, the gene responsible for the most common cause of the bare lymphocyte syndrome, a MHC class II immunodeficiency. *Immunity* 10:153-162.
14. Morris, A.C., Spangler, W.E., and **Boss, J.M.** 2000. Methylation of class II transactivator promoter IV prevents gene expression in trophoblast cells. *Journal of Immunology* 164: 4143-4149.
15. Beresford, G.W., and **Boss, J.M.** 2001. CIITA binding in vivo increases acetylation at the HLA-DRA promoter and upstream nucleosomes. *Nature Immunology* 2: 652-657.
16. Morris, A. C., Beresford, G.W., Mooney, M., **Boss, J.M.** 2002. Kinetics of a gamma interferon response: Expression and assembly of CIITA promoter IV and inhibition by methylation. *Mol. Cell. Biol.* 22 4781-4791.
17. Fujita, N., Jaye, D.L., Giegerman, C., Akyildiz, A., Mooney, M.R., **Boss, J.M.**, and Wade, P.A. 2004. MTA3 and the Mi-2/NuRD complex regulate cell fate during B-lymphocyte differentiation. *Cell* 119: 75-86.
18. Impey, S., McCorkle, S.R., Cha-Molstad, H., Dwyer, J.M., Yochum, J.S., **Boss, J.M.**, McWeeney, S., Dunn, J.J., Mandel, G., and Goodman, R.H. 2004. Defining the CREB regulon: a genome-wide analysis of transcription factor regulatory regions. *Cell* 119: 1041-1054.
19. Kersh, E.N., Fitzpatrick, D.R. Murali-Krishna, K., Shires, J., Speck, S.H., **Boss, J.M.** and Ahmed, R. 2006. Epigenetic regulation of the IFN γ gene during memory CD8 T cell differentiation in vivo. *Journal of Immunology* 176: 4083-4093.
20. Teferedegne, B.A., Mooney, M.A., Guo, Z., and **Boss, J.M.** 2006. Mechanism of action of an NF- κ B dependent enhancer. *Molecular and Cellular Biology* 26: 5759-5770.
21. Green, M.M. Yoon, H., and **Boss, J.M.** 2006. Epigenetic regulation during B cell differentiation controls accessibility to all CIITA promoters. *Journal of Immunology* 177:3865-3873. *Featured in "In this Issue" of JI.*
22. Majumder, P., Gomez, J.A., and **Boss, J.M.** 2008. The insulator factor CTCF controls MHC class II gene expression and is required for the formation of long-distance chromatin interactions. *Journal of Experimental Medicine* 205: 785-798. PMID: 18347100. PMCID: PMC2292219. ****Article chosen for commentary feature**
23. Oestreich, K.J., Yoon, H., Ahmed, R., and **Boss, J.M.** 2008. NFATc1 regulates PD-1 expression upon T cell activation. *Journal of Immunology* 181: 4832-4839. PMID: 18802087. PMCID: PMC2645436
24. Ting, J.P., Lovering, R.C., Alnemri, E.S., Bertin, J., **Boss, J.M.**, Davis, B.K., Flavell, R.A., Girardin, S.E., Godzik, A., Harton, J.A., Hoffman, H.M., Hugot, J.P., Inohara, N., Mackenzie, A., Maltais, L.J., Nunez, G., Ogura, Y., Otten, L.A., Philpott, D., Reed, J.C., Reith, W., Schreiber, S., Steimle, V., Ward, P.A. 2008. The NLR gene family: a standard nomenclature. *Immunity* 28: 285-287. PMID: 18341998. PMCID: PMC2630772
25. Oestreich, K.J., Yoon, H., Ahmed, R., and **Boss, J.M.** 2008. NFATc1 regulates PD-1 expression upon T cell activation. *Journal of Immunology* 181: 4832-4839. PMID: 18802087. PMCID: PMC2645436
26. Garvie CW, Boss JM. 2008. Assembly of the RFX complex on the MHCII promoter: Role of RFXAP and RFXB in relieving autoinhibition of RFX5. *Biochim Biophys Acta.* 1779:797-804. PMID: 18723135.
27. Pollack BP, Sapkota B, **Boss JM.** 2009. Ultraviolet Radiation-induced Transcription Is Associated with Gene-specific Histone Acetylation. *Photochem Photobiol.* 85: 652-662. PMID: 19076306. PMCID: Journal in process.
28. Palmer, M.B., Majumder, P., Cooper, J.C., Yoon, H., Wade, P.A., **Boss, J.M.** 2009. Yin yang 1 regulates the expression of snail through a distal enhancer. *Molecular Cancer Research* 7: 221-229. PMID: 19208738. PMCID: PMC2819842
29. Collins CM, **Boss JM,** Speck SH. 2009. Identification of infected B cell populations using a recombinant murine gammaherpesvirus 68 expressing a fluorescent protein. *Journal of Virology* 83:6484-6493. PMID: 19386718. PMCID: PMC2698576
30. Briggs L, Laird K, **Boss JM,** Garvie CW. 2009. Formation of the RFX gene regulatory complex induces folding of the interaction domain of RFXAP. *Proteins-Structure Function and Bioinformatics* 76:655-664. PMID: 19274739. PMCID: PMC2700855
31. Yoon, H. and **Boss, J.M.** 2010. PU.1 binds to a distal regulatory element that is necessary for B cell-specific expression of CIITA. *The Journal of Immunology* 184(9):5018-5028. PMID: 20363966 PMCID: PMC3472449.
32. Majumder, P. and **Boss, J.M.** 2010. CTCF Controls Expression and Chromatin Architecture of the Human Major Histocompatibility Complex Class II Locus. *Molecular and Cellular Biology* 17: 4211-4223. PMID: 20584980. PMCID: PMC2937552.
33. Laird, K.M., Briggs, L.L., **Boss, J.M.**, Summers, M.F., and Garvie, C.W. 2010. Solution structure of the heterotrimeric complex between the interaction domains of RFX5 and RFXAP from the RFX gene regulatory complex. *Journal of Molecular Biology* 405(3): 40-51. PMID: 20732328. PMCID: PMC2949527.
34. Majumder, P. and **Boss, J.M.** 2011. DNA methylation dysregulates and silences the HLA-DQ locus by altering chromatin architecture. *Genes and Immunity* 12: 291-299. PMID: 21326318. PMCID: PMC3107363.

35. Kao C, Oestreich KJ, Paley MA, Crawford A, Angelosanto JM, Ali MA, Intlekofer AM, **Boss JM**, Reiner SL, Weinmann AS, Wherry EJ. 2011. Transcription factor T-bet represses expression of the inhibitory receptor PD-1 and sustains virus-specific CD8(+) T cell responses during chronic infection. *Nature Immunology* 12(7):663-71. PMID: 21623380. PMCID: PMC3306165
36. Majumder, P. and **Boss, J.M.** 2011. Cohesin Regulates MHC Class II Genes through Interactions with MHC Class II Insulators. *The Journal of Immunology* 187: 4236-4244. PMID: 21911605. PMCID: PMC3186872
37. Youngblood, B.A., Oestreich, K.J., Ha, S.-J., Duraiswamy, J., Akondy, R.S., West, E., Wei, J., Riley, J.L., ***Boss, J.M.**, and ***Ahmed, R.** 2011. Chronic Virus Infection Enforces Demethylation of the Locus that Encodes PD-1 in Antigen-Specific CD8(+) T Cells. *Immunity* 35: 400-412. PMID: 21943489. PMCID: PMC3183460 ***Co-**responding authors who contributed equally to the supervision of this work. Faculty 1000 selected. **Paper highlighted in Nature Immunology**
38. Choi, N., Majumder, P., and **Boss, J.M.** 2011. Regulation of major histocompatibility complex class II genes. *Current Opinions in Immunology* 23: 81-87. PMID: 20970972. PMCID: PMC3033992.
39. Zinzow, W., Bushey-Long, A., Youngblood, B., Rosenthal, K.M., Butler, R., Mohammed, A.U.R., Skountzou, I., Ahmed, R., Evavold, B.D., and **Boss, J.M.** 2012. CIITA promoter I CARD-deficient mice express functional MHC class II genes in myeloid and lymphoid compartments. *Genes & Immunity* 13: 299-310. PMID: 22218223.doi: 10.1038/gene.2011.86. PMCID: PMC3366023
40. Choi, N.M., and **Boss, J.M.** 2012. Multiple Histone Methyl and Acetyltransferase Complex Components Bind the HLA-DRA Gene. *PLoS One* 7(5): e37554. PMID: 22701520. PMCID: PMC3365104
41. Yoon, H., Scherer, C.D., Majumder, P., Davis, C.W., Butler, R., Zinzow-Kramer, W., Skountzou, I., Koutsonanos, D.G., Ahmed, R., and **Boss, J.M.** 2012. ZBTB32 Is an Early Repressor of the CIITA and MHC Class II Gene Expression during B Cell Differentiation to Plasma Cells. *The Journal of Immunology* 189:2393-2403. PMID: 22851713. PMCID: PMC3424359.
42. Gokcumen, O., Zhu, Q., Mulder, L.C.F., Iskow, R.C., Austermann, C., Steward, M. Scharer, C.D., Raj, T., **Boss, J.M.**, Sunyaev, S., Price, A.I., Stranger, B., Simon, V., Lee, C. 2013. Balancing selection on a regulatory region exhibiting ancient variation that predates human-neandertal divergence. *PLoS Genetics* 9(4):e1003404. doi: 10.1371/journal.pgen.1003404. PMID: 23593015. PMCID: PMC3623772.
43. Youngblood, B.A., Noto, A., Porichis, F., Akondy, R.S. Ndhlovu, Z.M. Austin, J.W., Bordi, R., Procopio, F.A., Walker, B.D., Ahmed, R., **Boss, J.M.** Sekaly, R.-P., and Kaufmann, D.E. 2013. Cutting Edge: Prolonged Exposure to HIV Reinforces a Poised Epigenetic Program for PD-1 Expression in Virus-Specific CD8 T Cells. *The Journal of Immunology – Cutting Edge* 191(2):540-544. PMID: 23772031. PMCID: in progress.
44. Scharer, C.D., Barwick, B.G., Youngblood, B.A., Ahmed, R., and **Boss, J.M.** 2013. Global DNA Methylation Remodeling Accompanies CD8 T Cell Effector Function. *Journal of Immunology* 191: 3419-3429. PMID: 23956425; PMCID in process. **Manuscript Featured in "In This Issue" section.**
45. Lu, P., Youngblood, B., Austin, J.W., Rasheed-Mohammad, A. Ur, Butler, R., Ahmed, R., and **Boss, J.M.** 2013. Blimp-1 suppresses PD-1 activated expression using a feed forward repression circuit. *Journal of Experimental Medicine.* Provisionally accepted. Revision submitted– 12-8-2013.

D. Research Support

Ongoing Research Support

1) 5 R01 GM47310-16 P.I. Jeremy M. Boss
NIH/NIGMBS, AI 8/1/1993 - 4/01/2015

Regulation of the human MHC class II genes.

2) T32 NIGMS GM008490-21 Program Director: Jeremy M. Boss
NIH NIGMS 6/2013 – 5/2018

Predoctoral Training in Genetics This training grant supports students and activities in the Graduate Program in Genetics and Molecular Biology.

3) 1 PO1AI 080192-05 P.D. Rafi Ahmed Project 2, PI Jeremy M. Boss 0% effort
NIH/NIAID 9/08-9/14 - in no cost extension.

PD-1 Function, Signaling, and Regulation During Viral Infection; Project 2, Regulation and Expression of PD-1.

This Program Project (PO1) with Rafi Ahmed, Bruce Walker and Daniel Kaufmann (Harvard U.), Rafick Sekaly (U. Montreal), James Riley (U. Penn), Gordon Freeman (Dana Farber Cancer Inst), Arlene Sharpe (Harvard Med School), and Michael Dustin (NYU) seeks to understand the regulation of PD-1 and its function with respect to HIV infection.

4) 2U19 AI05726-09 NIAID P.D. Rafi Ahmed Project 1, Co-Investigator Jeremy M. Boss 10%
NIH/NIAID 5/1/09-4/31/14

NIH/NIAID Vaccine Induced Immunity in the Young and Aged, Project 1, Immune Memory –

5) Michael J. Fox Foundation for Parkinson's Research (PI: Tansey, MG; Co-Inv: Boss, JM)
2014 –2016 Waiting on contract for start date

“Age-related alterations in LRRK2 expression and function in immune cells and risk for idiopathic PD” The overall goal of this application is to test the hypotheses that age- or PD- related changes in LRRK2 expression result in a skewed immune cell repertoire, dysregulated signal transduction coupling, and altered activation responses of innate and adaptive immune cells.

Pending Support:

R21 1R21NS084647-01 (PI: Tansey, M; Co-Inv, Boss)
NIH/NINDS 4/1/14-3/31/16

Immunophenotyping in LRRK2 mutation carriers The overall goal of this application is to test the hypothesis that pathogenic LRRK2 mutations a) disrupt monocyte and T-cell homeostasis and/or the ability to respond to activation.

Role: co-inv, 10% effort

To be funded – impact score 14 with 2%tile.

1U19AI110483-01 (PD: I. Sanz; Proj Lead – Collaborative Project, Boss, JM)

NIH/NIAID 4/1/2014 – 3/31/2019 \$250,000 annual direct

U19 Autoimmunity Centers of Excellence: B cell autoimmunity in human SLE; Collaborative Project: Epigenetic Regulation of Autoimmunity. This collaborative project will create epigenetic maps of autoimmune cells and compare gene expression patterns to identify novel biomarkers and specific epigenetic programming events that lead to autoimmune disease. **Slated for funding.**

2U19 AI05726-11 (PD: R. Ahmed; Project 1, Co-Inv JM Boss) 5% effort

NIH/NIAID 5/1/14-4/31/19 salary only

NIH/NIAID Vaccine Induced Immunity in the Young and Aged

Project 1, Immune Memory – The epigenetic relationship in T cells produced during vaccination will be studied through whole genome approaches.

Slated for funding

New -RO1 – (PI: Boss, JM)

NIH/NIAID 7/1/2014 – 6/30/2019

Regulation of PD-1 gene expression: This program will examine the cis-regulatory elements that function to regulate PD-1 during acute and chronic infection, determine the interplay between the transcription factors NFATc1, Blimp-1, and STAT3, and examine the role that the chromatin modifier LSD1 plays in regulating PD-1 expression in T cells.

Received an impact score of 20 and is in the 7th %tile.