BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors. Follow this format for each person. **DO NOT EXCEED FIVE PAGES.**

NAME: **MINTER, Lisa M.**

eRA COMMONS USER NAME (credential, e.g., agency login): **LMINTER**

POSITION TITLE: **Professor and Department Head**

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Catholic University of America, Washington, DC	B.S.	08/1981	Medical Technology
University of Massachusetts, Amherst, MA	Ph.D.	09/2001	Animal Biotech/Biomed Sciences
University of Massachusetts, Amherst MA	Post-doc	08/2004	Immunology

A. Personal Statement

As an immunologist, I have extensive work creating “humanized” mouse models consisting of reconstituting immune deficient “NSG” mice with human peripheral blood mononuclear cells, to create either humanized mouse models of disease or mice with functional human immune systems. My expertise extends to flow cytometric analysis of rare cell populations, including analysis of immune cells recovered from tumor tissues (*Yang et al., 2018*).

My background in T cell signaling includes extensive training in *in vitro* and *in vivo* experimental design, procedures, animal model creation, and data analyses. I have developed highly representative models of disease, including both all murine and humanized mouse models, and have contributed to the knowledge base through publications in high impact journals such as *Nature Immunol, Blood*, *J Exp Med*, and *Sci Transl Med.*

I also have a successful track record of productive collaborations with academic (*Raman et al. 2023*) and industry partners, including utilizing pre-clinical “humanized” models of Graft-vs-Host Disease to test novel therapeutic agents (*Ozay et al.,2019; Geiger et al., 2019*).

a. Yang, H., W. Wang, K.A. Romano, M. Gu, K.Z. Sanidad, D. Kim, J. Yang, B. Schmidt, D. Panigrahy, R. Pei, D.A. Martin, E.I. Ozay, Y. Wang, M. Song, B.W. Bolling, H. Xiao, **L.M. Minter**, G.Y. Yang, Z. Liu, F.E. Rey, and G. Zhang (2018) A common antimicrobial additive increases colonic inflammation and colitis-associated colon tumorigenesis in mice. *Sci Transl Med*. [PMID: 29848663; PMCID: PMC6343133].

b. Raman, V., L.M. Howell, S.M.K. Bloom, C.L. Hall, V.E. Wetherby, **L.M. Minter**, A.A. Kulkarni, and N.S. Forbes (2023) Intracellular Salmonella delivery of an exogenous immunization antigen refocuses CD8 T cells against cancer cells, eliminates pancreatic tumors and forms antitumor immunity. *Front Immunol.* 14:1228532. [PMID: 37868996; PMCID: PMC10585021].

c. Ozay, E.I., J. Vijayaraghavan, G Gonzalez-Perez, S. Shanthalingam, H.L. Sherman, D.T. Garrigan, Jr., K. Chandiran, J.A. Torres, B.A. Osborne, G.N. Tew, I.I. Slukvin, R.A. Macdonald, K. Kelly, and **L.M. Minter** (2019) Cymerus™ iPSC-MSCs significantly prolong survival in a pre-clinical, humanized mouse model of Graft-vs-Host disease. *Stem Cell Res*. [PMID: 30738321; PMCID: PMC6544140].

d. Geiger, S*., E. I. Ozay*, U. Geumann, M.K. Hereth, T. Magnusson, S. Shanthalingam, D. Hirsch, S. Kälin, C. Günther, B.A. Osborne, G.N. Tew, F.G. Hermann, and **L.M. Minter** (2019) Alpha-1 Antitrypsin-Expressing Mesenchymal Stromal Cells Confer a Long-Term Survival Benefit in a Mouse Model of Lethal GvHD. *Mol Ther.* A27:1436-1451. [PMID: 31138510; PMCID: PMC6698199].

B. Positions, Scientific Appointments, and Honors

2004 – 2007	Adjunct Research Assistant Professor, Dept. of Veterinary & Animal Sciences
2007 – 2009	Research Assistant Professor, Dept. of Veterinary & Animal Sciences University of Massachusetts/Amherst, Amherst, MA
2009 – 2015	Assistant Professor, Dept. of Veterinary & Animal Sciences University of Massachusetts/Amherst, Amherst, MA
2010 – 2016	Director, Flow Cytometry Core Facility University of Massachusetts/Amherst, Amherst, MA
2011 – present	Adjunct Assistant Professor, Dept. of Biomedical Sciences, University of Illinois, Rockford College of Medicine, Rockford, IL
2015 – 2021	Associate Professor, with tenure, Dept. of Veterinary & Animal Sciences University of Massachusetts/Amherst, Amherst, MA
2021 – present	Professor, Dept. of Veterinary & Animal Sciences University of Massachusetts/Amherst, Amherst, MA
2022 – present	Department Head, Dept. of Veterinary & Animal Sciences University of Massachusetts/Amherst, Amherst, MA
2009 – present	Ad Hoc Reviewer, *Blood* (since 2009); *Cellular & Molecular Immunology* (since 2011); *Am J Pathol* (since 2011); *Future Medicine* (since 2011); *Arch Industrial Hygiene Toxicol* (since 2012); *Biorg Medicinal Chem Letters* (since 2013); *FEBS Letters* (since 2013); *Biol Reproduction* (since 2013); *J Biosciences & Medicine* (since 2015), *Biomarkers Med* (since 2016); *Int J Mol Med* (sin Expce 2016); *J Integrative Med* (since 2015); *J Immunol* (since 2016); *PLoS One* (since 2016); *J Translational Med* (since 2017); *J Leukocyte Biol* (since 2017); *Hematologica* (since 2017); *ASH Hematology 2017*; *Exp Therapeutic Med* (since 2018); *Immunol Letters* (since 2018); *Acta Hematologica* (since 2018); *BMC Cancer* (since 2018)
2008	Member, Scientific Review Panel DOD Bone Marrow Failure Research Program
2009 – 2015	Member, Programmatic Review Panel DOD Congressional Medical Research Program/Bone Marrow Failure Research Program
2011 – 2012	Chair, Programmatic Review Panel DOD Congressional Medical Research Program/Bone Marrow Failure Research Program
2011 – present	Ad Hoc Member, Scientific Review Panel, NSF Major Research Instrumentation Grants
2013 – present	Editorial board, Journal of Biosciences and Medicine
2015	Ad Hoc Scientific Reviewer, Wellcome Trust/DBT India Alliance
1998	University of Massachusetts Graduate Fellowship Award
2000	Snoeyenbos Prize for Excellence in Graduate Research and Academics
2001	Phi Kappa Phi Graduate Student Honor Society
2001	Ruth L. Kirschstein National Research Service Award Postdoctoral Fellowship
2009	Charles H. Hood Foundation Award for Child Health Research

C. Contributions to Science

The public URL for My Bibliography collection:
https://www.ncbi.nlm.nih.gov/myncbi/1RQWhskUavEAb/bibliography/public/

Identifying a potential mechanism for increased risk of breast cancer in pre-adolescent girls exposed to ionizing radiation

The highest risk of radiation-induced breast cancer occurs within a small population of women who have undergone therapeutic radiation for either malignant or non-malignant diseases prior to the onset of puberty. During my graduate studies I identified a correlation between epithelial proliferation (which is lacking in pre-adolescent mammary tissue) and responsiveness of the tumor suppressor protein p53 to ionizing radiation. My results indicated that inducing proliferation in pre-adolescent, quiescent mammary tissue, through hormonal or non-hormonal mitogens, resulted in the nuclear translocation of p53, enabling it to initiate apoptotic responses to ionizing radiation. These findings help to explain the increased risk of breast cancers associated with exposure to ionizing radiation in pre-pubescent girls.

a. **L. M. Minter,** E. S. Dickinson, S. P. Naber and D. J. Jerry (2002) Epithelial cell cycling predicts p53 responsiveness to gamma-irradiation during post-natal mammary gland development. *Development*. 129(12):2997-3008. [PMID: 12050146].

b. J. Jerry**, L. M. Minter,** K. A. Becker and A. C. Blackburn (2002) Hormonal control of p53 and chemoprevention. *Breast Cancer Res.* 4(3):91-94. [PMID: 12052250; PMCID: PMC138728].

Exploring novel delivery platforms to modulate T cell signaling

Together with my UMass Amherst colleague, Dr. Greg Tew (Department of Polymer Sciences & Engineering) we have successfully delivered immune response-modulating cargo to human peripheral mononuclear cells (hPBMCs) and can do so with higher efficiency than any commercially available product. Most recently, we altered pPKCθ cellular localization by delivering anti-pPKCθ, *ex vivo*, using a cell-penetrating protein transduction domain mimic. This treatment conferred a durable phenotype to hPBMCs cells that translated to a significant survival benefit when treated cells were used to induce graft-versus-disease in a "humanize" mouse model. This collaboration continues to push the boundaries of intracellular cargo delivery for the purposes of immune modulation as we develop efficient platforms to deliver siRNA, proteins and antibodies, and plasmid DNA. These publications highlight the potential for translational applications for the scientific discoveries stemming from my research program.

a. Tezgel, A. O., G. Gonzalez-Perez, J. C. Telfer, B. A. Osborne, **L. M. Minter**, and G. N. Tew (2013) Novel protein transduction domain mimics as nonviral delivery vectors for siRNA targeting *NOTCH1* in human T cells**.** *Mol Ther*. 21:201–209. [PMID: 23070119; PMCID: PMC3538314].

b. Ozay, E. I., G. Gonzalez-Perez, J. A. Torres, J. Vijayaraghavan, R. Lawlor, H. L. Sherman, D. T. Garrigan, Jr., A. S. Burnside, B. A. Osborne, G. N. Tew, and **L. M. Minter** (2016) Intracellular delivery of anti-pPKCθ (Thr538) via protein transduction domain mimics for immunomodulation. *Mol Ther*. [PMID: 27633441; PMCID: PMC5167783].

c. Ozay, E.I., S. Shanthalingam, H.L. Sherman, J.A. Torres, B.A. Osborne, G.N. Tew, and **L.M. Minter** (2020) Cell-Penetrating Anti-Protein Kinase C Theta Antibodies Act Intracellularly to Generate Stable, Highly Suppressive Regulatory T Cells. *Mol Ther.* 28:1987-2006. [PMID: 32492367; PMCID: PMC7474270].

d. Ozay, E.I., S. Shanthalingam, J.A. Torres, B.A. Osborne, G.N. Tew, and **L.M. Minter** (2020) Protein Kinase C Theta Modulates PCMT1 through hnRNPL to Regulate FOXP3 Stability in Regulatory T Cells. *Mol Ther.* 28:2220-2236. [PMID: 32592691; PMCID: PMC7544975].

First to identify a role for transmembrane receptor NOTCH1 in TH1 cell differentiation *in vitro* and *in vivo*.

As a post-doctoral fellow in the laboratory of Dr. Barbara Osborne, I was the lead author on a seminal paper that was the first to describe a role for NOTCH signaling in the differentiation of peripheral T cells to a T helper (TH) type I cell fate. I further contributed to studies that also described the importance of NOTCH signaling to differentiation of regulatory T cells as well as to TH17 cells. These studies were significant in that they introduced the concept that NOTCH is a regulator of cell fate in mature peripheral T cells and that its aberrant expression might play a role in autoimmune conditions. Extensive work in T cell activation and differentiation highlights my expertise in this area of fundamental immunological research.

a. **L. M. Minter,** *et al.* (2005) Inhibitors of γ-secretase block *in vivo* and *in vitro* T helper type 1 polarization by preventing Notch upregulation of *Tbx21, Nat. Immunol.* 6(7):680-688. [PMID: 15991363].

b. J. B. Samon, A. Champhekar, **L. M. Minter**, J. C. Telfer, L. Miele, A. Fauq, P. Das, T. E. Golde and B. A. Osborne (2008) Notch1 and TGFβ1 cooperatively regulate Foxp3 expression and the maintenance of peripheral regulatory T cells. *Blood*. 112:1813-1821. [PMID: 18550850; PMCID: PMC2518888].

c. S. Keerthivasan, R. Suleiman, R. Lawlor, J. Roderick, T. Bates, **L. Minter**, J. Anguita, I. Juncadella, B.J. Nickoloff, I.C. Le Poole, L. Miele and B.A. Osborne (2011) Notch signaling regulates mouse and human Th17 differentiation. *J Immunol.*187:692-701. [PMID: 21685328; PMCID: PMC3131467].

d. Dongre, L. Surampudi, R. G. Lawlor, A. H. Fauq, L. Miele, T. E. Golde, **L. M. Minter,** and B. A. Osborne (2014) Non-Canonical Notch Signaling Drives Activation and Differentiation of Peripheral CD4(+) T Cells. *Front Immunol*. 5:54. doi: 10.3389/fimmu.2014.00054. [PMID: 24611064; PMCID: PMC3921607].

Detailing NOTCH1 signaling in peripheral T cells

During my post-doctoral tenure and beyond, I was a key contributor on several publications that helped to elucidate the molecular mechanisms by which the transmembrane protein NOTCH1 can regulate activation, survival, and proliferation in peripheral CD4+ and CD8+ T cells. These findings were significant because they identified a previously undescribed role for NOTCH1 as having important functions during the activation of mature T cells, not just during thymic development, as had been extensively studied. Collectively, my work on NOTCH1 signaling in T cells prepares me well to perform the studies outlined in this application.

a. H. M. Shin, **L. M. Minter**, O. H. Cho, S. Gottipati, T. E. Golde, G. E. Sonenshein, and B. A. Osborne (2006) Notch1 Augments NF-κB Activity by Facilitating its Nuclear Retention. *EMBO J* 25, 129-138. [PMID: 16319921; PMCID: PMC1356346].

b. O. H. Cho, H. M. Shin, L. Miele, T.E. Golde, A. Fauq, **L. M. Minter** and B. A. Osborne (2009) Notch Is Required for Cytolytic Effector Function in $CD8^+$ T Cells *J Immunol.* 82:3380-3389. [PMID: 19265115; PMCID: PMC4374745].

c. Dongre, L. Surampudi, R. G. Lawlor, A. H. Fauq, L. Miele, T. E. Golde, **L. M. Minter,** and B. A. Osborne (2014) Non-Canonical Notch Signaling Drives Activation and Differentiation of Peripheral CD4(+) T Cells. *Front Immunol*. 5:54. doi: 10.3389/fimmu.2014.00054. [PMID: 24611064; PMCID: PMC3921607].

d. Shin, H.M., M.E. Tilahun, O.H. Cho, K. Chandiran, C.A. Kuksin, S. Keerthivasan, A.H. Fauq, T.E. Golde, L. Miele, M. Thome, B.A. Osborne, and **L. M. Minter** (2014) NOTCH1 Can Initiate NF-κB Activation via Cytosolic Interactions with Components of the T Cell Signalosome. *Front Immunol.* 5:249-263. [PMID: 24904593; PMCID: PMC4033603].

Probing the mechanisms of immune-mediated bone marrow failure

As a tenure track professor, mine was the first lab to describe a role for NOTCH1 as a driver of disease in the human autoimmune bone marrow failure disease, aplastic anemia. This finding, with high clinical relevance, was made using a novel murine model of aplastic anemia developed in my lab and which closely recapitulates the human disease at the symptomatic, cellular, and molecular levels, and verified following analysis of human patient samples. We have further utilized this model to investigate the potential contribution of various other mediators of disease, including aberrant expression of chemokine receptors which may mediate trafficking to the bone marrow during disease. My extensive background using animal models of disease positions me well to design, perform, and interpret results from the *in vivo* experiments detailed in this application.

a. Roderick, J.E., G. Gonzalez-Perez, C. Arieta Kuksin, A. Dongre, E. Roberts, J. Srinivasin, C. Andrzejewski, Jr., A. H. Fauq, T. E. Golde, L.Miele and **L. M. Minter** (2013) Therapeutic targeting of Notch signaling ameliorates immune-mediated bone marrow failure of aplastic anemia. *J Exp Med.* 210:1311-1329. [PMID: 23733784; PMCID: PMC3698520]. *FEATURED ON THE COVER*.

b. Arieta Kuksin, C., G. Gonzalez Perez, and **L. M. Minter** (2015). CXCR4 expression on pathogenic T cells facilitates their bone marrow-infiltration in a mouse model of aplastic anemia. *Blood.* 125(13):2087-94. doi:10.1182/blood-2014-08-594796. [PMID: 25647836; PMCID: PMC4375106].